ASSOCIATIONS OF PHTHALATE EXPOSURE WITH SELF-REPORTED SLEEP DISRUPTIONS IN MENOPAUSAL WOMEN

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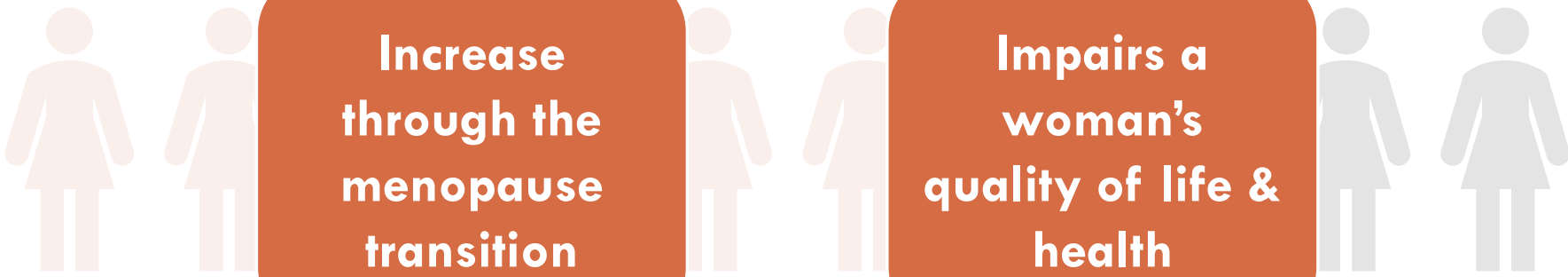
Hatcher *et al, submitted*

UP TO 60% OF MIDLIFE WOMEN EXPERIENCE POOR SLEEP QUALITY



Increase through the menopause transition

Impairs a woman's quality of life & health

Identifying risk factors is critical for creating potential interventions or therapies

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ENDOGENOUS HORMONES ARE ASSOCIATED WITH POOR SLEEP ACROSS MENOPAUSE

↑**FSH**

↓ **Estradiol**

↑ **Inhibin B**

↓ **Progesterone**

↑ **Testosterone:estradiol**

↑↓ **Estradiol:progesterone**

Endocrine disrupting chemicals?

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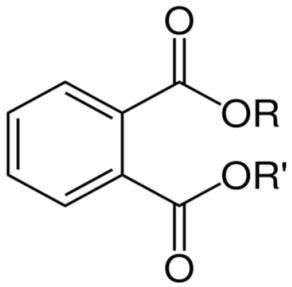
IS PHTHALATE EXPOSURE ANOTHER RISK FACTOR FOR MENOPAUSE SYMPTOMS?



- Exposure modulates hormones known to influence sleep quality
- Higher exposure increases nighttime awakenings in adults
- Associated with increased hot flashes in midlife women
- Phthalates → Class of plasticizers
  - Polyvinyl chloride plastics, chemical stabilizers
- Multiple sources of exposure

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WHAT IS KNOWN ABOUT THE IMPACT OF PHTHALATE EXPOSURE ON SLEEP?

Not a lot…

Evidence from the National Health and Nutrition Examination Survey

↑ Monocyclohexyl phthalate → Waking up at night

adult men and women

Preliminary results from the Midlife Women's Health Study

↑ Mono-(3-carboxypropyl) phthalate → Restless sleep

↑ Monomethyl phthalate → Insomnia

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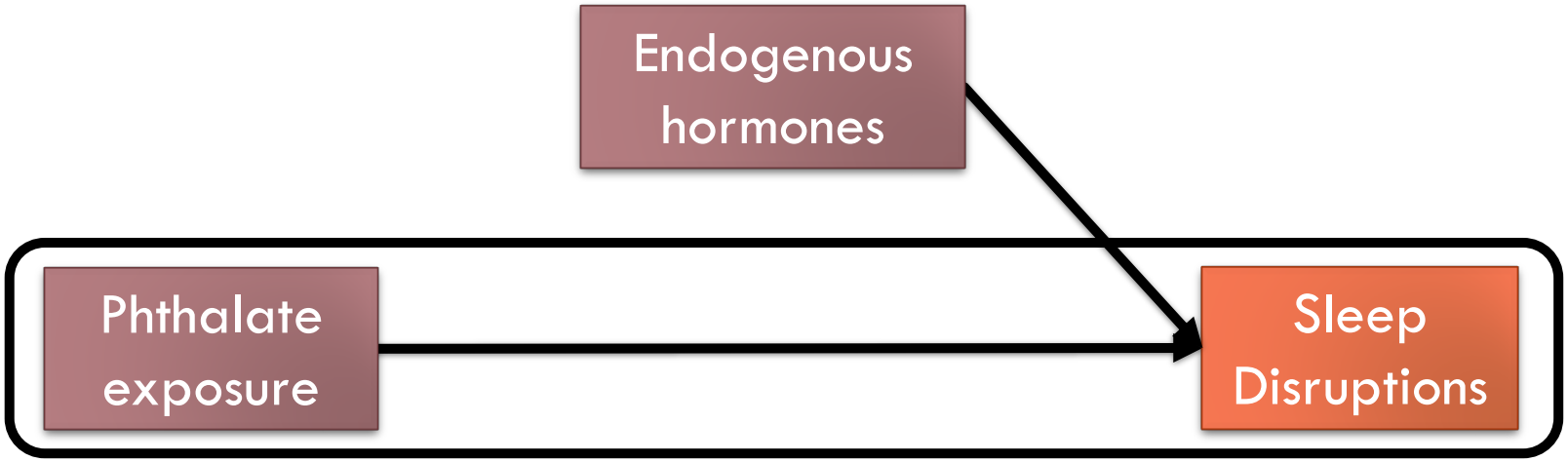
GAPS IN KNOWLEDGE & HYPOTHESIS



Hypothesis: Increased phthalate exposure will be associated with increased frequency of sleep disruptions.

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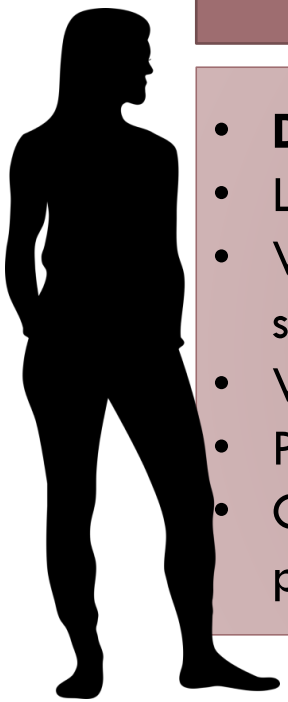
OVERVIEW OF THE MIDLIFE WOMEN'S HEALTH STUDY (MWHS)



Midlife Women's Health Study (MWHS)

- **Dr. Jodi Flaws**
- Longitudinal study
- Women recruited from Baltimore, MD and surrounding counties
- Women aged 45-54
- Pre- and perimenopausal
- Goal to identify risk factors for hot flashes in perimenopause

Exclusion Criteria

- Hormone therapy (including botanical therapy)
- Oophorectomy and/or hysterectomy
- Previously diagnosed with reproductive cancers

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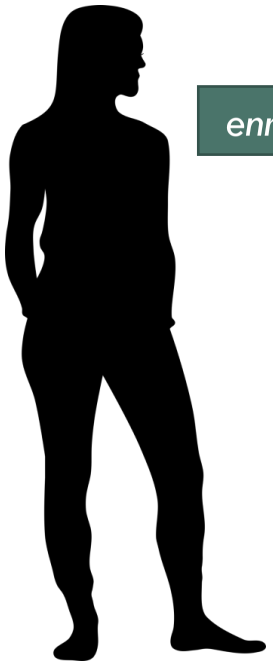
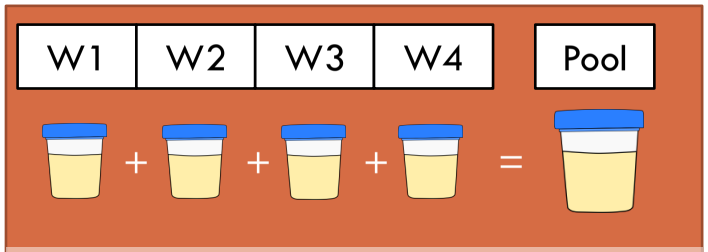
OVERVIEW OF SAMPLING METHODS FOR THE MWHS



enrolled

Clinic Visit

1. Demographics & symptoms survey
2. Depression indices (CES-D)
3. Subjective sleep indices



HPLC-MS/MS: Urine phthalate metabolite levels on pooled sample

Subjective Sleep Questions

Frequency of sleep disruptions:

1. Sleep disturbances
2. Insomnia
3. Restless sleep

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SELECTION OF SUMMARY PHTHALATE MEASURES

Summary phthalates	Description
sumPCP	Metabolites from personal care products
sumDEHP	Di-(2-ethylhexyl) phthalate metabolites
sumAA	Metabolites with known antiandrogenic activity
sumPLASTIC	Metabolites from plastic sources
sumALL	All calculated phthalate metabolites

Metabolite levels are similar to a national sample of adult women (National Health and Nutrition Examination Survey)

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OVERVIEW OF STATISTICAL MODEL: PHTHALATES → SLEEP DISRUPTIONS?

Summary Phthalates
sumPCP, sumDEHP, sumAA, sumPLASTIC, sumALL

Ordinal logistic regression

Frequency of Sleep Disruptions
Sleep disturbances, insomnia, restless sleep

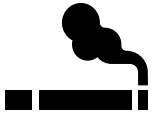
Never Rarely Sometimes Frequently Regularly

Adjusted for

- Menopause status (pre- or perimenopausal)
- Body mass index (BMI)
- Self-reported hot flashes at night (Yes/No)
- Present quality of life
- Depressive symptoms (CES-D Score)

Stratified by

- Self-reported smoking status
  - Nonsmokers
  - Former smokers
  - Current smokers



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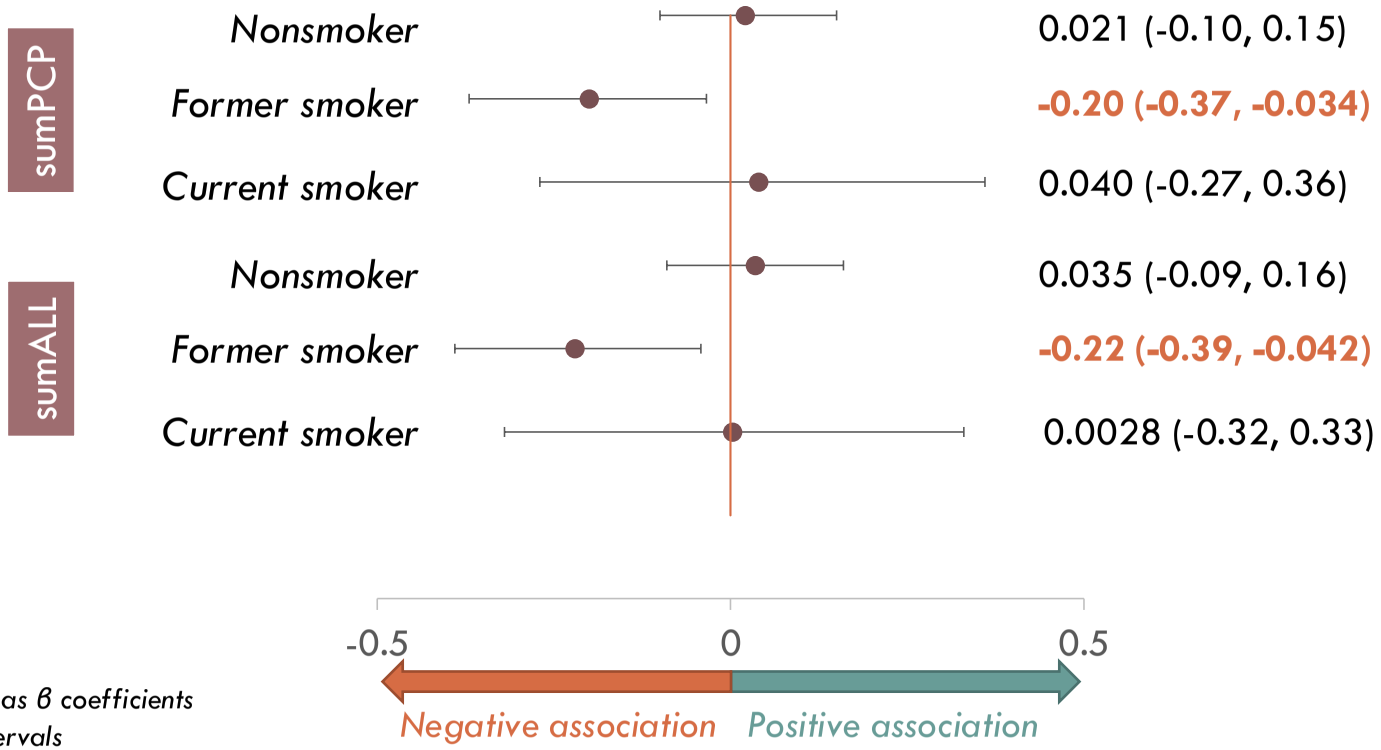
SUMPCP AND SUMALL ARE NEGATIVELY ASSOCIATED WITH SLEEP DISTURBANCES IN FORMER SMOKERS

Sleep Disturbances



All data are represented as β coefficients and 95% confidence intervals

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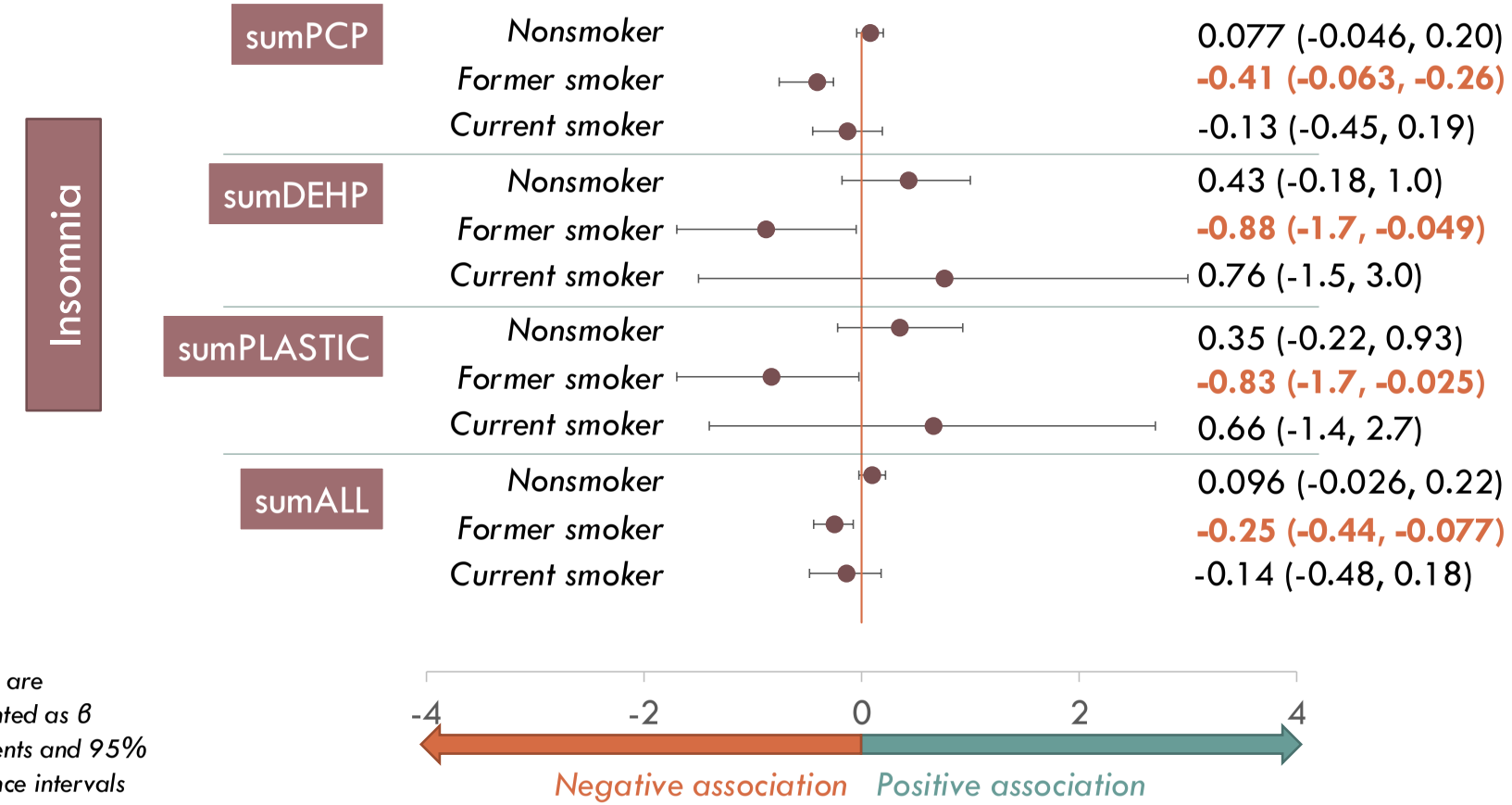
SUMPCP, SUMDEHP, SUMPLASTIC, AND SUMALL ARE ASSOCIATED WITH INSOMNIA IN FORMER SMOKERS



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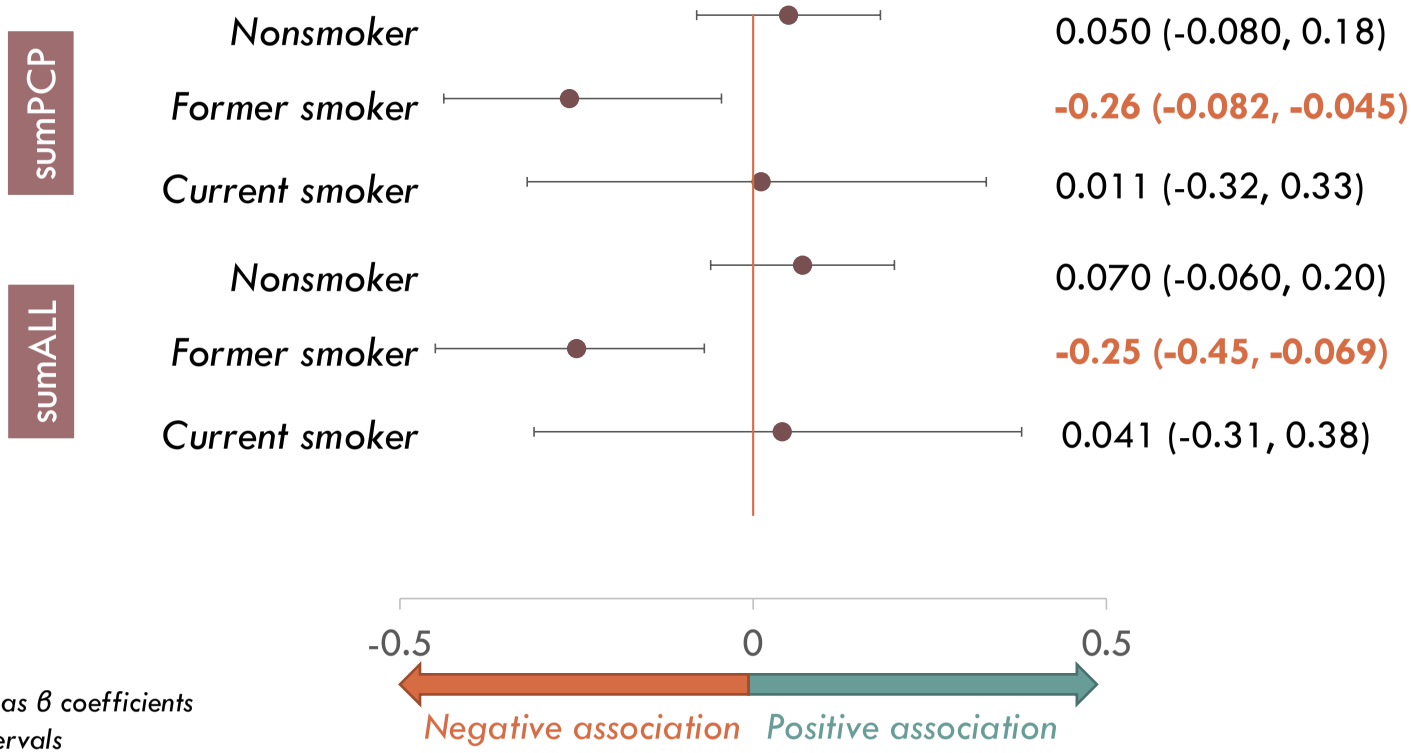
SUMPCP AND SUMALL ARE ASSOCIATED WITH RESTLESS SLEEP IN FORMER SMOKERS

Restless sleep



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OVERVIEW OF STATISTICAL MODEL: DOSE OF PHTHALATE → SLEEP DISRUPTIONS?

Summary Phthalates
sumPCP, sumDEHP, sumAA, sumPLASTIC, sumALL

Quartile 1 (Q1) vs. Quartiles 2-4 (Q2-4)

Ordinal logistic regression

Frequency of Sleep Disruptions
Sleep disturbances, insomnia, restless sleep

Never Rarely Sometimes Frequently Regularly

Adjusted for
- Menopause status (pre- or perimenopausal)
- Body mass index (BMI)
- Self-reported hot flashes at night (Yes/No)
- Present quality of life
- Depressive symptoms (CES-D Score)

Stratified by
- Self-reported smoking status
  - Nonsmokers
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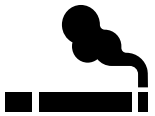
  - Current smokers



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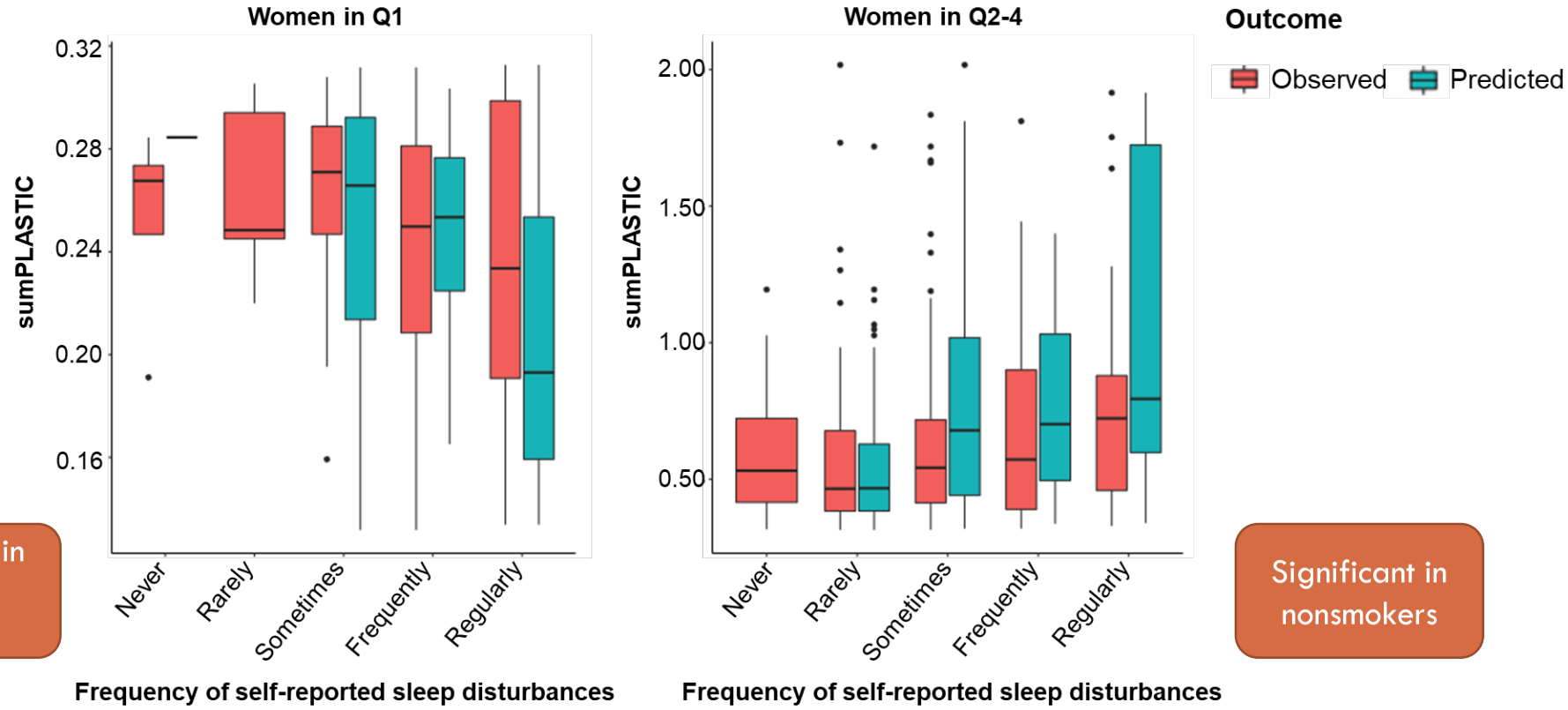
SUMPLASTIC IS ASSOCIATED WITH FREQUENCY OF SLEEP DISTURBANCES IN A DOSE-DEPENDENT MANNER



Significant in former smokers

Significant in nonsmokers

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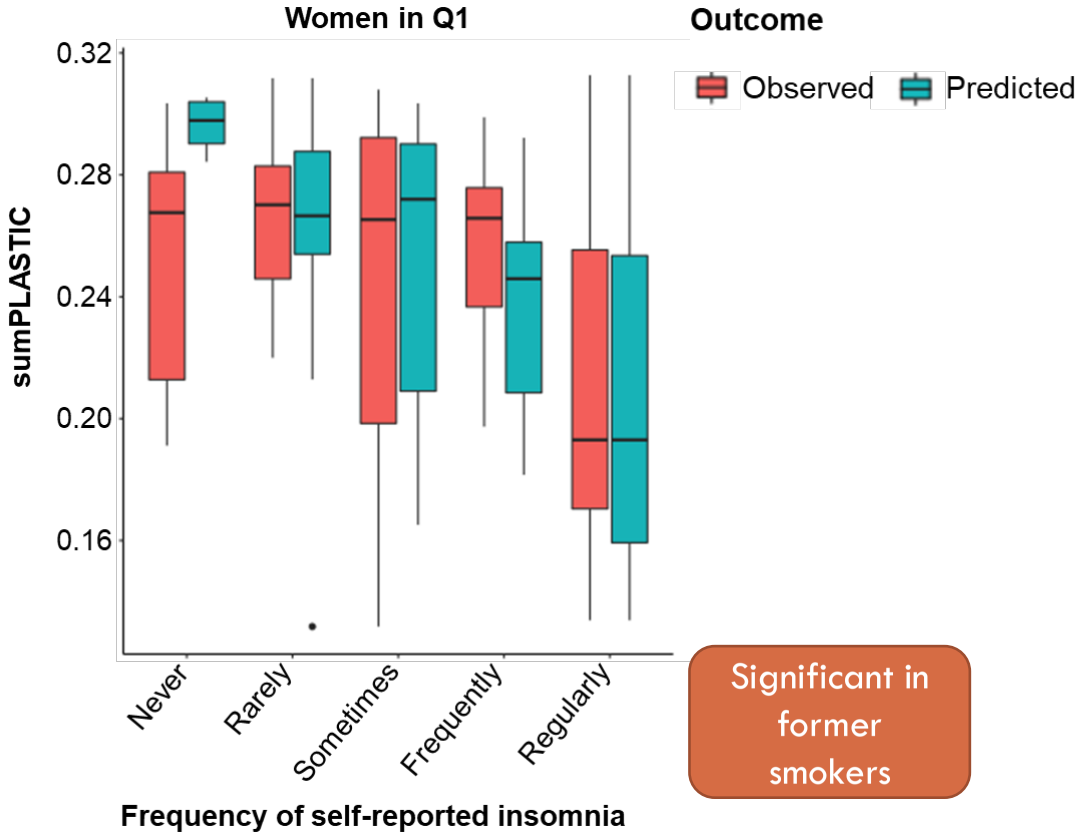
SUMPLASTIC IS NEGATIVELY ASSOCIATED FREQUENCY OF INSOMNIA IN QUARTILE 1



Significant in former smokers

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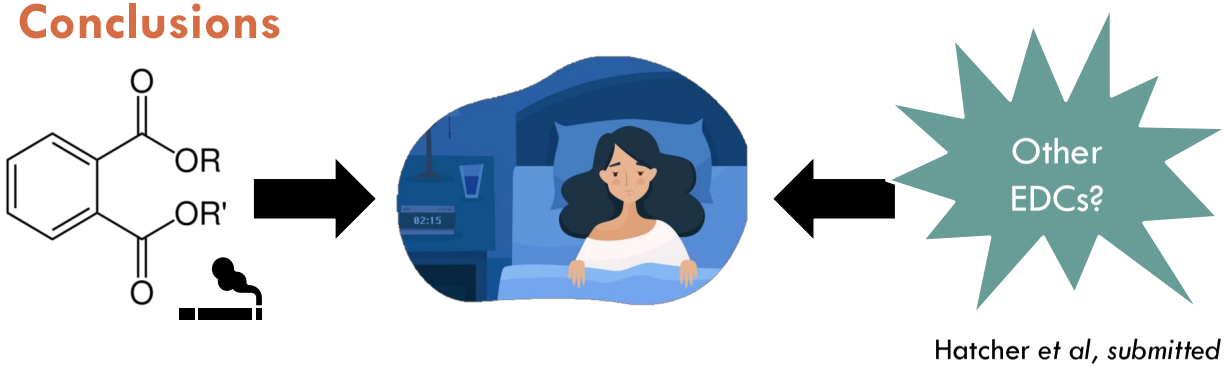
SUMMARY AND CONCLUSIONS

Measure	Sleep disturbances	Insomnia	Restless sleep
sumPCP	↓	↓ (Q1)	↓
sumDEHP		↓	
sumAA			
sumPLASTIC	↑ (Q2-4)	↓ (Q1)	
sumALL	↓	↓	↓

1. **sumPCP, sumDEHP, sumPLASTIC,** and **sumALL** – negative association with frequency of sleep disruptions
2. **Direction of association** – depends on smoking status and quartile

Conclusions



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MWHS

All participants of the MWHS

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THANK YOU!