



Sleep and Health

Saturday May 16, 2015
Nashville, TN

Eve Van Cauter, Ph.D.



SLEEP • METABOLISM AND HEALTH CENTER



Conflicts of Interest

- Investigator-initiated industry-sponsored research grants
 - Amylin/Astra Zeneca
 - Philips/Respironics
 - Merck
- Consultant
 - Pfizer Inc.
 - Shire/Viropharma
 - Philips/Respironics



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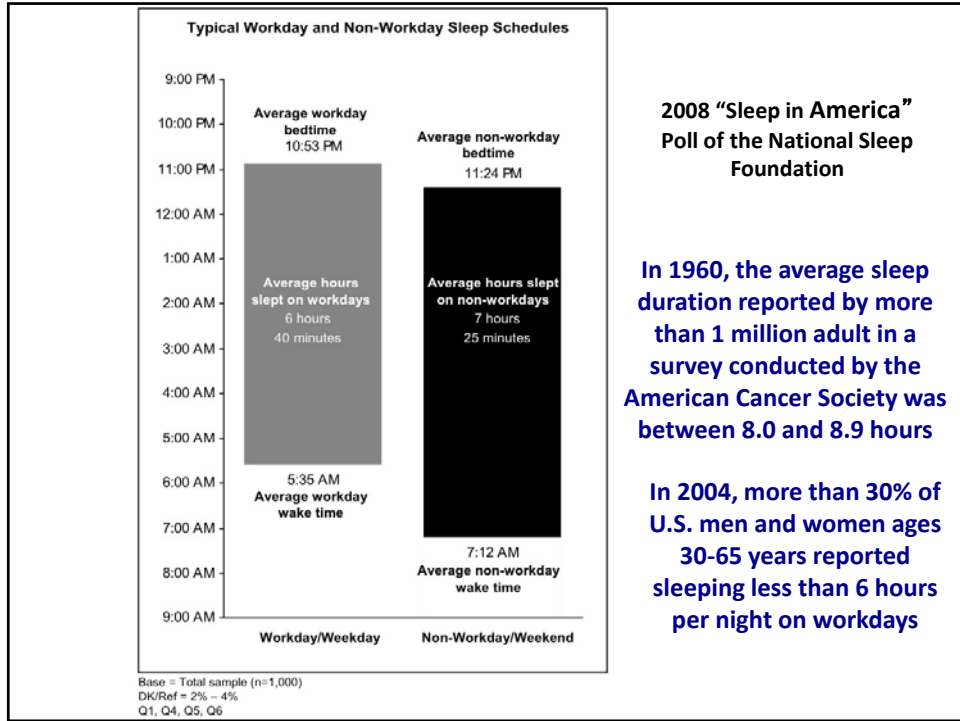


Sleep Disturbances

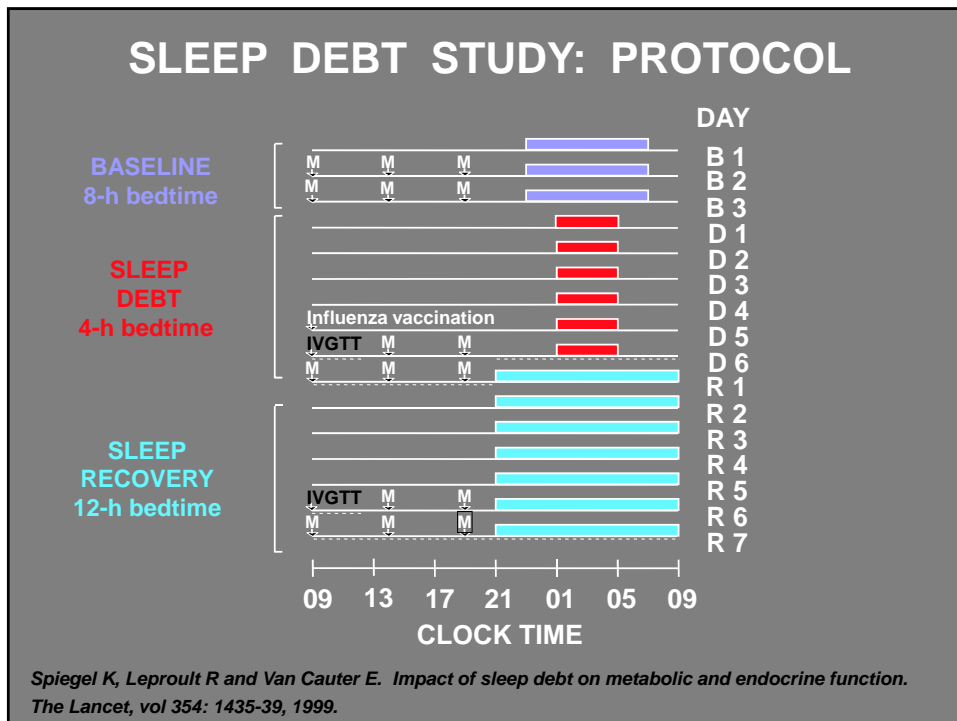
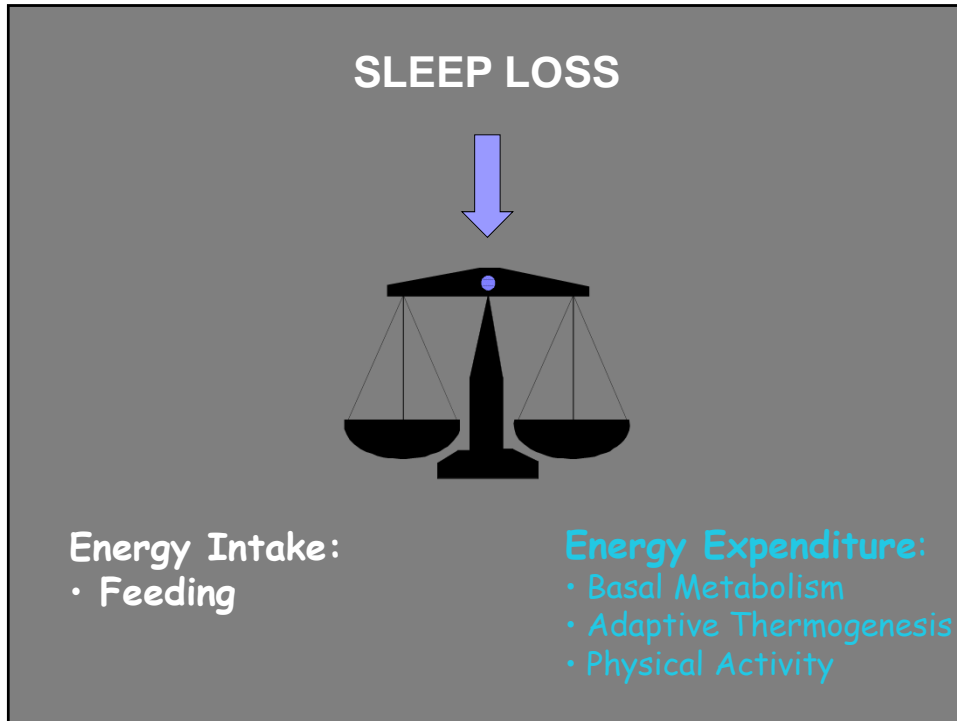
- **Insufficient sleep**
- **Poor sleep quality**
- **Obstructive sleep apnea**
- **Abnormal timing of sleep**

Outline

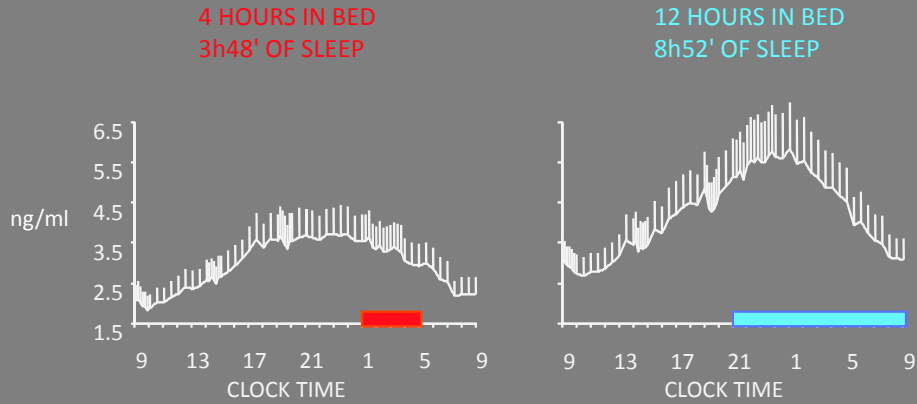
- **An introduction to SLEEP**
- **Sleep disturbances**
- **Sleep disturbances, obesity and diabetes: Interacting epidemics**
- **Sleep disorders in type 2 diabetes: Impact on glycemic control**



Insufficient Sleep and Obesity : Interacting Epidemics ?



IMPACT OF A SLEEP DEBT ON LEPTIN

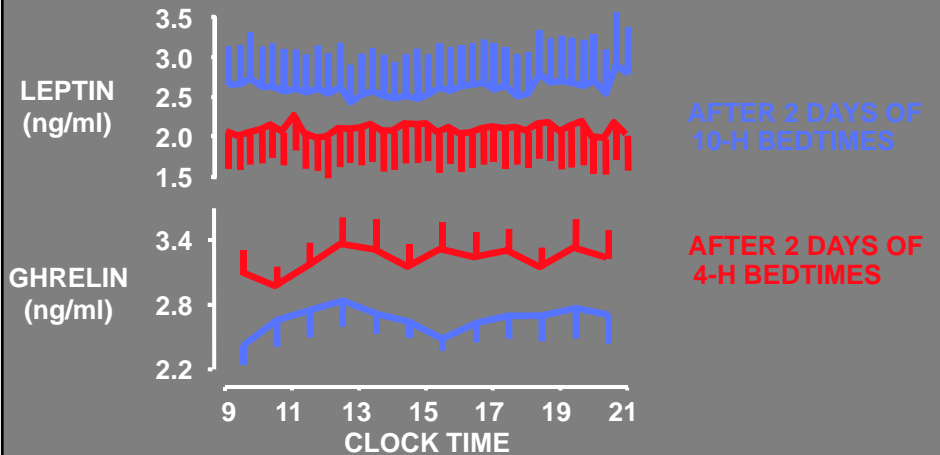


Difference between “sleep debt” and “fully rested” corresponds to underfeeding by ± 1000 Kcal for 3 days

Spiegel et al, JCEM, 89(11):5762-5771, 2004

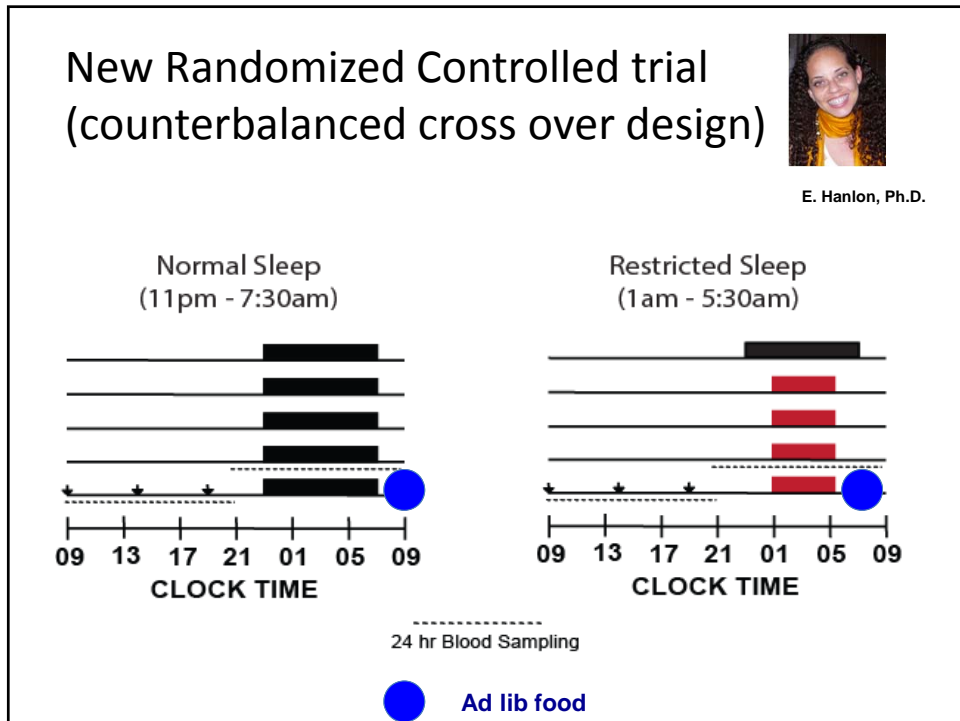
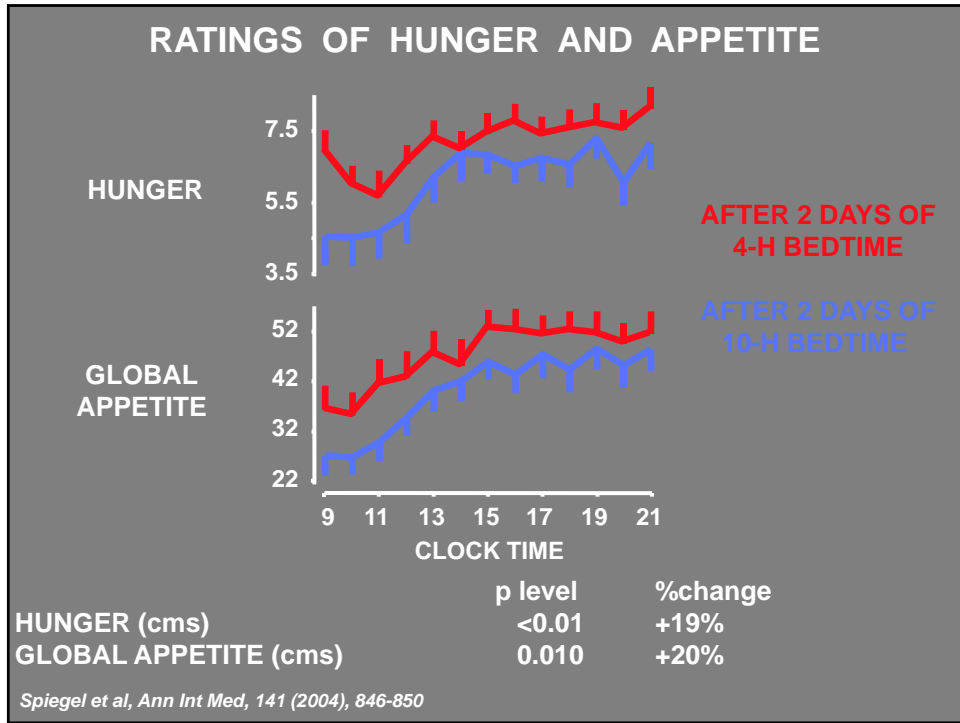
DAYTIME LEPTIN AND GHRELIN LEVELS

Randomized cross-over design in lean subjects



| | p level | % change |
|---------|---------|----------|
| leptin | 0.041 | -19% |
| ghrelin | 0.038 | +24% |

Spiegel et al, Ann Int Med, 141 (2004), 846-850

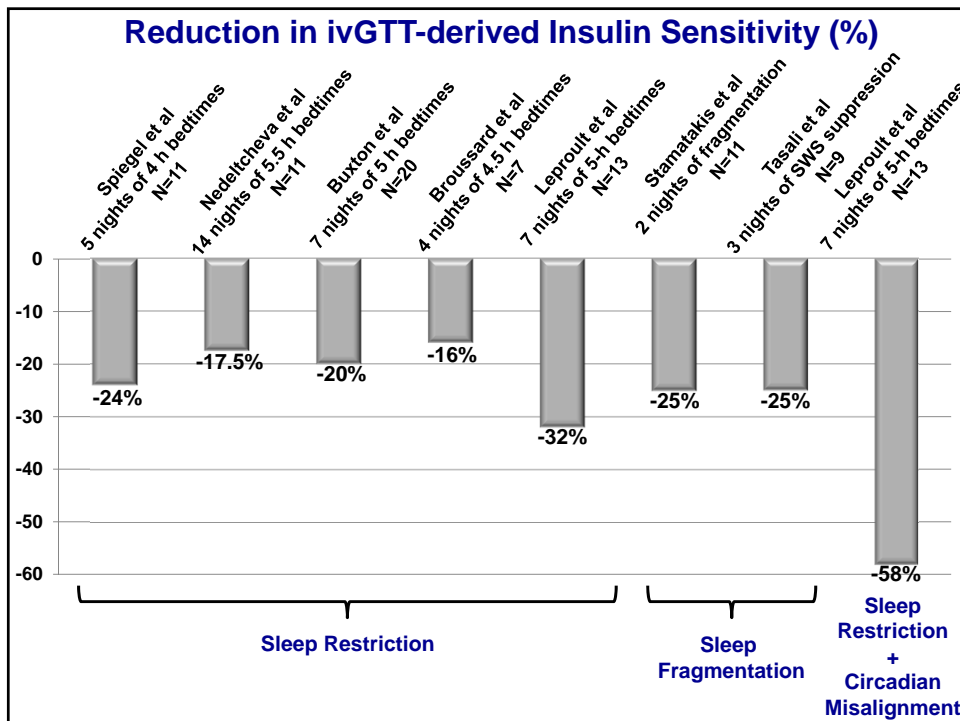


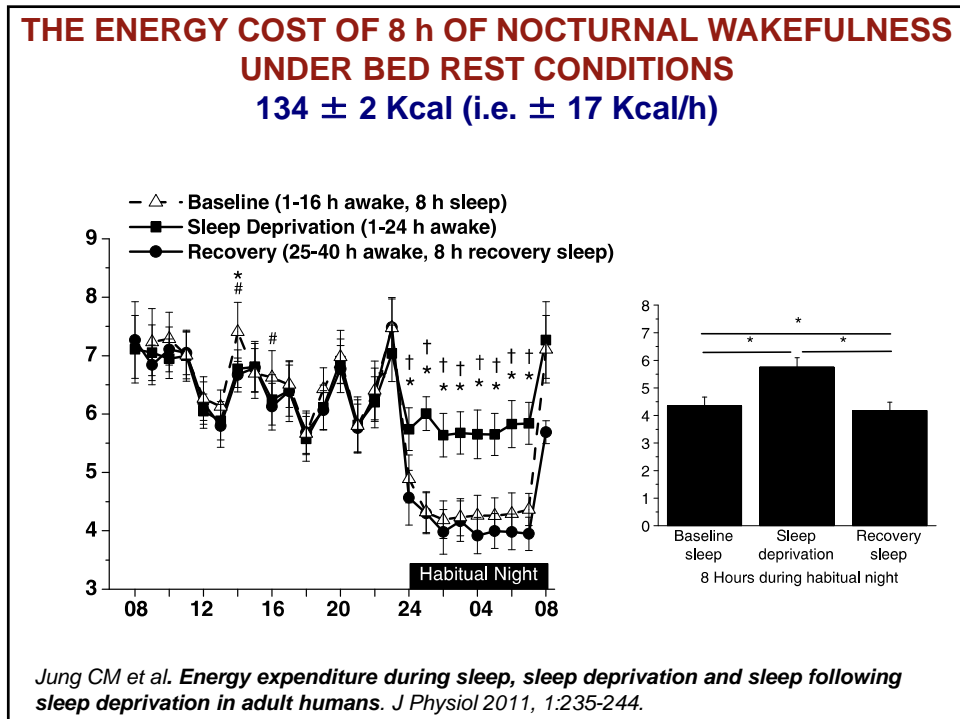
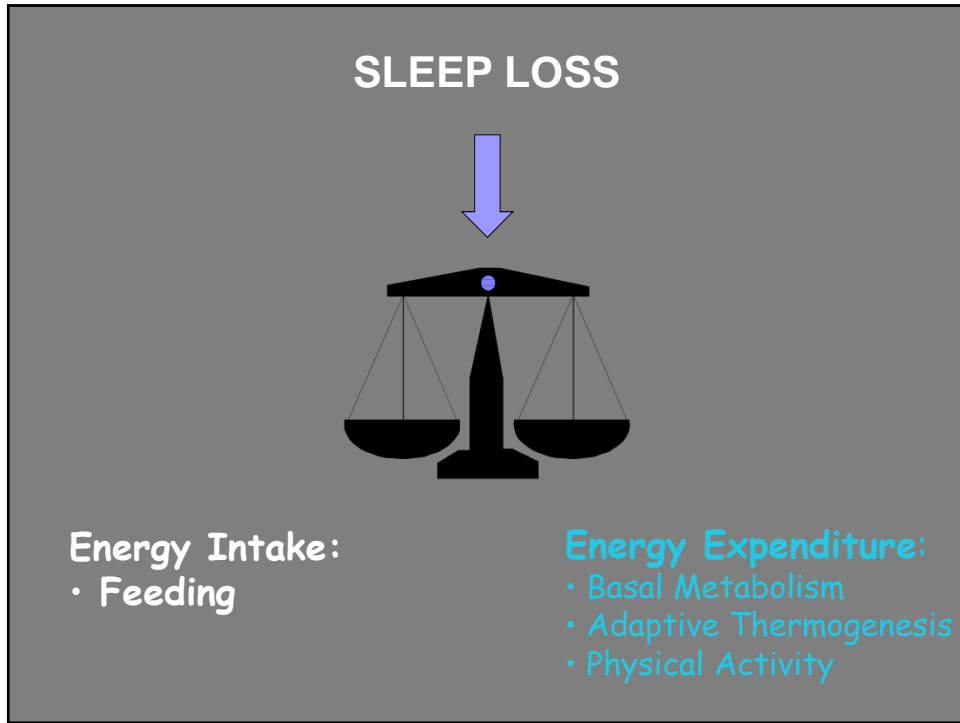
Short sleep duration increases energy intakes but does not change energy expenditure in normal-weight individuals^{1,2}

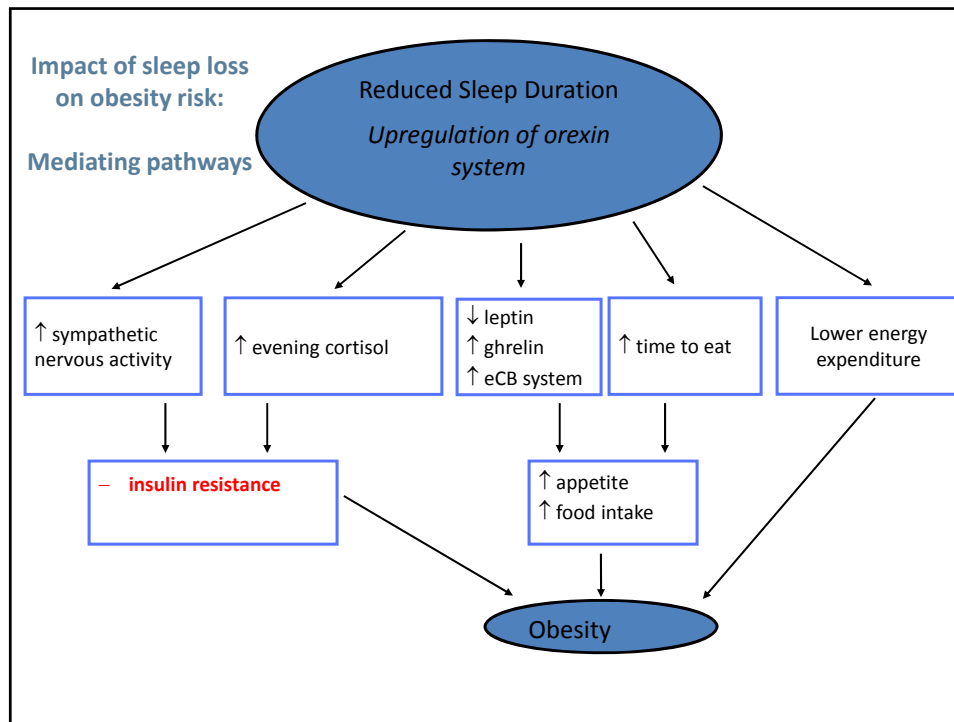
Marie-Pierre St-Onge, Amy L Roberts, Jinya Chen, Michael Kelleman, Majella O’Keeffe, Arindam RoyChoudhury, and Peter JH Jones

| | Short Sleep (± 3h45/night) | Normal Sleep (± 7h38/night) | Difference | P level |
|-------------------|-------------------------------|--------------------------------|------------|---------|
| Calories consumed | 2818 ± 593 | 2518 ± 593 | + 296 Kcal | 0.023 |
| Calories spent | 2589 ± 527 | 2611 ± 529 | - 22 Kcal | ns |

Am J Clin Nutr 2011;94:410–6.



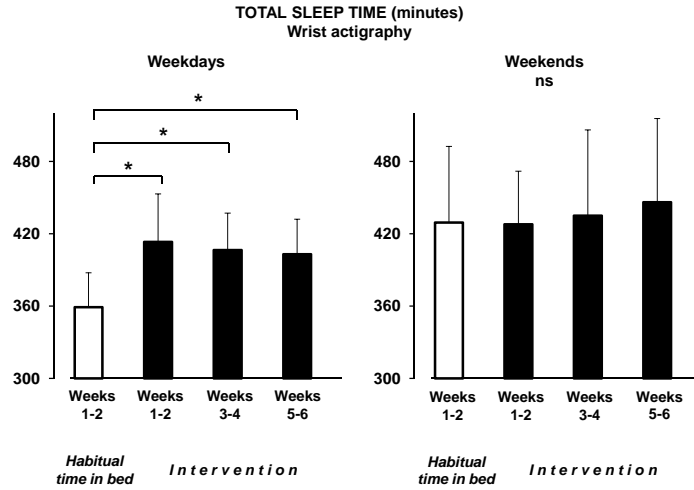




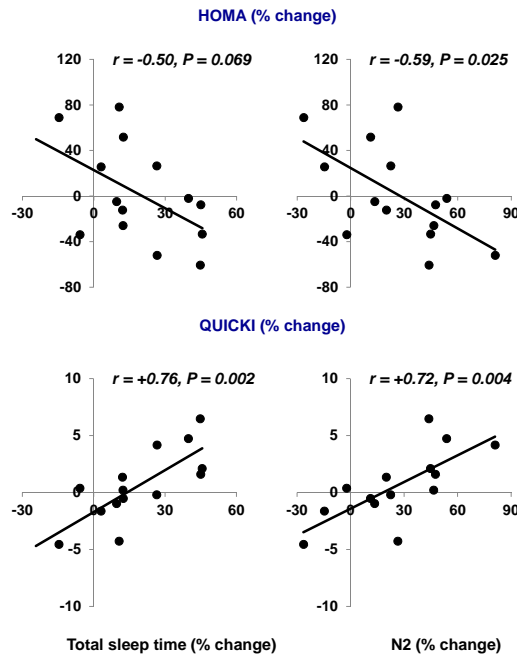
Major questions

- Can sleep extension in restricted sleepers have beneficial effects on obesity risk ?
- Can sleep extension in restricted sleepers facilitate weight loss ?

Beneficial Impact of Sleep Extension on Fasting Insulin Sensitivity in Adults with Habitual Sleep Restriction.

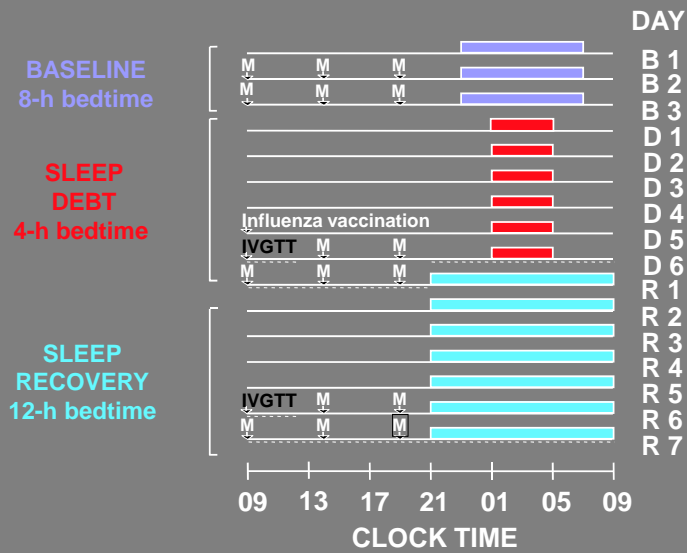


Leprout R et al, Sleep. 2014 Oct 28. [Epub ahead of print]

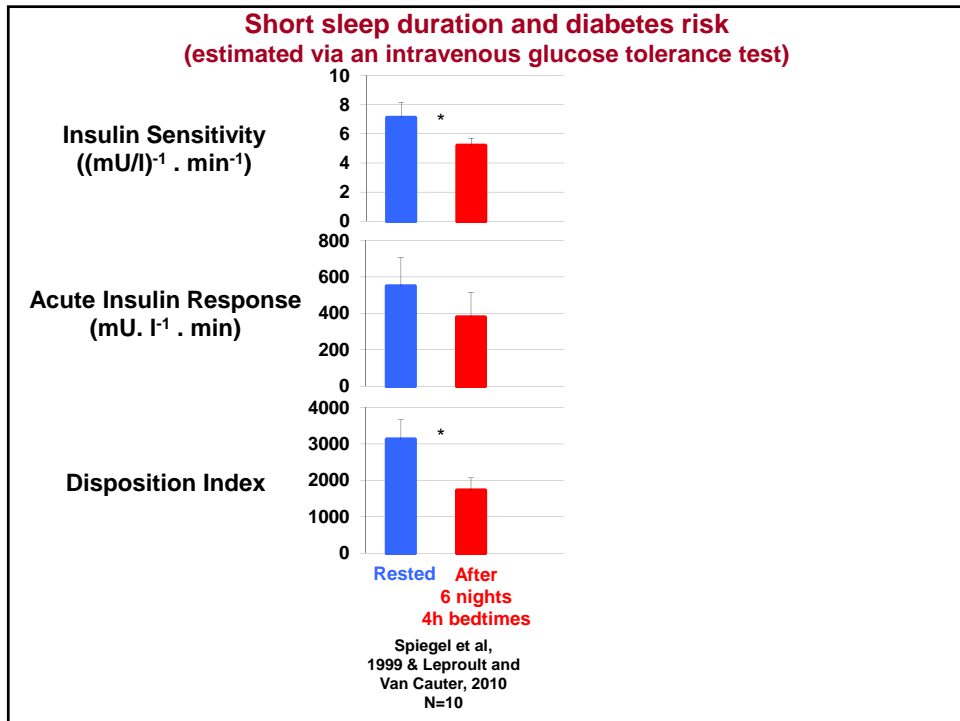
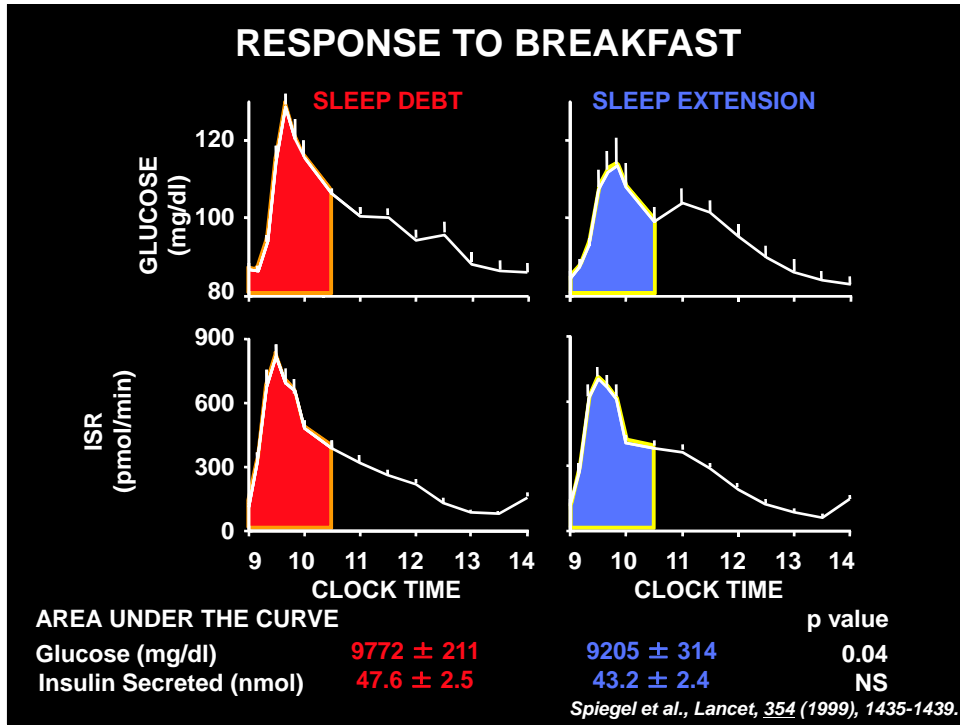


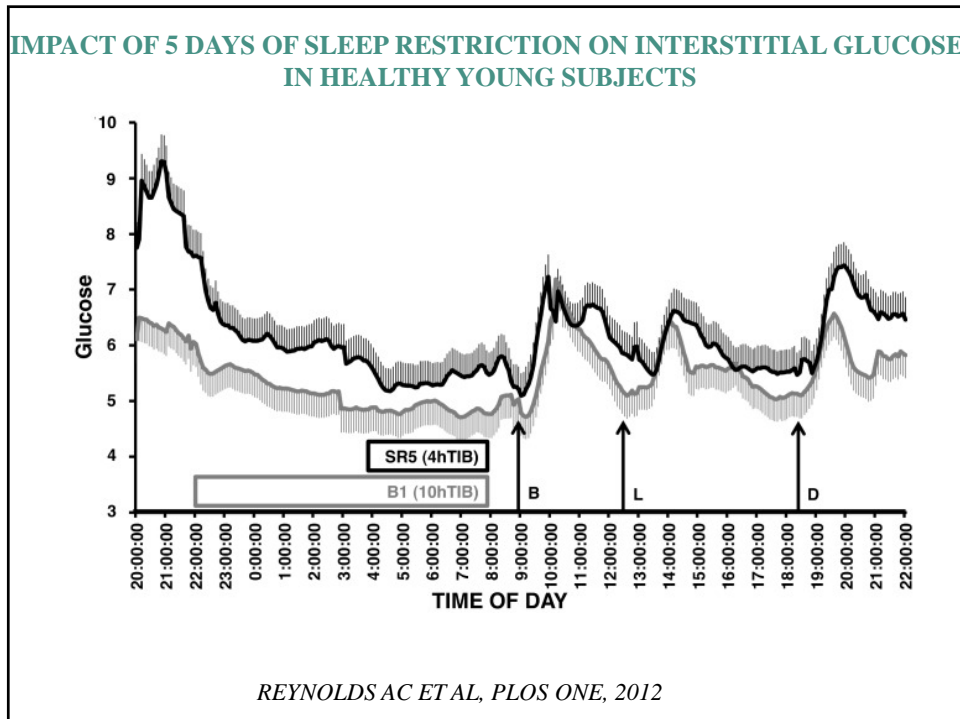
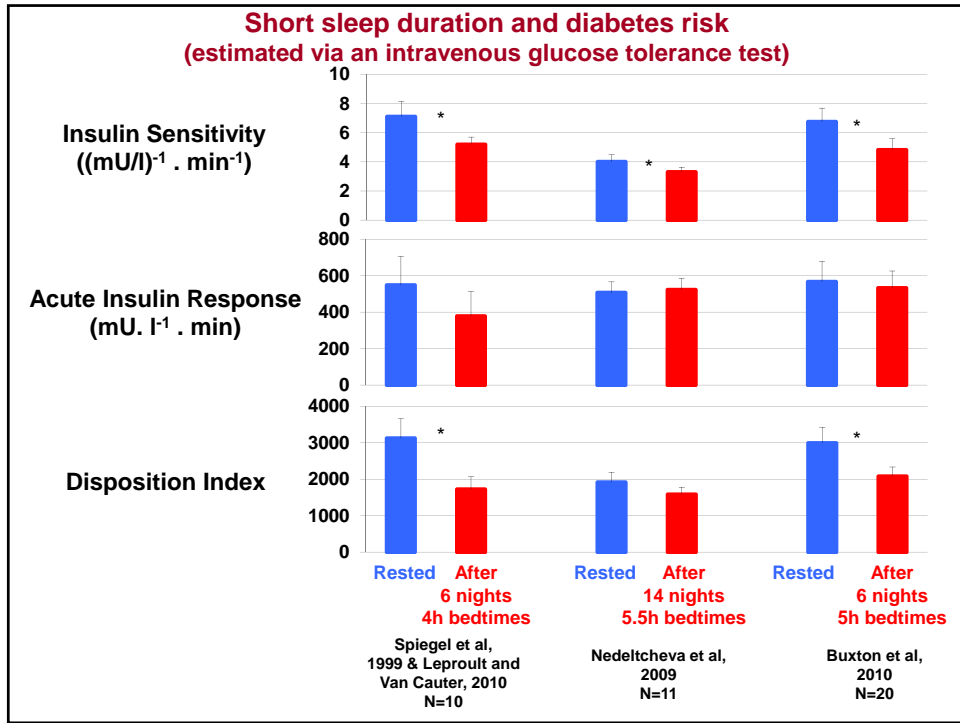
Insufficient, Obesity and Diabetes: Interacting Epidemics ?

SLEEP DEBT STUDY: PROTOCOL



Spiegel K, Leproult R and Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *The Lancet*, vol 354: 1435-39, 1999.





Assessment of insulin resistance at the level of the adipocyte: Does fat need sleep ?

- Biopsy of subcutaneous abdominal fat after 4 nights of sleep restriction and 4 nights of normal sleep
- Adipocytes isolated and viable up to one week in culture
- Phospho-Akt and Akt are measured by immunoblotting

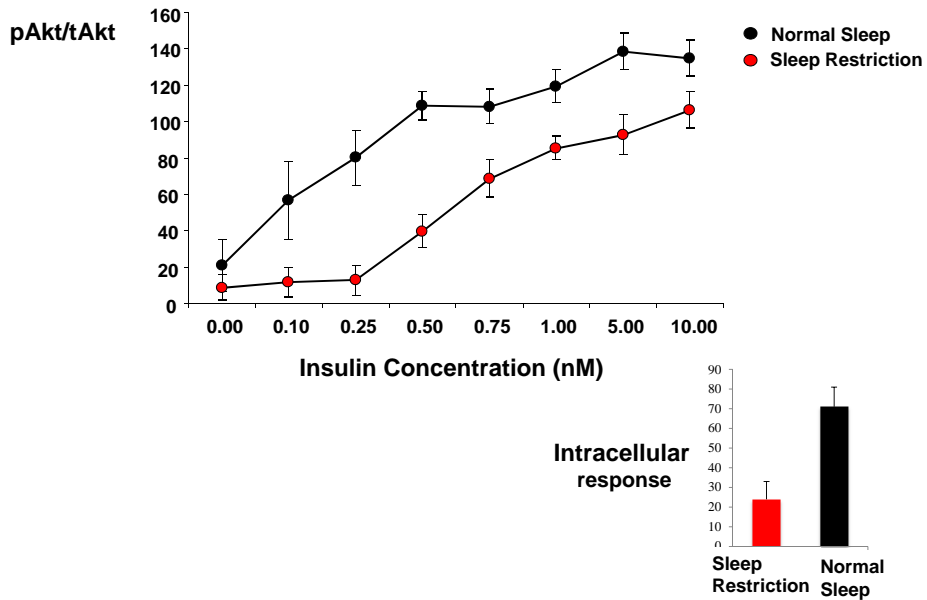
*Broussard JL et al.
Ann Inter Med 2012; 157: 549-57*

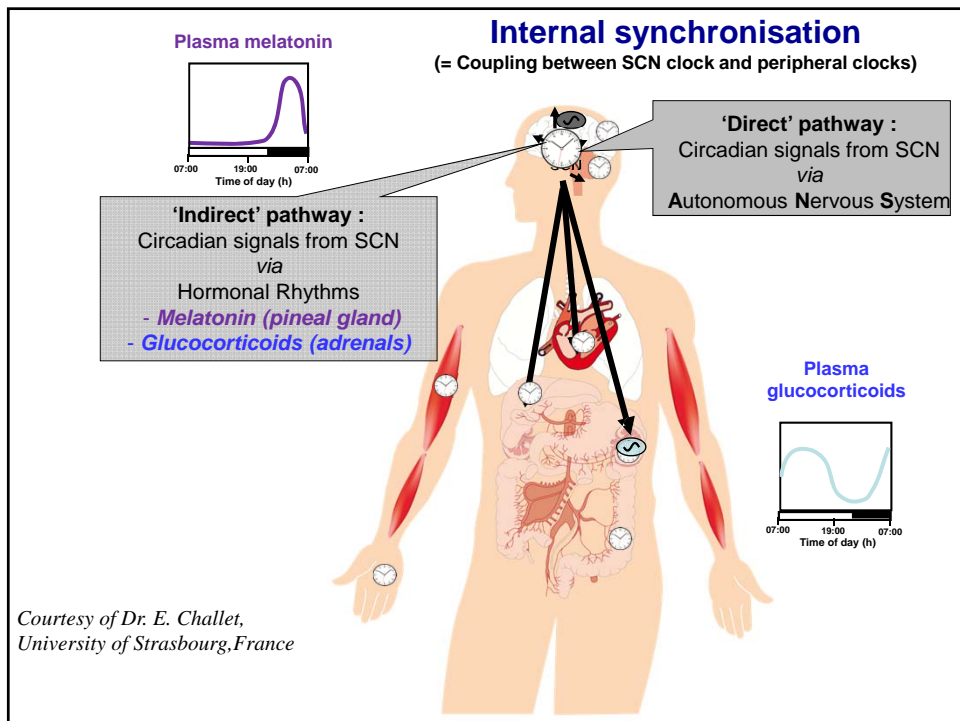
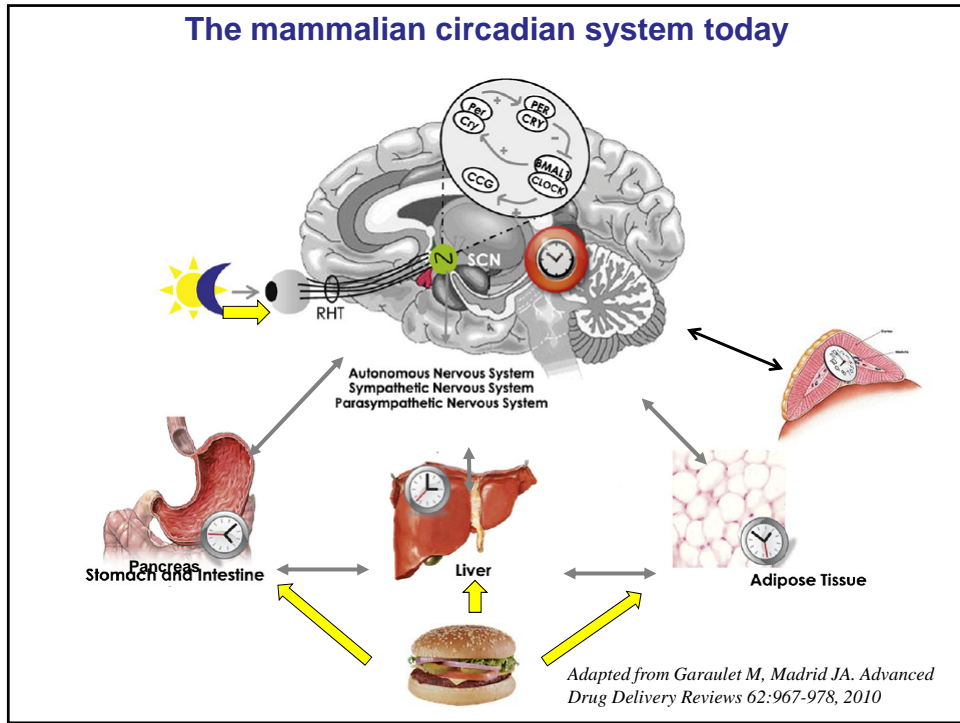
J. Broussard

E. Tasali

M. Brady

Assessment of insulin resistance in adipocytes



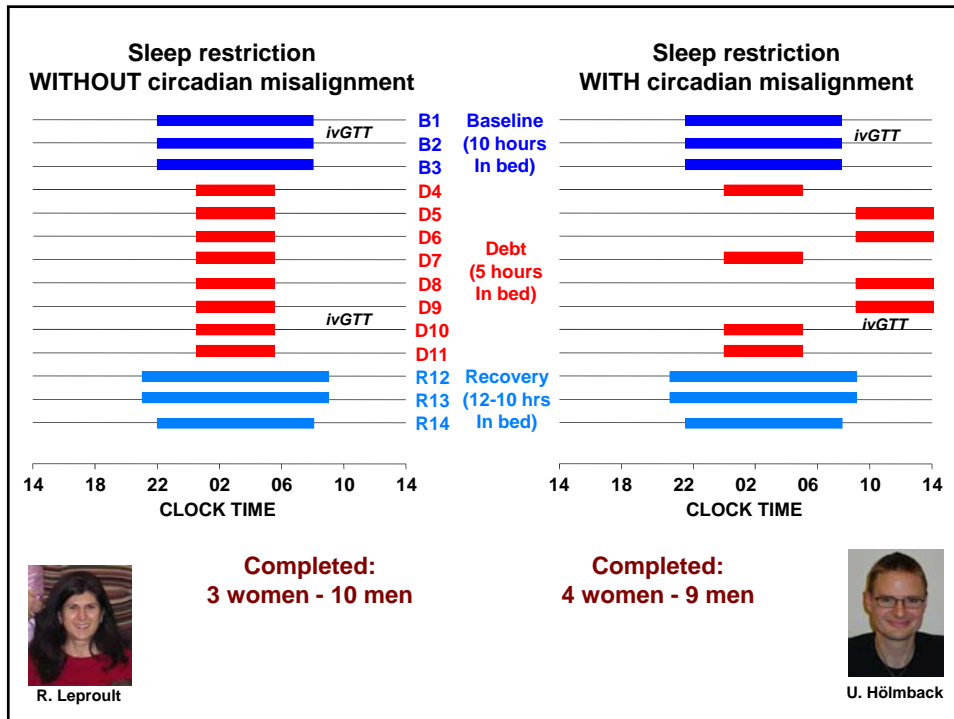


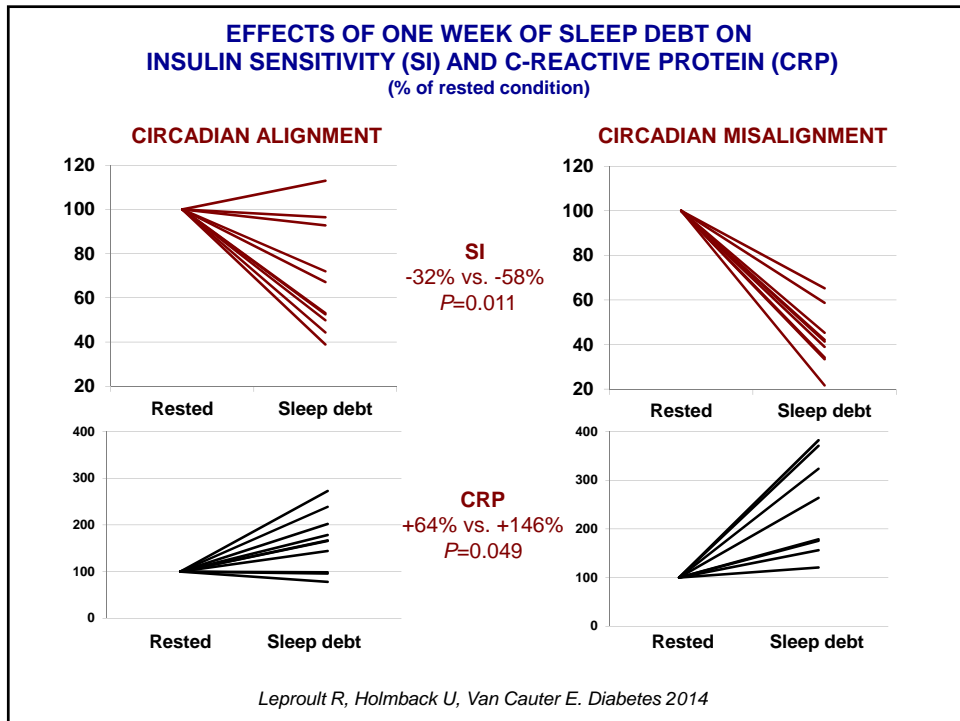
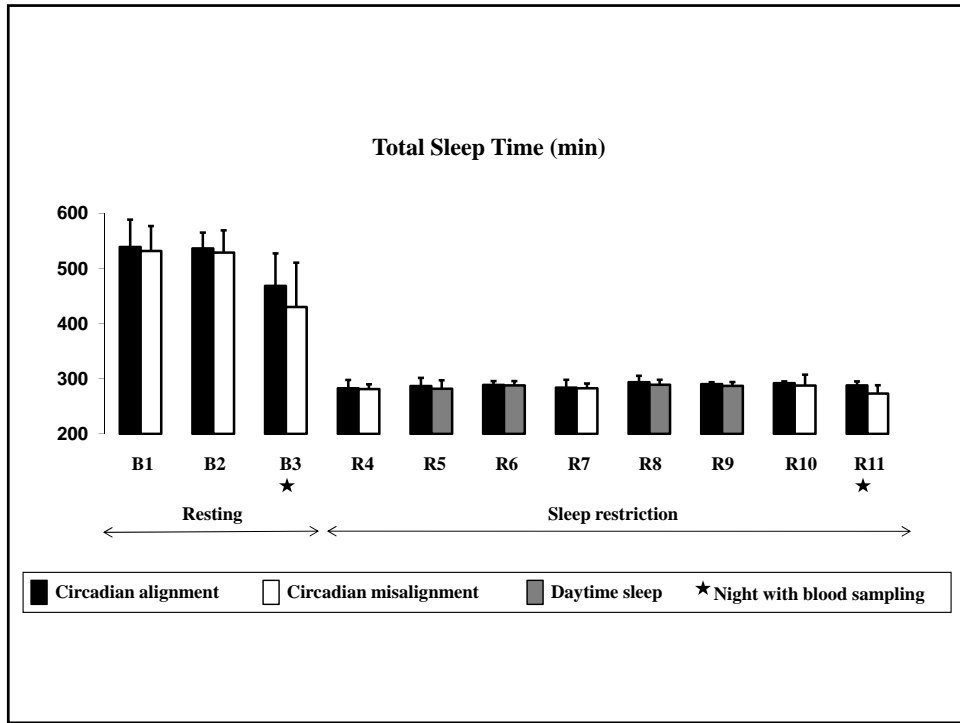
Cardio-Metabolic Impact of Circadian Misalignment

- Is the cardio-metabolic risk of circadian misalignment independent of sleep loss ?
- Does habitual circadian alignment impact glucose control in patients with diabetes ?

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THE UNIVERSITY OF CHICAGO
 MEDICINE & BIOLOGICAL SCIENCES
AT THE FOREFRONT OF MEDICINE



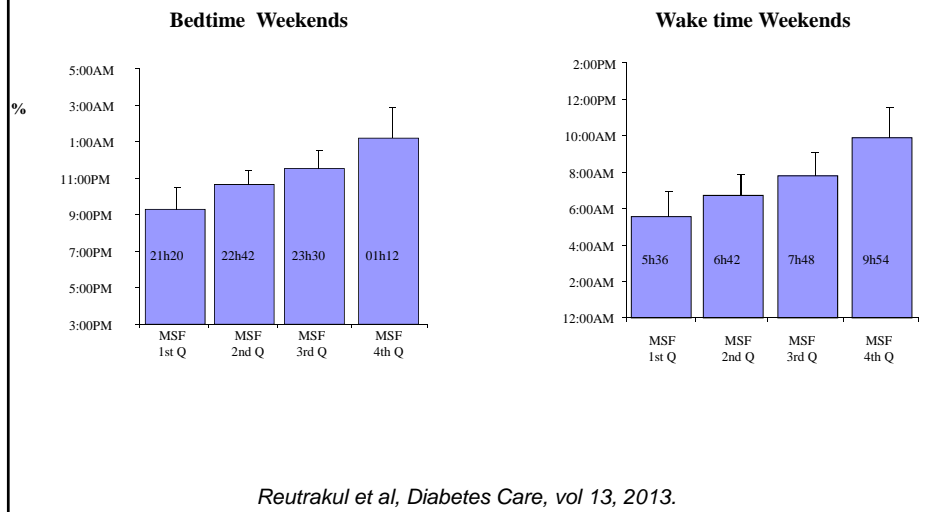


Chronotype Is Independently Associated With Glycemic Control in Type 2 Diabetes

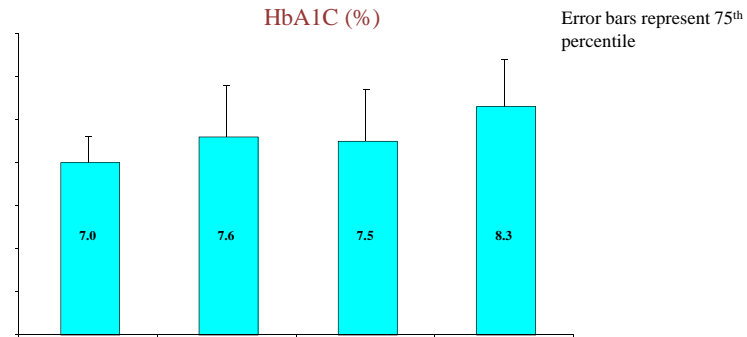
- 194 patients with T2DM had a structured interview and completed questionnaires to collect information on diabetes history and habitual sleep duration, quality, and timing. Shift workers were excluded.
- A recently validated construct derived from mid-sleep time on weekends was used as an indicator of chronotype (early vs late person)

Reutrakul S et al, Diabetes Care, vol 36, 2013

Chronotype in patients with T2DM



Chronotype & Glycemic Control



$P=0.001$, after adjustment for age, sex, race, BMI, insulin use, depression, diabetes complications, and perceived sleep debt

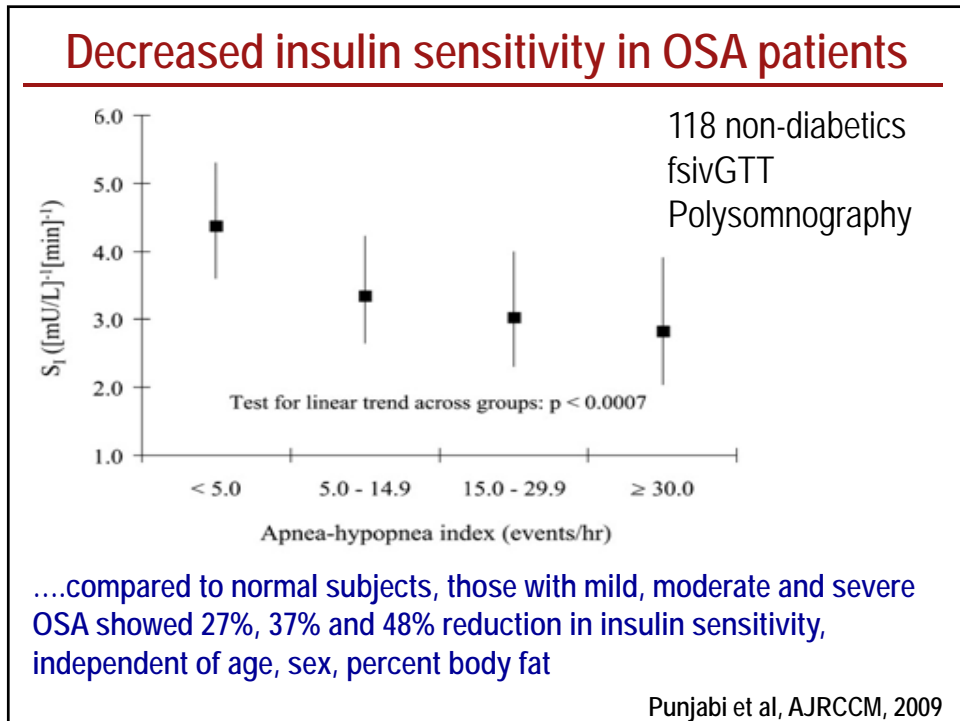
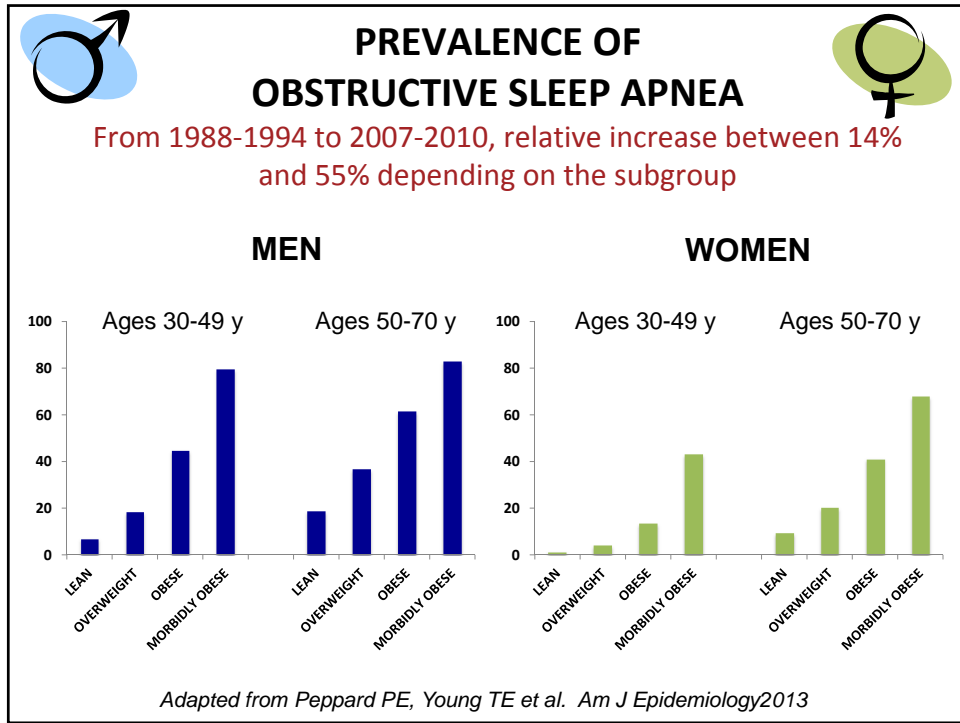
Reutrakul et al, Diabetes Care, 2013, in press

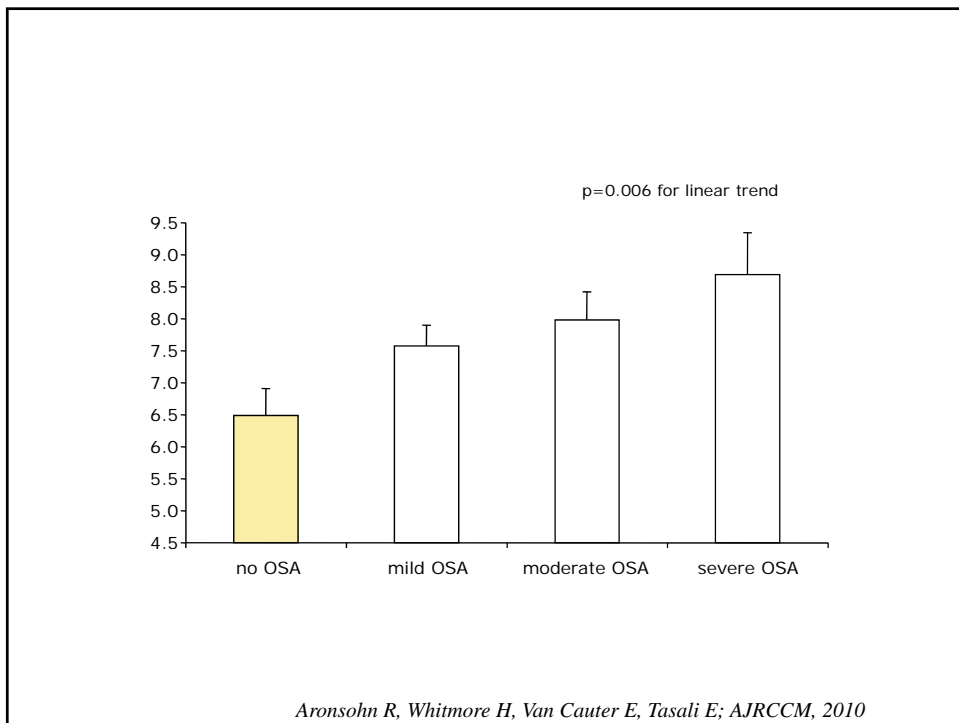
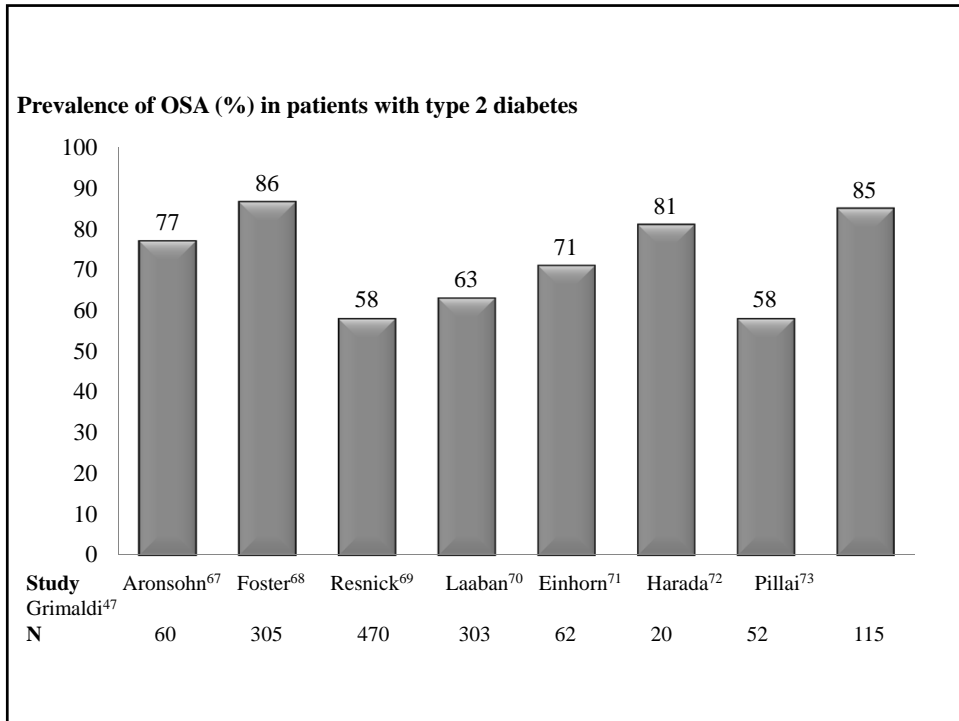
Sleep Disturbances

- Insufficient sleep
- Poor sleep quality
- Abnormal timing of sleep
- Obstructive sleep apnea

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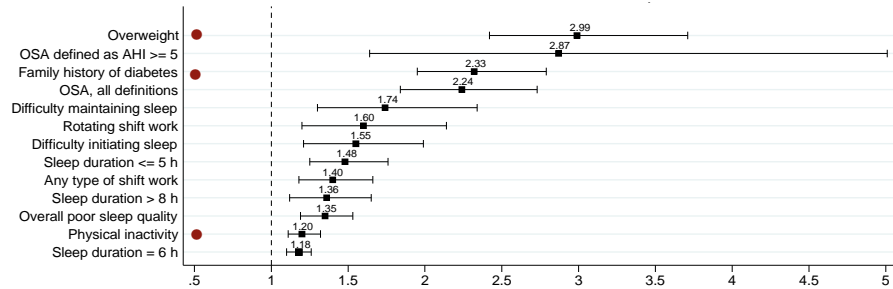


MAJOR QUESTIONS

Does effective treatment of OSA improve glycemic control in patients with type 2 diabetes ?

Does effective treatment of OSA prevent or delay the development of type 2 diabetes in patients with pre-diabetes ?

RISK ASSOCIATED WITH SLEEP DISTURBANCES COMPARED TO TRADITIONAL RISK FACTORS



Anothaisintawee T et al, unpublished data, under review, 2015