

# Sex Differences in Oral Appliance Therapy and Treatment Outcomes

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# Conflict of Interest Disclosure

1. I do not have any potential conflicts to disclose.

2. I wish to disclose the following potential

Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	Vivisol BV and Health Holland TKI
Consultant	
Speakers' Bureaus	
Financial Support	
Other	

3. The material presented in this lecture has no relationship with any of these potential conflicts, **OR**

4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:

# Objectives

1. Compare common assumptions about sex differences with evidence
2. Understand how sex-related factors affect OSA presentation and oral appliance therapy response

# Interactive Session

- Audience questions
- Participation by raising hands
- Purpose: assumptions vs evidence



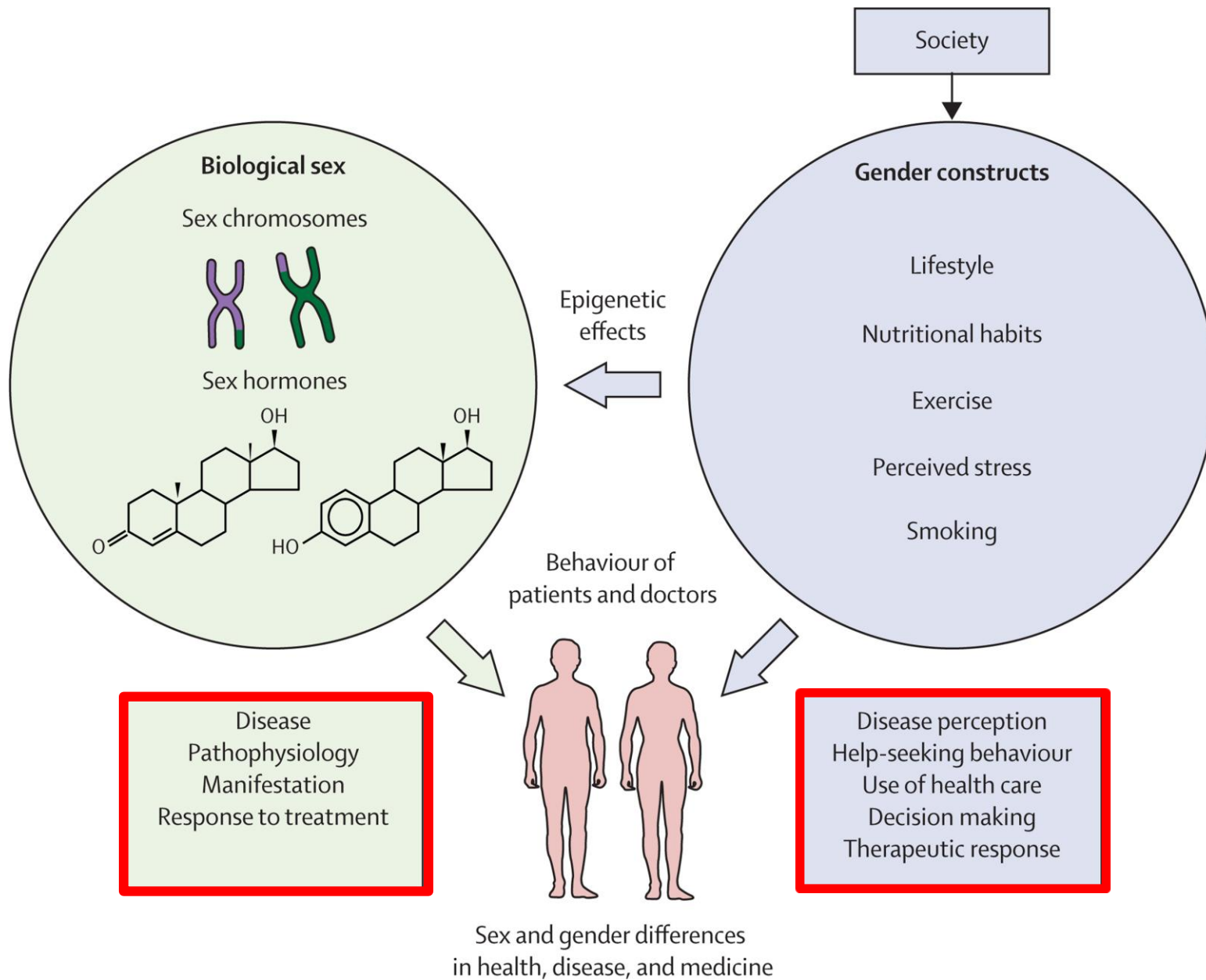


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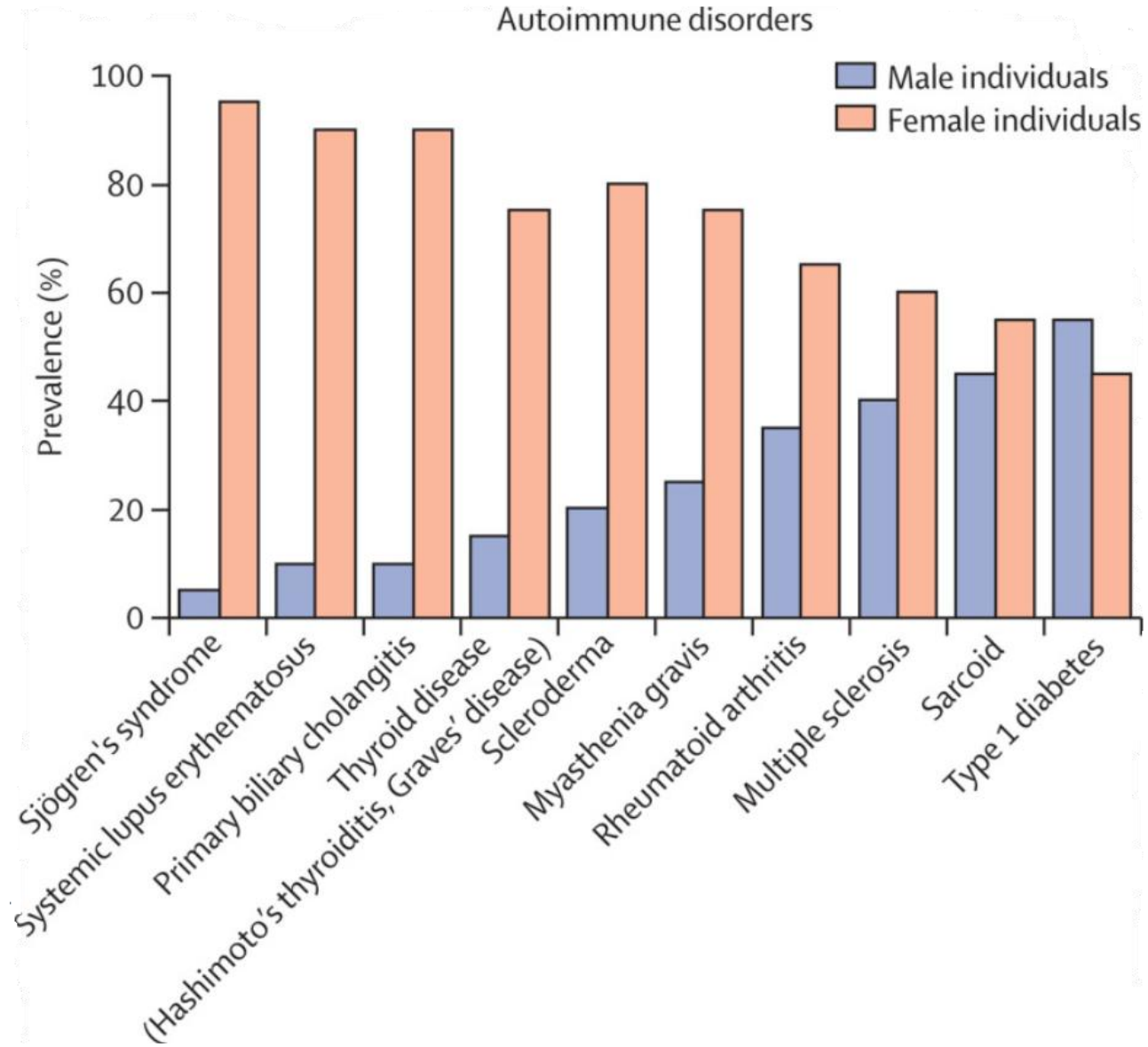
# Sex and gender: modifiers of health, disease, and medicine



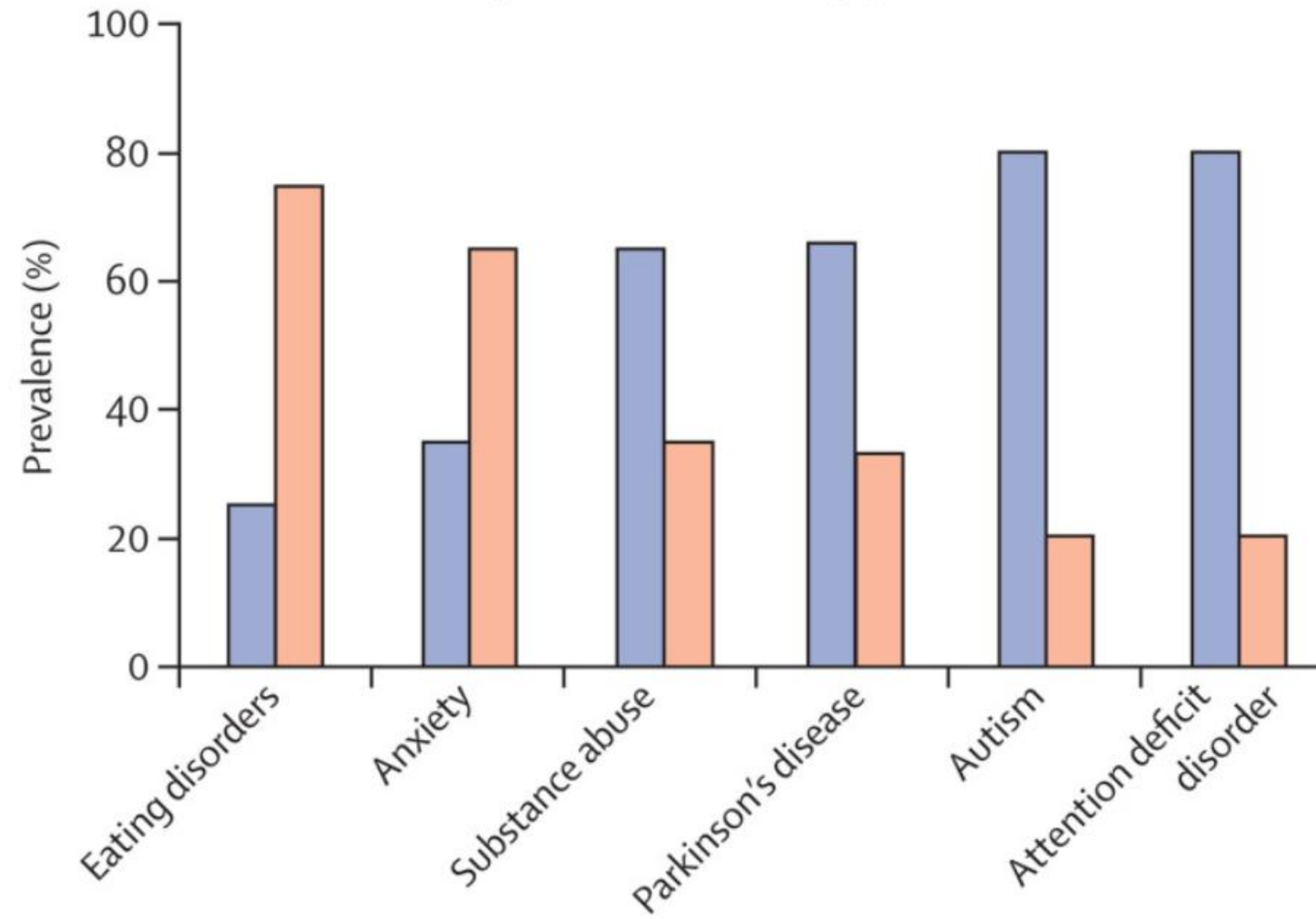
*Franck Mauvais-Jarvis, Noel Bairey Merz, Peter J Barnes, Roberta D Brinton, Juan-Jesus Carrero, Dawn L DeMeo, Geert J De Vries, C Neill Epperson, Ramaswamy Govindan, Sabra L Klein, Amedeo Lonardo, Pauline M Maki, Louise D McCullough, Vera Regitz-Zagrosek, Judith G Regensteiner, Joshua B Rubin, Kathryn Sandberg, Ayako Suzuki*

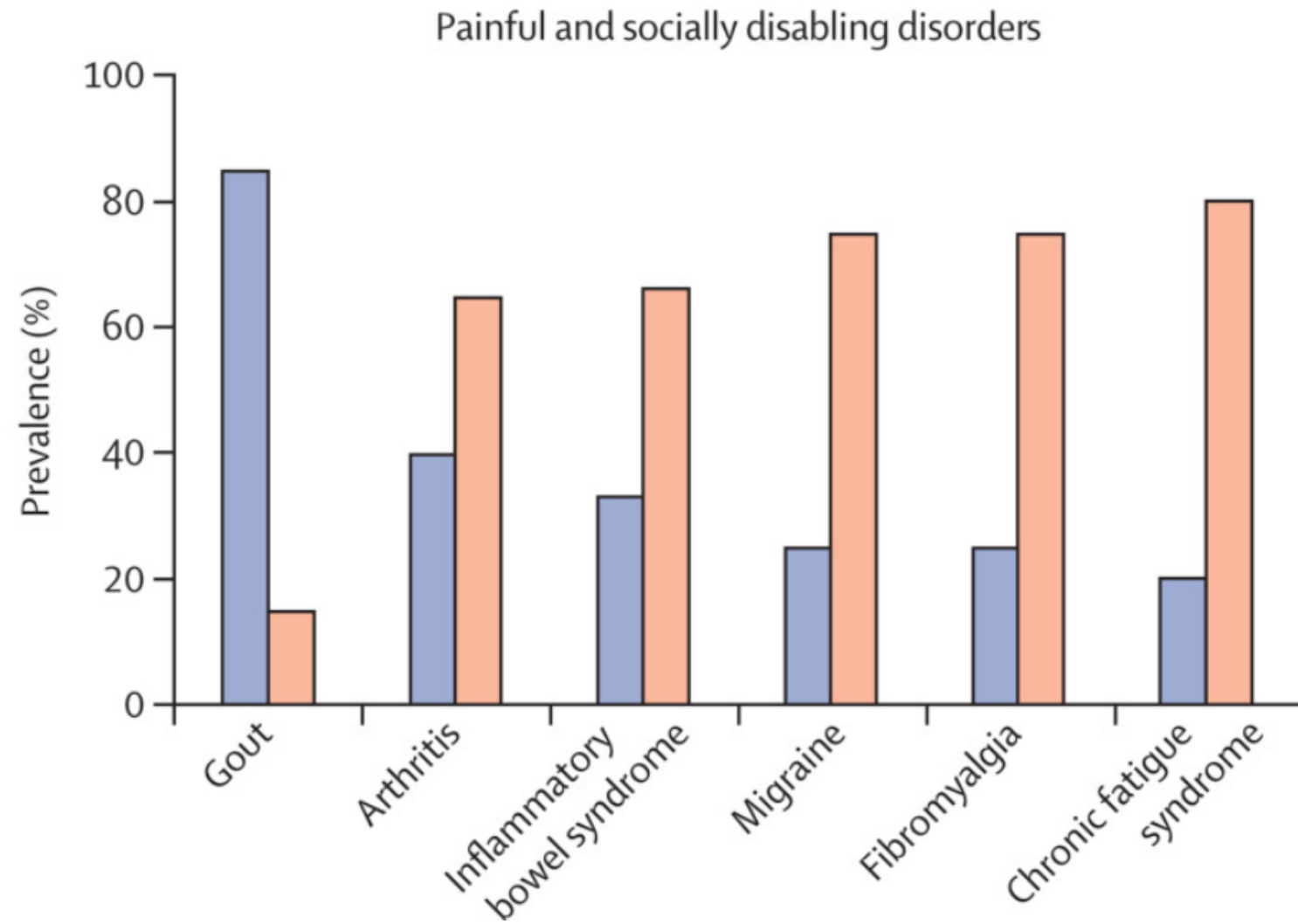


Medical research and care have been centered on male physiology!

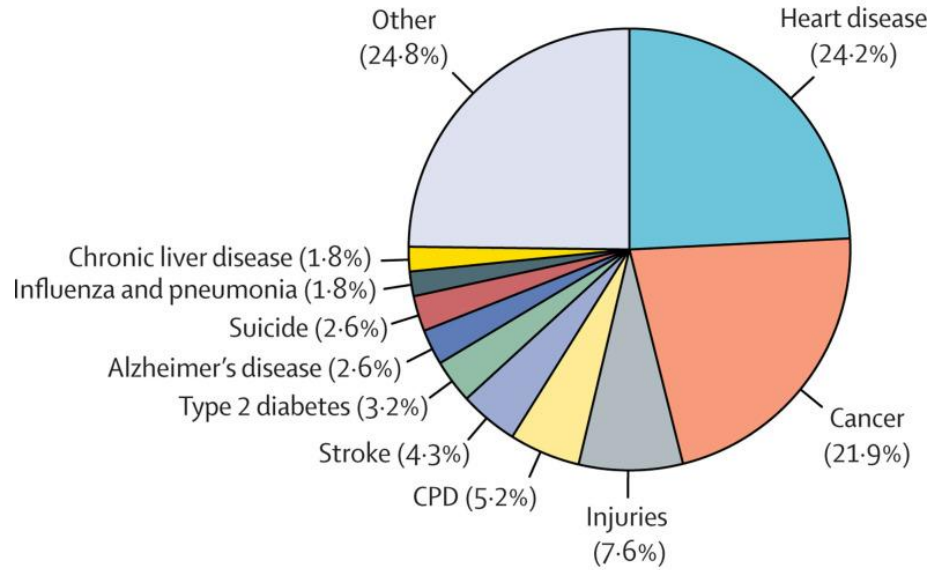


## Neurodegenerative and neuropsychiatric disorders

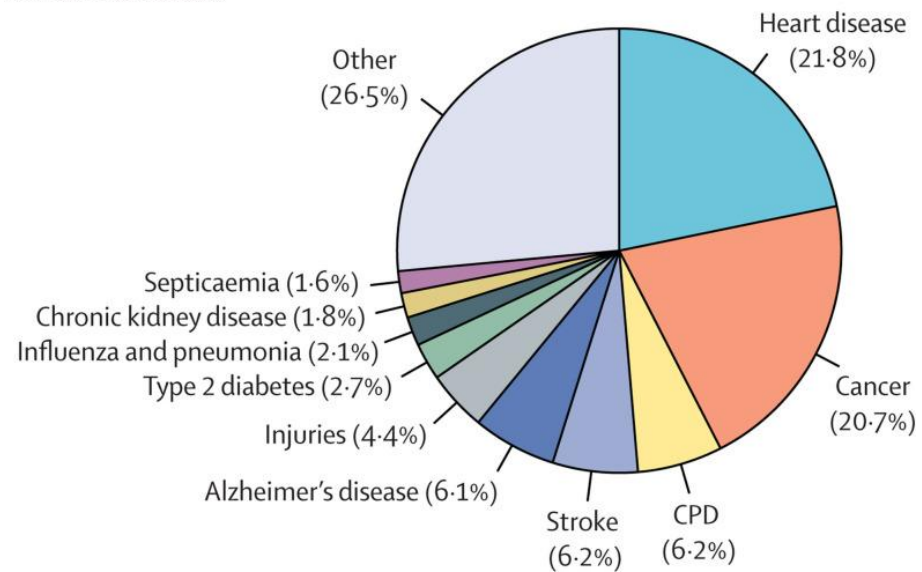




**Male individuals**



**Female individuals**



Percent distribution of the ten leading causes of death, by sex: USA, 2017

“Considering sex and gender in clinical and research practice is essential for true precision medicine . ”

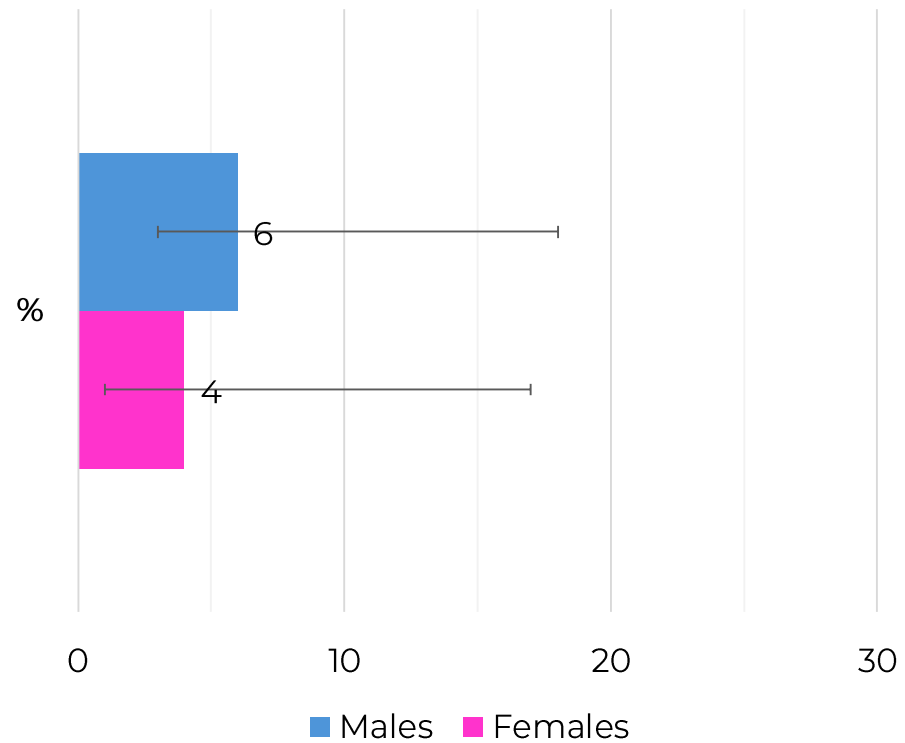
***How do sex differences shape the epidemiology, pathophysiology, clinical presentation, and therapeutic outcomes of OSA?***

# **Q1. Which statement best describes the prevalence of OSA in adults?**

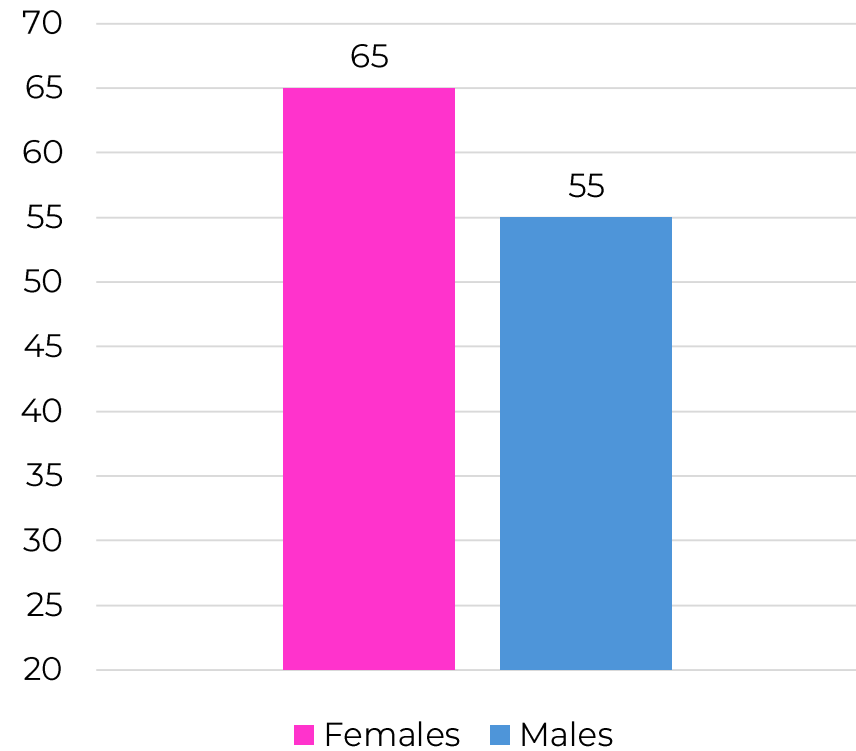
- A. OSA is more prevalent in males than in females
- B. OSA is equally prevalent in males and females
- C. OSA is more prevalent in females than in males

# Epidemiology

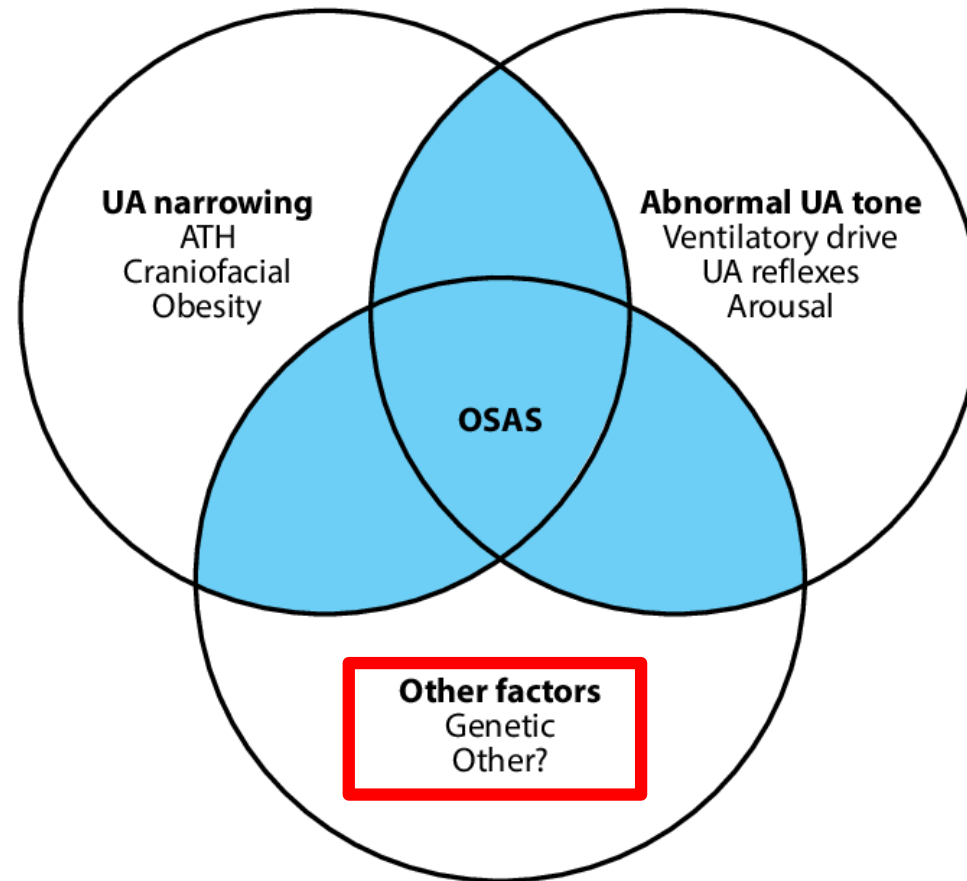
Prevalence clinically significant OSA



Peak age



# Role of Sex in Pathophysiology of OSA



## **Q2. Which anatomical and physiological features contribute to reduced upper-airway collapse in females during sleep?**

- A. Longer upper airway and increased neuromuscular activity
- B. Shorter upper airway, less neck and abdominal fat, and hormonally mediated airway protection
- C. Increased arousal threshold and reduced respiratory drive

## ♀ Pathophysiology

- **Shorter upper airway**
- **Less visceral fat deposition**
- **Protective effects of female sex hormones**
- **Increased upper-airway stability with a more active compensatory response and preserved respiratory drive**
- **Menopause: reduced respiratory drive and upper-airway stability**



Contents lists available at [ScienceDirect](#)

## Sleep Medicine Reviews

journal homepage: [www.elsevier.com/locate/smr](http://www.elsevier.com/locate/smr)



### CLINICAL REVIEW

# Role of menopause and hormone replacement therapy in sleep-disordered breathing

Eva Lindberg <sup>a, \*</sup>, Maria R. Bonsignore <sup>b, c</sup>, Päivi Polo-Kantola <sup>d</sup>

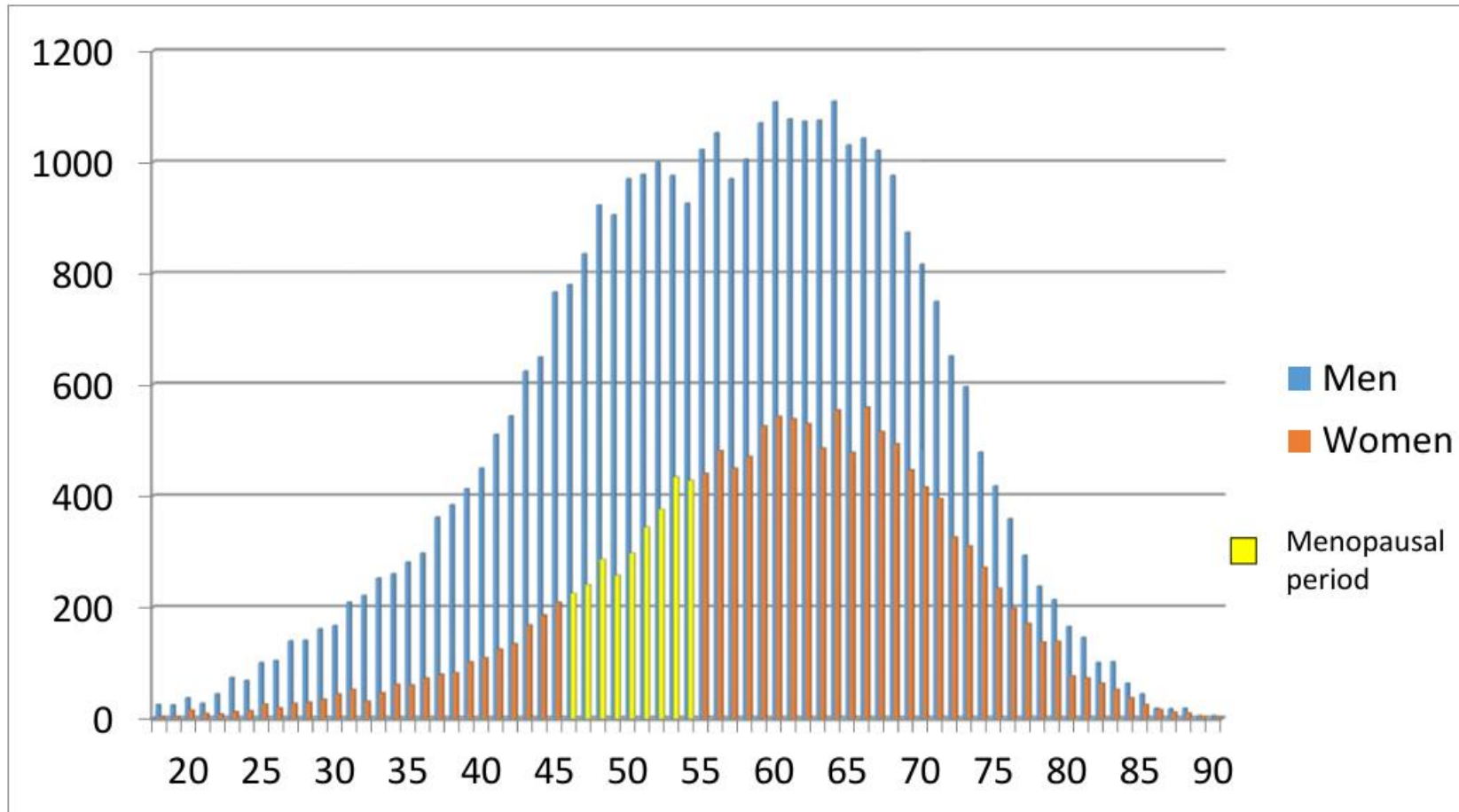
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<sup>c</sup> IBIM-CNR, Palermo, Italy

<sup>d</sup> Department of Obstetrics and Gynaecology and Sleep Research Unit, Turku University Hospital and University of Turku, Turku, Finland





**Fig. 1.** Number of men and women starting CPAP treatment by age. The data are based on 51,767 patients reported to the Swedish National Register, Swedevox.

# Conclusion Lindman et al., 2019

- The increase in SDB during the menopausal transition is mainly explained by aging and changes in weight gain and fat distribution.
- No evidence that menopausal sex hormone changes per se cause SDB.
- Evidence on the effect of hormonal replacement therapy on SDB is limited and inconclusive.

Q3. Compared with males, females with OSA generally present with:

- A. Higher AHI and fewer symptoms
- B. Lower AHI but similar symptom severity
- C. Lower AHI and more atypical symptoms

# ♀ Respiratory events

**Lower AHI**

**Respiratory events:**

- **Shorter**
- **Predominance of partial upper-airway obstruction**
- **Arousals are associated with less respiratory instability**
- **Prolonged apneas lead to greater oxygen desaturation**

## Lower AHI and more "atypical" symptoms



**Tiredness**



**Lack of energy**



**Mood disorders**



**Insomnia**



**Morning headache**



**Nightmares**

# THERAPY EVALUATION

**Objective**

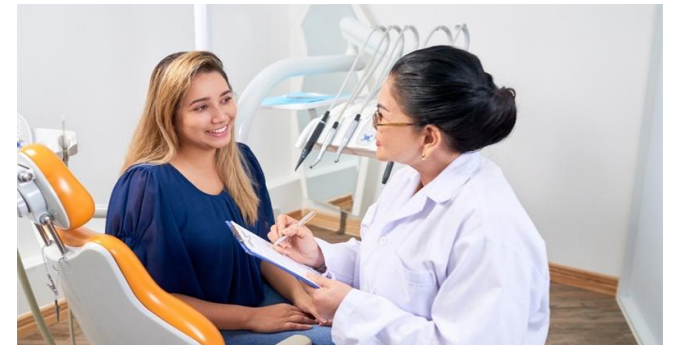


**Subjective**



# Subjective outcomes

- Reflects changes in symptom burden and treatment-related side effects.
- The patient's subjective experience is crucial for long-term treatment adherence.



# CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)



**Objective outcomes show no sex-related differences**

**Subjective outcomes (mood and cognitive function) are similar**

**Treatment adherence is comparable between sexes**

**Women require lower CPAP pressures**

Q4. Which statement best reflects the current evidence on sex-related differences for MAD treatment ?

A. Males and females respond similarly to MAD when OSA severity is considered

B. Females have, on average, a higher likelihood of successful MAD therapy

C. Males show a greater objective reduction in AHI with MAD compared with females

## Mandibular Advancement Device



**Objective outcomes: females show a greater reduction in AHI**

**Subjective outcomes: sex-related differences are unknown**

**Adherence: comparable between males and females**

# Summary

- Sex differences present in OSA: prevalence, AHI, OSA-related symptoms, MAD treatment <sup>2-4</sup>
- Limited research suggests that MAD treatment has better objective outcomes in female patients. <sup>5</sup>
- No research has evaluated sex differences in subjective outcomes of MAD treatment.
- Subjective outcomes reflects improvement in symptoms, and subjective experience is of importance for adherence. <sup>6,7</sup>

# Sex-related differences in subjective outcomes of mandibular advancement device treatment in adults with obstructive sleep apnea

**Joey Chung**; Zhengfei Huang; Frank Lobbezoo; Jean-Pierre T.F. Ho; Ning Zhou; Lisette Venekamp; Marjolein A.J. van Looij; J. Peter van Maanen; Jerryll Asin; Ghizlane Aarab



**AADSM Student Excellence Award!**

# Aim

- To assess short-term sex-related differences in subjective outcomes of MAD treatment among patients with OSA
- Hypotheses:
  - better subjective treatment outcomes in females
  - more pain-related side effects in females
  - no sex difference in adherence

# METHODS

- Prospective longitudinal study
- Patients referred for MAD treatment
- Approval by Ethics Review Board of ACTA under file number 2023-51736
  
- OSA Diagnosis (AHI  $\geq 5$ )
- MAD treatment started
- Permission to use data for research

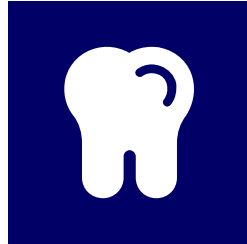


# METHODS

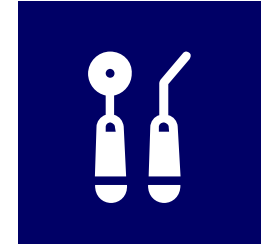
REFERRAL



INTAKE



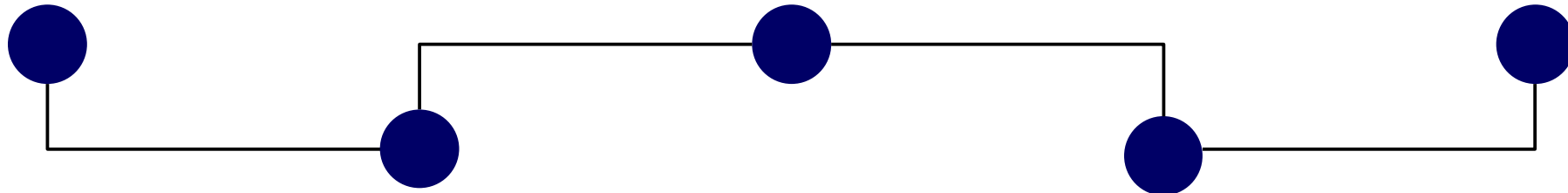
FOLLOW-UP



QUESTIONNAIRES



MAD PLACEMENT



# INTAKE

- Medical history, **incl. OSA-related symptoms**, dental history
- Intra-oral and extra-oral examination, panoramic radiograph (OPT)
- Informed consent

**Klinisch Onderzoeksformulier Intake OSAS / MRA** **ACTA**  
Crocifaciale Pijn & Disfunctie • Versie 2023.10.19

Ruimte voor stickers  
Patiëntnaam: \_\_\_\_\_ Datum: \_\_\_\_\_  
Geboortedatum: \_\_\_\_\_ Onderzoeker: \_\_\_\_\_  
Geslacht: \_\_\_\_\_ Patiëntnummer: \_\_\_\_\_

**Anamnese**

**Verwijzing**  
Verwijzer: \_\_\_\_\_ Reden verwijzing: \_\_\_\_\_  
AHI: \_\_\_\_\_ ESS: \_\_\_\_\_ BMI: \_\_\_\_\_ Verzekeraar: \_\_\_\_\_

**Algemene gezondheid**  
Medische anamnese: \_\_\_\_\_  
Medicatie: \_\_\_\_\_  
Onder behandeling: \_\_\_\_\_  
Allergieën: \_\_\_\_\_ Trauma: \_\_\_\_\_

Genotsmiddelen:	Roken	Alcohol	Drugs	Cafeïne

**OSAS / snurken**  
Eerdere behandeling OSAS / snurken: nee / ja: MRA / CPAP / chirurgie \_\_\_\_\_  
Overmatige slaperigheid overdag: nee / ja \_\_\_\_\_  
Herhaald wakker schrikken gedurende de slaap: nee / ja \_\_\_\_\_  
Snurken: nee / ja \_\_\_\_\_  
Niet verfrissende slaap: nee / ja \_\_\_\_\_  
Vermoeidheid overdag: nee / ja \_\_\_\_\_  
Concentratieverlies: nee / ja \_\_\_\_\_  
Stokkende ademhaling gedurende de slaap: nee / ja \_\_\_\_\_

**Tandheelkundig**  
Laatste bezoek TA: \_\_\_\_\_ Frequentie: ... x / jaar Tandborstel: hand / elektrisch ... x / dag ... min  
Geplande tandheelkundige behandeling(en): nee / ja \_\_\_\_\_

**Orofaciale pijn en disfunctie**  
Klachten: \_\_\_\_\_  
Sinds hoelang: \_\_\_\_\_  
Intensiteit: gevoelig / milde pijn / matige pijn / ernstige pijn  
Verloop over de dag: fluctuerend / constant  
Aard: zuarend / scherp / brandend  
Functieafhankelijk: nee / ja \_\_\_\_\_ Hoofdpijn: nee / ja \_\_\_\_\_  
Nekpijn: nee / ja \_\_\_\_\_ Pijn elders: nee / ja \_\_\_\_\_  
Beperkte mondopening: incidentieel / permanent Luxaties: nee / ja R / L  
Knappen bij bewegen: nee / ja R / L Crepitaties: nee / ja R / L

Blz. 1

## MAD design

The patient chooses from several MRA types selected by the clinician.



## Bite registration

Intra-oral scan and George Gauge



## MAD placement

Start position:

60% of the protrusive range (PR)



## Titration

Standardized protocol:

- 45% - 60% - 75% - 90% of PR
- Follow-up interval of 4 weeks



# DATA COLLECTION

## Referral

- AHI

## Questionnaires

- Sex
- Age
- BMI

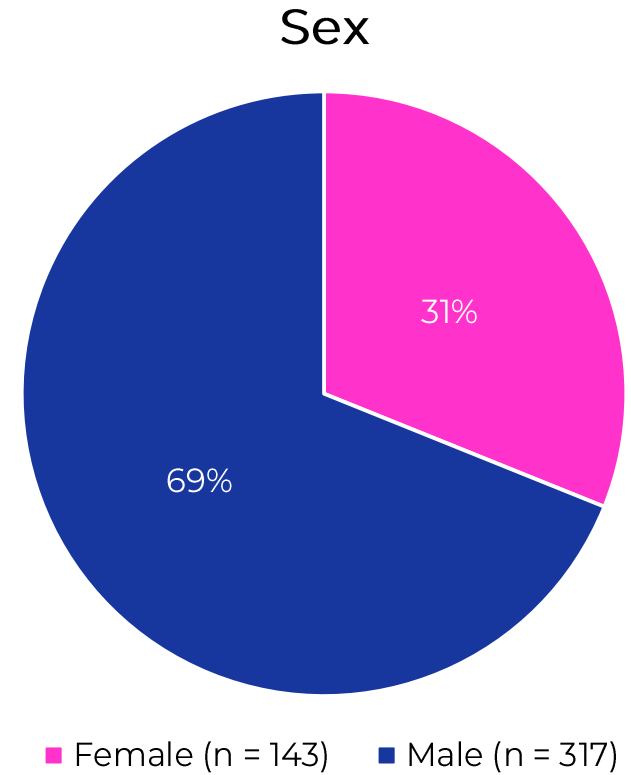
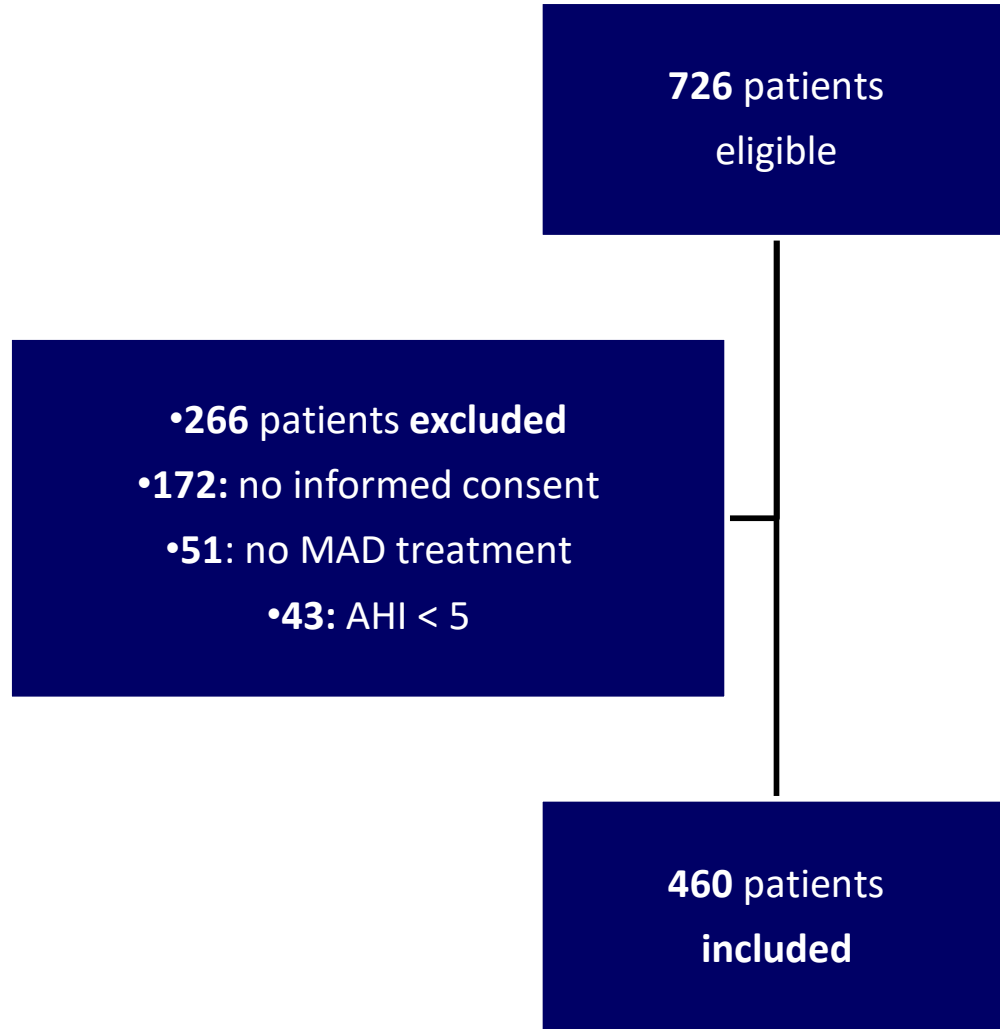
## Intake

- OSA-related symptoms

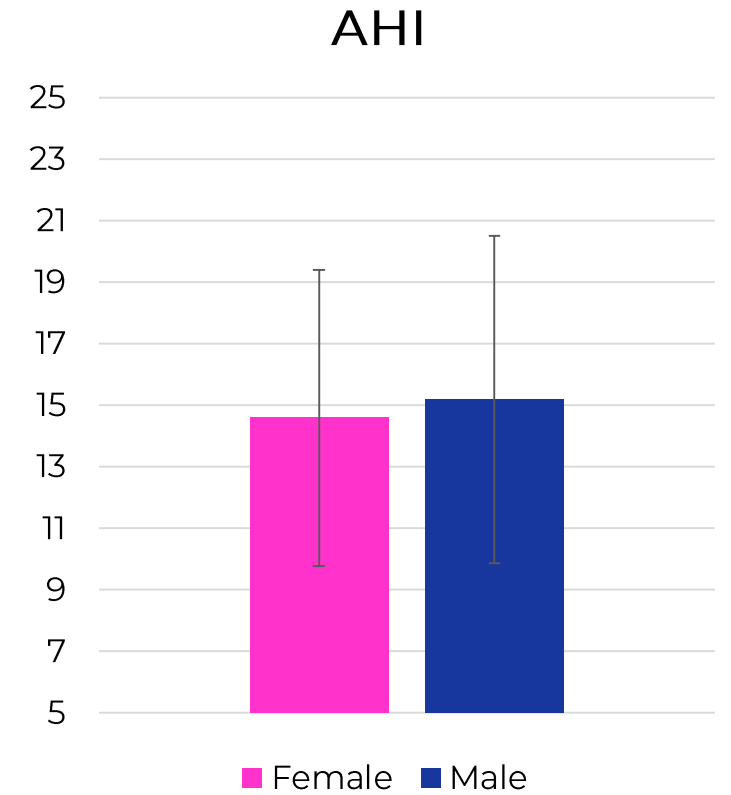
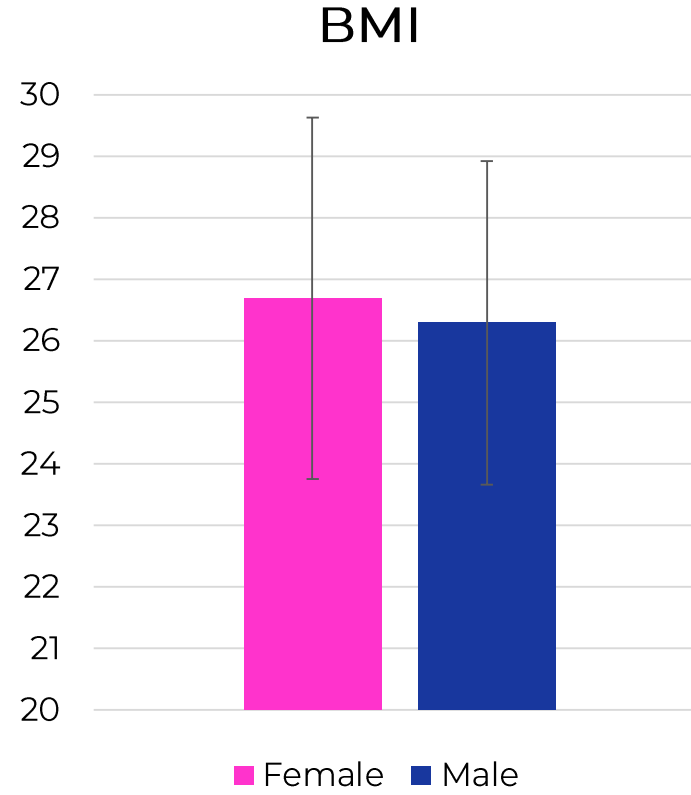
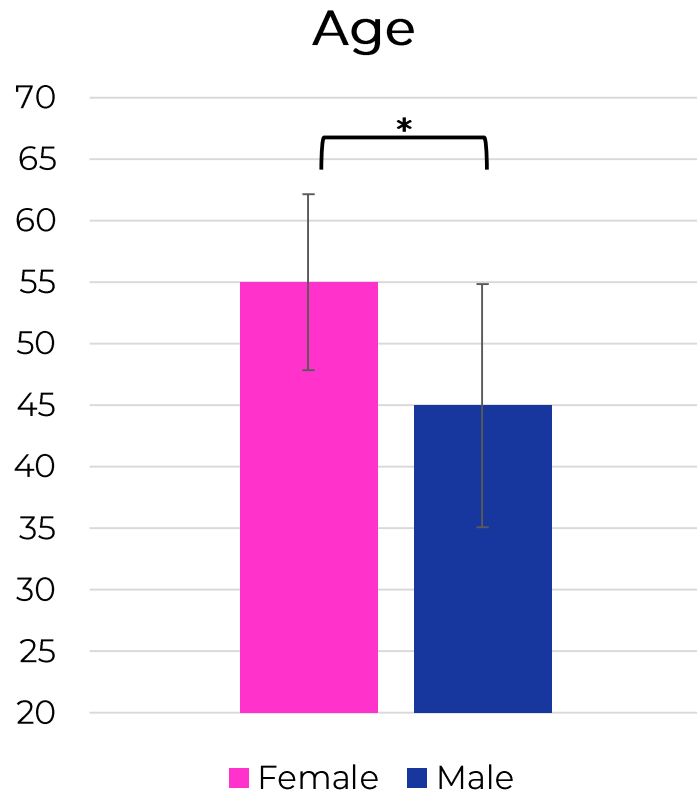
## Follow-up

- OSA-related symptoms
- Side effects MAD
- Treatment adherence

# PERIOD 2017-2024

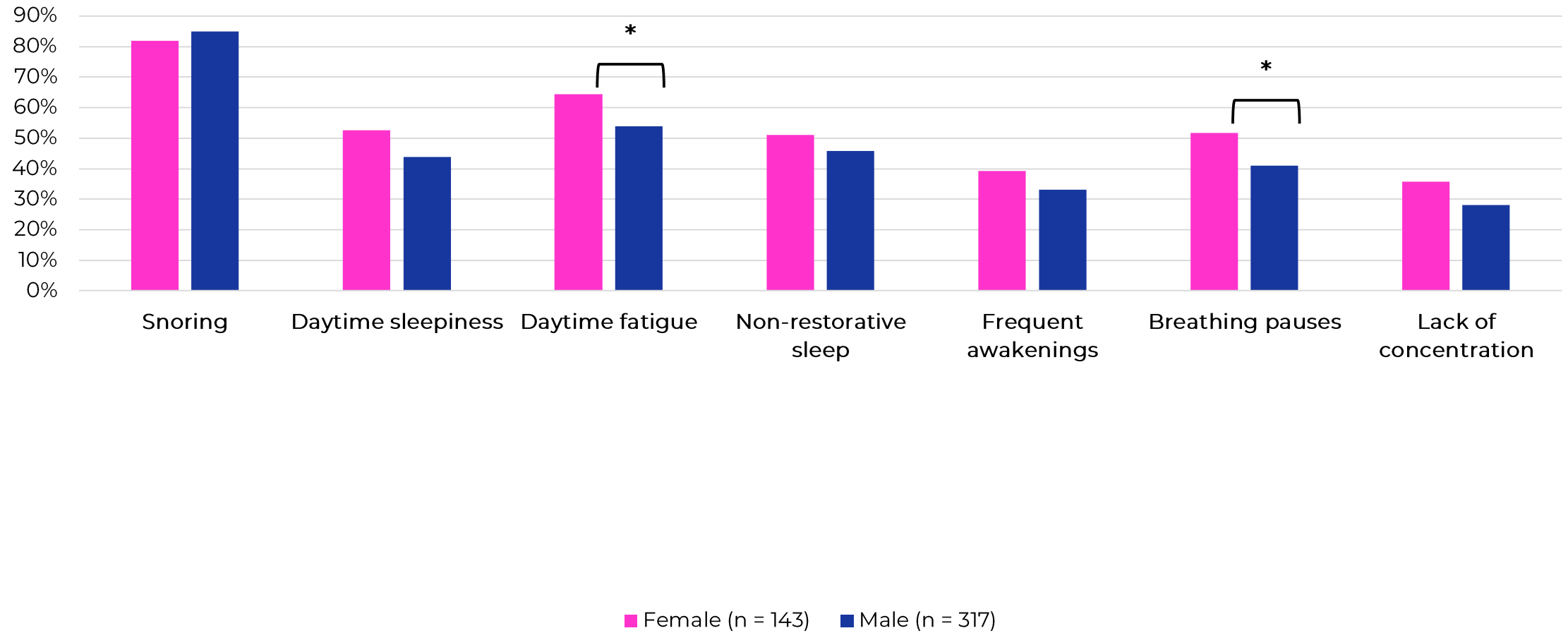


# DEMOGRAPHICS



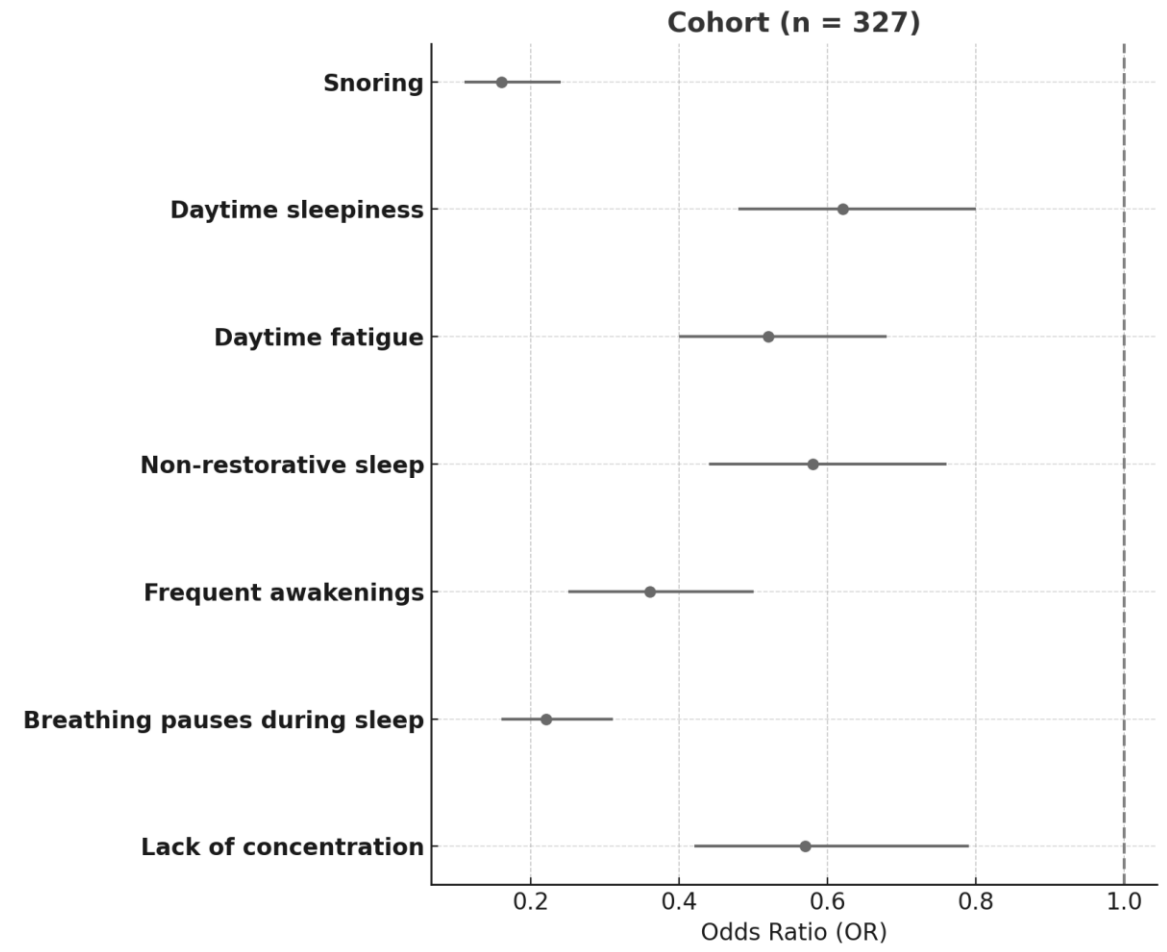
Mann-Whitney U test : \*  $P < .05$

# SYMPTOMS AT INTAKE



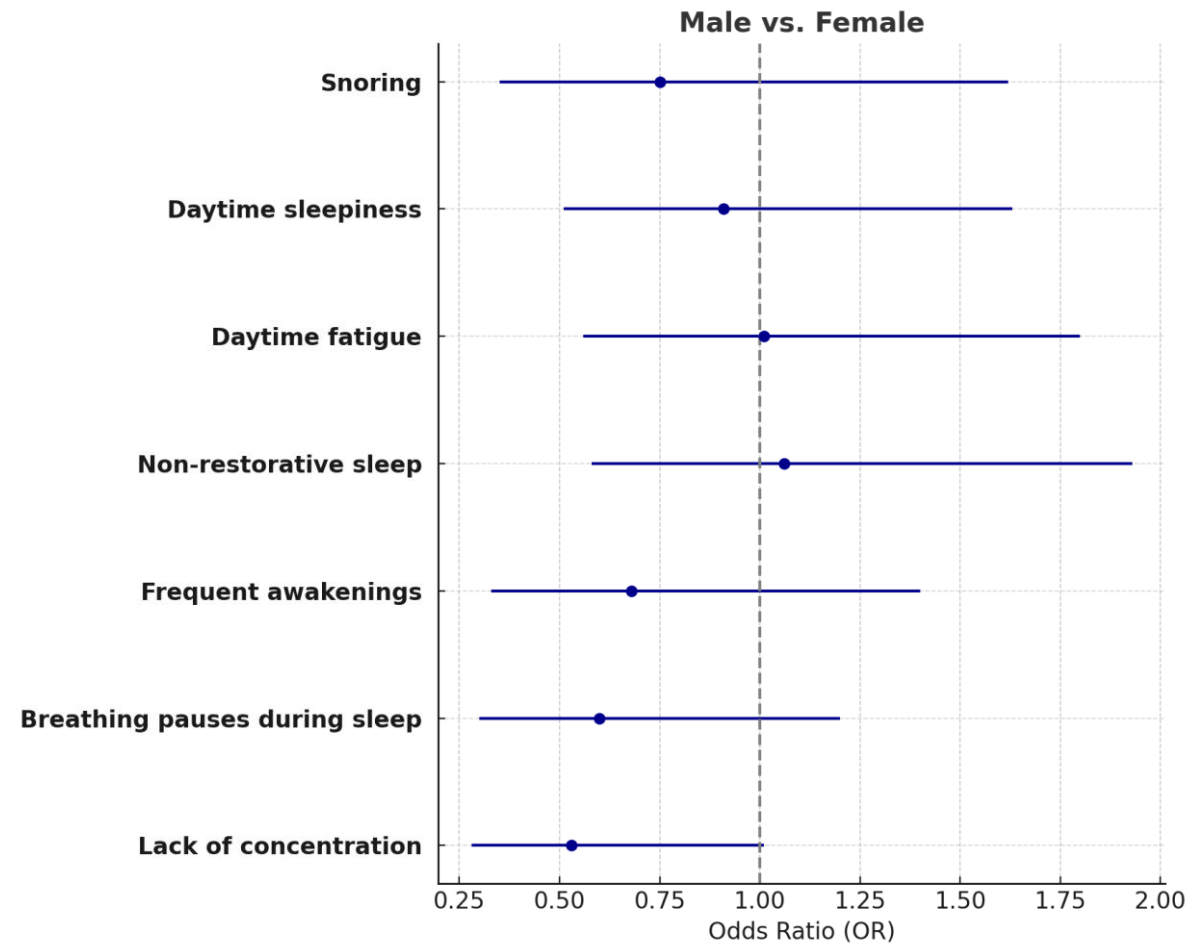
Chi-square test: \*  $P < .05$

# SYMPTOMS AT FOLLOW-UP: TOTAL GROUP



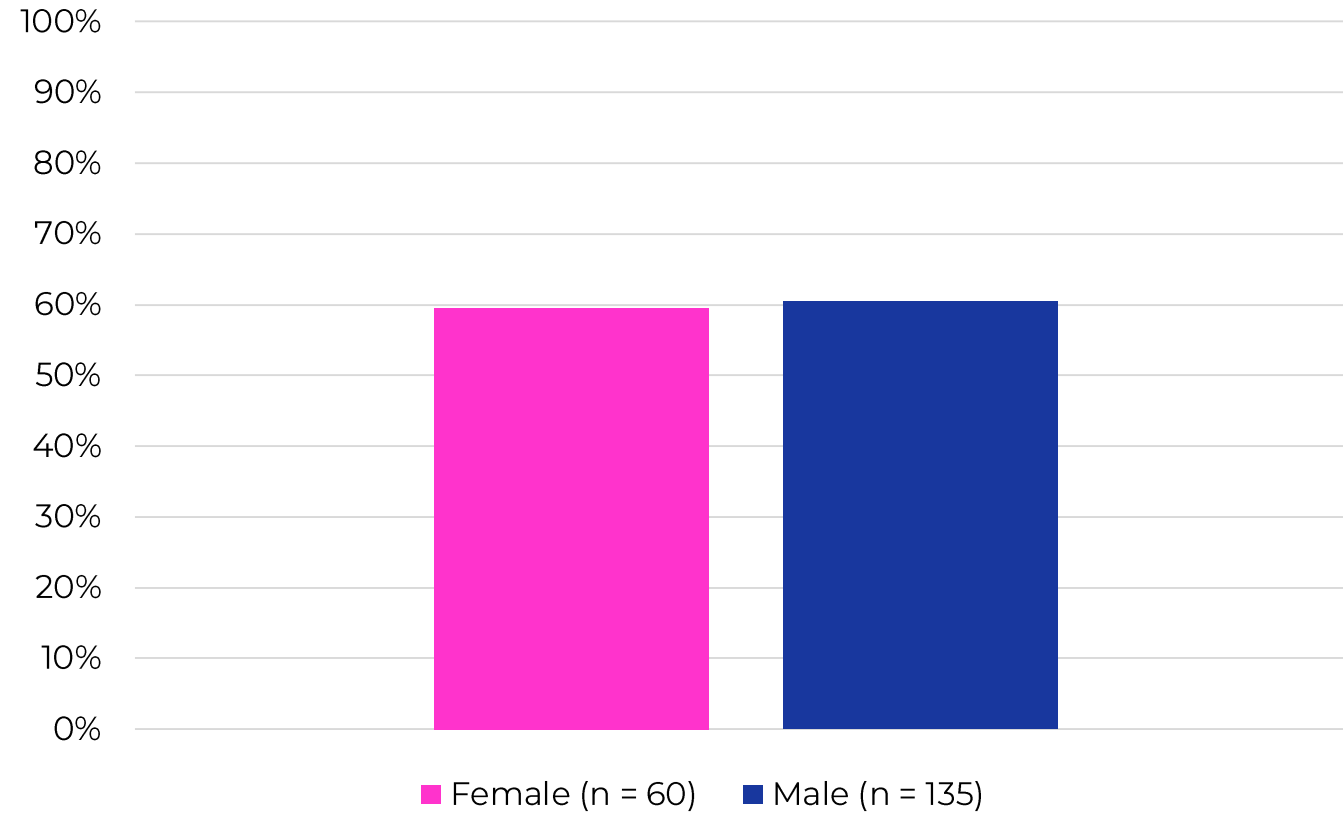
*Repeated binary regression models*

# SYMPTOMS AT FOLLOW-UP: MALES VS. FEMALES



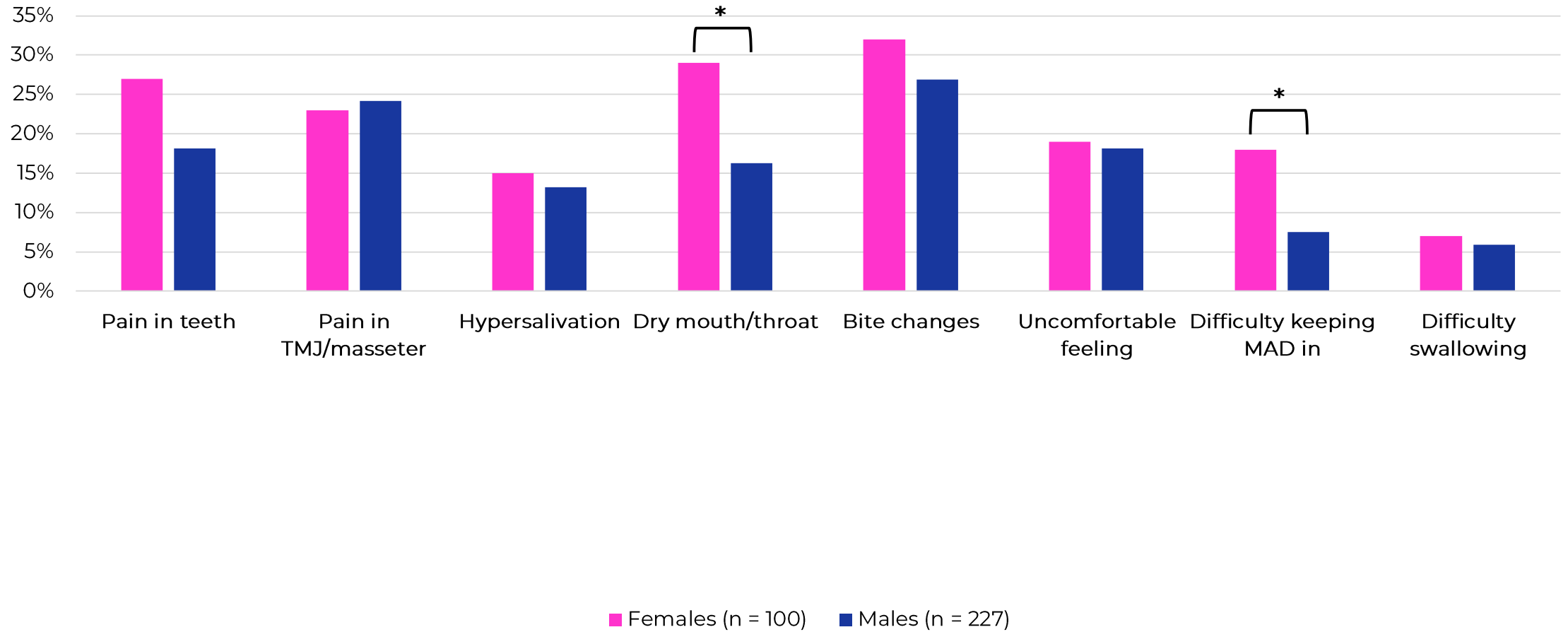
*Repeated binary regression models*

# COMPLETE ADHERENCE



Chi-square test:  $P = .36$

# SIDE EFFECTS



Chi-square test: \*  $P < .05$

## CONCLUSIONS

- MAD treatment is an effective treatment method for reducing OSA-related symptoms in both females and males.
- There is no significant sex difference in adherence to MAD treatment for OSA.
- Females report more daytime fatigue and breathing stops at intake, and more dry mouth/throat and difficulty keeping the MAD in the mouth at follow-up than males.

# Key Takeaways

1. OSA presents differently in females and males, whereas the effectiveness of MAD therapy appears comparable across sexes.
2. Adherence to MAD is comparable between females and males, despite differing symptom profiles and side-effect reporting.
3. Sex differences mainly emerge in symptom reporting at baseline and side-effects at follow-up, underscoring the need for tailored counseling and side-effect management.

# References

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