

# Nocturia

## Prevalent, Bothersome, CoMorbid, Undertreated

### Musings of a PCP

Martin Miner MD

Founder Men's Health Center The Miriam Hospital

Clinical Professor Family Medicine and Urology

Warren Alpert School of Medicine

Brown University

Providence, RI

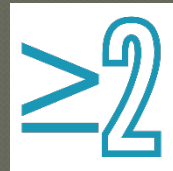
# Nocturia

---

- ◉ What is it?
- ◉ Why should we care?
- ◉ Evaluating the causes?
- ◉ How to treat?
- ◉ Who is in charge of nocturia?

NOCTURIA is defined as waking at night to urinate, with each voiding episode preceded and followed by sleep

Clinically Meaningful



with  $\geq 2$   
episodes/night<sup>2</sup>

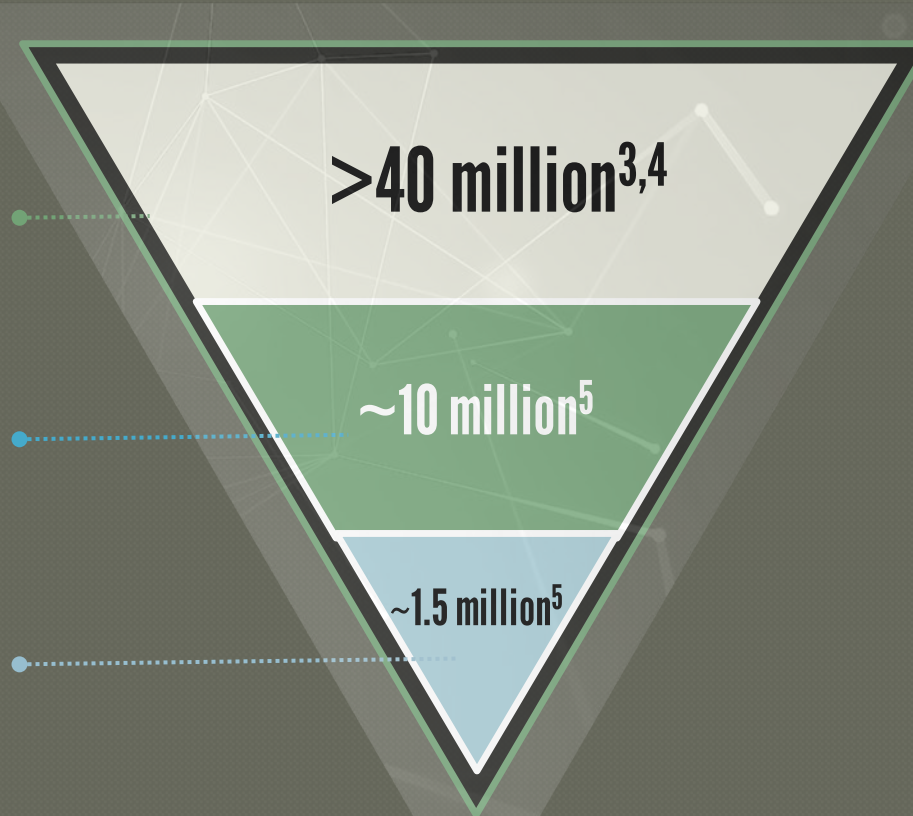


# Prevalent and Undertreated

Prevalence rate: up to **60%**<sup>1,2,\*</sup>

Diagnosis rate: **26%**<sup>5</sup>

Treatment rate: up to **18%**<sup>5,†</sup>



\*Prevalence rates of men and women older than 70 years old with  $\geq 2$  nightly voids (range in men, 29-59%; range in women, 28-62%).<sup>1,2</sup>

†Desmopressin treatment (melt or tablet) among patients with nocturia only.

1. Bosch JL, Weiss JP. *J Urol*. 2013;189(1 Suppl):S86-92. 2. Weiss JP. *Rev Urol*. 2012;14(3-4):48-55. 3. Fitzgerald MP, et al. *J Urol*. 2007;177(4):1385-1389.

4. KFF. <https://www.kff.org/other/state-indicator/distribution-by-age>. Accessed March 23, 2018. 5. Oelke M, et al. *Int J Clin Pract*. 2016;70(11):940-949.

# The Burden of Nocturia Is Broad and Substantial

## ASSOCIATIONS



Reduced quality of life<sup>1,2</sup>



Poorer overall and mental health<sup>1</sup>



Reduced work productivity<sup>1</sup>



Increased falls and fractures<sup>3-6</sup>



Increased mortality<sup>5</sup>

## Short-Term Consequences<sup>8</sup>

- Increased daytime sleepiness
- Reduced daytime energy
- Longer reaction time
- Reduced psychomotor performance
- Decreased concentration/memory/cognitive function
- Poor mood

**= SLEEP DEPRIVATION**

## Long-Term Consequences<sup>8</sup>

- Depression
- Susceptibility to somatic disease
- Risk of cardiovascular disease
- Risk of car accidents

1. Kobelt G, et al. *BJU Int.* 2003;91(3):190-195. 2. van Dijk MM, et al. *BJU Int.* 2010;105(8):1141-1146. 3. Asplund R. *Arch Gerontol Geriatr.* 2006;43(3):319-326. 4. Stewart RB, et al. *J Am Geriatr Soc.* 1992;40(12):1217-1220. 5. Nakagawa H, et al. *J Urol.* 2010;184(4):1413-1418. 6. Temml C, et al. *Neurol Urodyn.* 2009;28(8):949-952. 7. Kupelian et al. *Am Urol Assoc Edu Res.* 2011;185:571-577. 8. Abrams P. *Eur Urol Suppl.* 2005;3(6):1-7.



# NOCTURNAL POLYURIA: DEFINITION AND ETIOLOGIES

- Defined as nighttime urine production  $>20\%$  of the total urine output for younger adults and  $>33\%$  for older adults
- Etiologies – Treat the cause

## OVERCONSUMPTION

*Behavioral*  
*Environmental*  
*Diabetes insipidus*  
*Diabetes mellitus*

## OVERDIURESIS

*Third-space fluid resorption*  
*Fluid shifts*  
*Medications (eg, diuretics)*  
*Sleep disorders or apnea*  
*Congestive heart failure*  
*Renal conditions*  
*Diabetes mellitus*

## TOO LITTLE ANTIDIURESIS

*Circadian defect in secretion  
or action of vasopressin*  
*Renal conditions*  
*Cerebrovascular damage*  
*Central diabetes insipidus*  
*Nephrogenic diabetes insipidus*  
*Neurodegenerative diseases eg Parkinsons*

Is this an ideal urological problem? No surgical solution.....

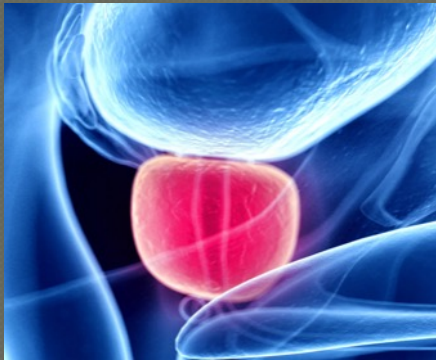
# How much does the etiology matter?

- The etiology of nocturia is multifactorial but >80% of patients with nocturia have nocturnal polyuria (NP)
- Regardless of the frequency or cause, nocturia results from a production of nocturnal urine that exceeds the capacity of the urinary bladder to comfortably store it



# CAUSES OF NOCTURIA

**BPH**



**OAB**



**Nocturia due to  
nocturnal polyuria**



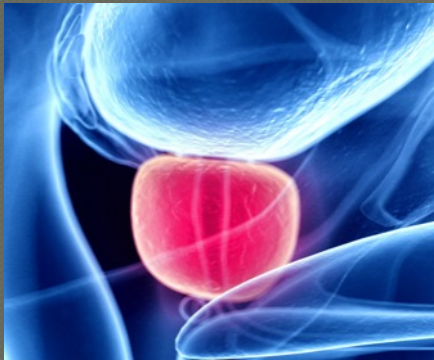
**Sleep Disorders**





# SYMPTOMS DIRECT TREATMENT

**BPH**



**OAB**



**Nocturia due to  
nocturnal polyuria**



**Sleep Disorders**



Alpha Blockers  
5 ARIs  
PDE 5

Antimuscarinics  
Beta 3s  
Botox

Behavioral  
Desmopressin

CPAP

# What Nocturia and Nocturnal Polyuria are **Not**

---

- ⦿ Merely a symptom of other urologic conditions (OAB, BPH)
- ⦿ Normal part of aging (or is it?)



# Prevalence: Higher Younger Women; Older Men

Table describes a global review (43 studies) of nocturia prevalence estimates between 1990 and 2009. (Bosch)

Men	One nightly void	Two or more nightly voids
20-40 years	11-35.2%	2-16%
>70 years	68.9-93%	29-59.3%
Women	One nightly void	Two or more nightly voids
20-40 years	20.4-43.9%	4.4-18%
>70 years	74.1-77.1%	28.3-61.5%

# Obstacles to Clinical Presentation Leads to Undertreatment

---

- ⦿ **Patients may not recognize nocturia as a medical condition**
  - 60.7% of patients assumed it was part of aging process
- ⦿ **Embarrassment and reluctance**
  - 66.4% with <3 nocturnal voids perceived it as a minor problem
- ⦿ **Failure of medical professionals to acknowledge and treat**
  - Of those who had consulted a doctor, 37.2% were not offered any treatment.
- ⦿ **Delay in diagnosis**
  - 12 weeks to make a diagnosis
  - 37 weeks until first prescribed treatment.
  - Time from the onset of symptoms to beginning treatment 105.5 weeks

Oelke M, Anderson P, Wood R, et al. Nocturia is often inadequately assessed, diagnosed and treated by physician: results of an observation, real-life practice dataset containing 8659 European and US-American patients. Int J Clin Pract. 2016;70:940-949. : Oelke M, De Wachter S, Drake MJ, et al. A practical approach to the management of nocturia. Int J Clin Pract. 2017 Nov; 71(11)

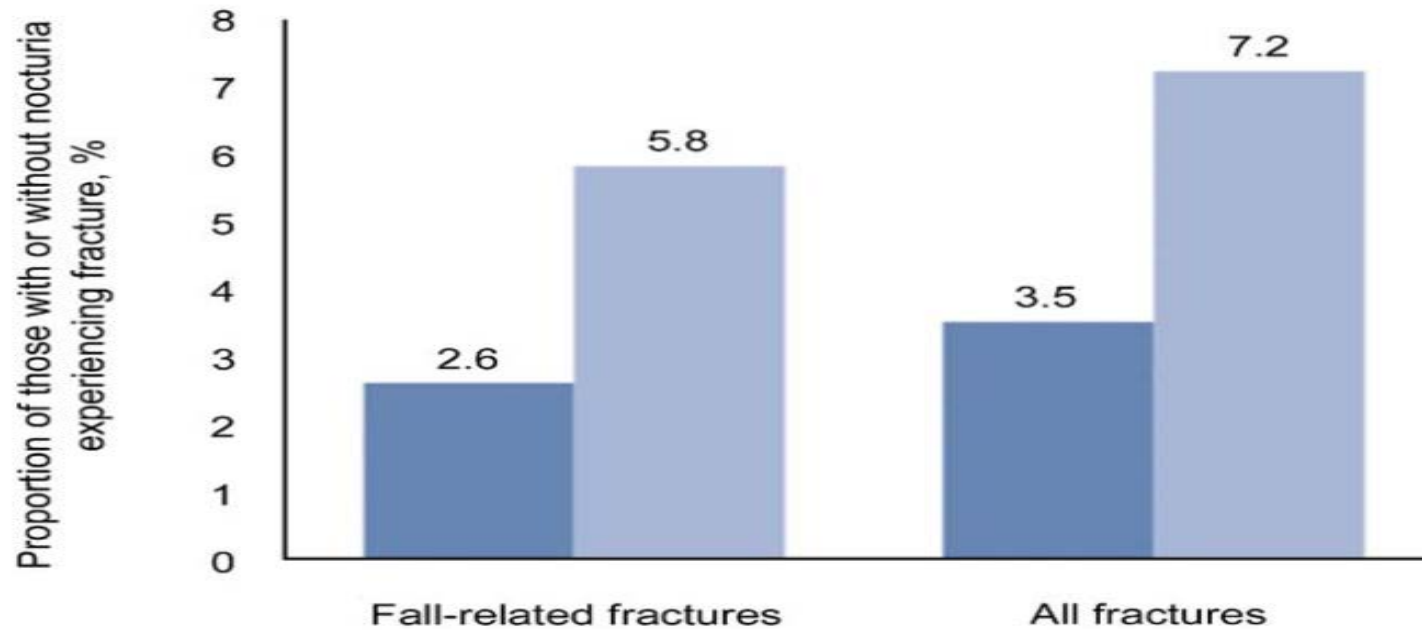
\*Population based study of 8659 patients, data reflects women



# Nocturia means poor sleep

- ⦿ Restorative or deep sleep happens in first 3 - 4 hours
- ⦿ Awakenings during the first 3 - 4 hours are most bothersome
- ⦿ Nocturia  $\geq 2$  correlates with disruption of deep sleep

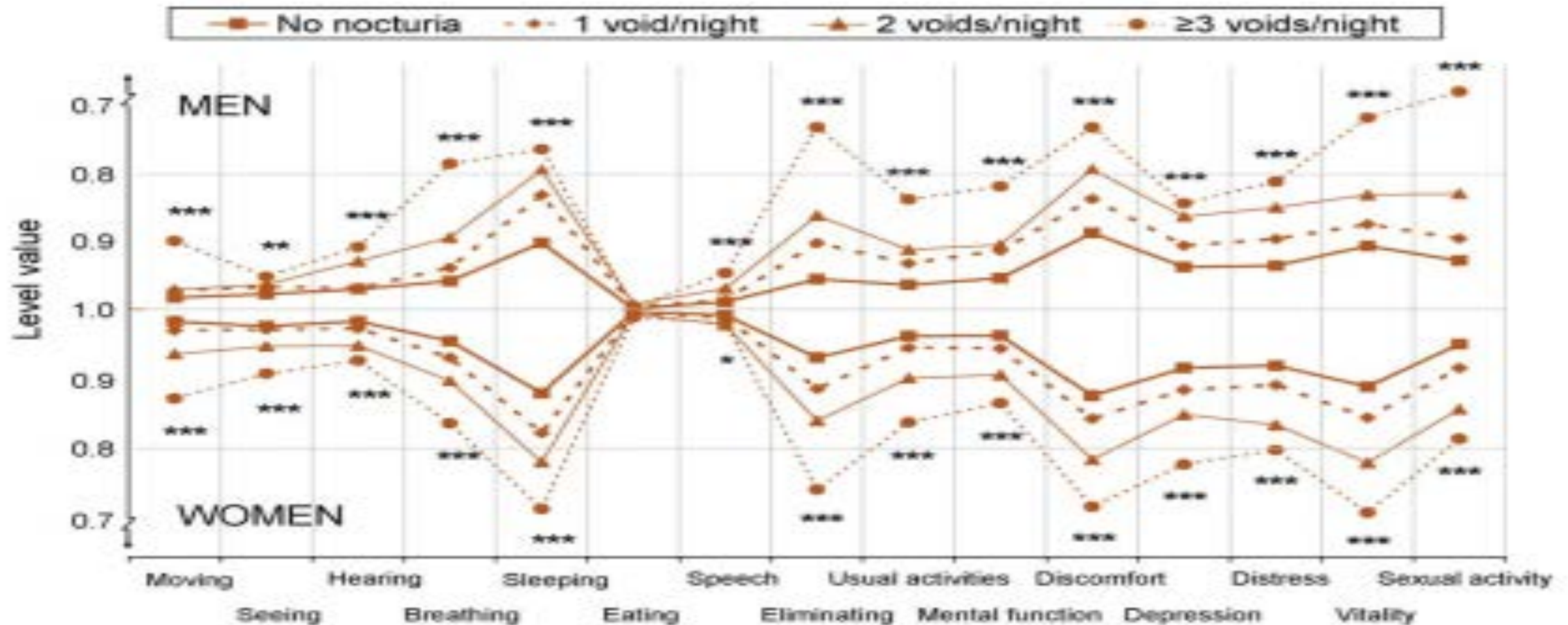
# Impact of Nocturia on Bone Fracture and Falls in Older Individuals



**Figure 1.** Incidence of all and fall related fractures in 359 patients with (light blue bars) and in 425 without (dark blue bars) nocturia was significantly higher in former (each  $p = 0.03$ ).



# Increasing Nocturnal Voids Decreases Most HRQoL Dimensions

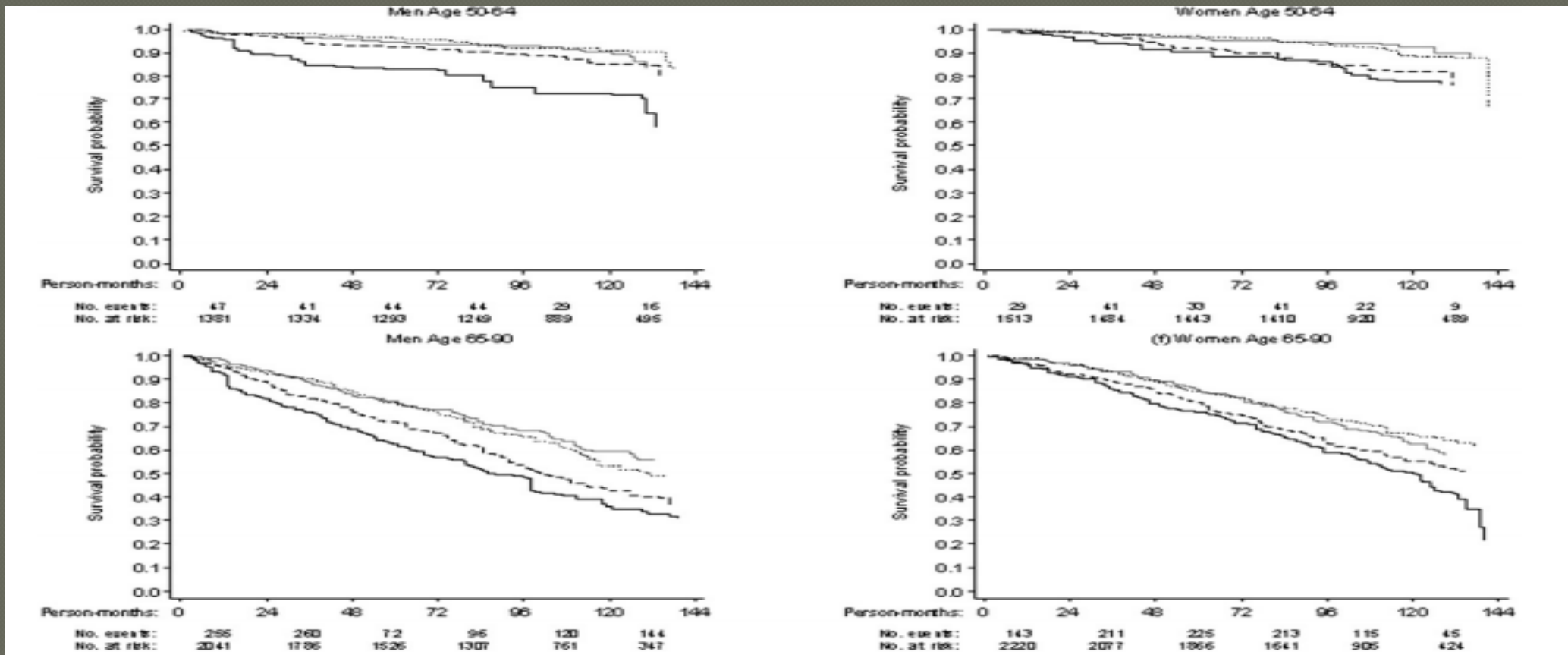


**Degree of bother increased with nocturia frequency ( $p < 0.01$ )**

Tikkinen K, Johnson T, Tammela T, et al. Nocturia Frequency, Both, and Quality of Life: How Often is Too Often? A Population-Based Study in Finland. Eur Uro 2010; 57:488-498

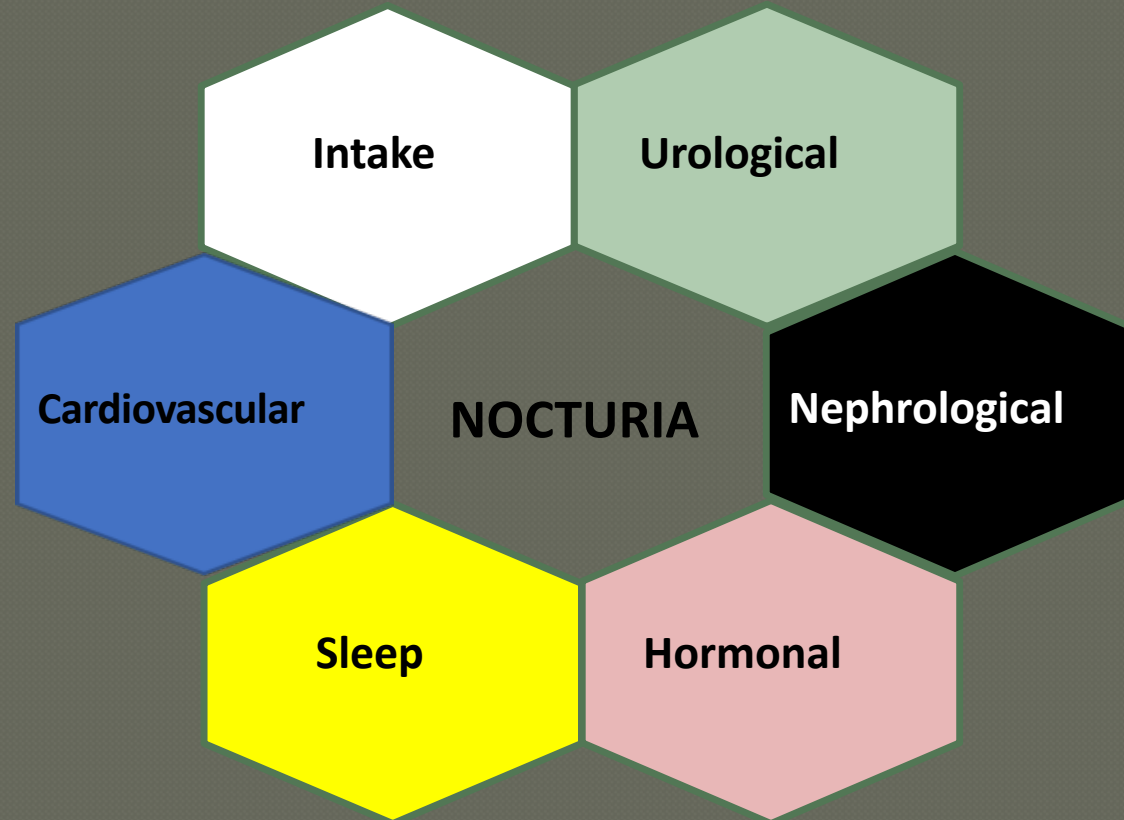
# Survival Probability with Nocturia

— 0 voiding episodes/night    ..... 1 voiding episode/night  
 - - - 2 voiding episodes/night    — 3+ voiding episodes/night





# Cause of Nocturia is Multifactorial and Multidisciplinary



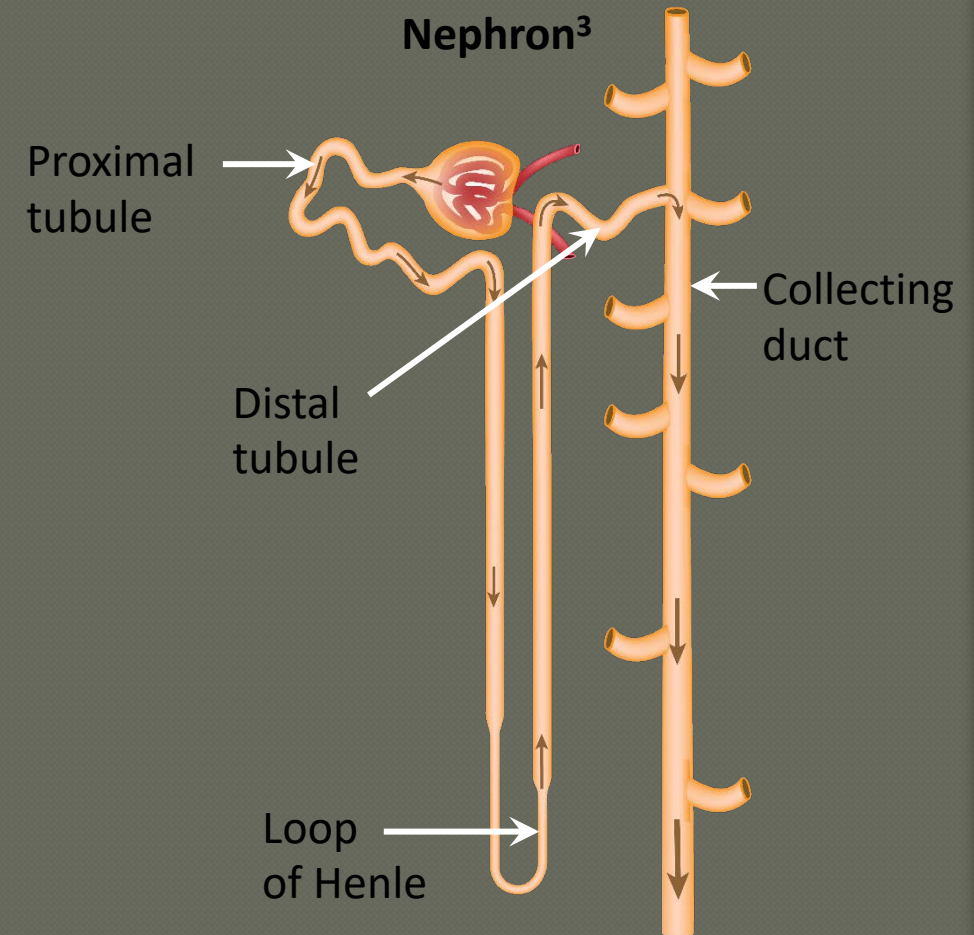


# WHEN TREATMENT CALLS FOR PAUSING URINE PRODUCTION

## Desmopressin

- Desmopressin is a synthetic analog of AVP (Arginine Vasopressin) and a selective  $V_2$  receptor agonist
- *It increases water reabsorption in the distal tubule and collecting ducts, concentrates the urine, and decreases urine production*

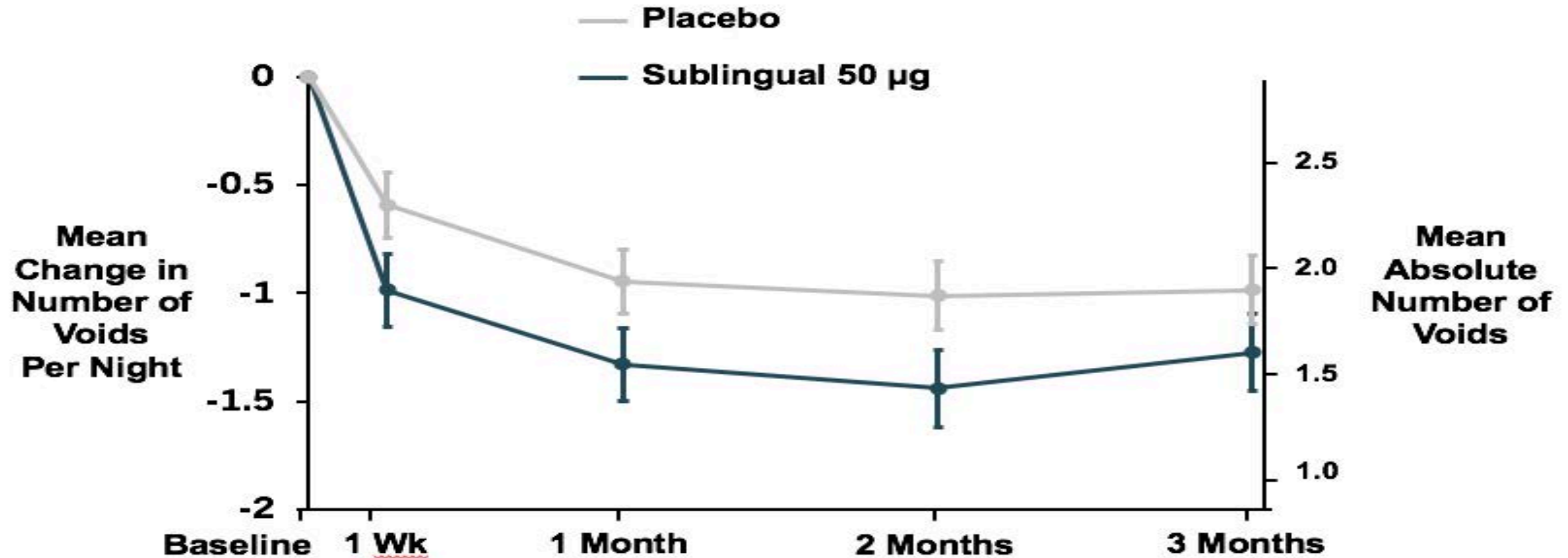
**DESMOPRESSIN FORMULATIONS  
REDUCE NOCTURIA BUT ARE ASSOCIATED  
WITH A RISK FOR HYPONATREMIA<sup>1,2</sup>**



AVP=arginine vasopressin.

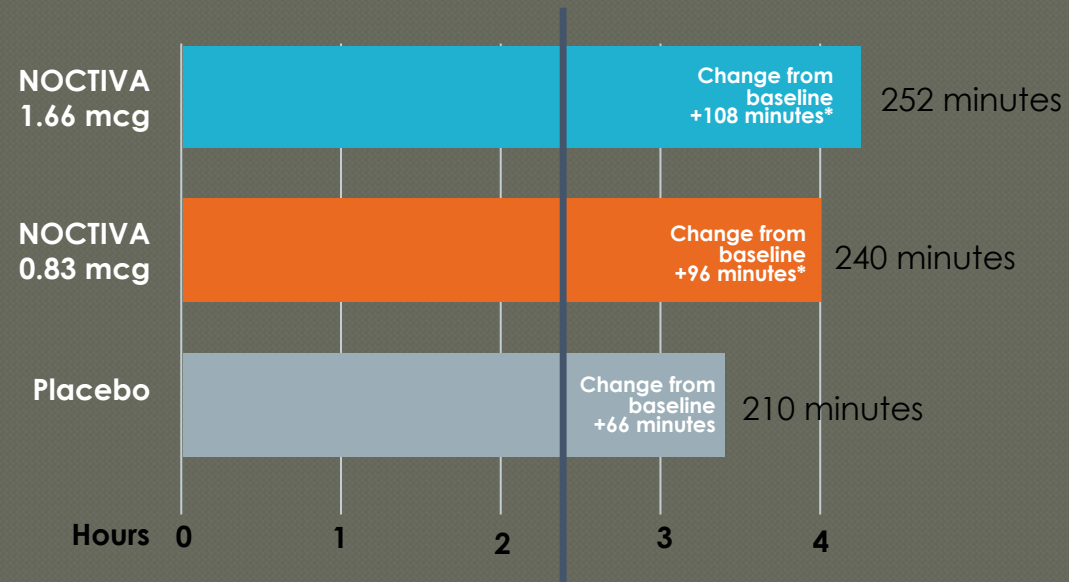
1. Weiss JP, et al. *BJU Int.* 2011;108(1):6-21.
2. Ebell MH, et al. *J Urol.* 2014;192(3):829-835.
3. Amerman E. In. *Human Anatomy and Physiology.* 2nd ed; 2018:941-984.

# Sublingual Desmopressin in Men: Mean Decrease in Nocturnal Voids





# Decreased Urine Production Equals Increased Bladder Filling



Baseline:  
2.4 hours

The **first 4 hours of sleep**  
are the most important  
for a **restful night**.<sup>2</sup>

# HISTORICAL FEARS ABOUT DESMOPRESSIN

---

- ◉ DECREASING SODIUM
- ◉ DECREASING SODIUM
- ◉ DECREASING SODIUM
- ◉ DECREASING SODIUM
- ◉ DECREASING SODIUM
- ◉ DECREASING SODIUM



# Incidence of Hyponatremia in Women and Men Long-term (Up to 3 Years)

Post baseline Serum Sodium (mmol/L)	Pooled Data: Safety Analysis Set	
	Women (25 µg)	Men (50 µg)
	N=67	N=78
	n (%)	n (%)
≥ 135	52 (78)	45 (58)
130-134	12 (18)	24 (31)
126-129	3 (4)	8 (10)
≤ 125	0	1 (1)



# Risk Factors for Hyponatremia

- ⦿ Age (single best predictor)
- ⦿ Lower serum sodium at baseline
- ⦿ Higher dose
- ⦿ Decreased GFR

# Monitoring Sodium

## FDA Recommendations

- Prior to initiation
- 7 days
- 30 days
- Periodically thereafter

## Expert Opinion

- Prior to initiation
- 7 days
- 30 days
- 60 days
- 90 days
- Every 3 months? 6 mo?  
Yearly?

# Conclusions



- Nocturia may have a complicated etiology but simply results from a production of nocturnal urine that exceeds the functional bladder capacity
- The prevalence is significant
- Behavioral therapy and treating underlying medical conditions is essential but may fall short
- Short acting versions of desmopressin reduce nocturia by decreasing urine production during sleeping hours
- Attention to contraindications and monitoring recommendations regarding serum sodium are critical



# Nocturia in Primary Care: Hx-Taking

---

**The recommended questions are:**

- After you fall asleep, on average, how many times do you urinate at night?
- Does the nocturia bother you?
- Would you like to discuss treatments for nocturia?

# DOES ANY SPECIALTY OWN URINE?

---



DOES ANY SPECIALTY OWN URINE? **NO**

---

A PERFECT  
OPPORTUNITY FOR  
SHARED CARE





# Urologists and Primary Care Must Work Together on This

---

- Must be able to effectively evaluate and differentiate other diseases
- Must be able to safely treat and monitor

# What This Men's Health Doc Believes

---

- Adequate treatment of nocturia requires shared care
- Regardless of the frequency or cause, nocturia results from a production of nocturnal urine that exceeds the capacity of the urinary bladder to comfortably store it
- Therefore, whether nocturia is a symptom or disease is of little relevance in choosing to treat