Prediabetes cohort study

Assist.Prof. Thunyarat Anothaisintawee, M.D., Ph.D.
Department of Family Medicine,
Ramathibodi Hospital, Mahidol University
Email: thunyarat.ano@mahidol.ac.th

Background and rationale

- Diabetes is the major public health burden in Thailand.
- Diabetes is the significant cause of CVDs and CKD.
- Prevalence of diabetes in Thai population is 8.9% in year 2014.
- Prevalence of prediabetes in Thai population is 14.2% in year 2014.
- The annual risk of progression to DM in prediabetes people was 4 times greater than people with normal glucose level.
- However, there has been no evidence about the risk of progression to DM in prediabetes people in Thailand.

Background and rationale

- In addition, currently there are new risk factors of DM apart from traditional risk factors such as sleep factors and serum uric acid level.
- Systematic review of Sleep Disturbances Compared to Traditional Risk Factors for Diabetes Development

Contents lists available at ScienceDirect

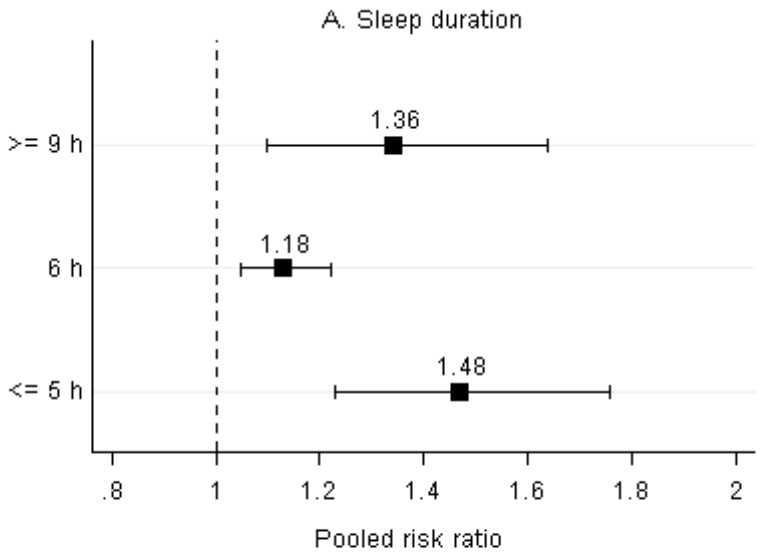
Sleep Medicine Reviews

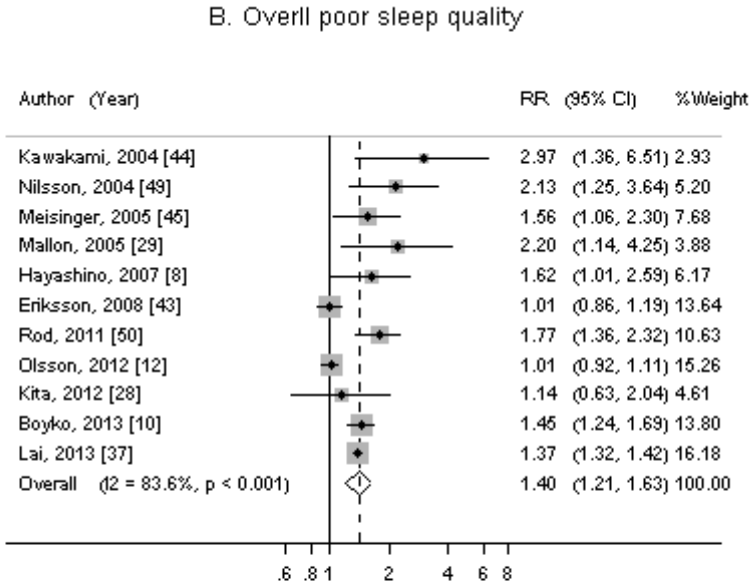
journal homepage: www.elsevier.com/locate/smrv

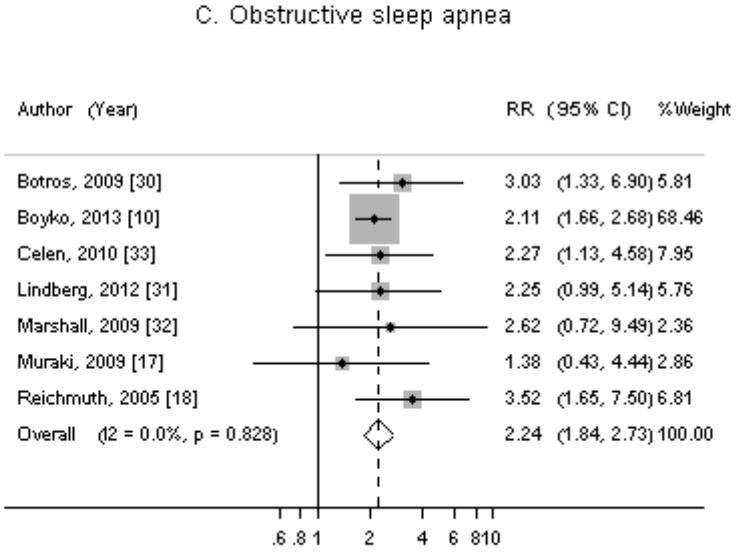
CLINICAL REVIEW

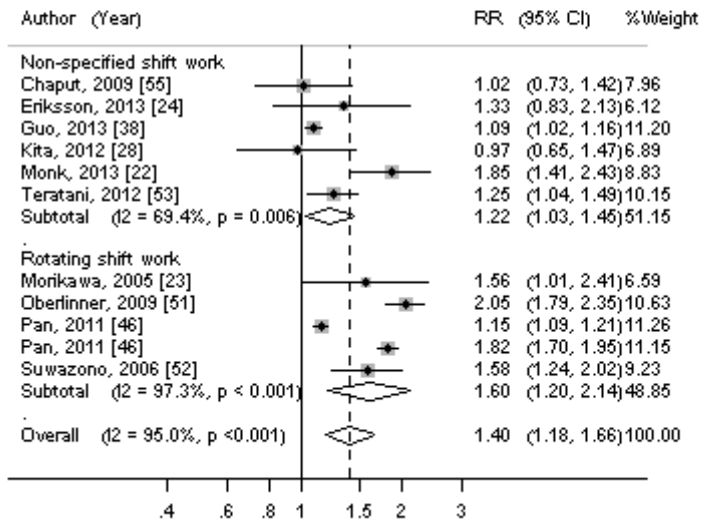
Sleep disturbances compared to traditional risk factors for diabetes development: Systematic review and meta-analysis

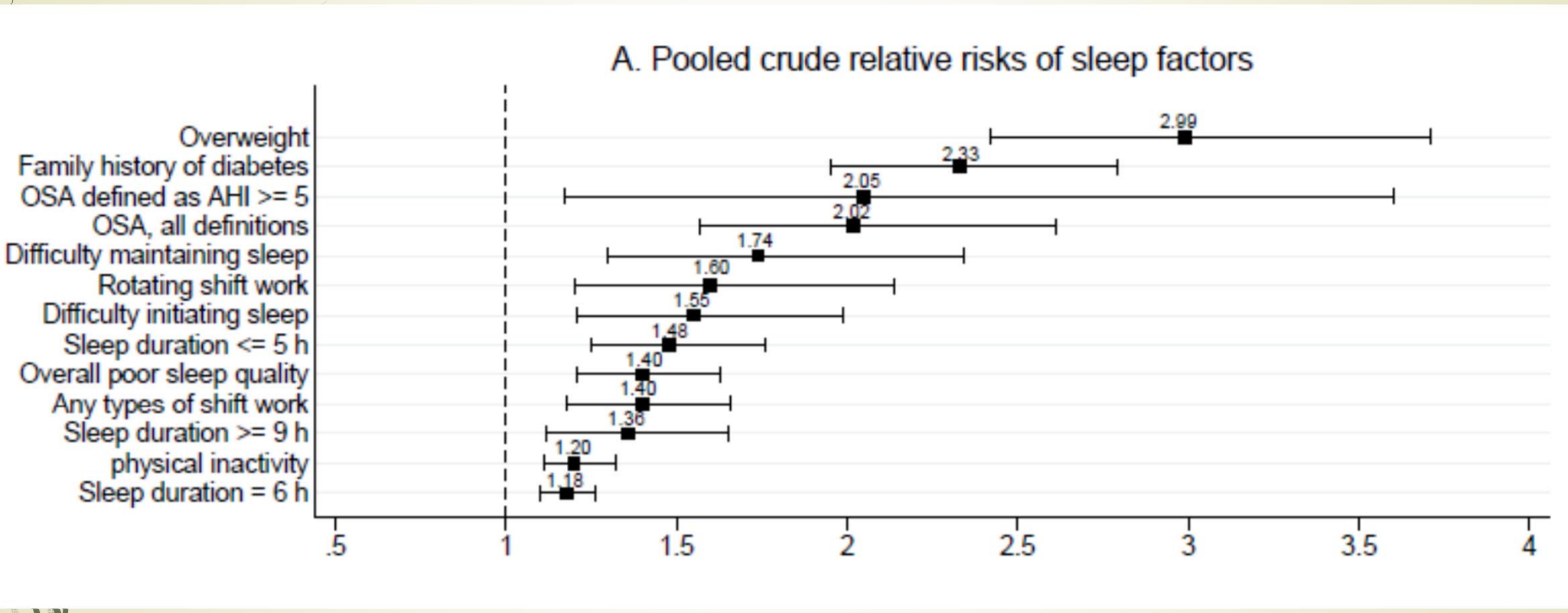
Thunyarat Anothaisintawee [a, b, 1], Sirimon Reutrakul [c, *, 1], Eve Van Cauter [d], Ammarin Thakkinstian [b]


A. Sleep duration
>= 9 h
6 h
<= 5 h
1.36
1.18
1.48
.8
1
1.2
1.4
1.6
1.8
2
Pooled risk ratio


B. Overll poor sleep quality
Author (Year)
RR (95% CI)
%Weight
Kawakami, 2004 [44] 2.97 (1.36, 6.51) 2.93
Nilsson, 2004 [49] 2.13 (1.25, 3.64) 5.20
Meisinger, 2005 [45] 1.56 (1.06, 2.30) 7.68
Mallon, 2005 [29] 2.20 (1.14, 4.25) 3.88
Hayashino, 2007 [8] 1.62 (1.01, 2.59) 6.17
Eriksson, 2008 [43] 1.01 (0.86, 1.19) 13.64
Rod, 2011 [50] 1.77 (1.36, 2.32) 10.63
Olsson, 2012 [12] 1.01 (0.92, 1.11) 15.26
Kita, 2012 [28] 1.14 (0.63, 2.04) 4.61
Boyko, 2013 [10] 1.45 (1.24, 1.69) 13.80
Lai, 2013 [37] 1.37 (1.32, 1.42) 16.18
Overall (I2 = 83.6%, p < 0.001) 1.40 (1.21, 1.63) 100.00
.6 .8 1 2 4 6 8


C. Obstructive sleep apnea
Author (Year)
RR (95% CI)
%Weight
Botros, 2009 [30] 3.03 (1.33, 6.90) 5.81
Boyko, 2013 [10] 2.11 (1.66, 2.68) 68.46
Celen, 2010 [33] 2.27 (1.13, 4.58) 7.95
Lindberg, 2012 [31] 2.25 (0.99, 5.14) 5.76
Marshall, 2009 [32] 2.62 (0.72, 9.49) 2.36
Muraki, 2009 [17] 1.38 (0.43, 4.44) 2.86
Reichmuth, 2005 [18] 3.52 (1.65, 7.50) 6.81
Overall (I2 = 0.0%, p = 0.828) 2.24 (1.84, 2.73) 100.00
.6 .8 1 2 4 6 810


D. Shift work
Author (Year)
RR (95% CI)
%Weight
Non-specified shift work
Chaput, 2009 [55] 1.02 (0.73, 1.42) 7.96
Eriksson, 2013 [24] 1.33 (0.83, 2.13) 6.12
Guo, 2013 [38] 1.09 (1.02, 1.16) 11.20
Kita, 2012 [28] 0.97 (0.65, 1.47) 6.89
Monk, 2013 [22] 1.85 (1.41, 2.43) 8.83
Teratani, 2012 [53] 1.25 (1.04, 1.49) 10.15
Subtotal (I2 = 69.4%, p = 0.006) 1.22 (1.03, 1.45) 51.15
Rotating shift work
Morikawa, 2005 [23] 1.56 (1.01, 2.41) 6.59
Oberlinner, 2009 [51] 2.05 (1.79, 2.35) 10.63
Pan, 2011 [46] 1.15 (1.09, 1.21) 11.26
Pan, 2011 [46] 1.82 (1.70, 1.95) 11.15
Suwazono, 2006 [52] 1.58 (1.24, 2.02) 9.23
Subtotal (I2 = 97.3%, p < 0.001) 1.60 (1.20, 2.14) 48.85
Overall (I2 = 95.0%, p <0.001) 1.40 (1.18, 1.66) 100.00
.4 .6 .8 1 1.5 2 3

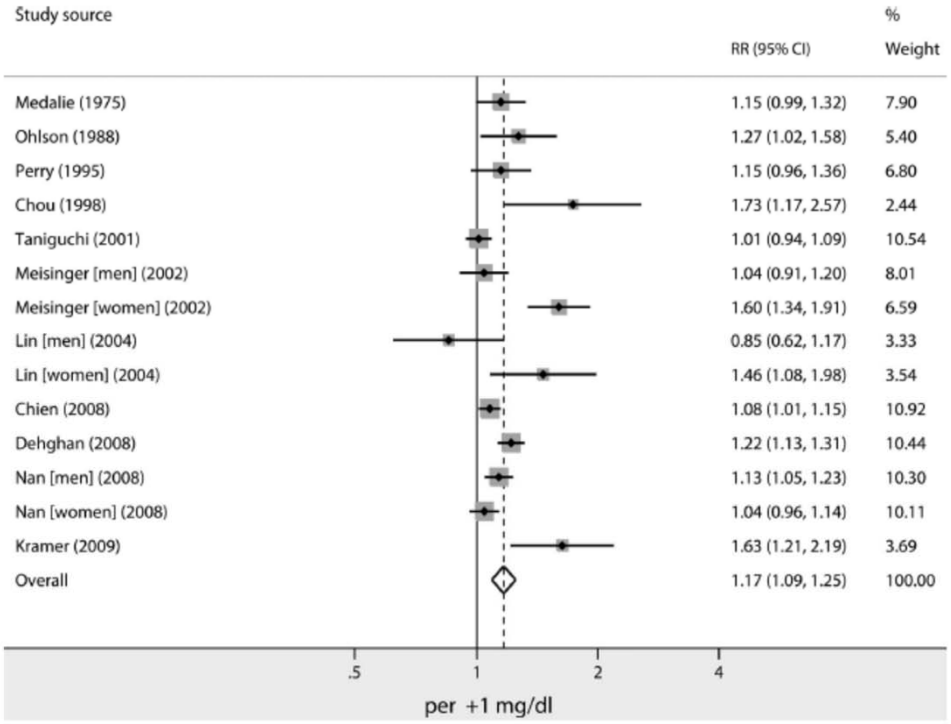

A. Pooled crude relative risks of sleep factors
Overweight
Family history of diabetes
OSA defined as AHI >= 5
OSA, all definitions
Difficulty maintaining sleep
Rotating shift work
Difficulty initiating sleep
Sleep duration <= 5 h
Overall poor sleep quality
Any types of shift work
Sleep duration >= 9 h
physical inactivity
Sleep duration = 6 h
2.99
2.33
2.05
2.02
1.74
1.60
1.55
1.48
1.40
1.40
1.36
1.20
1.18
.5
1
1.5
2
2.5
3
3.5
4

Reviews/Commentaries/ADA Statements
META-ANALYSIS

Association Between Serum Uric Acid and Development of Type 2 Diabetes

SATORU KODAMA, MD, PHD
KAZUMI SAITO, MD, PHD
YOKO YACHI, RD
MIHOKO ASUMI, MS
AYUMI SUGAWARA, RD
KUMIKO TOTSUKA, RD
AKI SAITO, RD
HIROHITO SONE, MD, PHD, FACP

systematic literature search of Medline (31 March from 1966 to 2009) and Embase (31 March from 1980 to 2009) for observational cohort studies examining the association between SUA level and



Objectives of PreDM cohort

1) To estimate the annual progression rate to DM in prediabetes people
2) To investigate the association between sleep factors and HbA1c level in prediabetes people
3) To investigate the association between serum uric acid and HbA1c level in prediabetes people

Prediabetes cohort study

- Outpatient clinic of Family Medicine Department, Ramathibodi Hospital, Mahidol University
- October 2014-March 2018
- Prediabetes defined according to ADA guideline as
  - FPG = 100-125 mg/dL or
  - 2-hour OGTT = 140-199 mg/dL or
  - HbA1c = 5.7%-6.4%
- Exclusion criteria: cognitive impairment

Data collection

Interested factors

- **Demographic data:** age, sex, educational level, F.H. of DM
- **Underlying diseases:** HT, DLP, GDM, depression, CKD, CVDs
- **Health risk behavior:** smoking, alcohol drinking
- **Physical examination:** BP, BW, WC, NC, HC, Height

Sleep factors

- **Sleep quality:** Pittsburgh Sleep Quality Index (PSQI)
- **Sleep duration:**

  [(sleep duration on weekdays × 5) + (sleep duration on weekend × 2)]/7
- **Risk of OSA:** Berlin questionnaire
- **Circadian parameters:**
  - Mid sleep time on free day (MSF)
  - Morningness and eveningness preference: Thai composite scale of morningness (CSM) score
  - Social jetlag: absolute difference of mid sleep time between weekday and weekend

Data collection

- **Depressive symptoms:** Center for Epidemiological Studies-Depression (CES-D)
- **Diet:** Food Frequency Questionnaire (FFQ)
- **Physical activity:** Global Physical Activity Questionnaire (GPAQ)
- **Laboratory tests:**
  - Serum uric acid
  - Serum creatinine
  - Lipid profile
- **Outcomes of interest**
  - Fasting plasma glucose
  - HbA1c level

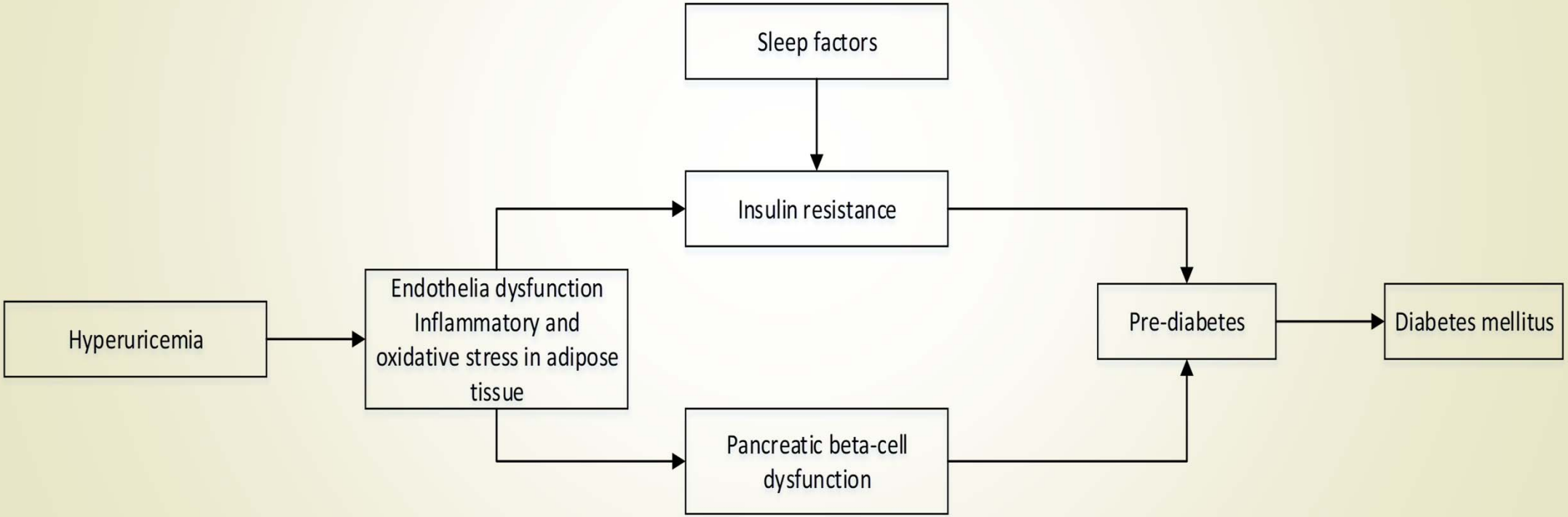
Results

- Total participants: 2,836
- Serum collection: 2,174

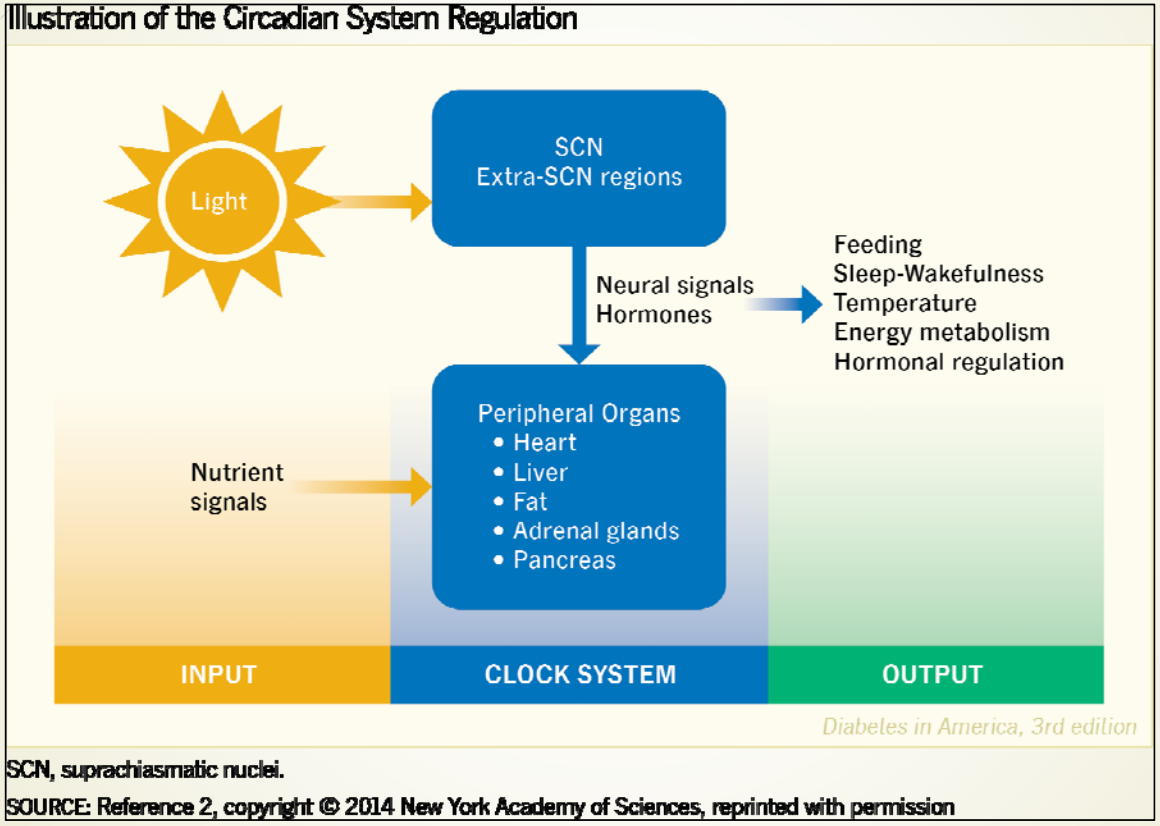
1. Relationship between sleep factors and HbA1c level in prediabetes people
2. Relationship between serum uric acid and HbA1c level in prediabetes people

Relationship between sleep factors and HbA1c level in prediabetes people

Mechanism of short sleep duration, poor sleep quality, OSA, and risk of DM



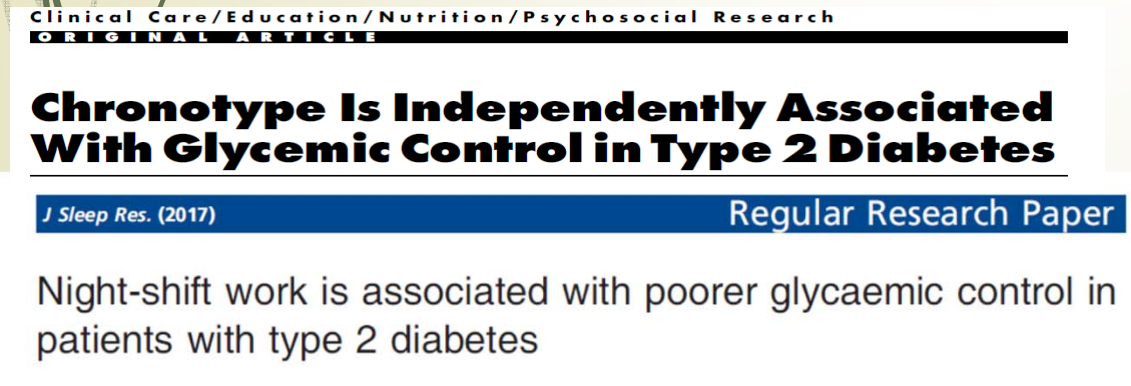
Circadian system



Reutrakul S, Punjabi NM, Van Cauter E: Impact of Sleep and Circadian Disturbances on Glucose Metabolism and Type 2 Diabetes. Chapter 25 in Diabetes in America, 3rd ed. Cowie CC, Casagrande SS, Menke A, Cissell MA, Eberhardt MS, Meigs JB, Gregg EW, Knowler WC, Barrett-Connor E, Becker DJ, Brancati FL, Boyko EJ, Herman WH, Howard BV, Narayan KMV, Rewers M, Fradkin JE, Eds. Bethesda, MD, National Institutes of Health

Circadian disruption and glucose metabolism

- Shift work, a form of circadian misalignment, increases diabetes risk
- T2DM patients who work night shift had poor glycemic control
- Late chronoytpe “later sleep time and wake time” has been shown to be associated with poorer glycemic control in T2DM


Clinical Care/Education/Nutrition/Psychosocial Research

ORIGINAL ARTICLE

Chronotype Is Independently Associated With Glycemic Control in Type 2 Diabetes

J Sleep Res. (2017) Regular Research Paper

Night-shift work is associated with poorer glycaemic control in patients with type 2 diabetes


Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

ELSEVIER

CLINICAL REVIEW

Sleep disturbances compared to traditional risk factors for diabetes development: Systematic review and meta-analysis

Thunyarat Anothaisintawee [a, b, 1], Sirimon Reutrakul [c, *, 1], Eve Van Cauter [d], Ammarin Thakkinstian [b]

Objectives

- To examine whether sleep duration, sleep quality, OSA risk, and chronotype assessed by MSF and social jetlag associated with HbA1c level
- Multiple linear regression analysis

Results from univariate linear regression (N= 1,014)

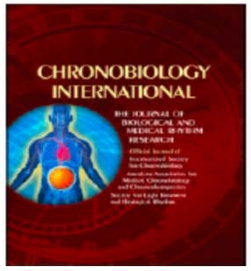
Factor	B	95% CI	P-value
Chronotype (MSF)	**0.020**	**0.002, 0.038**	**0.028**
OSA risk	**0.08**	**0.03, 0.12**	**0.001**
Social jet lag	0.02	-0.03, 0.06	0.484
Sleep duration (h)	-0.01	-0.02, 0.01	0.420
Modified PSQI	-0.0004	-0.008, 0.007	0.911
Female	0.09	0.04, 0.13	<0.001
Alcohol drinking	-0.06	-0.12, -0.01	0.023
BMI	0.011	0.005, 0.016	<0.001
Triglyceride	0.0004	0.0001, 0.0007	0.007

Results from multivariate linear regression

Factor	B	95% CI	P-value
Chronotype (MSF)	**0.019**	**0.00001, 0.038**	**0.049**
OSA risk	**0.071**	**0.023, 0.119**	**0.004**
Female	0.082	0.034, 0.130	0.001
Alcohol drinking	-0.065	-0.124, -0.007	0.029
BMI	0.007	0.002, 0.013	0.009
Triglyceride	0.0004	0.0001, 0.0007	0.007

Conclusion

- Later chronotype and OSA risk were independently associated with higher HbA1c level in people with prediabetes after adjusting for sex, BMI, alcohol drinking, triglyceride level and other sleep factors.



Taylor & Francis
Taylor & Francis Group

Chronobiology International
The Journal of Biological and Medical Rhythm Research

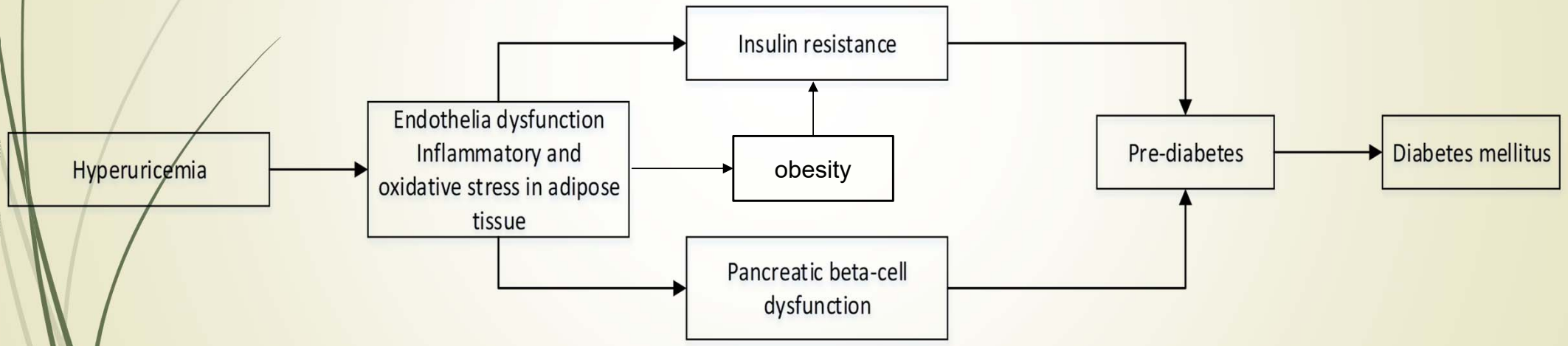
ISSN: 0742-0528 (Print) 1525-6073 (Online) Journal homepage: http://www.tandfonline.com/loi/icbi20

Later chronotype is associated with higher hemoglobin A1c in prediabetes patients

Thunyarat Anothaisintawee, Dumrongrat Lertrattananon, Sangsulee Thamakaison, Kristen L. Knutson, Ammarin Thakkinstian & Sirimon Reutrakul

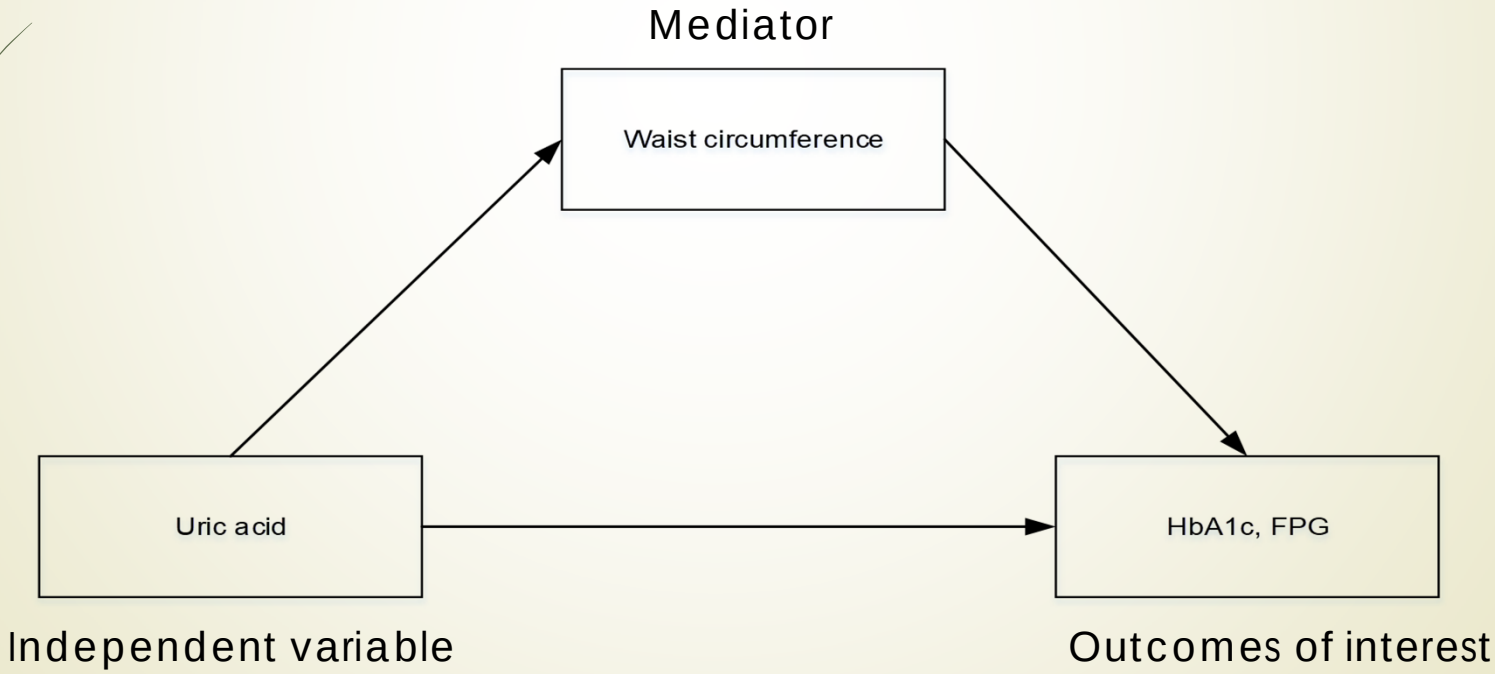
Relationship between serum uric acid and HbA1c level in prediabetes people

Mechanisms of serum uric acid and risk of diabetes



Objectives

- To estimate indirect effect of serum uric acid on FPG and HbA1c level through waist circumference
- To estimate direct effect of serum uric acid on FPG and HbA1c level
- Mediation analysis

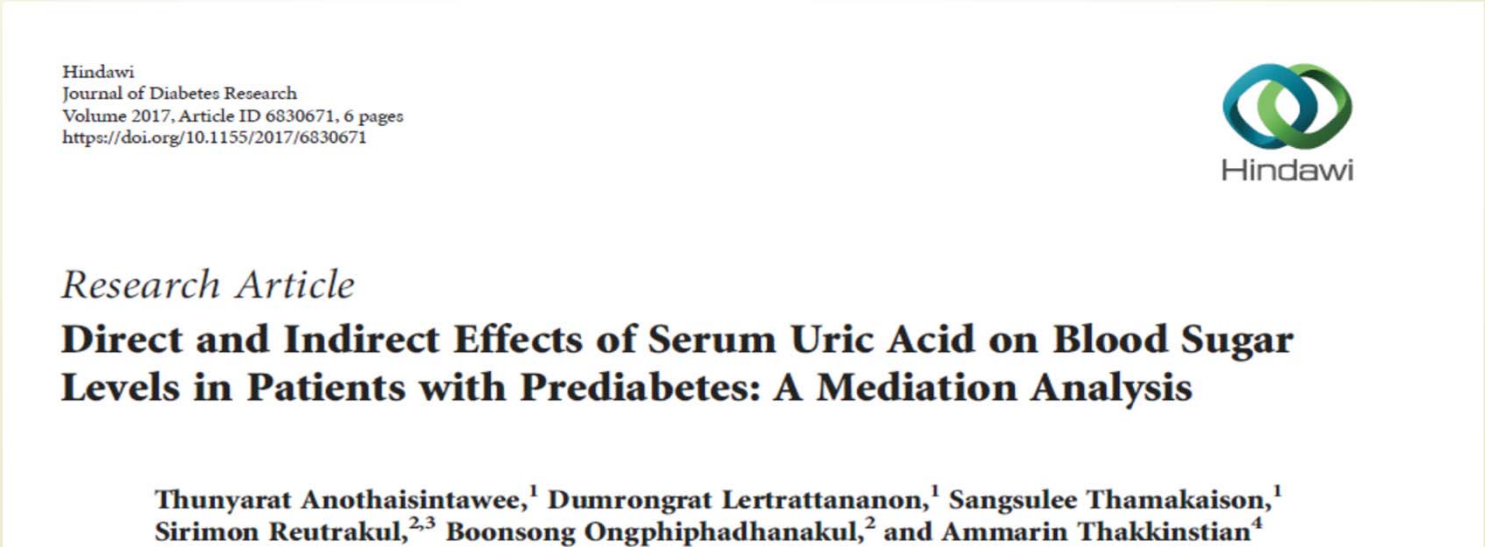


Results from mediation analysis (N = 1,633)

Effects	Pathway	β	P-value	95% CI
Fasting plasma glucose				
Indirect	**UA → WC → FPG**	**0.082**	**0.026**	**0.010, 0.154**
Direct	**UA → FPG**	**0.413**	**0.026**	**0.049, 0.776**
HbA1c				
Indirect	**UA → WC → HbA1c**	**0.006**	**0.001**	**0.003, 0.010**
Direct	UA → HbA1c	0.014	0.111	-0.003, 0.030

Conclusion

- An increase in serum uric acid level was associated with increased FPG by both direct and indirect effect through WC.
- However, the association between serum uric acid and FPG was mainly explained by the direct effect of uric acid on FPG.
- In addition, serum uric acid did not have a direct effect on HbA1c.
- The effect of uric acid on HbA1c level was shown only when it was mediated through waist circumference.



Hindawi
Journal of Diabetes Research
Volume 2017, Article ID 6830671, 6 pages
https://doi.org/10.1155/2017/6830671

Hindawi

Research Article

Direct and Indirect Effects of Serum Uric Acid on Blood Sugar Levels in Patients with Prediabetes: A Mediation Analysis

Thunyarat Anothaisintawee,[1] Dumrongrat Lertrattananon,[1] Sangsulee Thamakaison,[1] Sirimon Reutrakul,[2,3] Boonsong Ongphiphadhanakul,[2] and Ammarin Thakkinstian[4]

Another work from the PreDM cohort

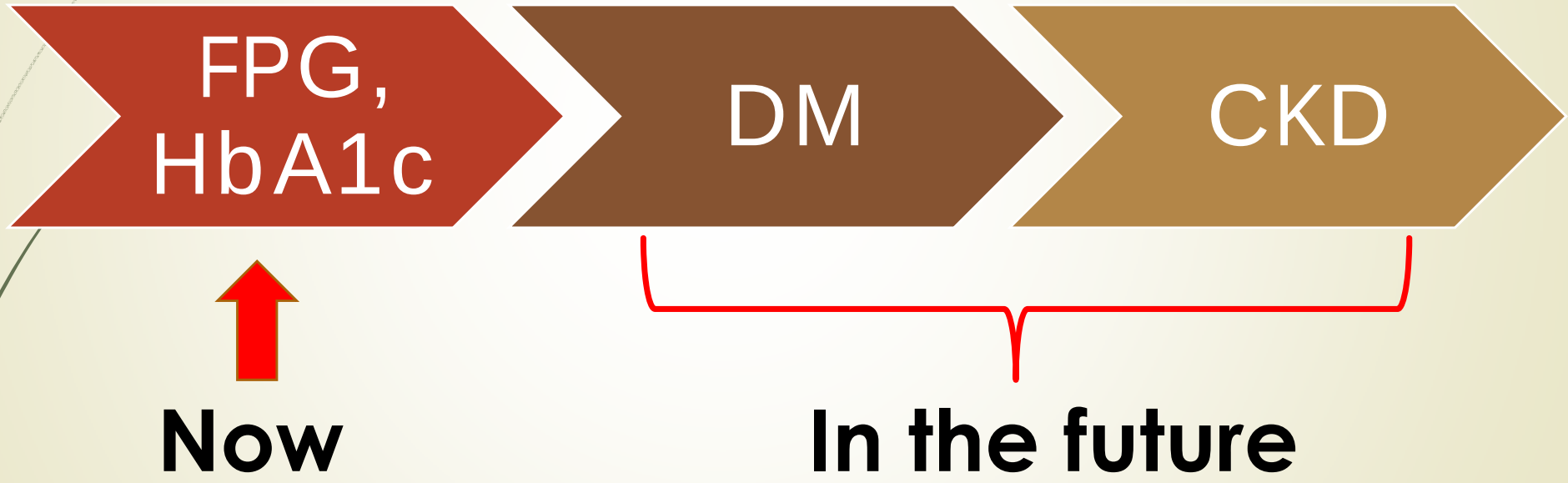
frontiers in Endocrinology

ORIGINAL RESEARCH
published: 15 August 2018
doi: 10.3389/fendo.2018.00435

The Relationship Among Morningness-Eveningness, Sleep Duration, Social Jetlag, and Body Mass Index in Asian Patients With Prediabetes

Thunyarat Anothaisintawee[1,2], *Dumrongrat Lertrattananon*[3], *Sangsulee Thamakaison*[3], *Ammarin Thakkinstian*[3] *and Sirimon Reutrakul*[3,4]*

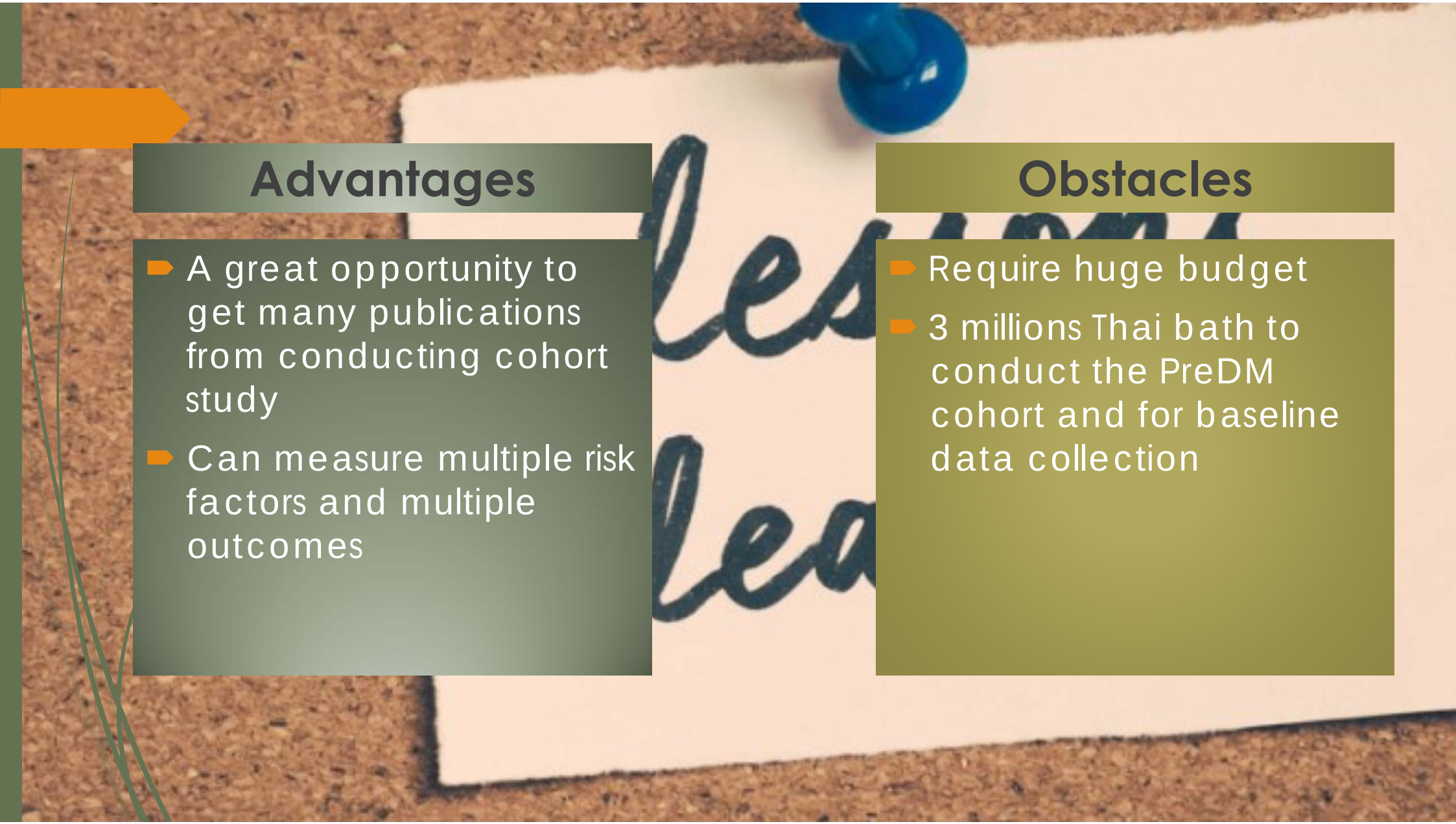
Future plan



Future plan

- Progression rate to DM in prediabetes people and the different progression rate between FPG 100-109 mg/dl and FPG 110-125 mg/dl
- Metabolomics of T2DM
- Genetic studies about sleep factors, serum uric acid and risk of T2DM and CKD


lessons
learned



Advantages

- A great opportunity to get many publications from conducting cohort study
- Can measure multiple risk factors and multiple outcomes

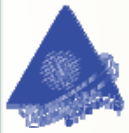
Obstacles

- Require huge budget
- 3 millions Thai bath to conduct the PreDM cohort and for baseline data collection

Funding support

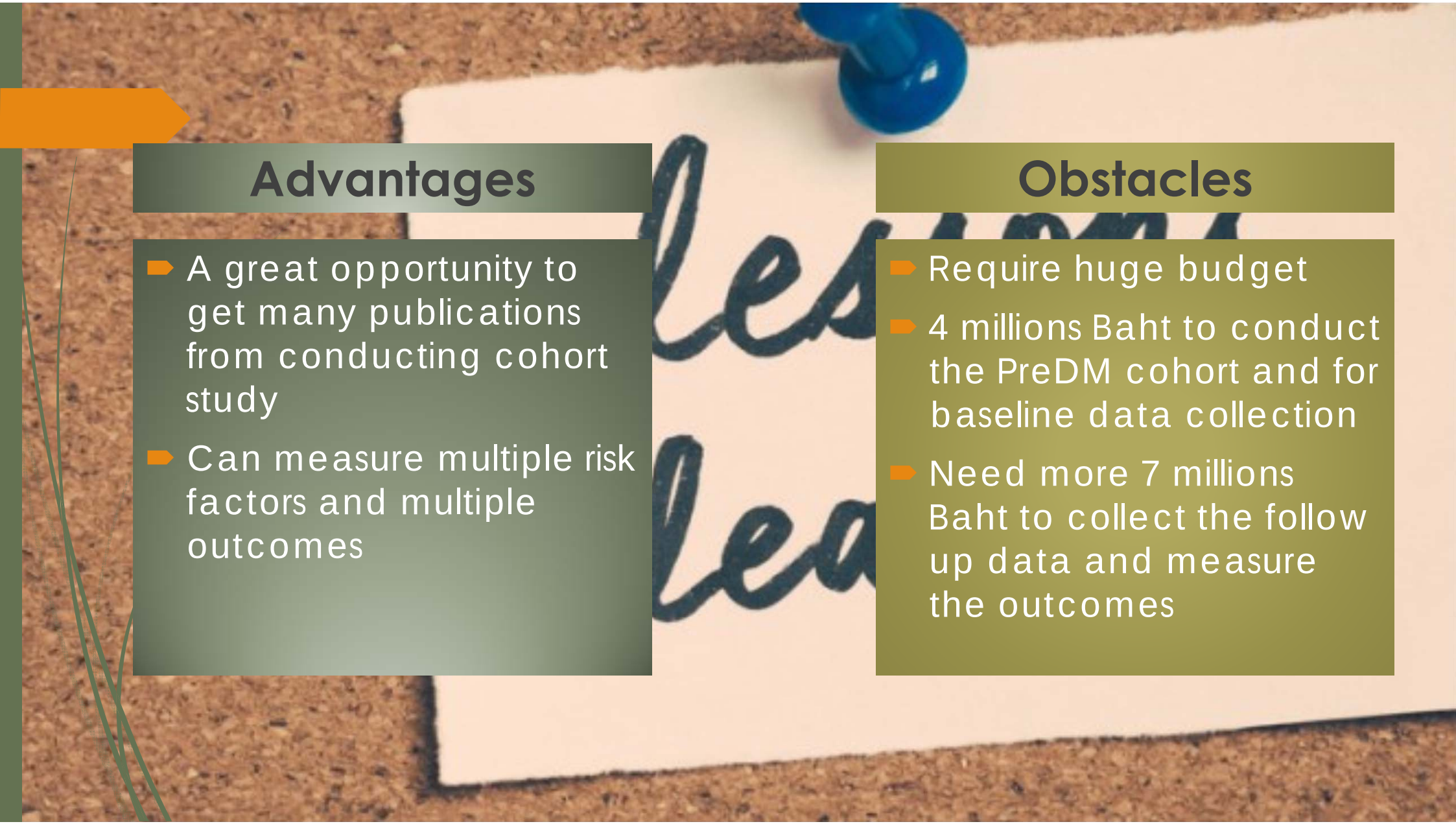
MSD

Year 2014-2015



สถาบันวิจัยระบบสาธารณสุข (สวรส.)
Health Systems Research Institute (HSRI)

Year 2015-2018



Advantages

- A great opportunity to get many publications from conducting cohort study
- Can measure multiple risk factors and multiple outcomes

Obstacles

- Require huge budget
- 4 millions Baht to conduct the PreDM cohort and for baseline data collection
- Need more 7 millions Baht to collect the follow up data and measure the outcomes

ทุนสนับสนุนกลุ่มวิจัยมุ่งเป้า

~~National Clinical Research Center~~

~~Health System Research Institute~~

Need teamwork

Great Colleagues

Prof. Ammarin Thakkinstian

Prof. Sirimon Reutrakul

Great Colleagues

Dr. Dumrongrat Lertrattananon

Assist. Prof. Sangsulee Thammakrisorn

Great Research Assistants

Mooktida Vaiyaput

Marisa Cheunchom

For all of prediabetes patients