

Start	End	Topic	Speakers
09:00	09:20	Phenotyping Nocturia – Judge a Book by its Cover?	An-Sofie Goessaert
09:20	09:40	Sleep and Nocturia – Central Mechanisms into Business?	Karlien Dhondt
09:40	10:00	Bladder and Kidney – Making the Bladder Gladder or Lowering the Water Levels?	Philip Van Kerrebroeck
10:00	10:20	Questionnaire on Nocturia – to TANGO or Not to TANGO?	Wendy Bower
10:20	10:30	Questions	All

Speaker Powerpoint Slides

Please note that where authorised by the speaker all PowerPoint slides presented at the workshop will be made available after the meeting via the ICS website www.ics.org/2017/programme. Please do not film or photograph the slides during the workshop as this is distracting for the speakers.

Aims of Workshop

Nocturia is a highly prevalent condition affecting both men and women of all ages. It is no longer a problem merely attributed to overactive bladder or benign prostate hyperplasia. There can be an impairment in one or more factors of the triad brain-kidney-bladder but also other factors such as obesity, hypertension, peripheral edema, sleep disturbance, depression, medication, etc can play a role.

The objective of this workshop is to provide an overview on causes and co-morbidities of nocturia and how to identify them.

Learning Objectives

This workshop should allow the attendant to know the answers to following questions:

1. What physical features can help you to identify possible causes or co-morbidities of nocturia?
2. How does sleep affect nocturia and how does nocturia affect sleep?
3. What not to miss in the work-up of nocturia?

Learning Outcomes

After this course the attendant should be aware of the most evident causes and co-morbidities of nocturia and he/she should be able to identify them in patients in clinical practice.

Target Audience

Urologists, Gynaecologists, Geriatricians and Nurses

Advanced/Basic

Basic

1. **Speaker 1: Phenotyping nocturia – judge a book by its cover?** - An-Sofie Goessaert, urology trainee, Ghent University Hospital Belgium

Nocturia is a complaint which seems to be invisible for anyone else but for the patient and for his or her bed partner, unless the patient is asked about it or mentions it him or herself. However, there are certain physical uitingen that can help you understand or suspect the underlying pathophysiology. It is obvious that you need a full medical history to get a direction on the pathophysiology, for example, the presence of kidney disease, diabetes, depression, etc., conditions that are also not necessarily clinically visible. But looking at your patient and examining your patient is as important for a good diagnostic workout.

What to do on a first consultation?

- Blood pressure > arterial hypertension?
- Weight assessment / waist circumference > obesity?
- Cardiovascular examination (shortness of breath, chronic coughing or wheezing, peripheral edema, confusion or impaired thinking, high heart rate) > cardiac failure?
- Digital rectal examination > benign prostate hypertrophy?

A few examples:

- Obesity:

Obesity is a multifactorial disease with adverse health consequences, such as cardiovascular disease, type 2 diabetes, hypertension, sleep apnea, and possibly depression, which may result independently in nocturia.

Lifestyle-related factors may also be more common among the obese. It is possible that nocturia in some obese persons is related to excessive nighttime eating or drinking, especially consumption of alcohol. This can cause nocturnal polyuria, leading to an increased nighttime voiding frequency.¹

- Arterial hypertension:

The link between hypertension and NP can be explained by its stimulating effect on glomerular filtration, inhibiting effect on the ADH and its effect on the pressure-natriuresis relation in the kidney. This is a feedback system to control blood pressure, whereby increases in renal perfusion pressure lead to a decrease in sodium reabsorption and more sodium excretion.²⁻⁴

Healthy adults show a nighttime drop in blood pressure of at least 10%, however this is lacking in people with non-dipping hypertension, who show an enhanced sodium excretion.³ Such non-dipping hypertension has been linked to physical activity during nighttime, which supports the finding that non-dipping hypertension is more prevalent in patients who wake up to go to the toilet at night.²

- Peripheral edema:

Peripheral edema are common in patients with venous insufficiency, heart failure, hypertension and autonomic dysfunction. These patients typically accumulate fluid in their lower extremities while standing during daytime, but when they change to the supine position when going to sleep in the evening, this fluid is reabsorbed into the circulation. This presents as a surplus of fluid to the circulatory system, which stimulates ANP and glomerular filtration and results in more nighttime urine production.^{5,6}

1. Aoki Y., Yokoyama O. Metabolic Syndrome and nocturia. LUTS. 2012; 4 (s1): 11-15.
2. Feldstein CA. Nocturia in arterial hypertension: a prevalent, underreported, and sometimes underestimated association. J Am Soc Hypertens. 2013;7(1):75-84.
3. McKeigue PM, Reynard JM. Relation of nocturnal polyuria of the elderly to essential hypertension. Lancet. 2000;355(9202):486-8.
4. Asplund R. Diuresis pattern, plasma vasopressin and blood pressure in healthy elderly persons with nocturia and nocturnal polyuria. Neth J Med. 2002;60(7):276-80.
5. Gulur DM, Mevcha AM, Drake MJ. Nocturia as a manifestation of systemic disease. Bju International. 2011;107(5):702-13.
6. Boongird S, Shah N, Nolin TD, Unruh ML. Nocturia and aging: diagnosis and treatment. Adv Chronic Kidney Dis. 2010;17(4):e27-40.

2. **Speaker 2: Sleep and nocturia – central mechanisms into business?** – Karlien Dhondt, Ghent University Hospital Belgium

The aim of this talk is to demonstrate some interesting aspects on nocturia by focussing on sleep. More specifically, sleep fragmentation and dopaminergic neurotransmission. Before going into detail, we start with a few aspects about sleep physiology first.

When studying sleep, one has to bear in mind that sleep physiology is influenced by two important factors, which are known as the circadian rhythm, and the sleep homeostasis. In this context, there is a range of neurotransmitters that are or sleep or wake promoting. The circadian rhythm is the hour glass in which we can sleep, it is independent from the previous nights. On the contrary, the sleep homeostasis is based on how we slept the nights before and reflects sleep pressure that has been built up during the day.

Research of sleep and uro/nephrology in our University Center, started in pediatrics. We explored sleep by performing a full polysomnography in children with therapy resistant or dependent nocturnal enuresis (NE). The observations were tantalizing : we found increased cortical arousals (sleep fragmentation) associated with periodic limb movements (PLMS). This was later confirmed in a case control study. Later, the study was repeated in a homogenous group of children with monosymptomatic NE, and the same observations were found. However, compared to the pilot study in which more children with reduced bladder capacity were included, the PLMS-index was significantly higher in the latter group (1).

A population based epidemiological study from Finland comprising a systematic evaluation of factors associated with nocturia in adults reported a correlate between RLS (strongly associated with PLMS in adults) and nocturia (2). One might suspect a persistent common pathophysiological mechanism with: sleep fragmentation, PLMS, NE or nocturia.

The observation of PLMS is of interest. PLMS are a well described feature in sleep medicine, they are seen on a PSG and are periodic short movements of the legs (flexion in the ankle, hip, knee). The pathophysiology of PLMS is caused by a disturbed dopaminergic neurotransmission. However, the cause of dopamine depletion can be variable. In case of dopaminergic

depletion, the effect on motor, sensory nerves and autonomic balance are hypothesized to be less inhibited. Moreover, dopamine has also an important role in the mictury center in the brain.

The second part is the role of sleep fragmentation. The amount of cortical arousals reflects sleep fragmentation and this is known to cause sleep deprivation. The autonomic nerve system with a higher sympathetic output (increased blood pressure, increased heart rhythm)

A good model for explaining how these factors might interact is Parkinson disease.

The final conclusion is that dopaminergic dysfunction might be an important mediating factor in some phenotypes of nocturia and NE. This will be further explored in the future.

(1) K. Dhondt et al. *J Urol*, 2009, *Acta Paediatr* 2014, *Ped Nephrol* 2015

(2) K. Tikkinen et al. *Am J Epidemiol* 2009

3. **Speaker 3: Bladder and kidney – making the bladder gladder or lowering the water levels?** – Philip Van Kerrebroeck, Professor of Urology, Maastricht University Medical Center, the Netherlands

The International Continence Society (ICS) defines nocturia as ‘the complaint that the individual has to wake at night one or more times to void...each void is preceded and followed by sleep.’ Patients experiencing <2 voids/night in general do not experience significant bother. However bother, as well as morbidity and mortality, will be significant with >2 voids/night. Nocturia is an underreported, underdiagnosed, and undertreated condition, with many patients believing it to be a natural consequence of aging. Nocturia is associated with multiple medical conditions, and conveys an increased mortality risk.

The treatment of nocturia advanced because of the understanding that it is a distinct clinical entity with a number of pathophysiologic causes. Nocturia may be sub classified into three categories, based on the causative mechanisms:

1. Reduced Voided Volume, a reduced capacity for the bladder to store urine, whether globally or only during sleep
2. Global (or 24 hour) Polyuria, an overabundant production of urine during the diurnal plus nocturnal periods, quantified as a volume of greater than 40 ml/kg in 24 hours
3. Nocturnal Polyuria (NP) overabundant production of urine only at night, with 24 hour urine output remaining within the normal range. NP is defined as nocturnal urine production of > 20 % of 24 hour output in younger adults (21–35) and > 33 % of 24 hour urine output in older adults

Traditionally nocturia was believed to be primarily the result of either overactive bladder (OAB) or benign prostatic hyperplasia (BPH). This was seemingly confirmed in the 1990s when the increase in prostate outlet reducing procedures occurred with a concomitant decline in nocturia. However, NP is now recognized as a major etiology of nocturia. Data obtained from cohorts of the NOCTUPUS and US/CANADA trials, indicated that the majority of nocturia patients were found to have nocturnal polyuria. The NOCTUPUS trials were three randomized controlled trials studying the effect of desmopressin tablet formulation on subjects with nocturia. Upon enrollment, subjects completed 7-day frequency volume charts (FVC) recording the volume and time of their voids. Examining this data, it was found that the NP prevalence in records included in analysis (641/846) was 76 %. If the FVCs discarded from analysis due to incompleteness were assumed not have nighttime polyuria, the proportion with NP was 64 % (641/1003).

Similarly, the United States/Canada trial was a phase III randomized double blind trial to evaluate efficacy of the treatment of nocturia with desmopressin Melt. This study indicated a NP prevalence in complete records (806/917) of 88 %. If the FVCs discarded from analysis assumed not have nocturnal polyuria, the proportion with NP was 57 % (806/1,412). Subgroup analysis showed increasing prevalence of NP with age, and a slightly higher occurrence in men compared to women. In the young (<65), NP affected 66 % (325/493) in the NOCTUPUS trial and 83 % (390/468) in the US/Canada trial, while the prevalence in patients >65 years old was 90 % (316/353) in the NOCTUPUS trial and 93 % (416/449) in the US/Canada Trial.

4. **Speaker 4: Questionnaire on nocturia – to TANGO or not to TANGO?** – Wendy Bower, Department of Medicine and Community Care, Melbourne Health and Department of Medicine, Dentistry and Health Science the University of Melbourne.

The causal pathway of nocturia is multi-factorial and differs between patients. There are significant interactions between voiding at night and markers of poor health. A comprehensive multidisciplinary assessment metric that identifies co-existing causes of nocturia beyond the urinary tract was warranted.

This presentation describes the development and use of TANGO a screening tool to target the aetiology of nocturia and guide outcomes. A Cochrane-style review identified variables carrying a significant risk in relation to nocturia severity. Discriminating items in robust tools measuring co-morbidities were collected; pertinent clinical measures were added. After removal of item duplication, the self-completed 57 item questionnaire (TANGO) was piloted (n=22), modified, then completed by 300 patients ≥ 40 years of age with nocturia who were presenting to the sleep disorder, diabetes, rehabilitation, continence or falls and balance clinics, or in-patients of aged care or rehabilitation wards.

Endorsement of items was analysed; those with a high floor effect (i.e. $>70\%$ of responses "never" or its equivalent), an inter-relationship >0.8 (i.e. redundant) or $>50\%$ missing data were removed. Measures included in their entirety were subject to exploratory factor analysis to identify items with multiple loadings. Psychometric properties were used to reduce the initial TANGO metric to a short form.

Non-urinary tract factors identified on the causal pathway of nocturia clustered into the domains of mental health, cardiovascular, metabolic, sleep and inflammatory conditions and medication. List 1 shows the metrics from which TANGO items were drawn. A medical history checklist was added to the questionnaire along with a clinician-completed section of physical measures (height; weight; neck, waist and hip circumferences; heart rate; blood pressure; TUG Test).

List1: Metrics from which TANGO items were sourced:

- Overactive Bladder Symptom Score
- International Prostate Symptom Score
- Epworth Sleepiness Scale
- Pittsburg Sleep Quality Index
- Insomnia Severity Index
- STOPBang Obstructive Sleep Apnea Questionnaire
- AUSDRISK Diabetes Risk Assessment Tool
- Hospital Anxiety and Depression Scale
- EQ-5D-3L Health Status Questionnaire
- SF-36 Health Status Questionnaire
- Brief Pain Inventory (Short Form)
- Psoriatic Arthritis Screening and Evaluation Questionnaire
- General Practitioner Cognitive Screening Test

The TANGO Short Form was developed from items significantly associated with high frequency nocturia. Patient self-completion required between 30 seconds and 2 minutes. Test-retest reliability of this new metric demonstrated substantial to excellent agreement (Kappa 0.6 to 0.79 and 0.8 to 1.00 respectively). This tool has the potential to improve evaluation across disciplines and medical specialties and to smooth inequalities associated with current care of patients with nocturia.

Workshop 10

ICS 2017 FLORENCE

Causes & Co-morbidities of nocturia

12 September – ICS 2017

Workshop 10 – Causes & Co-morbidities of Nocturia

ICS 2017 FLORENCE

An-Sofie Goessaert



Country: Belgium


Profession: Urology trainee, postdoc researcher

Experience & Qualifications: MD, PhD. PhD on nocturia in adults, with special emphasis on pathogenesis of nocturnal polyuria and potential therapeutic strategies. Member of the International Nocturnal Polyuria Research Group.

Workshop 10 – Causes & Co-morbidities of Nocturia

ICS 2017 FLORENCE

Karliën Dhondt



Country: Belgium

Profession: Child & adolescent psychiatrist, somnologist

Experience & Qualifications: MD, PhD, Child & adolescent psychiatrist, somnologist. Main experience in the link between sleep disorders and nocturnal enuresis.

Workshop 10 – Causes & Co-morbidities of Nocturia

ICS 2017 FLORENCE

Philip Van Kerrebroeck



Country: The Netherlands


Profession: Professor of Urology at the University of Maastricht, and works as a urologist at the Maastricht University Medical Centre, the Netherlands.

Experience & Qualifications: MD, PhD, professor. Professor Van Kerrebroeck was for 8 years Chairman of the Standardisation Committee of the International Continence Society and was first author of the Standardisation report on Nocturia and is past Chairman of the ICI-RS Nocturia Think Tank.

Workshop 10 – Causes & Co-morbidities of Nocturia

ICS 2017 FLORENCE

Wendy Bower



Country: Australia

Profession: continence physiotherapist, currently PI investigator of the TANGO study

Experience & Qualifications: MD, PhD, continence physiotherapist. Main experience in incontinence issues in children. She is the Principle Investigator of the TANGO study, an initiative targeting underlying aetiology to guide treatment in people with nocturia.

Workshop 10 – Causes & Co-morbidities of Nocturia

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Workshop 10 – Causes & Co-morbidities of Nocturia

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****NEW FOR 2017****

Please complete the in-app evaluation in the workshop before leaving.

Workshop 10 – Causes & Co-morbidities of Nocturia

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Workshop 10 – Causes & Co-morbidities of Nocturia

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- A shortened version of the handout has been provided on entrance to the hall
- A full handout for all workshops is available via the ICS website.
- Please silence all mobile phones
- Please refrain from taking video and pictures of the speakers and their slides. PDF versions of the slides (where approved) will be made available after the meeting via the ICS website.

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

Phenotyping nocturia

Judge a book by its cover?

An-Sofie Goessaert

ICS 2017 FLORENCE

Affiliations to disclose*:

Nothing to declare

* All financial ties (over the last year) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

Self-funded

Institution (non-industry) funded

Sponsored by:

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

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An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

PHIL BETTER SOON Phil Collins rushed to hospital after gashing his head in horror fall forcing him to cancel London shows

The 66-year-old musician was taken to a London hospital at the accident.

Phil Collins is recovering well and 'doing good' after toilet fall, says daughter Lily at Okja premiere

By Claire Rathor for Metro.co.uk Friday 9 Jan 2017 8:57 am

182

Comeback: Phil Collins takes nasty fall in bathroom, suffers "head gash"

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

To know

The obvious

- Age¹
- Gender²
- Ethnicity³

The background

- Risk of nocturia increases with age
- Men & women are equally affected
- Higher prevalence rates in blacks and Hispanics compared to Caucasians

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

AGAINST ALL ODDSBINS Phil Collins reveals he's back on the booze – despite saying alcohol was killing him

Rock superstar, 66, had quit drinking for three years after being hospitalised in 2012

EXCLUSIVE By Steven Brule, Associate Editor

Phil Collins has revealed he is drinking again despite saying alcohol was killing him.

The rock legend, 66, makes a comeback tonight at

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

Genesis - Dreaming While You Sleep

4 Comments 8 Tags

"Dreaming While You Sleep" as written by and Michael Collins

Rehearsed...

Read More - 1 Edit Wiki

In and out of awareness, in and out of sleep
 Trying to keep my hands upon the wheel
 Never saw the corner in the driving can
 I never saw her step stop the street

Dreaming while you sleep
 Dreaming while you sleep
 Memories to keep
 Dreaming while you sleep

I can never understand what went through my mind
 I didn't stop to see what I had done
 I had to keep on driving deep into the night
 The rules between would somehow put it right

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

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To ask

The obvious

- Alcohol / drinking habits⁴
- Medication⁵ (Diuretics, β-blockers, SSRIs)
- Sleep⁶

The background

- Suppression of ADH
- Increase of 24h urine production
- Increase of ANP (sleep apnea)

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

Frail Phil Collins hobbles around Miami with a walking stick as he continues his recovery from major back surgery last year

By JOHANA CRANLEY FOR WALLTOPELIVE
 PUBLISHED: 10:30 AM EST | UPDATED: 10:30 AM EST | 27 January 2016

Phil Collins is relying on the use of a walking stick after undergoing major surgery on his back last autumn.

The 64-year-old singer was spotted hobbling around his home city of Miami last week, using the stick.

The star opened up about his emergency surgery in an interview with Rolling Stone in October, admitting doctors had to take his back apart.

Scroll down for video

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

Phil Collins, 66, rushed to HOSPITAL after fall on the way to the toilet - as he's forced to postpone remaining London shows at the Royal Albert Hall

Phil Collins has been rushed to hospital after a horror fall on his way to the bathroom.

By Nicole Douglas
Thursday, June 08, 2017

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

To see

<p>The obvious</p> <ul style="list-style-type: none"> • Mobility⁷ • Peripheral edema⁸ • Obesity⁹ 	<p>The background</p> <ul style="list-style-type: none"> • Neurological damage • Nocturnal fluid redistribution • Cardiovascular disease, diabetes mellitus, hypertension, sleep apnea,...
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An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

ICS 2017 FLORENCE

Phil Collins Uses Hypertensive Chamber for Diabetic Foot Abscess
January 30, 2017

340 PHIL COLLINS

One night, pumped full of opiates and completely wired up, I try to rip the whole lot out. Alarms ring and in rush the nurses. I'm given a stern telling-off. Little wonder—it seems these cables and wires are keeping me going; they're literally plugging me into life's backup generator.

Eventually I'm discharged and I start to have something like a relatively normal life. I'm on various medications—for hypertension, my pancreas, my heart. And against all medical advice, non-medical advice and sanity, I start to drink again—slowly. Slowly at

After experiencing a bit of a reveal in the popular Collins recently, Phil Collins has been working hard at getting the word out about homelessness by lending his weight to the Young & Homeless appeal with Centropoint

What does this have to do with hypertensive medicine you ask? Well in Collins' interview on the Young & Homeless appeal on The Independent records he explained that the reason for his last minute absence at the Centropoint Christmas gala, was due to an abscess on his foot that he'd developed from suffering with Type 2 Diabetes. Luckily for Collins, who lives in Spain for the majority of the year, the consultant partner straight into a hypertensive chamber for a weeks worth of HBCT sessions, and the abscess quickly healed.

An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

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To examine

<p>The obvious</p> <ul style="list-style-type: none"> • Enlarged prostate¹⁰ • Hyperglycemia¹¹ • Hypertension¹² 	<p>The background</p> <ul style="list-style-type: none"> • Decreased bladder capacity • Glucosuria • Nocturnal natriuresis
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An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

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<p>To know</p> <p>Age Gender ethnicity</p>	<p>To ask</p> <p>Drinking habits Medication Medical history Quality of sleep Quality of life Daily activities</p>	<p>To see</p> <p>Mobility Peripheral edema Obesity/cachexia Skin colour (pink, puffy/blue bloater)</p>	<p>To examine</p> <p>Prostate Urinary flow Heart rate Blood pressure Blood sugar Creatinine Breathing</p>
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An-Sofie Goessaert – Urology Dept., Ghent University Hospital, Belgium

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To continue... frequency volume chart¹³

<p>The obvious</p> <ul style="list-style-type: none"> • Reduced bladder capacity • 24h polyuria • Nocturnal polyuria 	<p>The background</p> <ul style="list-style-type: none"> • OAB, BPH, bladder stone, bladder cancer • Diabetes, polydipsia • Impairment ADH, RAAS, ANP
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Questions?

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 NOPIA, INPRG

References

1. Boonrod S, Shah N, Nalin TD, Unruh ML. Nocturia and aging: diagnosis and treatment. *Adv Chronic Kidney Dis.* 2010;17(4):e27-40.
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100 YEARS
Ghent University

UZ

Sleep and Nocturia – are central mechanisms into business ?

ICS Firenze
12th of september 2017
Karlien Dhondt, MD, PhD
Center for Neurophysiological Monitoring
Ghent University Hospital, Belgium

SLEEP

NOCTURIA

K. Dhondt

OUTLINE

- The impact of nocturia on sleep AND wakefulness
- The association of nocturia and sleep disorders
- Potential underlying central mechanisms in nocturia

K. Dhondt

OUTLINE

- The impact of nocturia on sleep AND wakefulness
- The association of nocturia and sleep disorders
- Potential underlying central mechanisms in nocturia

K. Dhondt

- Reasons for nocturnal awakenings (US, by age group)

- Nocturia is an independent predictor of insomnia and of deterioration of sleep quality
 - difficulties falling back to sleep
 - fewer hours of sleep
- Nocturia is known to impair mental functioning, quality of life and productivity
- Patients with two or more voids a night have a higher risk of mortality

Assouline et al. Sleep Med Rev. 2013

K. Dhondt

- First uninterrupted sleep period (FUSP) Blivisic et al. Sleep Med 2015, J Clin Sleep Med 2015

PSQI Variable	First (Shortest) Time to First Void Quartile Mean (SE)	Second Time to First Void Quartile Mean (SE)	Third Time to First Void Quartile Mean (SE)	Fourth (Longest) Time to First Void Quartile Mean (SE)	p
Global Score	9.62 (0.27)	8.54 (0.28)	7.75 (0.28)	7.39 (0.27)	< 0.0001
Quality	1.62 (0.05)	1.57 (0.05)	1.43 (0.05)	1.34 (0.05)	0.0015
Latency	1.70 (0.07)	1.39 (0.07)	1.19 (0.07)	1.11 (0.07)	< 0.0001
Duration	1.16 (0.07)	0.98 (0.07)	0.83 (0.07)	0.80 (0.07)	0.0020
Efficiency	1.50 (0.08)	1.24 (0.08)	1.04 (0.08)	1.10 (0.08)	0.0005
Sleep Disturbance	1.68 (0.05)	1.63 (0.05)	1.54 (0.05)	1.50 (0.05)	0.0358
Sleep Medication	0.73 (0.07)	0.47 (0.07)	0.50 (0.07)	0.50 (0.07)	0.0486
Daytime Dysfunction	1.37 (0.06)	1.26 (0.06)	1.18 (0.06)	1.12 (0.06)	0.0241

When comparing the average PSQI scores among those in the lowest compared to the highest quartile of time to first void, there was a statistically significant difference among all PSQI subscales.

K. Dhondt

OUTLINE

- The impact of nocturia on sleep AND wakefulness
- The association of nocturia and sleep disorders
 - PLMS in sleep
 - OSAS
- Potential underlying central mechanisms in nocturia

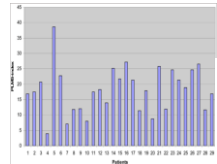
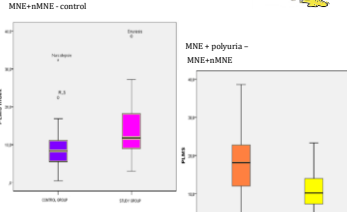
K. Dhandt

I. Obstructive sleep apnea and nocturia Ancoisi-Inaroi et al. Sleep Med Rev. 2015

- Decreased nocturnal plasma renin and aldosterone secretion
- Increase in atrial natriuretic peptide (severe cases)
 - Nocturnal natriuresis
 - Increased diuresis
- Treatment with C-pap
 - Reverses effects of decreased plasma renin/aldosterone secretion
 - Normalizing sodium output
 - Normalizing nocturnal diuresis
- Increase in sleep fragmentation
 - Increase in autonomic arousal
 - Sympathetic outflow ++

K. Dhandt

II. Nocturnal enuresis in childhood and sleep: the presence of Periodic limb movements in sleep (PLMS)

K. Dhandt et al. J Inorg Biochem 2009, Acta Paediatr 2014, Ped Nephrol 2015

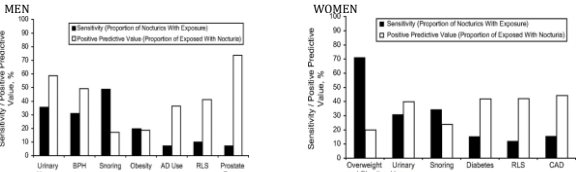
K. Dhandt

Nocturia and NE: continuum ? K. Dhandt

- Similarities, differences (L.S. Grunze et al)

Epidemiological study




- Sensitivity and positive predictive value for correlates of nocturia among men/women in the population-based Finnish National Nocturia and Overactive Bladder Study, Finland, 2003-2004. (Kari A. G. Tikkanen et al. Am J Epidemiol. 2009)
- Strong association with RLS symptoms and PLMS findings on PSG



K. Dhandt

Restless leg syndrome (RLS) and PLMS ?

- movement disorder: PLMS-index (per hour of sleep) >5
 - Causes sleep fragmentation
 - Cortical arousal / Autonomic arousal
- dopaminergic neurotransmission hypofunction hypothesis:
 - At least, PLMS are partially under dopaminergic control
 - Pharmacological trials with DA agonists reduce PLMS
 - Neuro-imaging studies
 - Down regulation of flurodopa binding in putamen/caudate nucleus
 - SPECT: D2 receptor binding impaired throughout the striatal brain region
- But:
 - no differences in dopamine/metabolites concentration in CSF
 - no differences in dopamine transporter (SPECT)

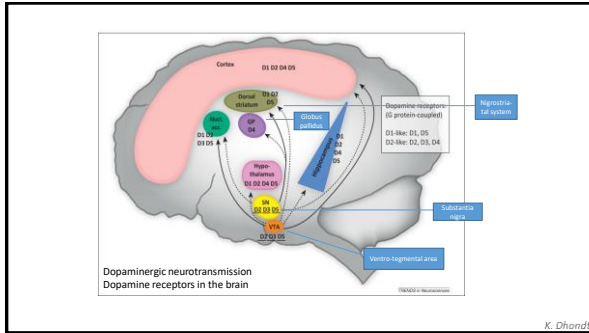




K. Dhandt

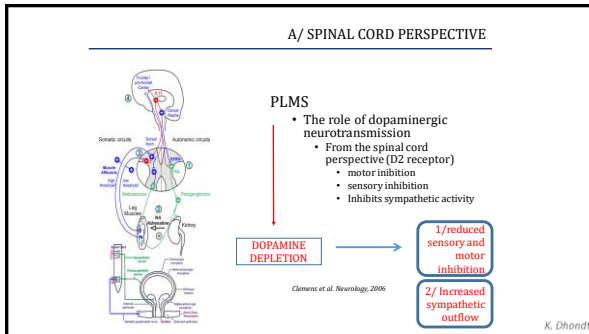
OUTLINE

- The impact of nocturia on sleep AND wakefulness
- The association of nocturia and sleep disorders
- Potential underlying central mechanisms in nocturia

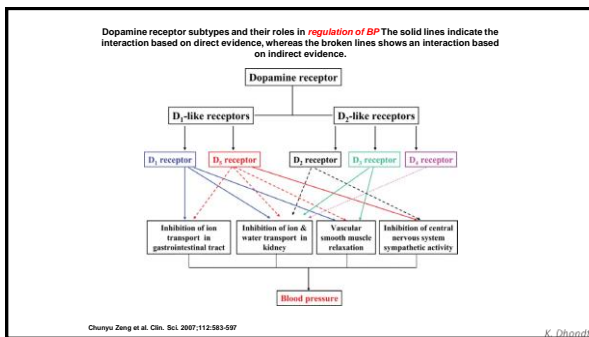
K. Dhandt



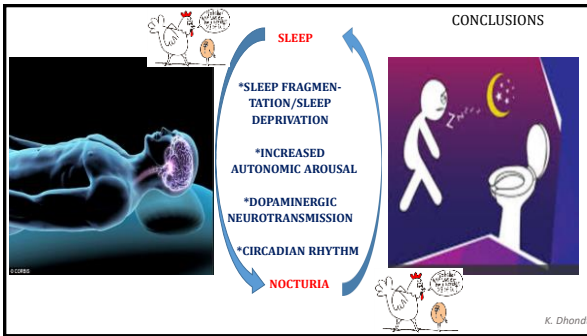
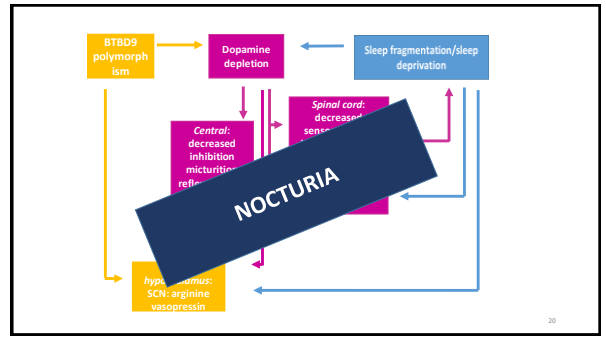
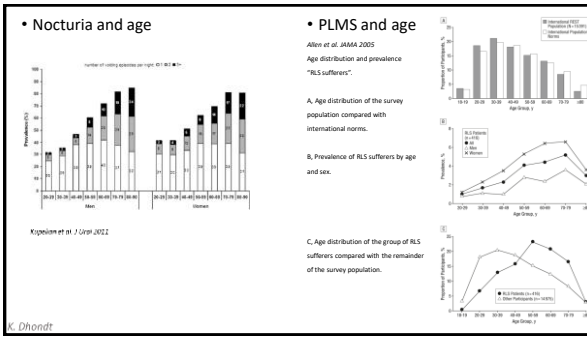
- Dopaminergic neurotransmission
 - Two types of receptors: D1 like (D1,D5), D2 like (D2,D3,D4)
 - D1 receptors are more abundant than D2 receptors in neocortical areas, particularly in prefrontal regions
 - Cortical D1 receptor system plays a key role in **executive functioning, working memory, attention, and inhibition**, which depends on frontal lobe integrity
 - Projections:
 - From the spinal cord perspective (A)
 - Central brain regions (B)
- Complex, dose dependent interactions...
- K. Dhondt



- B/ CENTRAL DOPAMINERGIC SYSTEM
- D1, D2 receptor
 - D1 inhibits micturition reflex
 - D2 relaxes urethral sfincter
 - Animal pharmacological studies (cats)
 - Increasing DA during bladder filling phase
 - DA controls bladder function
 - D1 antagonist: bladder hyperactivity
 - D2 antagonist: no effect on urethral sfincter
-
- K. Dhondt



- Causes of dopaminergic hypofunction ?
- Genetics
 - BTBD9 polymorphism *Stefansson et al. N Engl J Med 2007; Moore et al. Sleep 2014*
 - Iron storage
 - Circadian disorder (hypothalamus)
 - Sleep deprivation (animal studies): decrease of tyrosine hydroxylase
 - Aging; loss of dopaminergic neurotransmission
 - Human molecular imaging studies have consistently found an age-related decrease of D2 receptor markers in the magnitude of 5–10% per decade, starting in early adulthood *Ishikawa et al. Synapse 2009*
 - Losses of D1 receptor densities in the striatum of around 8% per decade *Riekmann et al. Cereb Cortex 2011*
- Model: Parkinson's disease
- K. Dhondt




Maastricht UMC+

BLADDER and KIDNEY

Making the bladder gladder or lowering the water levels?

Philip E.V. Van Kerrebroeck, MD, PhD, MMSc
Professor of Urology, Maastricht University Medical Center+



Maastricht UMC+

ICS 2017 FLORENCE

Affiliations to disclose[†]:
Astellas, Astra-Zeneca, Axonics, Ferring, Medtronic

* All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

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Nocturia is a multifactorial medical condition

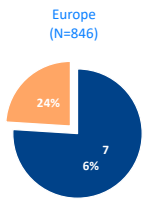
Nocturnal polyuria impaired circadian rhythm of AVP, diuretics, congestive heart failure, obstructive sleep apnoea, peripheral oedema, excessive nocturnal fluid intake	Global polyuria diabetes mellitus/insipidus, primary polydipsia, medication, excessive fluid intake
Reduced bladder capacity benign prostatic hyperplasia (BPH), neurogenic bladder, idiopathic nocturnal detrusor overactivity, other urological conditions/disorders/malignancies, anxiety disorders, medication (e.g. beta blockers)	Sleep disorders primary or secondary sleep disorders, neurologic conditions, psychiatric disorders, chronic pain, medication, alcohol

Nocturia

Maastricht UMC+ Dani H et al. *Nat Rev Urol* 2016;13:573-83; Nimeh T et al. *Curr Urol Rep* 2015;16:66 AVP: arginine-vasopressin

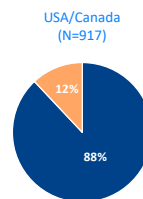
Nocturia is primarily caused by nocturnal polyuria

Europe (N=846)



74% with nocturnal polyuria
24% without nocturnal polyuria (other causes)

USA/Canada (N=917)



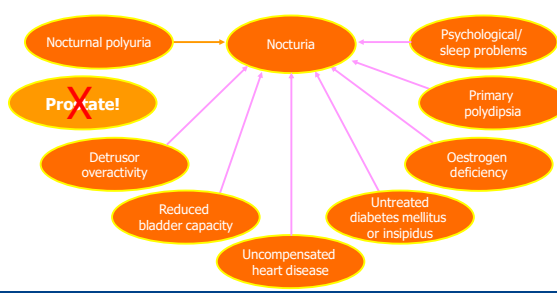
88% with nocturnal polyuria
12% without nocturnal polyuria (other causes)

Nocturnal polyuria based on data from 3- or 7-day frequency-volume charts completed by patients as part of screening for inclusion in subsequent trials of nocturia therapy

Maastricht UMC+ Weiss JP et al. *J Urol* 2011;196:1358-63

What causes nocturia in women?

Nocturia in women often attributed to overactive bladder (OAB)



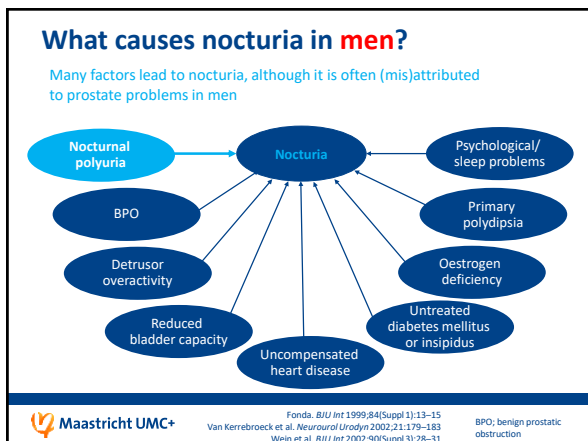
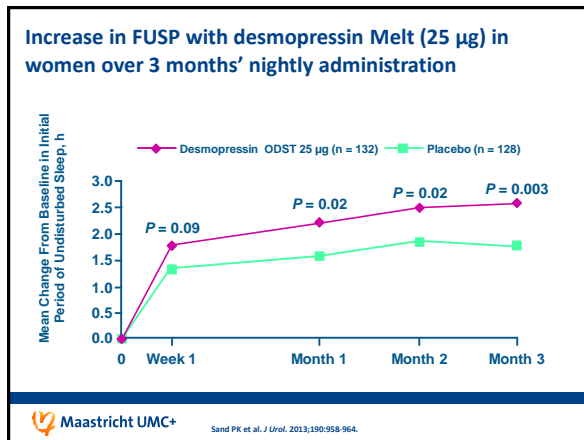
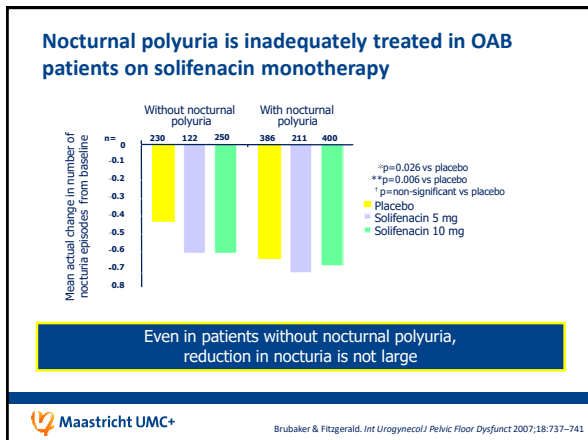
Maastricht UMC+ Fonda, *BJU Int* 1999;84(Suppl 1):13-15 van Kerrebroeck et al. *Neurosci Urodyn* 2002;23:179-183 Wein et al. *BJU Int* 2002;90(Suppl 3):28-31

Overactive bladder diagnosis does not exclude nocturnal polyuria

- In EPIC,¹ 12.8% of women responders had OAB and amongst women with OAB, 74% had nocturia²
- Overall, about 62% of patients with OAB + nocturia (male and female) have nocturnal polyuria (NP)³
- Rate of NP in women with OAB + nocturia increases with age
Prevalence aged 65-74=0.86 [95% CI: 0.62-1.00]⁴

62% of patients diagnosed with OAB and nocturia have nocturnal polyuria

Maastricht UMC+ 1. Irwin et al. *Eur Urol* 2006;50:1306-1314. 2. Irwin et al. *BJU Int* 2008; 3. Brubaker & Fitzgerald. *Int Urogynecol J Public Floor Dysfunct* 2007;18:737-741. 4. Drake et al. *Am J Obstet Gynecol* 2005;192:1682-1686



Thinking beyond the prostate

- Nocturia in men traditionally regarded as due to detrusor overactivity or bladder outlet obstruction (BOO) – caused by BPO
- However, ~83% of male patients with nocturia have nocturnal polyuria (NP)

Causes of male nocturia (total n=41)	Patients (%)
Single isolated causes	
NP	8 (19.51)
Small nocturnal bladder capacity	2 (4.88)
BOO	1 (2.44)
Sleep apnoea syndrome	0 (0)
Double combinations	
NP + small nocturnal bladder capacity	6 (14.63)
NP + BOO	8 (19.51)
Small nocturnal bladder capacity + BOO	4 (9.76)
Triple combinations	
NP + small nocturnal bladder capacity + BOO	10 (24.39)
NP + small nocturnal bladder capacity + sleep apnoea syndrome	2 (4.88)

Maastricht UMC+ | Chang et al. *J Urol* 2006;67:541-544

- ### Are classical BPO treatments good enough?
- Various methods of treating BPO – based on assumption that all symptoms caused by prostate problems
 - α-adrenoceptor antagonists
 - 5α-reductase inhibitors
 - TURP
 - Phytotherapy
 - Combination therapy
 - These can be effective for some LUTS, but nocturia – rated the most bothersome of LUTS – may not be significantly improved¹
- Maastricht UMC+ | TURP, transurethral resection of the prostate; LUTS, lower urinary tract symptoms; 1. Djavan et al. *Eur Urol Suppl* 2005;4:61-68

TURP has limited effect on nocturia

- 118/138 (85.5%) patients with BPO had nocturia before TURP
- After treatment, 91 of these (77.1%) still reported nocturia
- Improvement in nocturia score (1.0) significantly inferior to improvements for all other IPSS symptoms

	Patients scoring ≥2 score before TURP	Patients scoring ≥2 score after TURP	Rate of response (%)
Emptying	102	27	54.3
Voiding frequency	116	63	38.4
Intermittency	101	33	49.3
Urgency	103	70	37.0
Weak stream	122	35	63.0
Hesitancy	84	18	47.8
Nocturia	118	91	19.6

TURP not the answer – are other mechanisms involved?

Maastricht UMC+ | IPSS, International Prostate Symptom Score; Yoshimura et al. *Urology* 2003;61:4786-790

Tamsulosin OCAS not significantly better than placebo in reducing nocturnal voids

- 8-week study, n=117
- Some improvements in overall IPSS scores BUT
 - Mean reduction in number of nocturnal voids **not** significantly greater with tamsulosin OCAS than placebo (p=0.10)
 - Increase in duration of undisturbed sleep **not** significantly greater with tamsulosin OCAS than placebo (p=0.20)

Maastricht UMC+ OCAS: oral controlled absorption system Djavan et al. Eur Urol Suppl 2005;4:61-68

NP often underlies failure of α_1 -blocker treatment for nocturia

- Of 41 patients with nocturia which was not responsive to α_1 -blocker treatment, 85.4% found to have nocturnal polyuria
- Treatment specifically for nocturnal polyuria may improve nocturia

n=41 (α_1 -blocker-resistant males)

Category	Percentage
Nocturnal polyuria	85.4%
Polyuria	9.8%
Normal nocturnal output	4.8%

Maastricht UMC+ Yoong et al. Med J Malaysia 2005;60:294-296

Up to 95% of BPE patients have NP and nocturia resistant to α_1 -blocker therapy

- 55/58 patients (95%) with LUTS suggestive of BPE found to have NP
- Of these, 20 received α_1 -blocker therapy for 6 weeks
 - NP unchanged in 75%
 - No significant difference in mean nocturnal urine production before and during therapy

Maastricht UMC+ BPE: benign prostatic enlargement NP: nocturnal polyuria Koseoglu et al. J Urol 2005;67:1188-1192

For once ...

... men aren't so different from women

They may benefit similarly from desmopressin treatment for nocturia!

Maastricht UMC+

Increase in FUSP with desmopressin Melt (50 μ g) in men over 3 months' nightly administration

Time Point	Desmopressin ODSST 50 μ g (n = 119)	Placebo (n = 142)
0	0.0	0.0
Week 1	~1.1	~0.5
Month 1	~1.6	~0.9
Month 2	~2.1	~1.2
Month 3	~1.8	~1.3

P-values: Week 1 (P=0.0004), Month 1 (P=0.0017), Month 2 (P<0.0001), Month 3 (P=0.0064)

Maastricht UMC+ Weiss JP et al. J Urol. 2013;190:965-972S.

Combination therapy may also be used for patients with nocturnal polyuria

- Combination therapy should also take NP into account to alleviate nocturia
- Patients may have:
 - BPO + NP
 - OAB + NP
 - BPO + OAB + NP
- Therefore:
 - antimuscarinic + α_1 -blocker + desmopressin may be required for successful nocturia treatment
- Clinical studies to evaluate benefits of combination therapy are warranted

Maastricht UMC+ NP: nocturnal polyuria; BPO: benign prostatic obstruction; OAB: overactive bladder

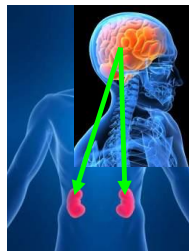
Nocturia needs to be treated according to its causes

- If a patient has nocturia and diagnosis of OAB or BPO, they may ALSO have NP
- If NP present, consider combination therapy:

Diagnosis	Desmopressin	Anticholinergic	α_1 -blocker
NP	✓		
OAB		✓	
BPO			✓
NP + OAB	✓	✓	
NP + BPO	✓		✓
OAB + BPO		✓	✓
NP + OAB + BPO	✓	✓	✓

Conclusions

Think on the bladder and the kidneys!



- >80% of patients with nocturia have nocturnal polyuria (NP)
- NP comorbid with BPO and/or OAB must be addressed
- desmopressin successfully treats nocturia caused by NP
- combination therapy (desmopressin + anticholinergics + α_1 -blockers) is feasible to improve nocturia in patients with BPO and/or OAB with NP

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NOCTURIA
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improve the diagnosis
and treatment of Nocturia



www.europeanurology.com/nocturia

Development of **TANGO**, a screening tool to identify co-existing causes of Nocturia

A/Prof Wendy Bower FACP

Department of Medicine and Community Care, Melbourne Health
Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne



Affiliations to disclose[†]:

Ferring Pharmaceuticals

Funding for speaker to attend:

- Self-funded
- Institution (non-industry) funded
- Sponsored by: *Ferring*

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

.. nocturia is outside the category of a storage lower urinary tract symptom (LUTS)



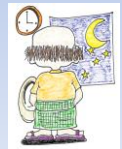
Gulur 2011; Drake 2015

Frequency, Urgency and Nocturia

“...no single variable affected 50% or more of men with nocturia

...in women multiple correlates predictive of night voiding”

Tikkinen 2010



Targeting **A**etiology of **N**octuria **G**uides **O**utcomes

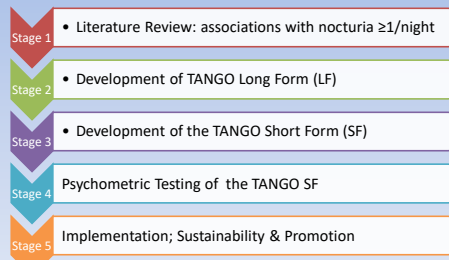
AIM: To develop a brief patient-completed screening tool to capture all-causes of nocturia

To be used in conjunction with

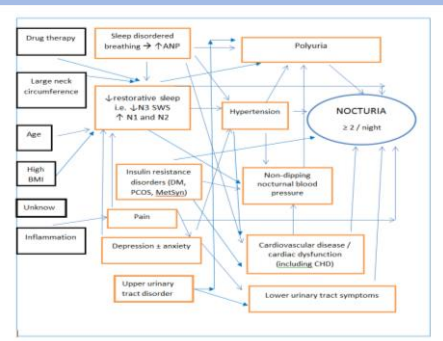
- Bladder diary
- Sleep measures
- Renal function tests
- Urine flow dynamics
- Patient-Reported Outcomes



TANGO Study Overview



Nocturia: Causal inter-relationships



Stage 2: Development of TANGO LF



Process

- Expert panel selected validated & reliable questionnaires that captured the comorbidities identified in Stage 1.
- Discriminating items were added to an item bank.



TANGO LF

- 57 self-reported questionnaire items
- 10 clinical measures



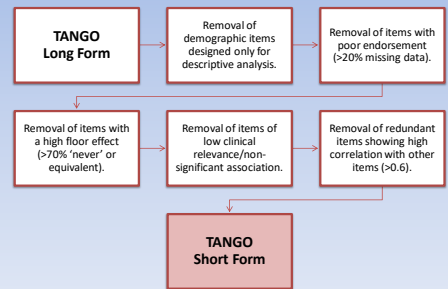
Pilot

- n=21 individuals ≥40 years
- Feedback → modifications to wording and formatting

Stage 2: Development of TANGO LF

- Variables having a significant risk association with nocturia of ≥ 1 /night identified
- TANGO Long Form developed
 - 6 domains
 - 57 items, 10 clinical measures
 - self-completed questionnaire
- Sample size: N=250 patients
- ≥ 40 years age, nocturia ≥ 1 /night,
- Recruited from Sleep / Continence / Falls and Balance / Rehabilitation services at RMH

Stage 3: Development of TANGO SF



TANGO: Methods



Short form:

- Retained items with:
 - Direct causal link to nocturia
 - High endorsement
 - Significant association with nocturia ≥ 2
 - Significant association with high bother
- Items worded according to cut-off from analysis
- Pilot of Short Form on 10 adults → modification of wording when problematic

TANGO NOCTURIA SCREEN

Number of times wake up to urinate? _____ (0=1 Patient/Doctor Note)

Please an 'X' beside each statement to indicate whether or not it is true for you. True False

Category	Statement	True	False
CARDIO-METABOLIC	My ankles, feet or legs swell during the day	<input type="checkbox"/>	<input type="checkbox"/>
	I take heart tablets (e.g. Lasix)	<input type="checkbox"/>	<input type="checkbox"/>
	I have kidney disease	<input type="checkbox"/>	<input type="checkbox"/>
	I take tablets to control my blood pressure	<input type="checkbox"/>	<input type="checkbox"/>
	I often get dizzy when standing up	<input type="checkbox"/>	<input type="checkbox"/>
SLEEP	I have high blood sugar (Diabetes)	<input type="checkbox"/>	<input type="checkbox"/>
	My blood sugar levels are difficult to keep stable	<input type="checkbox"/>	<input type="checkbox"/>
	I have 7 hours or less sleep per night	<input type="checkbox"/>	<input type="checkbox"/>
URINARY TRACT	I need to get up to pass urine within 3 hours of going to sleep	<input type="checkbox"/>	<input type="checkbox"/>
	I experience a sudden urge to urinate on most days	<input type="checkbox"/>	<input type="checkbox"/>
	I have a bladder urgency accident once or more a week or more	<input type="checkbox"/>	<input type="checkbox"/>
	I often need to strain or push to start urinating	<input type="checkbox"/>	<input type="checkbox"/>
	I have an enlarged prostate gland (BPH/LEU/ENLTY)	<input type="checkbox"/>	<input type="checkbox"/>
GENERAL	In general, I would say that my health is not good	<input type="checkbox"/>	<input type="checkbox"/>
	I have trouble staying awake while driving, sitting or during social activities	<input type="checkbox"/>	<input type="checkbox"/>
	I often wake up at night in the last 3 months	<input type="checkbox"/>	<input type="checkbox"/>

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The TANGO Short Form Screening Questionnaire

Stage 3: Development of TANGO SF

Cardio/Metabolic Domain

<input type="checkbox"/>	My ankles, feet or legs swell during the day.
<input type="checkbox"/>	I take fluid tablets (e.g. Lasix).
<input type="checkbox"/>	I have kidney disease.
<input type="checkbox"/>	I take tablets to control my blood pressure.
<input type="checkbox"/>	I often get dizzy when standing up.
<input type="checkbox"/>	I have high blood sugar OR diabetes.
<input type="checkbox"/>	My blood sugar levels are difficult to keep stable.

CARDIO / METABOLIC

Stage 3: Development of TANGO SF

Sleep Domain

<input type="checkbox"/>	I have 5 hours or less sleep per night.
<input type="checkbox"/>	I would describe my sleep quality as bad.
<input type="checkbox"/>	It takes me longer than 30 minutes to fall asleep at night.
<input type="checkbox"/>	I have difficulty staying asleep at night because of my bladder.
<input type="checkbox"/>	I often experience pain at night.
<input type="checkbox"/>	I have been told I snore loudly OR stop breathing at night.

SLEEP

Stage 3: Development of TANGO SF

Urinary Tract Domain

<input type="checkbox"/>	I need to get up to pass urine within 3 hours of going to sleep.
<input type="checkbox"/>	I experience a sudden urge to urinate on most days.
<input type="checkbox"/>	I have a bladder urgency accident once a week or more.
<input type="checkbox"/>	I often need to strain or push to start urinating.
<input type="checkbox"/>	I have an enlarged prostate gland. (MALES ONLY)

URINARY TRACT

Stage 3: Development of TANGO SF

Wellbeing Domain

<input type="checkbox"/>	In general, I would say that my health is <i>not</i> good.
<input type="checkbox"/>	I have trouble staying awake while driving, eating or during social activities.
<input type="checkbox"/>	I have had a fall in the last 3 months.
<input type="checkbox"/>	I don't look forward to things with as much enjoyment as I used to.

WELLBEING

TANGO SCREENING QUESTIONNAIRE
Place a tick next to each statement which is TRUE for you.
If the statement does not apply, leave the box blank *One of 5*

<input type="checkbox"/>	My ankles, feet or legs often swell during the day.
<input type="checkbox"/>	I take fluid tablets (e.g. Lasix).
<input type="checkbox"/>	I have kidney disease.
<input type="checkbox"/>	I take tablets to control my blood pressure.
<input type="checkbox"/>	I often get dizzy when standing up.
<input type="checkbox"/>	I have high blood sugar OR diabetes.
<input type="checkbox"/>	My blood sugar levels are difficult to keep stable.
<input checked="" type="checkbox"/>	I would usually have 8 hours or less sleep per night.
<input type="checkbox"/>	I would describe my sleep quality as 'very bad'.
<input type="checkbox"/>	It usually takes me longer than 30 minutes to fall asleep at night.
<input type="checkbox"/>	I often have difficulty staying asleep at night.
<input type="checkbox"/>	I have difficulty staying asleep at night, but only because of my bladder.
<input type="checkbox"/>	I often experience pain at night. (Pain \neq TIS).
<input checked="" type="checkbox"/>	I have been told I snore loudly OR stop breathing at night.
<input checked="" type="checkbox"/>	I often need to get up to pass urine within 3 hours of going to sleep.
<input type="checkbox"/>	I experience a sudden urge to urinate on most days.
<input type="checkbox"/>	I have a bladder urgency accident once a week or more.
<input type="checkbox"/>	I often need to strain/push to start urinating.
<input type="checkbox"/>	I have an enlarged prostate gland. (MALES ONLY)
<input type="checkbox"/>	In general, I would say that my health is fair to poor.
<input type="checkbox"/>	I have trouble staying awake while driving, eating or during social activities.
<input type="checkbox"/>	I have had a fall, slip or trip in the last 3 months.
<input type="checkbox"/>	I look forward with enjoyment to things less than I used to.

CARDIO/METABOLIC
SLEEP
URINARY TRACT
WELLBEING

TANGO SCREENING QUESTIONNAIRE
Place a tick next to each statement which is TRUE for you.
If the statement does not apply, leave the box blank *Not a tick*

<input type="checkbox"/>	My ankles, feet or legs often swell during the day.
<input type="checkbox"/>	I take fluid tablets (e.g. Lasix).
<input type="checkbox"/>	I have kidney disease.
<input checked="" type="checkbox"/>	I take tablets to control my blood pressure.
<input checked="" type="checkbox"/>	I often get dizzy when standing up.
<input checked="" type="checkbox"/>	I have high blood sugar OR diabetes.
<input checked="" type="checkbox"/>	My blood sugar levels are difficult to keep stable.
<input checked="" type="checkbox"/>	I would usually have 8 hours or less sleep per night.
<input checked="" type="checkbox"/>	I would describe my sleep quality as 'very bad'.
<input checked="" type="checkbox"/>	It usually takes me longer than 30 minutes to fall asleep at night.
<input checked="" type="checkbox"/>	I often have difficulty staying asleep at night.
<input checked="" type="checkbox"/>	I have difficulty staying asleep at night, but only because of my bladder.
<input checked="" type="checkbox"/>	I often experience pain at night. (Pain \neq TIS).
<input checked="" type="checkbox"/>	I have been told I snore loudly OR stop breathing at night.
<input checked="" type="checkbox"/>	I often need to get up to pass urine within 3 hours of going to sleep.
<input checked="" type="checkbox"/>	I experience a sudden urge to urinate on most days.
<input checked="" type="checkbox"/>	I have a bladder urgency accident once a week or more.
<input checked="" type="checkbox"/>	I often need to strain/push to start urinating.
<input checked="" type="checkbox"/>	I have an enlarged prostate gland. (MALES ONLY)
<input checked="" type="checkbox"/>	In general, I would say that my health is fair to poor.
<input checked="" type="checkbox"/>	I have trouble staying awake while driving, eating or during social activities.
<input checked="" type="checkbox"/>	I have had a fall, slip or trip in the last 3 months.
<input checked="" type="checkbox"/>	I look forward with enjoyment to things less than I used to.

CARDIO/METABOLIC
SLEEP
URINARY TRACT
WELLBEING

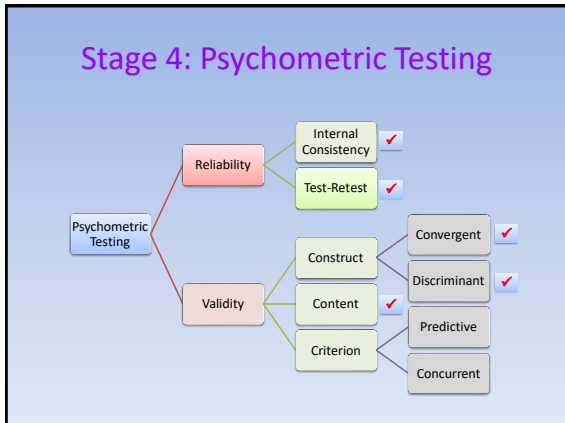
TANGO SCREENING QUESTIONNAIRE
 Place a tick next to each statement which is TRUE for you. If the statement does not apply, leave the box blank. I prefer to leave blank

N=2

<input type="checkbox"/> My ankles, feet or legs often swell during the day.	CARDIOVASCULAR
<input type="checkbox"/> I take fluid tablets (e.g. Lasix).	
<input type="checkbox"/> I have kidney disease.	
<input type="checkbox"/> I take tablets to control my blood pressure.	
<input type="checkbox"/> I often get dizzy when standing up.	SLEEP
<input type="checkbox"/> I have high blood sugar (diabetes).	
<input type="checkbox"/> My blood sugar levels are difficult to keep stable.	
<input checked="" type="checkbox"/> I would usually have 6 hours or less sleep per night.	
<input checked="" type="checkbox"/> I would describe my sleep quality as 'very bad'.	URINARY TRACT
<input checked="" type="checkbox"/> I usually take more than 30 minutes to fall asleep at night.	
<input checked="" type="checkbox"/> I often have difficulty sleeping at night.	
<input checked="" type="checkbox"/> I have difficulty staying asleep at night, but only because of my bladder.	
<input checked="" type="checkbox"/> I often experience pain at night (pain <u>at night</u>).	HEARING
<input checked="" type="checkbox"/> I have been told I have nocturia (I get up to urinate at night).	
<input checked="" type="checkbox"/> I often need to get up to pass urine within 3 hours of going to sleep.	
<input checked="" type="checkbox"/> I experience a sudden urge to urinate on most days.	
<input type="checkbox"/> I have a bladder urgency accident once a week or more.	
<input type="checkbox"/> I often need to strain/push to start urinating.	
<input type="checkbox"/> I have an enlarged prostate gland. (MALES ONLY)	
<input checked="" type="checkbox"/> In general, I would say that my health is fair to poor.	
<input type="checkbox"/> I have trouble staying awake while driving, walking or during social activities.	
<input type="checkbox"/> I have had a fall, slip or trip in the last 3 months.	
<input type="checkbox"/> I look forward with enjoyment to things less than I used to.	

Interpretation Guidelines: Primary Care & Hospital

CARDIOVASCULAR	<input type="checkbox"/> My ankles, feet or legs often swell during the day.	<input type="checkbox"/> I take fluid tablets (e.g. Lasix).	<input type="checkbox"/> I have kidney disease.	<input type="checkbox"/> I take tablets to control my blood pressure.
SLEEP	<input checked="" type="checkbox"/> I would usually have 6 hours or less sleep per night.	<input checked="" type="checkbox"/> I would describe my sleep quality as 'very bad'.	<input checked="" type="checkbox"/> I usually take more than 30 minutes to fall asleep at night.	<input checked="" type="checkbox"/> I often have difficulty sleeping at night.
URINARY TRACT	<input checked="" type="checkbox"/> I have difficulty staying asleep at night, but only because of my bladder.	<input checked="" type="checkbox"/> I often experience pain at night (pain <u>at night</u>).	<input checked="" type="checkbox"/> I have been told I have nocturia (I get up to urinate at night).	<input checked="" type="checkbox"/> I often need to get up to pass urine within 3 hours of going to sleep.
HEARING	<input checked="" type="checkbox"/> In general, I would say that my health is fair to poor.	<input type="checkbox"/> I have trouble staying awake while driving, walking or during social activities.	<input type="checkbox"/> I have had a fall, slip or trip in the last 3 months.	<input type="checkbox"/> I look forward with enjoyment to things less than I used to.



Reliability Testing of TANGO

Objective: To establish test-rest reliability of the TANGO SF

Setting & Participants: 40 rehabilitation inpatients

- Inclusion Criteria:
 - ≥ 40 years of age
 - LOS ≥ 5 days from initial contact by RA
- Exclusion Criteria:
 - Conditions associated with atypical nocturia; urinary catheterisation; cognitive impairment or limited English that precluded questionnaire completion

Results: Substantial to perfect agreement (Kappa 0.61-1.0) demonstrated on 17 of the 22 TANGO SF items

TANGO RESULTS

- 23 item screening tool for aetiology of nocturia
- Identifies clinically relevant causes of nocturia
- Minimum time burden
 - Patient completed
- Easy to interpret visually
 - interpretation guideline under development
- May direct treatment to underlying causes
 - Multi-modal therapy
 - Facilitate right treatment for right patient

Development of a long-form screening tool to identify clinically relevant comorbidities of nocturia

Nocturia as a Marker of Poor Health: Causal Associations to Inform Care

Re-Reliability testing of the TANGO

TANGO - a screening tool to identify comorbidities on the causal pathway of nocturia

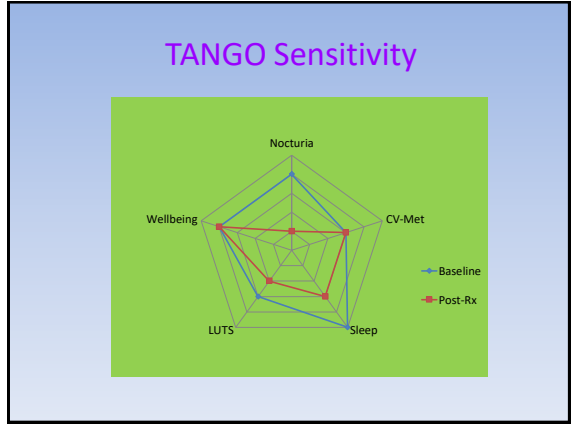
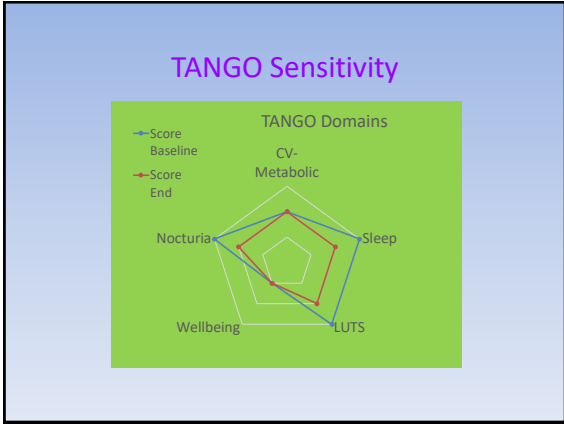
Objective: To identify a short screening tool for use in identifying risk factors for nocturia... **Results:** The majority (80%) of the sample are included... **Conclusions:** A short screening tool for identifying risk factors for nocturia...

GENDER-SPECIFIC VERSIONS

- Low testosterone levels in men and oestrogen in women is associated with ↑ water and salt diuresis
 - Sex hormones stimulate ANP → to reduce sodium load → ↑ GFR → ↑ urine production
- Testosterone deficiency is associated with:
 - Hot flushes and sweating
 - Insomnia or other sleep disturbances
 - Lower sleep efficiency: ↑ nocturnal awakenings, ↓ time in slow-wave sleep? Modulated via adiposity (Barrett-Connor 2008).
- Low testosterone levels frequently coexist with obstructive sleep apnoea (men)
 - Higher apnea-hypopnea index
 - More sleep time with O₂ saturation levels < 90%.
- Progesterone and estrogen deficiency
 - Difficulty staying asleep
 - Night sweats

GENDER-SPECIFIC VERSIONS

- TANGO-M extra variables
 - I wake from sleep because of night sweats / feeling hot
 - I wake from sleep because of feeling cold
 - I have not had my testosterone levels checked
- TANGO-F extra variables
 - I have difficulty staying asleep at night because of feeling hot / sweating
 - My last menstrual period was more than 1 year ago
 - I do not take oestrogen (tablets or patches)



- ### TANGO extension
- Develop Patient Reported Outcomes from
 - Sleep
 - LUTS
 - QoL
 - Consumer perspective
 - Methodology: n=204 data sets that included
 - Pittsburgh Sleep Quality Index (PSQI),
 - ICIQ-Overactive Bladder
 - ICIQ-Female Lower Urinary Tract Symptoms Long Form
 - ICIQ-Male Lower Urinary Tract Symptoms Long Form
 - Nocturia Quality of Life
 - Associations between episode frequency, bother and variables

Descriptive findings (N=1 vs N≥2)

	1/night n=101	≥2/night n=124	OR ≥2/night Significance 1 vs
Urgency (n, % 2daily)	21 (34%)	103 (73%)	0.25, p<0.001
Urgency Incontinence (n, % 2daily)	12 (19%)	62 (44%)	0.23, p<0.001
Bother due to nocturia (n, % ≥ moderate bother)	17 (27%)	105 (74%)	0.35, p<0.001
FUST in hrs (median, IQR)	4.1 (3.5-5.4)	2.5 (2.0-3.0)	0.26, p<0.001
Sleep Efficiency (median, IQR)	88 (76-97)	81 (64-94)	0.97, p=0.010
Overall sleep quality (n, % fairly to very bad)	15 (24%)	61 (43%)	0.37, p= 0.012
Discomfort breathing whilst sleeping (n, % ≥weekly)	2 (3%)	24 (17%)	0.24, p=0.018
Sleep Latency (≥30mins)	18 (29%)	62 (44%)	1.91, p=0.050

- Establish “predictors” of nocturia:
 - High frequency and nocturia-related bother
-
- What matters to patients?
 - on-line data collection of ranked bother of Nocturia

TANGO Uno

You Know. We Want to Understand.

UnO – We want to Know (n=500)

Link through our new TANGO Research Group Facebook page

<https://www.surveymonkey.com/r/TANGO-OS>

Bother Reasons Ranked		
	n	%
Trouble getting back to sleep	32	27.8
Disturbed/disrupted/broken sleep	31	27.0
Having to get out of bed	19	16.5
Fatigue/tiredness next day	12	10.4
Other	7	6.0
Bother to others	6	5.2
No or very little bother	3	2.6
Getting to the toilet on time	1	0.9
Grumpy/bad mood next morning	1	0.9
Bladder Discomfort	1	0.9
Concern re: falling in dark	1	0.9
Worry that condition will worsen	1	0.9

Current work

- Translation of TANGO
- Establishing concurrent validity
- Developing an in-patient version: TANGO-NOW



Thank
you

For more information:

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