

睡眠时间与成年人代谢综合征相关性的 Meta 分析

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【摘要】目的 对睡眠时间与成年人 MS 之间的关系进行定量评估,以期为 MS 的防治提供科学依据。**方法** 检索中英文数据库,纳入 2019 年 10 月以前已发表的相关文献。采用 Stata 11.0 软件对纳入的文献进行 Meta 分析。**结果** 最终纳入 38 篇文献,包含研究对象共计 656 319 例,其中 MS 患者共 150 638 例。睡眠时间与 MS 存在“U”形关联,短睡眠时间者患 MS 风险是正常睡眠者的 1.11 倍(95%CI: 1.07~1.16),长睡眠时间者患 MS 风险是正常睡眠者的 1.10 倍(95%CI: 1.03~1.18)。亚组分析显示,横断面研究中,相对于正常睡眠时间组,短睡眠时间使男性、<60 岁人群、亚洲人及白种人患 MS 风险分别增加 6%、14%、9% 和 24%,长睡眠时间使女性和<60 岁人群患 MS 风险分别增加 13% 和 19%。队列研究中观察到亚洲人短睡眠时间与 MS 呈正相关($RR=1.10$, 95%CI: 1.07~1.13),白种人长睡眠时间与 MS 呈正相关($RR=1.56$, 95%CI: 1.08~2.26)。**结论** MS 与长睡眠时间和短睡眠时间之间均存在关联。睡眠是可以改变的行为习惯,因此通过干预睡眠以降低 MS 患病风险具有重要的公共卫生意义。

【关键词】 睡眠时间; 代谢综合征; Meta 分析; 观察性研究

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A Meta-analysis on the association between sleep duration and metabolic syndrome in adults

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【Abstract】Objective To quantitatively evaluate the relationship between sleep duration and metabolic syndrome in adults in order to set up programs on prevention and treatment of metabolic syndrome in this population. **Methods** Relevant studies were identified by systematically searching databases before October 2019. All statistical analyses were under the use of Stata 11.0. **Results** A total of 656 319 participants including 150 638 cases with metabolic syndrome were involved in these 38 articles. A U-shaped relationship between sleep duration and metabolic syndrome was noticed. For short and long sleep duration, the $OR=1.11$ (95% CI: 1.07~1.16) and 1.10 (95% CI: 1.03~1.18), respectively. Subgroup analyses on cross-sectional studies revealed that factors as men, aged under 60 years, being Asians or Caucasians would increase the risk of metabolic syndrome by 6%, 14%, 9%, and 24%, respectively for those with short sleep duration. Factors as aged 60 years and above, being black and with long sleep duration, would increase the risks of metabolic syndrome by 13% and 19%, respectively in women. In subgroup analyses on cohort studies, positive correlation between short sleep duration and metabolic syndrome was observed in both Asian ($RR=1.10$, 95% CI: 1.07~1.13) and in Caucasians ($RR=1.56$, 95% CI: 1.08~2.26) populations. **Conclusions** Results of this study revealed an association between metabolic syndrome and the duration of sleep. We understand that sleep is a behavior that can be changed step by step, through adequate intervention programs, to reduce the risk of metabolic syndrome which has become an important public health issue.

【Key words】 Sleep duration; Metabolic syndrome; Meta-analysis; Observational study

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MS是一组心血管代谢危险因素的集合,包括腹部肥胖、糖代谢异常、血压升高和血脂异常等^[1],其中以腹部肥胖和胰岛素抵抗为临床特征。这些危险因素在人群中易感并在个体中聚集。有研究证实,MS可使患2型糖尿病的风险增加5倍,使患心血管疾病的风险增加3倍^[2]。尽管没有精确统一的定义,但无可争议的是MS及其危险因素相互作用增加了个体不良心血管疾病结果的风险。近来有研究表明,睡眠时间过长或过短可能与MS风险增加有关^[3-5],但是目前研究结论并不一致,为此,本研究将对睡眠时间与成年人MS之间的关系进行定量评估,以期为MS的防治提供科学依据。

材料与方法

1. 文献检索策略:检索中国知网、万方、PubMed、Embase、Cochrane数据库,检索时间为2019年10月以前已发表的相关文献。英文检索词以“Metabolic Syndrome”“sleep duration”为Mesh主题词,与“Metabolic Syndromes”“Insulin Resistance*”“Dysmetabolic Syndrome X”“Reaven*”“Cardiovascular Syndrome, Metabolic”“sleep duration”等自由词组合,中文检索词为“睡眠”、“代谢综合征”或“胰岛素抵抗”。语言限制为中文和英文。为避免遗漏,另对纳入研究中的参考文献进行手工检索。

2. 纳入排除标准:纳入标准:①与睡眠时间和MS有关的观察性研究;②MS定义明确;③有可提取的风险效应值;④研究人群为≥18岁成年人;排除标准:①综述或Meta分析等;②病理机制性研究。

3. 数据提取:由2名研究人员独立提取纳入文献中的相关数据。若有分歧,则通过共同商讨或咨询第三人解决。提取信息包括:第一作者、发表年份、研究对象国别、种族、MS诊断标准、年龄、性别、样本量、病例数、暴露测量、测量时段、睡眠时间和MS的风险效应值等。

4. 统计学分析:采用Stata 11.0软件对纳入的文献进行Meta分析。横断面研究选用OR值及其95%CI进行描述,队列研究将OR值及HR值近似等于RR值,选用RR值及其95%CI进行描述。长睡眠时间及短睡眠时间按原文中定义,参照睡眠时间一般为6~8 h,否则根据Hamling等^[6]研究进行参照组转换。异质性评估采用Q检验,当P>0.1且I²≤50%时采用固定效应模型;反之,则认为存在异质性,采用随机效应模型。采用Egger's检验和Begg's检验评价潜在发表偏倚(P<0.05,认为存在发表偏倚),并

进行敏感性分析。按研究设计(横断面研究和队列研究)、种族(白种人、亚洲人及黑种人)、性别、年龄组(<60岁和≥60岁)、测量睡眠时段(24 h和夜晚)进行亚组分析。

结 果

1. 文献检索结果:通过中国知网、万方、PubMed、Embase及Cochrane library数据库,共检索到1 600篇文献。排除重复、不相关、综述性及无可用数据的文献后,最终纳入38篇文献[3-5, 7-41],中文文献3篇,英文文献35篇。检索流程见图1。

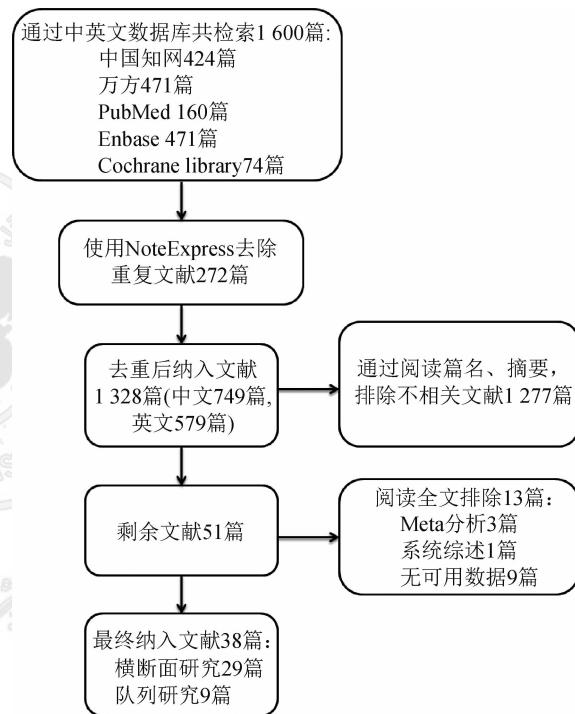


图1 纳入文献筛选流程图

2. 纳入文献基本情况:纳入的38篇文献中29篇为横断面研究,其余9篇为队列研究。研究对象均为成年人,共计656 319例,其中MS患者150 638例。MS诊断标准主要采用2005年和2009年美国心脏协会/美国国家心肺血液研究所(American Heart Association/National Heart, Lung, and Blood Institute, AHA/NHLBI),此外还有美国成年人胆固醇教育计划(national cholesterol education program adult treatment panel III, NCEP ATP III)、中华医学会糖尿病学分会、日本MS诊断标准评估委员会(Japanese Committee to Evaluate Diagnostic Standards for Metabolic Syndrome, JCEDSMS)、日本肥胖研究协会(Japan Society for the Study of

Obesity, JASSO)。17篇测量睡眠时间为夜晚,21篇为24 h。见表1。

3. 睡眠时间与成年人MS关联:

(1)短睡眠时间与MS:研究短睡眠时间与MS关联的文献共37篇,其中横断面研究28篇,队列研究9篇,Q检验结果显示存在异质性($P<0.1$, $I^2=66.7\%$),故采用随机效应模型,总合并效应量为1.11(95%CI:1.07~1.16),提示相对于正常睡眠组,短睡眠时间可使患MS风险增加11%。横断面研究中,

合并 $OR=1.10$ (95%CI:1.04~1.16);队列研究中,合并 $RR=1.13$ (95%CI:1.08~1.18),队列研究的风险值高于横断面研究。见图2。

在横断面研究的亚组分析中,短睡眠时间与MS的关联在白种人、亚洲人、男性、<60岁和测量睡眠时段的亚组中更强。在队列研究的亚组分析中,该关联在亚洲人、测量睡眠时段的亚组中更强。见表2。

(2)长睡眠时间与MS:研究长睡眠时间与MS关联的文献共34篇,其中横断面研究26篇,队列研

表1 纳入文献的基本特征

纳入研究	发表年份	国别	研究设计	MetS诊断标准	睡眠测量方法	测量睡眠时段	年龄(岁)	样本量	病例数
Hall ^[7]	2008	美国	横断面	AHA/NHLBI-2005	问卷调查	夜晚	30~54	1 214	284
Choi ^[8]	2008	韩国	横断面	NCEP ATP III-modified criteria	问卷调查	夜晚	≥20	4 222	1 171
Kobayashi ^[11]	2010	日本	横断面	JASSO	问卷调查	夜晚	≥20	27 792	2 418
左惠娟 ^[9]	2011	中国	横断面	中华医学会糖尿病学分会	问卷调查	24 h	18~45	4 937	329
Najafian ^[10]	2011	伊朗	横断面	NCEP-ATP III	问卷调查	24 h	≥19	12 492	2 936
Arora ^[13]	2011	中国	横断面	AHA/NHLBI-2009	问卷调查	24 h	≥50	29 333	8 222
Choi ^[12]	2011	韩国	队列	AHA/NHLBI-2005	问卷调查	夜晚	40~70	1 107	204
McCanlies ^[15]	2012	美国	横断面	AHA/NHLBI-2005	问卷调查	夜晚	39.61	98	14
Wu ^[14]	2012	中国	横断面	NCEP ATP III-modified criteria	问卷调查	夜晚	20~90	7 100	1 035
Sabanayagam ^[16]	2012	美国	横断面	AHA/NHLBI-2005	问卷调查	夜晚	≥20	6 122	2 284
Lee ^[19]	2013	韩国	横断面	NCEP ATP III-modified criteria	问卷调查	24 h	≥20	301	106
Chaput ^[20]	2013	加拿大	横断面	AHA/NHLBI-2005	问卷调查	夜晚	18~65	810	199
Yoo ^[17]	2013	美国	横断面	AHA/NHLBI-2005-modified criteria	问卷调查	24 h	22~60	106	35
Stefani ^[18]	2013	韩国	横断面	AHA/NHLBI-2009	问卷调查	24 h	20~79	24 511	6 103
Hung ^[21]	2013	中国	横断面	AHA/NHLBI-2005-modified criteria	问卷调查	24 h	50.8±11.8	3 435	899
Chaput ^[22]	2013	加拿大	队列	AHA/NHLBI-2005	问卷调查	夜晚	18~65	293	29
Yu ^[23]	2014	中国	横断面	NCEP ATP III-modified criteria	问卷调查	24 h	≥35	11 496	4 488
Ohkuma ^[24]	2014	日本	横断面	AHA/NHLBI-2009	问卷调查	24 h	≥20	4 402	281
Okubo ^[25]	2014	日本	横断面	JCEDSMS	问卷调查	24 h	20~80	1 481	168
Saleh ^[26]	2014	加拿大	横断面	AHA/NHLBI-2009	加速度测量法	夜晚	≥20	1 371	512
Chang ^[30]	2015	中国	横断面	AHA/NHLBI-2005	问卷调查	24 h	20~60	796	195
Wu ^[27]	2015	中国	横断面	AHA/NHLBI-2005-modified criteria	问卷调查	24 h	63.6	25 184	8 046
Kim ^[29]	2015	韩国	队列	AHA/NHLBI-2009	问卷调查	24 h	40~70	2 579	558
Li ^[28]	2015	中国	队列	AHA/NHLBI-2009	问卷调查	夜晚	30~65	4 774	1 506
Min ^[32]	2016	韩国	横断面	NCEP-ATP III	问卷调查	24 h	25~70	8 505	1 338
Yoon ^[5]	2016	韩国	横断面	NCEP ATP III-modified criteria	问卷调查	24 h	40~69	72 673	19 125
Lin ^[33]	2016	中国	横断面	AHA/NHLBI-2009	问卷调查	夜晚	51.05	4 197	880
Song ^[4]	2016	中国	队列	AHA/NHLBI-2005	问卷调查	夜晚	18~98	15 753	6 302
Yang ^[31]	2016	中国	队列	AHA/NHLBI-2009	问卷调查	夜晚	62.5±7.4	9 275	2 447
Suliga ^[34]	2017	波兰	横断面	AHA/NHLBI-2009	问卷调查	夜晚	37~66	10 367	5 333
Cole ^[35]	2017	非洲	横断面	AHA/NHLBI-2009	问卷调查	夜晚	≥25	263	52
Deng ^[3]	2017	中国	队列	AHA/NHLBI-2009	问卷调查	24 h	20~80	162 121	25 357
Itani ^[36]	2017	日本	队列	JCEDSMS	问卷调查	24 h	18~65	39 182	6 622
Kim ^[39]	2018	韩国	横断面	NCEP-ATP III	问卷调查	24 h	40~69	133 662	34 826
van der Pal ^[37]	2018	荷兰	横断面	NCEP-ATP III	问卷调查	24 h	40~75	1 679	447
Titova ^[38]	2018	瑞典	队列	WHO	问卷调查	24 h	≥45	19 691	4 941
陈梦雪 ^[41]	2019	中国	横断面	AHA/NHLBI-2005-modified criteria	问卷调查	夜晚	20~70	1 274	404
周娟 ^[40]	2019	中国	横断面	AHA/NHLBI-2009	问卷调查	24 h	≥18	1 721	542
合计								656 319	150 638

注:AHA/NHLBI:美国心脏协会/美国国家心肺血液研究所;NCEP ATP III:国家胆固醇教育计划成年人治疗小组;JASSO:日本肥胖研究协会;JCEDSMS:日本MS诊断标准评估委员会

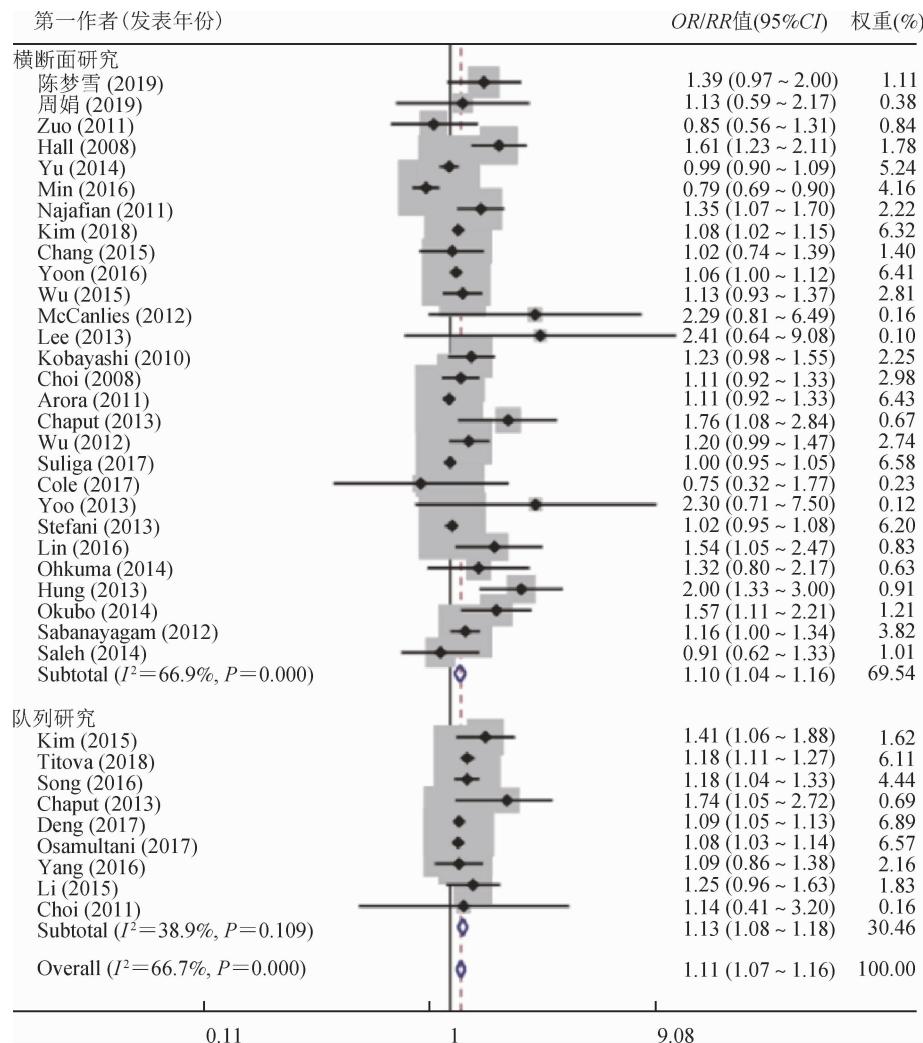


图2 短睡眠时间与MS关联的森林图

表2 睡眠时间与MS相关性研究的亚组分析

亚组	短睡眠时间				长睡眠时间			
	研究个数	OR/RR值(95%CI)	异质性检验P值	F值(%)	研究个数	OR/RR值(95%CI)	异质性检验P值	F值(%)
横断面研究								
种族								
白种人	7	1.24 (1.02 ~ 1.51)	0.001	74.50	6	1.18 (0.94 ~ 1.48)	0.002	73.60
亚洲人	20	1.09 (1.02 ~ 1.16)	0.000	66.90	19	1.07 (0.98 ~ 1.17)	0.000	83.30
黑种人	1	0.75 (0.32 ~ 1.76)	-	-	1	1.08 (0.99 ~ 1.17)	-	-
性别								
男	11	1.06 (1.00 ~ 1.14)	0.004	61.10	10	1.07 (0.98 ~ 1.16)	0.071	43.00
女	10	1.01 (0.95 ~ 1.07)	0.003	64.10	9	1.13 (1.02 ~ 1.17)	0.003	66.10
年龄组(岁)								
<60	10	1.14 (1.03 ~ 1.27)	0.000	70.30	10	1.19 (1.06 ~ 1.33)	0.000	62.90
≥60	5	0.96 (0.90 ~ 1.02)	0.763	0.00	5	1.07 (0.96 ~ 1.19)	0.125	35.30
测量睡眠时段								
24 h	16	1.10 (1.04 ~ 1.16)	0.000	69.20	15	1.06 (0.95 ~ 1.18)	0.000	87.40
夜晚	12	1.21 (1.07 ~ 1.36)	0.001	65.50	11	1.09 (0.98 ~ 1.23)	0.073	41.10
队列研究								
种族								
白种人	2	1.33 (0.94 ~ 1.89)	0.113	60.10	2	1.56 (1.08 ~ 2.26)	0.202	38.60
亚洲人	7	1.10 (1.07 ~ 1.13)	0.455	0.00	6	1.09 (0.95 ~ 1.26)	0.000	80.70
测量睡眠时段								
24 h	4	1.12 (1.06 ~ 1.18)	0.052	61.20	3	1.14 (0.72 ~ 1.79)	0.000	96.40
夜晚	5	1.19 (1.08 ~ 1.32)	0.536	0.00	5	1.19 (1.10 ~ 1.29)	0.745	0.00

究8篇, Q 检验结果显示存在异质性($P<0.1, I^2=83.6\%$),故采用随机效应模型,总合并效应量为1.10(95%CI:1.03~1.18),提示相对于正常睡眠组,长睡眠时间可使患MS风险增加10%。但按研究设计分组后并未观察到该结果。横断面研究中,合并 OR 值为1.08(95%CI:0.99~1.17);队列研究中,合并 RR 值为1.16(95%CI:0.97~1.39)。见图3。

在横断面研究的亚组分析中,长睡眠时间与MS的关联在女性和<60岁的亚组中更强。在队列研究的亚组分析中,该关联在白种人和测量睡眠时段为夜晚的亚组中更强。见表2。

4. 发表偏倚及敏感性分析结果:利用睡眠时间与MS关联文献绘制漏斗图,并进行Egger's检验和Begg's检验。短睡眠时间中Begg's检验 $P=0.07$,Egger's检验 $P=0.006$,提示存在发表偏倚;长睡眠时间中Egger's检验和Begg's检验 P 值分别为0.62和0.63,均 >0.05 ,提示不存在发表偏倚。敏感性分析结果显示,短睡眠时间与长睡眠时间研究中删除

任一篇文献对剩余文献合并效应值均无明显影响,证实了本研究最终结果的稳定性。见图4,5。

讨 论

睡眠行为可以调节人体激素分泌,对机体代谢也会产生影响。近年来有大量研究表明睡眠过长或过短与MS及其组分如肥胖、糖尿病、高血压等相关^[42~44]。本研究表明与正常睡眠相比,短睡眠时间使MS患病风险增加了11%,长睡眠时间使患病风险增加了10%,睡眠时间与MS呈“U”形关联。之前已发表了3项相关荟萃研究^[45~47],但纳入的文献主要为横断面研究,队列研究数目有限,本研究在此基础上,又加入了近5年新发表的文献,其中队列研究新增7篇,使结论因果关联更具说服力。与该3项荟萃分析一样,本研究也证实短睡眠时间使MS患病风险增加,其内在机制可能与睡眠不足导致瘦素降低,生长素释放肽增加,从而产生饥饿感摄入更多热量导致肥胖^[48],而肥胖除了是MS的组分外,也可以降

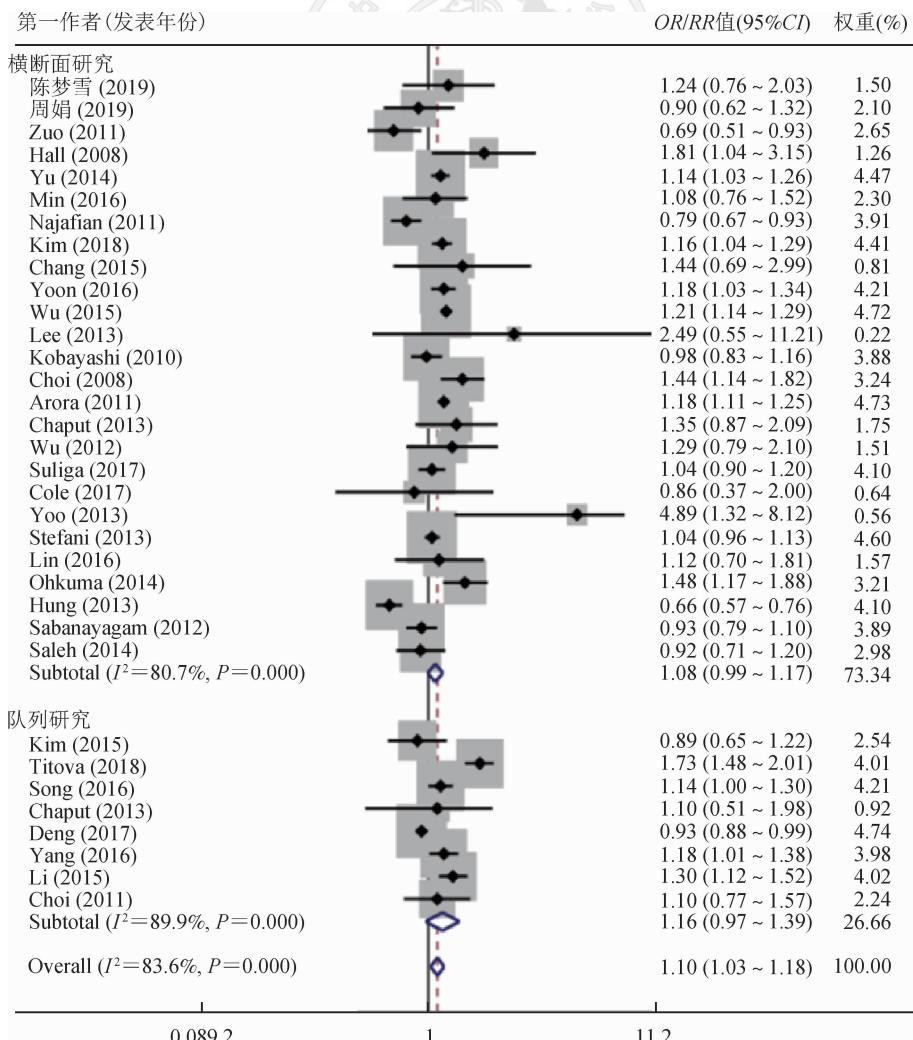


图3 长睡眠时间与MS关联的森林图

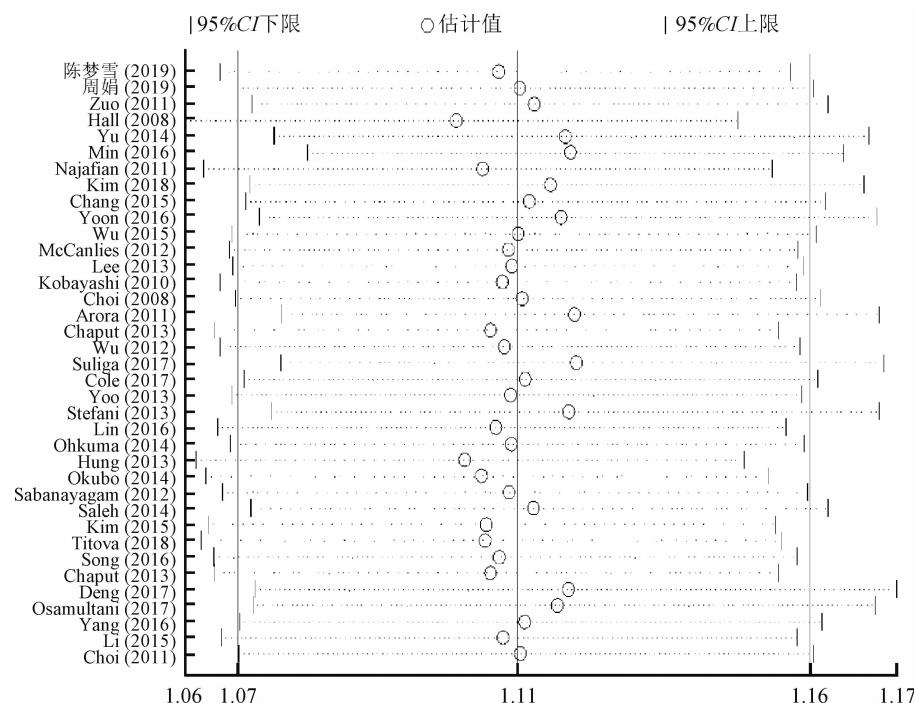


图4 短睡眠时间与MS研究的敏感性分析

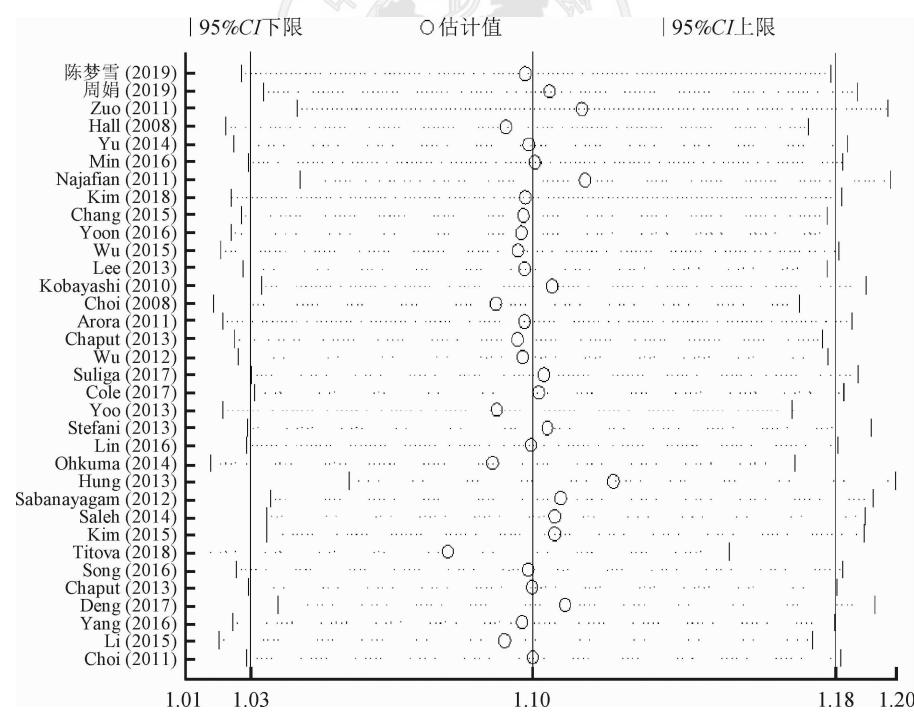


图5 长睡眠时间与MS研究的敏感性分析

低胰岛素的敏感性,与糖尿病的发生相关。此外,也有研究认为是下丘脑-垂体-肾上腺机制激活对睡眠和糖代谢产生影响^[49]。本研究中,所有模型中均观察到短睡眠时间与MS均存在关联,队列的风险值($RR=1.13, 95\%CI: 1.08 \sim 1.18$)略大于横断面研究($OR=1.10, 95\%CI: 1.04 \sim 1.16$),但Ju和Choi^[45]的研究中未发现短睡眠时间与MS相关($RR=1.62,$

$95\%CI: 0.74 \sim 3.55$),可能是由于相关文献数及样本量较少。

在总合并效应中,本研究显示长睡眠时间增加了MS患病风险($OR=1.10, 95\%CI: 1.03 \sim 1.18$)。Ju和Choi^[45]在横断面设计中得到该结论($OR=1.23, 95\%CI: 1.02 \sim 1.49$),但在队列中并未观察到相同结果。本研究在研究设计的分组中均未发现长睡眠时

间与 MS 的关联。这与 Iftikhar 等^[47]和 Xi 等^[46]的结论一致,二者纳入研究主要为横断面,风险值分别为 1.13 (95% CI: 0.97 ~ 1.32) 和 1.07 (95% CI: 0.87 ~ 1.32)。亚组中未发现关联可能是由于样本量相对较少,合并后样本量增大,才使亚组中微弱的关联得以显示。长睡眠时间意味着体育锻炼时间减少、卧床时间增加,这对于脂肪代谢会产生影响,在一定程度上可以解释长睡眠时间与 MS 的正相关性。

亚组分析中,不同的种族、性别、年龄组及测量睡眠时段与 MS 的关联不同。<60岁人群睡眠时间过长或过短都会增加 MS 患病风险,这一关联在老年人中并不明显,可能由于老年人慢性病发病率较高,需要长期服药,药物对睡眠会存在潜在影响,而且慢性病与 MS 相关,但由于所能提取的信息有限,无法获得慢性病分组结果,故还需进一步研究证实。有趣的是,本研究发现睡眠时间与 MS 的关联在性别分布上相反,男性短睡眠时间与 MS 正相关,而女性长睡眠时间与 MS 正相关。女性睡眠时间过长可能会导致超重肥胖的发生率增高,而女性超重肥胖多为腹型肥胖,产生的健康问题要比男性更大,如高血压和心血管疾病^[50],并且胰岛素抵抗与内脏肥胖密切相关。但由于亚组的研究数目不同,故应谨慎解释结果。

本研究存在局限性。首先,睡眠的测量方法大多为自我报告,导致得到的睡眠时间主观性较大;其次,MS 定义并不一致,主要表现在组成成分及腹部肥胖的定义上,这可能使结果存在较大异质性;第三,短睡眠时间进行漏斗图 Egger's 检验存在发表偏倚,但 Begg's 检验并未得出相同结论,有待更多文献进行佐证;第四,由于信息的有限性,一些混杂因素不能充分考虑,如是否使用药物治疗或睡眠质量,因此对于结论需谨慎解释。

综上所述,本研究结果显示 MS 与长睡眠时间和短睡眠时间之间均存在关联。睡眠是一种可以改变的行为习惯,因此通过干预睡眠以降低 MS 患病风险具有重要的公共卫生意义。

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