Norman R Zinner Debate:
"The ICS Standardisation of OA B 10 Years on: Are We Barking up the Wrong Tree?"
Thursday, 18th October 2012, 11:00-12:00

Moderators: Ted Arnold, Chris Chapple & Richard Millard

- Norman Zinner Tribute Jerry Blaivas
- OAB: The good, the bad, the ugly Alan Wein 15 mins
- OAB: Whom does the definition serve best? Kari Tikkinen 10 mins
- OAB: A urodynamic view Werner Schaefer 10 mins
- Do we need to have a brain to get OAB? Marcus Drake 10 mins
- Rebuttal, Discussion and Questions All 15 mins

OAB. Are We Barking up the Wrong Tree? A Lesson From My Dog, Norman Zinner, *Neurourology and Urodynamics* 30:1410–1411 (2011)

OAB: Whom does the definition serve best?

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Norman R Zinner Debate. The ICS Standardisation of OAB 10 Years on: Are We Barking up the Wrong Tree?

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Emory University, Atlanta, GA, USA

The ICS 2002/2006 definition of OAB[1-2]

Overactive bladder syndrome (OAB) is ‘‘urgency, with or without urgency incontinence usually with increased daytime frequency and nocturia.’’

- “These symptom combinations are suggestive of urodynamically demonstrable detrusor overactivity, but can be due to other forms of urethro-vesical dysfunction.”
- “These terms can be used if there is no proven infection or other obvious pathology.“
- 2002 document describes also as “urge syndrome or urgency-frequency syndrome”

1. Abrams et al. ***Neurourol Urodyn*** 2002:21:167 2. Abrams et al. ***Neurourol Urodyn*** 2006:25:293

Complex "scientific" terminology hampered by the lack of specificity

- Overactive bladder *syndrome* (OAB) is ''urgency, *with or without* urgency incontinence *usually with* increased daytime frequency and nocturia.''
  - "These symptom combinations are suggestive of urodynamically demonstrable detrusor overactivity, *but can be due to other forms* of urethro-vesical dysfunction."
  - "These terms can be used if there is no proven infection or *other obvious* pathology."

- "*urgency* is the complaint of a sudden compelling desire to pass urine which is difficult to defer."

1. Abrams et al. ***Neurourol Urodyn*** 2002:21:167 2. Abrams et al. ***Neurourol Urodyn*** 2006:25:293

comments

OVERACTIVE BLADDER: SYMPTOM OR SYNDROME? J.G. BLAIVAS

– Joan and Sanford Weil Medical College, Cornell University, USA

Blaivas. ***BJU Int*** 2003:92:521

European Urology

European Urology 47 (2005) 273–276

Editorial

Overactive Bladder: A Clinical Entity or a Marketing Hype?

Helmut Madersbacher

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Accepted 20 October 2004

Available online 10 November 2004

Madersbacher. ***Eur Urol*** 2004:47:273

Neurourology and Urodynamics

OAB. Are We Barking Up the Wrong Tree? A Lesson From My Dog

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Zinner. ***Neurourol Urodyn*** 2011:30:1410

Tikkinen & Auvinen. ***Eur Urol*** 2012:61:746

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Editorial

Does the Imprecise Definition of Overactive Bladder Serve Commercial Rather than Patient Interests?

Kari A.O. Tikkinen [a,b,*], *Anssi Auvinen* [c]

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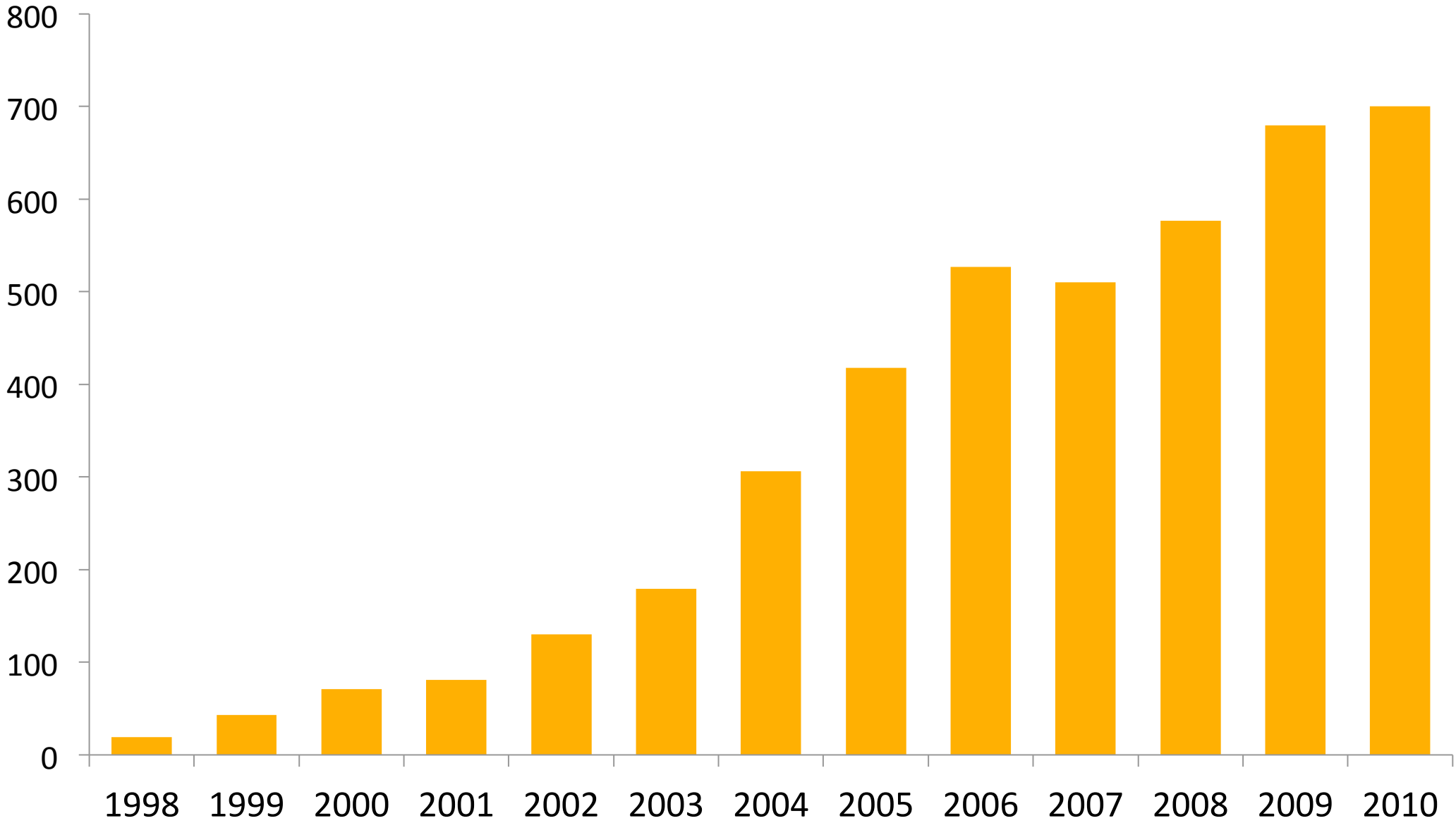
Number of overactive bladder publications[1]

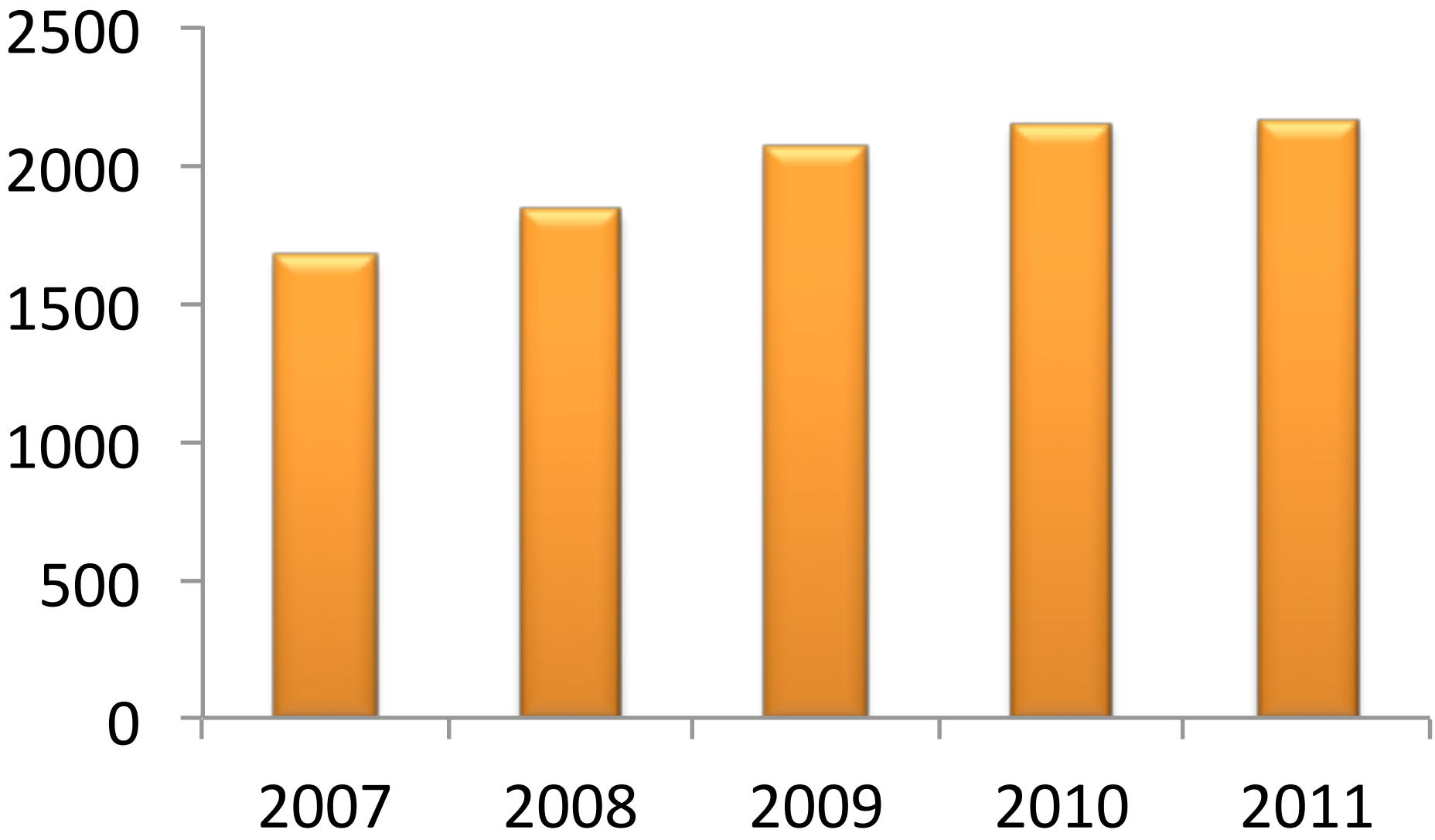


Publications across all journals indexed in Scopus, including the term "overactive bladder" 1998-2010

1. Tikkinen & Auvinen. ***Eur Urol*** 2012:61:746

Development of OAB market size in the US

in millions of US dollars



Data from *IMS Health*, available at http://www.imshealth.com/ims/Global/Content/Corporate/Press%20Room/IMS%20in%20the%20News/Documents/Overactive_Bladder_Market1.pdf

What about the patients - do OAB concept and treatments work for them?

- Antimuscarinics are the first-line drug treatment for OAB
  - However, benefits are small

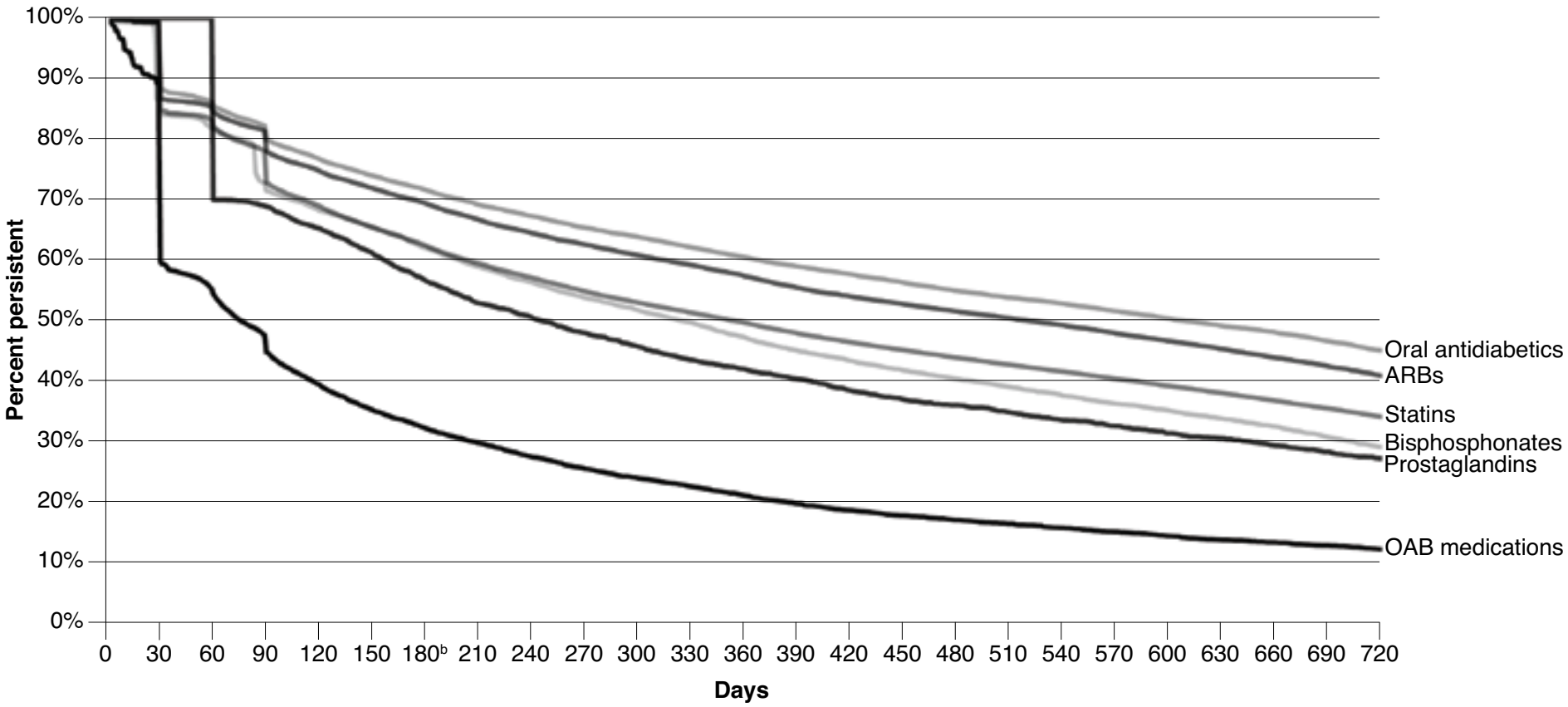
- Median symptom changes with antimuscarinics in RCTs

Urgency:	- 0.9 episodes/24 hours
Urgency incontinence:	- 0.5 episodes/24hours
Frequency:	- 0.8 episodes/24 hours
Nocturia:	- 0.1 episodes/night, NS

Buser et al. ***Eur Urol*** 2012 (in press) e-published Sept 7, 2012

Adherence to OAB medications (anticholinergics) is low

FIGURE 4 Time to Discontinuation[a] of 6 Chronic Therapy Classes, Allowing for 90-Day Treatment Gap



[a]*Discontinuation was defined as the end of days supplied for an index medication pharmacy claim immediately preceding a 90-day gap in therapy. A minimum of 12 months (maximum 24 months) continuous eligibility following the index date (day 0) was required. Beginning at day 390, the denominator for the calculation consisted of all remaining eligible patients with continuous enrollment through the end of the 30-day interval. Patients with continuous enrollment ending between day 360 and day 720 were censored at the point of their cessation of benefits.*

[b]*Using the 90-day gap, 6-month persistence rates were prostaglandin analogs 57%, statins 62%, bisphosphonates 62%, oral antidiabetics 72%, ARBs 69%, and OAB medications 32%.*

ARB = angiotensin II receptor blocker; OAB = overactive bladder.

Yeaw et al. ***J Manag Care Pharm*** 2009;15:728

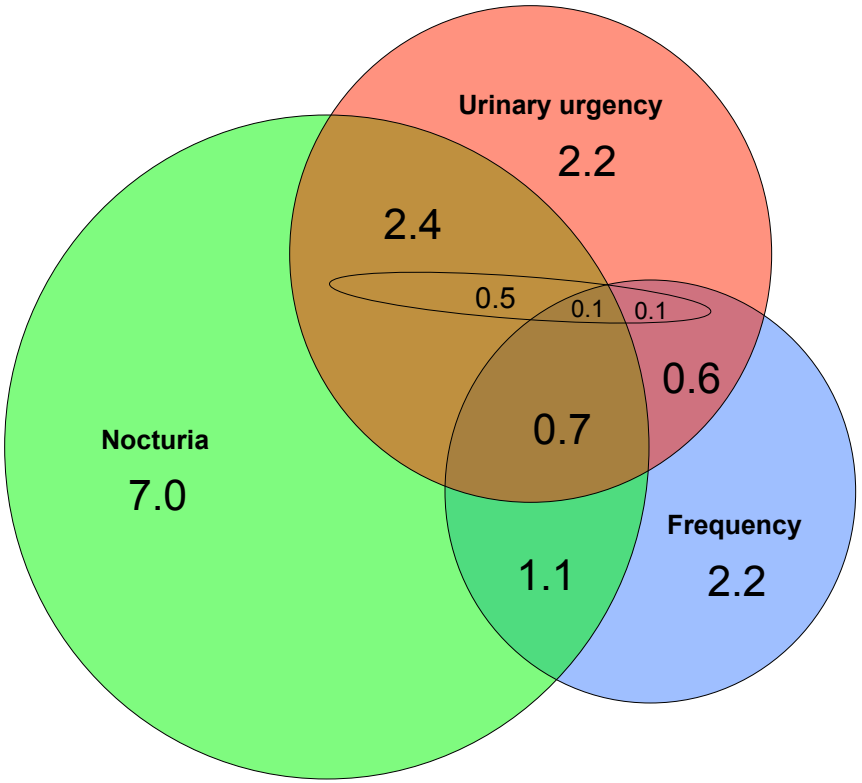
Reasons for discontinuing OAB medication
reported by >20% of those who discontinued

Reason	N (%)
Did not work as expected	611 (46.2)
Switched to a new medication	332 (25.1)
Learned to get by without medication	308 (23.3)
I had side effects	279 (21.1)

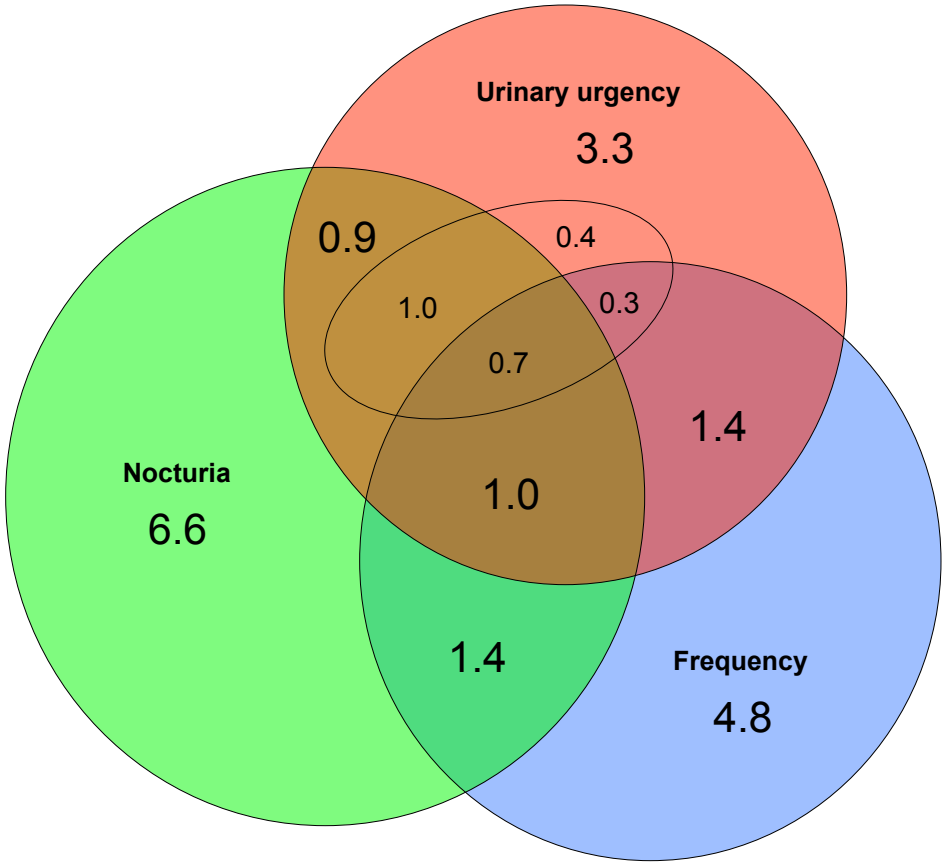
Benner et al. ***BJU Int*** 2010;105:1276

Age-standardized prevalence of overactive bladder symptoms

Urinary urgency without urgency incontinence (circle)
Urinary urgency with urgency incontinence (oval)
Frequency (>8)
Nocturia (>1)



MEN



WOMEN

Modified from Tikkinen et al. ***PLoS One*** 2007;2:e195.

"OAB is misleading because it makes it too easy for clinicians to feel they have made a diagnosis when they have not. In so doing, it curtails further thinking and does not promote the scientific pursuit of fact."

Norman R. Zinner. Neurourol Urodyn 2011

American Urological Association 2012 Guidelines on Overactive Bladder

"**OAB Diagnosis.** The review revealed insufficient publications to address OAB diagnosis from an evidence basis"

Available at http://www.auanet.org/content/media/OAB_guideline.pdf

Key Element of 'Marketing Disease'	Suggestions for Doing Better
1. Exaggerate the prevalence of disease	
Create a broad disease definition	Learn exact definition and question whether it is appropriately specific.
Publicize a large prevalence estimate.	Ask: "Does the sample truly represent the general population?"
Blur between mild and severe.	Be clear about the disease spectrum.

Modified from Woloshin S, Schwartz LM (2006) Giving Legs to Restless Legs: A Case Study of How the Media Helps Make People Sick. PLoS Med 3(4): e170. http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0030170

PLoS MEDICINE

Key Element of 'Marketing Disease'	Suggestions for Doing Better
2. Encourage more diagnosis	
Highlight that doctors fail to recognize	Acknowledge the problems of overdiagnosis.
Encourage people's self-diagnosis.	
Promote awareness 'uncritically'	Learn if awareness activities are industry sponsored.

Modified from Woloshin S, Schwartz LM (2006) Giving Legs to Restless Legs: A Case Study of How the Media Helps Make People Sick. PLoS Med 3(4): e170. http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0030170

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Key Element of 'Marketing Disease'	Suggestions for Doing Better
3. Suggest that all disease should be treated	
Exaggerate the benefits of the drug for everyone with disease.	Objectively report benefits and study populations; Learn industry ties.
Understate harms of treatments	Quantify side effects
Imply that long-term treatment is safe and effective.	Remember that studies are typically short-term.

Modified from Woloshin S, Schwartz LM (2006) Giving Legs to Restless Legs: A Case Study of How the Media Helps Make People Sick. PLoS Med 3(4): e170. http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0030170

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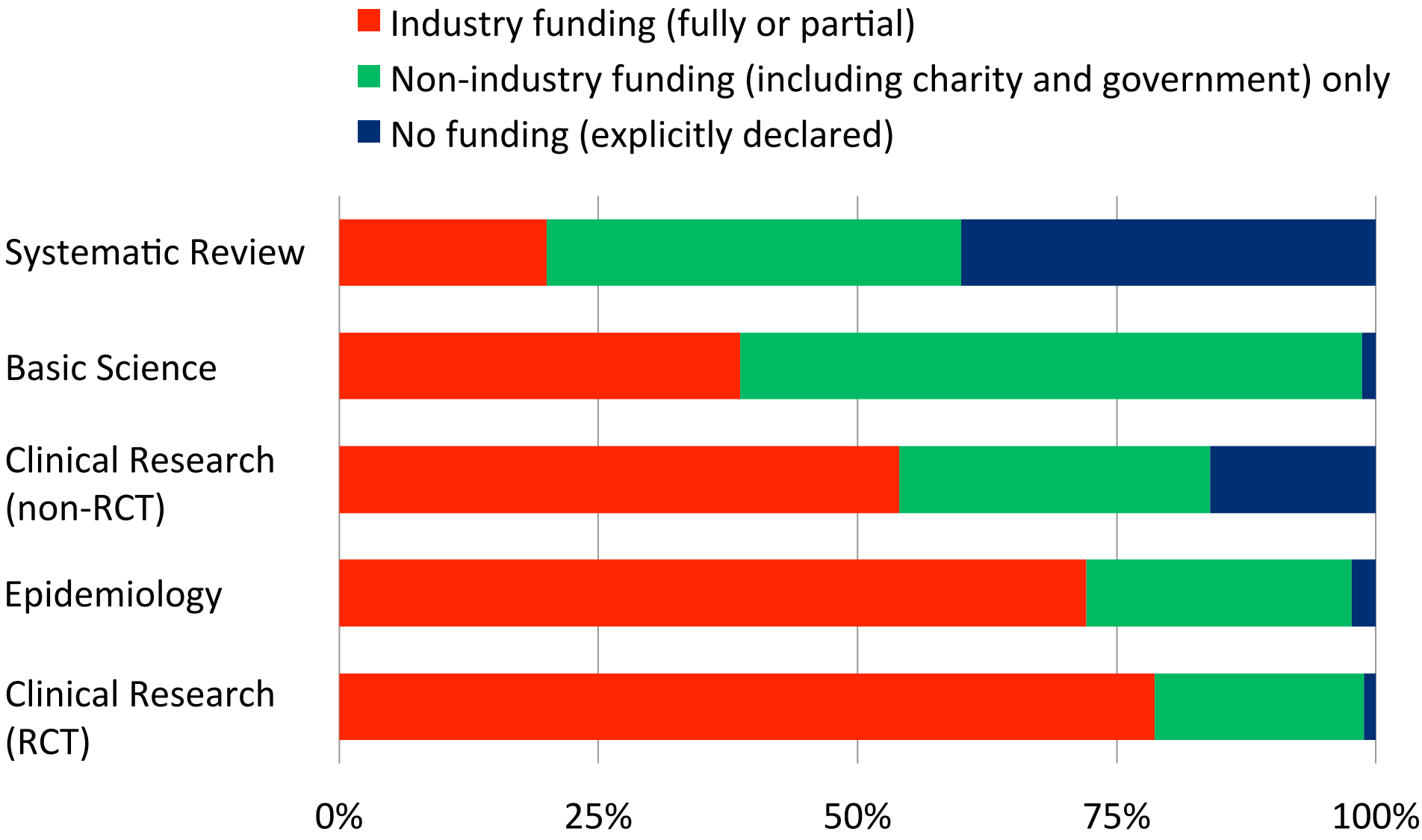
Reported funding sources for overactive bladder papers by subtype



1. Tikkinen & Auvinen. ***Eur Urol*** 2012:61:746

So, whom does the definition serve best?

1. Excellent for disease awareness campaigns but also for *disease mongering* and *selling sickness*

2. Does not optimally promote the scientific pursuit of fact
   - May be harmful for further thinking

3. Is ‘patient-friendly’ but maybe also (patient-) misleading

Take Home Messages

Be aware that

1. Overactive bladder is not a disease

- Overactive bladder is the name given to a group of troubling urinary symptoms
  - These symptoms may (or may not) have same etiology
- Term 'OAB' implies a mechanism
  - We often don't know the mechanism of these symptoms

2. Disease-branding and drug-mongering are common promotional practices of 'selling sickness'

- aim is to expand markets by widening the boundaries of diagnosable conditions

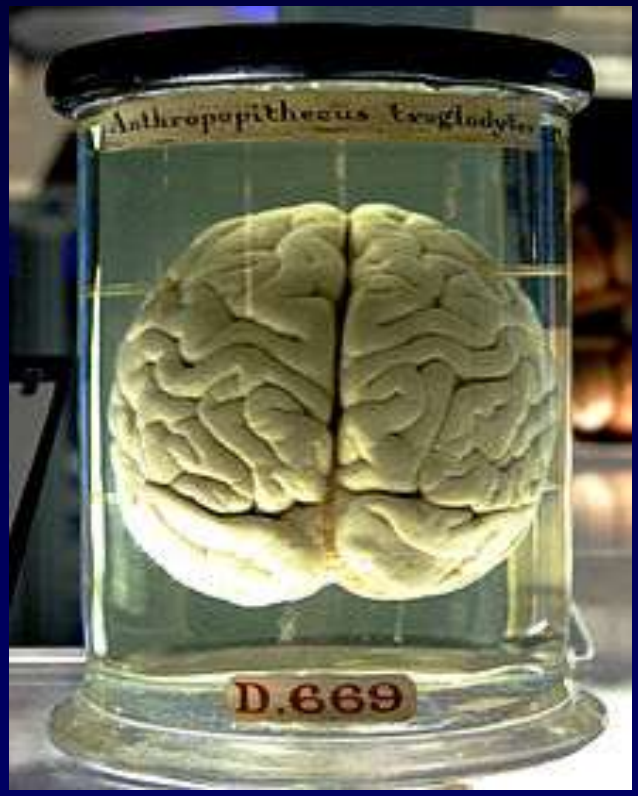
Do we need a brain to get an overactive bladder?

Marcus Drake

University of Bristol &
Bristol Urological Institute

Summary

- Consciousness, perception and attention
  - Intrusive urinary sensation
- Decision making- “free will”, or “volition”
  - Abnormal LUT muscle behaviour
- Personality



Perception is interpretation of sensory information to represent and understand the environment.

Where subconscious sensory information becomes a conscious sensation

Consciousness; the state of being aware of an external object or something within oneself

Perception and attention

- In the range of competing stimuli, only one is consciously attended to (“perceived”)
- *“Bottom-up” processing*- Sensory transduction and afferent signalling
- Stimulus-driven attention; stimuli like sudden loud noise unavoidably attract our attention. *Parietal & temporal cortex*
- *“Top-down“ processing*- Learning & expectation alter how sensory signals are perceived
- Endogenous attention; where we choose to concentrate attention- like a conversation *Frontal cortex, basal ganglia*

Clinical presentations

- OAB; urgency, with or without incontinence, usually with frequency and nocturia
  - Exclude other causes of similar symptoms

- Subconscious LUT sensory information receives disproportionate attention in the competing traffic of body and environment
- Intrusive urinary sensation

- *Brain function; to give LUT sensory traffic due precedence amongst the overall sensory load*

- How the transition occurs, when subconscious (sensory) becomes conscious (sensation), determines whether a person experiences the intrusive urinary sensations called “OAB”- *Endogenous versus stimulus-driven?*

Volition, or free will, is the cognitive process by which an individual decides on and commits to a course of action

Volitional control

- Actions are determined by your volition, all processes automatically adjusting to support what you decide to do
- Generally your actions require urine storage; an active maintenance of the LUT organs in the appropriate state
- When it is your will to pass urine, inhibition of the voiding reflex is switched off

Clinical presentations

- Detrusor overactivity; bladder contractions during the storage phase which may be spontaneous or provoked
- Non-volitional muscle activity counteracting the urine storage function
- Abnormal LUT muscle behaviour

- *Brain function; regulation of LUT smooth muscle control so it co-operates in carrying out the individual's volitional actions*
- Impaired volitional control allows expression of the involuntary detrusor contractions &/or urethral relaxations called "DO"

The “gatekeepers” of urgency-frequency syndrome

- Transition of subconscious sensory traffic into conscious sensation
- Emergence of non-volitional LUT muscle activity

- Pathophysiology should be evaluated from perspective of potential influence on the gatekeepers

Do we need a brain for OAB?

- The brain is the seat of consciousness; where LUT sensory traffic takes undue precedence, a person may experience urgency
- The brain is the seat of volition, emphasising storage roles of the LUT organs