Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 3
BLSME 2024

The impact of insomnia on depression: a prospective cohort study based on the UK Biobank

Zhiyu Wen *

Department of Biostatistics, School of Public Health, Nanjing Medical University, Nanjing 211166, China

* Corresponding Author Email: wenzy0701@stu.njmu.edu.cn

Abstract. Major Depressive Disorder (MDD) is a serious global mental health condition that has gotten worse recently due to its influence on well-being and quality of life. Data from the World Health Organization (WHO) reveal a prevalence of 3.8% for depression globally. Depression's link with various complications necessitates exploring its etiology for effective prevention and management. Insomnia, prevalent in 10-20% of adults, is closely associated with depression. The causal relationship between insomnia and depression is of particular interest. Using the UK Biobank database, a prospective cohort design investigated the independent association between insomnia and depression risk, adjusting for potential confounders. Data were analysed with descriptive statistics, ANOVA, χ^2 tests, and multivariable Cox models. Several models accounted for confounders and evaluated insomnia's relationship with depression. R Studio 2022.07.2 facilitated the analyses. The 173,809-participant cohort displayed diverse characteristics. This study, centered around Model 1, highlighted a significant association between depression and insomnia($P<0.05$). Model 2 and Model 3 further validated this connection, maintaining a statistically significant difference in insomnia($P<0.05$) after adjusting for additional factors. This study, utilizing the UK Biobank database, highlights the independent association between insomnia and depression risk. Findings underscore insomnia's pivotal role across demographics, reinforcing the multifaceted nature of this link.

Keywords: Depression; Insomnia; Prospective Studies; Multivariate Analysis.

1. Introduction

One of the most common mental health conditions affecting people worldwide is major depressive disorder, or MDD. Its severity has recently escalated and affects not only a person's physical and psychological well-being but also their overall quality of life. This concerning trend is underscored by the data compiled by the World Health Organization (WHO), revealing that depression afflicts an estimated 3.8% of the global population. This prevalence encompasses 5% of adults, further delineated by a gender distribution of 4% among males and 6% among females [1]. Notably, individuals aged 60 years and above are also profoundly affected, with 5.7% of this age cohort experiencing the burdens of depression [1].

In addition to its deleterious consequences on quality of life and social functioning, depression is intrinsically linked to heightened susceptibility to a range of complications [2]. Amid these challenging circumstances, a thorough exploration into the intricate etiological foundations of depression, encompassing the multifaceted interplay of genetics, environment, and social dynamics, is indispensable for devising effective prevention and management strategies [3].

Depression is commonly accompanied by insomnia. With a prevalence ranging between 10% and 20% among adults, insomnia is defined by its disruptive impact on sleep continuity and quality, including difficulties in sleep initiation, maintenance, and achieving restorative outcomes [4,5]. This affliction, often accompanied by daytime sleepiness and cognitive impairment, is associated with a range of adverse effects on daily functioning and overall well-being [4]. Remarkably, approximately half of those affected grapple with its chronic persistence, thereby further amplifying its societal significance.

Hence, whether insomnia serves as a causal factor for depression is a pivotal inquiry within this context.

The majority of evidence pertaining to the association between insomnia and depression is derived from observational studies [6-8]. Numerous studies have meticulously identified insomnia as a discrete and independent risk factor, exhibiting a compelling propensity to contribute to the emergence or recurrence of depression across varying age groups, encompassing young, middle-aged, and older adults [6]. Blanken TF et al. found that over a 6-year follow-up, 18.4% (141 individuals) developed first-onset MDD, with insomnia severity, particularly difficulty initiating sleep (DIS), being a significant predictor, independent of sleep duration and other depression symptoms; this underscores the potential of targeting DIS for preventing first-onset MDD [7]. According to research by Paunio T et al., inadequate sleep has a critical role in the onset of depression and the likelihood of disability retirement [8]. This emphasizes the importance of identifying and treating sleep disorders as soon as possible. However, the majority of studies exhibit limited sample sizes or insufficiently high levels of evidence.

Hence, this investigation employs the extensive UK Biobank database to elucidate the independent association between exposure to insomnia and the depression. This is achieved through the implementation of a cohort study, characterized by a heightened level of evidence, wherein the assessment of causality is rigorously examined. This endeavor aims to deepen the comprehension of the relationship between these two pivotal conditions, thereby contributing to collective efforts aimed at elucidating effective strategies for their prevention and management.

2. Methods

2.1. Study subjects

The principal data source for this investigation comes from the UK Biobank, a large and long-running health research project launched in the UK in 2006. Encompassing a vast and diverse cohort exceeding five hundred thousand volunteers hailing from every corner of the nation, the UK Biobank has seamlessly evolved into an invaluable resource for facilitating longitudinal investigations. Its establishment is firmly rooted in the bedrock of a population-based, forward-looking research cohort [9]. The demarcation of inclusion and exclusion parameters is visually explicated in Figure 1. Subsequent to a thorough evaluation, the ultimate assemblage of this study incorporates a total of 173,809 participants, each contributing substantively to the intricacy and robustness of the scrutinized dataset.

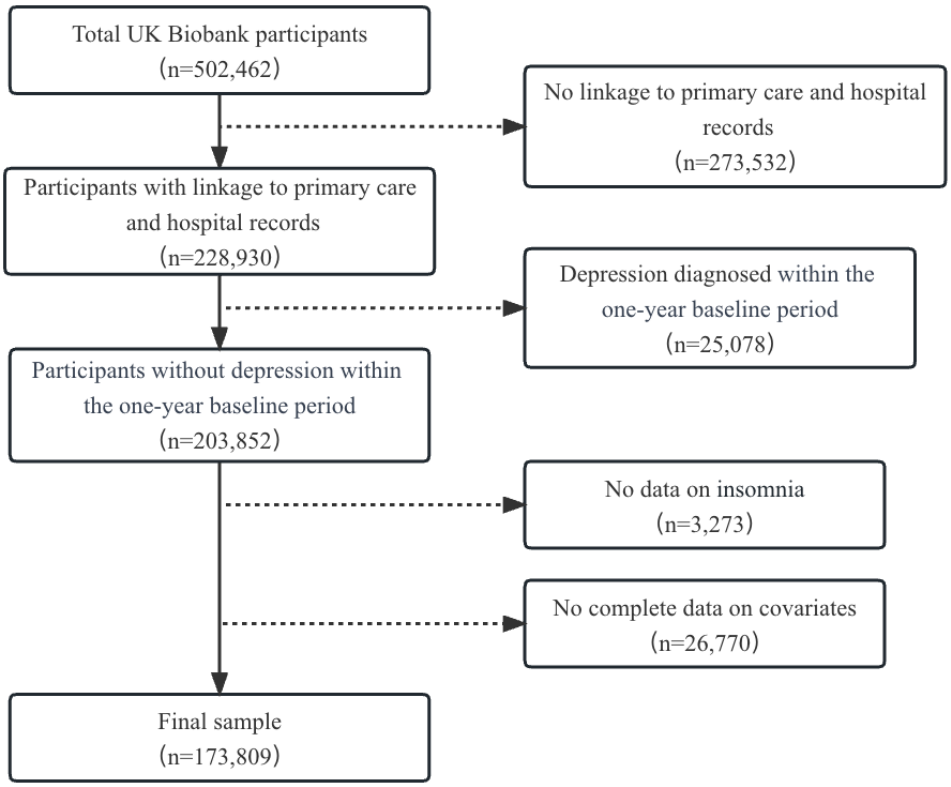

Figure 1. Enrollment flowchart for the current study's participants.

2.2. Outcome follow-up

In order to establish the precise delineation of instances involving depression, this investigation employed a cohort comprising individuals whose medical histories encompass primary care and hospital documentation. The participants were individuals who had received an official diagnosis from medical professionals who fulfilled the requirements set forth by the National Institute for Health and Care Excellence (NICE). Within the ambit of this study, the term "depression events" assumes a distinctly defined characterization, denoting the earliest documented occurrence that is categorized under the F32-F33 code range in the comprehensive framework of the International Classification of Diseases, Version 10 (ICD-10).

2.3. Insomnia

Within the boundaries of the UK Biobank, self-reported questionnaires obtained during the recruitment phase were used to evaluate insomnia. More specifically, by asking participants about their experiences with difficulties falling asleep at night or waking up during the night, the state of insomnia was assessed. Participants could choose from various response options to indicate the frequency of these experiences. Participants were also given a note that stated that if they had a great deal of variety in their experiences, then they should base their response on what they had experienced during the previous four weeks.

2.4. Covariates

During the initial assessment visit, socio-demographic variables such as age at recruitment, sex, and ethnicity were self-reported. The Townsend deprivation index, determined based on national census output areas prior to participant enrollment in the UK Biobank, assigned scores according to participant postcodes.

The Body Mass Index (BMI), calculated as the division of body weight by height squared (kg/m^2), is determined through measurements taken by trained nurses using individuals' weight and height. In

this study, the BMI categories for different weight statuses are as follows: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), and obesity (≥30.0).

The respondents self-reported their status as smokers and alcohol drinkers, classifying their behavior as never, former, or current. Dietary habits were assessed via touchscreen questionnaire, including fruit, vegetable, red meat consumption, and oily fish and processed meat intake.

Usual walking pace and TV viewing hours were provided, and diabetes diagnosis was self-declared. The 24-hour A-weighted equivalent sound level was used to quantify the amount of noise exposure, with a 10-decibel penalty applied between 23:00 and 07: 00.

2.5. Statistical methods

Continuous data were compared between groups using one-way ANOVA and were expressed as mean (SD). Using a $\chi 2$ test, categorical data were compared between groups and expressed as n (%). Potential confounders were taken into account using multivariable Cox proportional hazard models. Model 1 (primary model) took into account factors such as age at recruitment, sex, the Townsend deprivation index, and smoking status. Model 2 also included adjustments for factors such as alcohol drinker status, typical walking speed, average TV watching time, consumption of processed meat, and intake of oily fish. Model 3 further corrected for diabetes and BMI.

The entire statistical analysis was performed in the R Studio environment (version 2022.07.2). A significant threshold of $P < 0.05$ was established.

3. Results

3.1. Baseline characteristics

The research cohort for this cohort study consisted of 173,809 people, of which 79,999 were male (46.0%) and 93,810 were female (54.0%). At the time of recruitment, the subjects' ages ranged from 38 to 71 years old, with a median age of 58.0 years. To ensure the specificity of the investigation, instances of depression occurring within one year of baseline were excluded, resulting in the occurrence of 6,722 instances of depression ascertained during the follow-up period. The foundational characteristics of the subjects are succinctly presented in Table 1, encapsulating an overview of the collective attributes under scrutiny.

The empirical outcomes disclosed that various parameters, including age at recruitment, sex, BMI, Townsend deprivation index, smoking status, alcohol drinker status, usual walking pace, average TV watching time, diabetes status, consumption of processed meat and oily fish, exhibited statistically significant associations with depression ($P<0.05$). Conversely, race, cooking vegetable intake, fresh fruit intake, and exposure to noise pollution displayed no statistically significant correlations with depression ($P>0.05$).

Notably, the prevalence of insomnia differed significantly ($P<0.05$) between the groups with depression and those without (normal). This finding underscores the intricate interplay between insomnia and depression, reinforcing the potential clinical relevance of the relationship between these factors within the scope of the study.

Table 1. The baseline characteristics of the study participants.

Baseline Characteristics	Depression Events		P value
	No (n=167,087)	Yes (n=6,722)	
Age at recruitment (mean(SD), years)	56.87(8.03)	56.20(8.31)	<0.001
Males (n(%))	77,459(46.0)	2,540(54.0)	<0.001
BMI (mean(SD), kg/m2)	27.42(4.66)	28.33(5.36)	<0.001
Townsend deprivation index (mean(SD))	-1.54(2.90)	-0.92(3.16)	<0.001
Smoking status (n(%))			<0.001
Never	93,573(56.0)	3,235(48.1)	
Former	58,403(35.0)	2,440(36.3)	
Current	15,111(9.0)	1,047(15.6)	
Caucasian (n(%))	154,738(92.6)	6,231(92.7)	0.791
Alcohol drinker status (n(%))			<0.001
Never	6,823(4.1)	308(4.6)	
Former	5,066(3.0)	386(5.7)	
Current	155,198(92.9)	6,028(89.7)	
Usual walking pace (n(%))			<0.001
Slow	11,349(6.8)	999(14.9)	
Moderate	88,405(52.9)	3,592(53.4)	
Fast	67,333(40.3)	2,131(31.7)	
Average TV watching time (mean(SD), hours/day)	2.87(1.55)	3.15(1.78)	<0.001
Cooked vegetable intake (mean(SD), tablespoons/day)	2.77(1.85)	2.78(1.95)	0.556
Fresh fruit intake (mean(SD), pieces/day)	2.29(1.55)	2.26(1.78)	0.198
Processed meat intake (n(%))			0.008
Never	14,939(8.9)	657(9.8)	
Less than once a week	51,934(31.1)	2,069(30.8)	
Once a week	49,609(29.7)	1,883(28.0)	
2-4 times per week	44,436(26.6)	1,859(27.7)	
5-6 times per week	4,930(3.0)	195(2.9)	
At least once every day	1,239(0.7)	59(0.8)	
Oily fish intake (n(%))			<0.001
Never	17,622(10.5)	907(13.5)	
Less than once a week	54,196(32.4)	2,158(32.2)	
Once a week	64,782(38.8)	2,402(35.7)	
2-4 times per week	29,036(17.4)	1,183(17.6)	
5-6 times per week	1,099(0.7)	58(0.8)	
At least once every day	352(0.2)	14(0.2)	
Diabetes (n(%))	6,239(3.7)	483(7.2)	<0.001
Insomnia (n(%))			<0.001
Never/rarely	41,613(24.9)	1,057(15.7)	
Sometimes	80,677(48.3)	3,109(46.3)	
Usually	44,797(26.8)	2,556(38.0)	
24-hour A-weighted equivalent sound level (mean(SD), dB)	56.06(4.25)	56.11(4.23)	0.338

3.2. Association between insomnia and the risk of depression

Model 1 stands as the pivotal framework in this analysis. Within the realm of insomnia evaluation, the application of multivariate Cox hazard models was meticulously employed to account for

pertinent variables encompassing age at recruitment, sex, Townsend deprivation index, and smoking status. The outcomes of this rigorous analysis revealed a profound and statistically significant divergence in insomnia prevalence between the depression-affected cohort and the cohort displaying normal psychological well-being (P<0.05), a distinction succinctly outlined in Table 2.

Expanding the scrutiny of Model 1, a stratification approach was undertaken to dissect the results along the dimensions of sex, age at recruitment, and smoking status. Similar patterns were found in this analysis, explaining a statistically significant difference in the incidence of insomnia between the depressed group and the normal group (P<0.05). This pivotal revelation, showcased in Figure 2, bolsters the argument for the interconnectedness of insomnia and depressive tendencies across diverse subgroups, further underscoring the multifaceted nature of the relationship under investigation.

Table 2. Association between insomnia and the risk of depression.

	HR	95%CI	P value
Model 1[a]	1.4396	(1.3906,1.4904)	<0.001
Model 2[b]	1.3911	(1.3435,1.4404)	<0.001
Model 3[c]	1.3859	(1.3385,1.4350)	<0.001

CI, confidence interval; HR, hazard ratio.

[a] Main model, adjusted for age at recruitment, sex, Townsend deprivation index, smoking status.

[b] Additional adjustment for alcohol drinker status, usual walking pace, average TV watching time, processed meat intake, oily fish intake in model 1.

[c] Additional adjustment for diabetes, BMI in model 2.

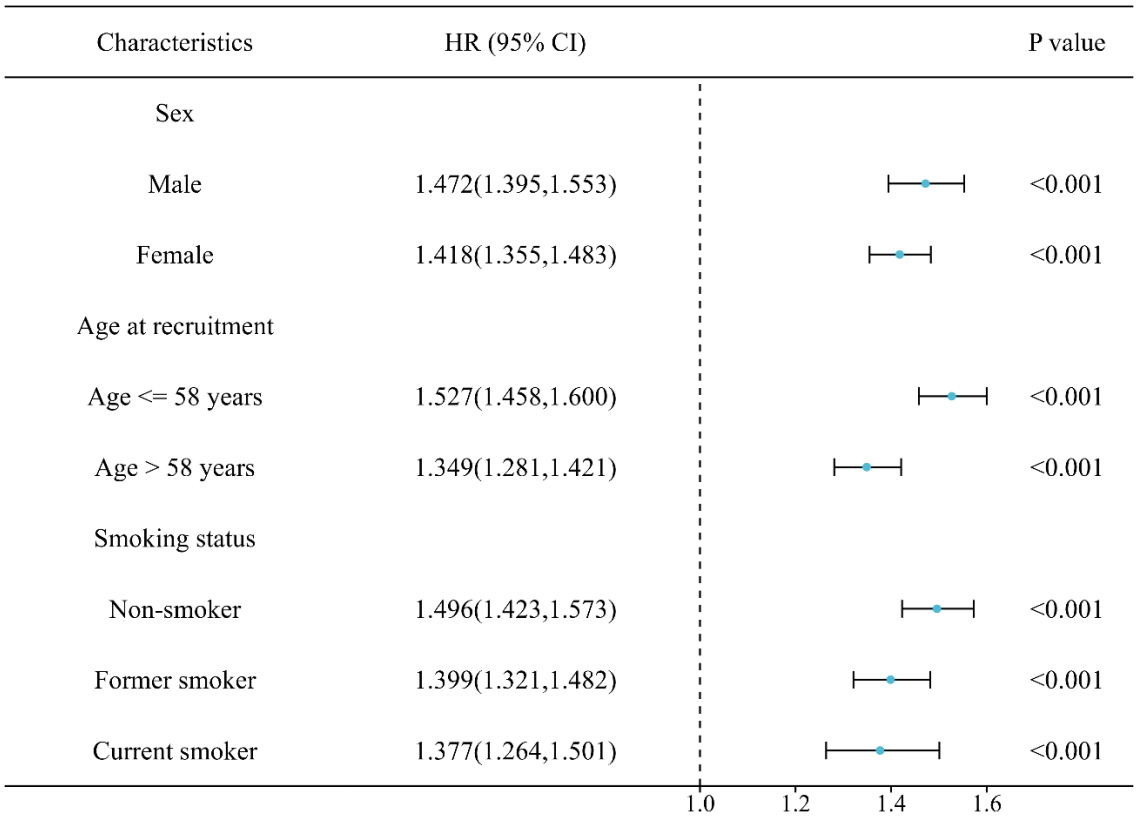

Figure 2. Forest plot of stratified analysis of insomnia on the risk of depression in the main model.

3.3. Sensitivity analysis

There was also a significant difference in insomnia between the two groups ($P<0.05$) in Model 2, which also corrected for alcohol drinker status, typical walking pace, average TV watching time, processed meat intake, and oily fish intake based on Model 1. (Table 2).

Advancing further to Model 3, which further adjusted for diabetes and BMI based on Model 2, the discernible distinction in insomnia prevalence endured, maintaining its statistically significant status ($P<0.05$) as evidenced by the findings encapsulated within Table 2.

After stepwise adjustment of different confounding factors, depression and insomnia were statistically significant($P<0.05$).

4. Discussion

Utilizing the comprehensive UK Biobank public database as its foundation, the present study adopted a prospective cohort methodology to meticulously investigate the independent associations between exposure to insomnia and the subsequent risk of depression. Through systematic adjustments for a range of potential confounding variables, a compelling and statistically significant causal correlation between insomnia and depression risk was ascertained. The robustness of these results was further corroborated by both stratified analysis and sensitivity analysis, affirming the reliability of the study's outcomes.

Previous scholarly investigations have suggested that the amelioration of insomnia may serve as an instrumental predictive marker for the trajectory of depression [10]. In alignment with these antecedent inquiries, the findings unveiled within this study provide a corroborative perspective, collectively accentuating the prospective value of insomnia intervention as a pivotal avenue for tackling the intricacies of depression.

The stratified analysis unfurls an intriguing revelation: the impact of insomnia on depression is comparatively diminished among current smokers in contrast to former smokers and non-smokers. Furthermore, former smokers exhibit a comparatively lower impact of insomnia on depression in comparison to non-smokers. Although this phenomenon could potentially be explained by the notion that smoking behavior or certain inherent components in tobacco might ameliorate insomnia, thus exerting a subtle and partially positive impact on the trajectory of depression development, this perspective contradicts both prior research [11] and the results of interaction analysis in this study, which indicate that the interaction between insomnia and smoking status lacks statistical significance.

The strengths of this study reside in its robust design as a large-scale prospective cohort investigation, orchestrated within the expansive landscape of the UK Biobank dataset. The adjustment for a multitude of potential confounding variables bolsters the comprehensive assessment of insomnia's impact on depression, thereby enhancing the persuasiveness of the study's findings compared to antecedent research. Nonetheless, the study harbors certain limitations. Firstly, the assessment of insomnia relies on self-report, thereby introducing potential uncertainties such as recall bias into the results. Secondly, the study's scope is confined to UK-based data, necessitating a cautious evaluation of its applicability to other international contexts.

While the level of evidence for causal relationships in cohort studies is relatively higher compared to cross-sectional and case-control studies, the precise causality within the current research remains unverified. Consequently, there arises a necessity for conducting randomized controlled trials to investigate the impact of insomnia amelioration on depression. Furthermore, given the limited evidence of an interaction between insomnia and smoking, it is important to emphasize the necessity for additional research to delve into the precise nature of this phenomenon in future studies.

5. Conclusion

In summation, a substantive and statistically significant correlation between insomnia and the risk of depression has been unveiled. This study furnishes vital epidemiological evidence underscoring the intricate link between insomnia and depression, thus directing the trajectory of future research endeavors. First off, since insomnia is a simple, low-cost indicator, it can be used to quickly identify people who are more likely to experience mental health problems. Secondly, to determine the effect of improved insomnia status on incident depression, randomized controlled trials should be conducted.

References

[1] World Health Organization. Depressive disorder(depression). World Health Organization;2023. Accessed August 18, 2023. https: //www.who.int/news-room/fact-sheets/detail/depression.

[2] Zhang Y, Chen Y, Ma L. Depression and cardiovascular disease in elderly: Current understanding. J Clin Neurosci. 2018; 47: 1 - 5. https: //doi.org/10.1016/j.jocn.2017. 09. 022.

[3] Eze IC, Foraster M, Schaffner E, et al. Incidence of depression in relation to transportation noise exposure and noise annoyance in the SAPALDIA study. Environ Int. 2020; 144: 106014. https: //doi.org/10.1016/j.envint.2020.106014.

[4] Yang Q, Borges MC, Sanderson E, et al. Associations between insomnia and pregnancy and perinatal outcomes: Evidence from mendelian randomization and multivariable regression analyses. PLoS Med. 2022; 19 (9): e1004090. Published 2022 Sep 6. https: //doi.org/10.1371/journal.pmed.1004090.

[5] Mirchandaney R, Barete R, Asarnow LD. Moderators of Cognitive Behavioral Treatment for Insomnia on Depression and Anxiety Outcomes. Curr Psychiatry Rep. 2022; 24 (2): 121 - 128. https: //doi.org/10.1007/s11920 - 022 - 01326 - 3.

[6] Fang H, Tu S, Sheng J, Shao A. Depression in sleep disturbance: A review on a bidirectional relationship, mechanisms and treatment. J Cell Mol Med. 2019; 23 (4): 2324 - 2332. https: //doi.org/10.1111/jcmm.14170.

[7] Blanken TF, Borsboom D, Penninx BW, et al. Network outcome analysis identifies difficulty initiating sleep as a primary target for prevention of depression: a 6-year prospective study. Sleep. 2020; 43 (5): zsz288. https: //doi.org/10.1093/sleep/zsz288.

[8] Paunio T, Korhonen T, Hublin C, et al. Poor sleep predicts symptoms of depression and disability retirement due to depression. J Affect Disord. 2015; 172: 381 - 389. https: //doi.org/10.1016/j.jad.2014.10.002.

[9] Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med. 2015; 12 (3): e1001779. Published 2015 Mar 31. https://doi.org/10.1371/journal.pmed.1001779.

[10] Riemann D, Krone LB, Wulff K, Nissen C. Sleep, insomnia, and depression. Neuropsychopharmacology. 2020; 45 (1): 74 - 89. https: //doi.org/10.1038/s41386 – 019 - 0411 - y.

[11] Jaehne A, Loessl B, Bárkai Z, et al. Effects of nicotine on sleep during consumption, withdrawal and replacement therapy. Sleep Med Rev. 2009; 13 (5): 363 - 377. https: //doi.org/10.1016/j.smrv.2008. 12. 003.