

The effect of cataract surgery on sleep quality: a systematic review and Meta-analysis

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Abstract

• **AIM:** To evaluate the effect of cataract surgery on sleep quality and to compare the difference between ultraviolet-blocking clear intraocular lens (UVB-IOL) and blue-filtering intraocular lens (BF-IOL) implantation.

• **METHODS:** Electronic search was performed of PubMed, MEDLINE, Embase and the Cochrane Library up to January 2016. Studies were eligible when they evaluated the sleep quality before and after cataract surgery by Pittsburgh sleep quality index (PSQI). A random/fixed-effects Meta-analysis was used for the pooled estimate. Heterogeneity was assessed with the I^2 test.

• **RESULTS:** Six studies were selected from 5623 references. Cataract surgery significantly reduced the PSQI scores at postoperative 0-3mo [mean difference (MD) = -0.62, 95%CI: -1.14 to -0.11, $P=0.02$, $I^2=66\%$] and 3-12mo (MD=-0.32, 95%CI: -0.62 to -0.02, $P=0.04$, $I^2=0$), respectively. Considering different intraocular lens (IOL) implantations, relative post-operative PSQI reduction was found for both UVB-IOL and BF-IOL, but a significant reduction was detected only for UVB-IOL. No significant difference was found with the effect of BF-IOL vs UVB-IOL on sleep quality.

• **CONCLUSION:** This study found that cataract surgery significantly improved the PSQI score-derived subjective sleep quality irrespective of the IOL type implanted. These findings highlight a substantial benefit of cataract surgery on systemic health with photoreceptive restoration in addition to visual acuity improvements.

• **KEYWORDS:** cataract surgery; intraocular lens implantation; sleep quality

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INTRODUCTION

Sleep quality is essential for maintaining health; conversely, sleep disorders or disruptions are associated with comorbidity management, medication administration and a personal burden^[1]. Cataract development interferes with the spectrum of light transmitted and reduces the amount of light reaching the retina, particularly in the short wavelength range of the visible spectrum (450-490 nm), accounting for the disruption of the human biological rhythm^[2]. However, only a few studies with limited subjects and study design have investigated the impact of cataract removal and artificial lens implantation on sleep quality^[3-13].

There exist two main classes of intraocular lens (IOL) currently implanted, which differ in light transmission properties: the ultraviolet-blocking clear intraocular lens (UVB-IOL) and the blue filtering intraocular lens (BF-IOL). The BF-IOL blocks the short wavelength spectrum blue light more efficiently than the UVB-IOL does, theoretically protecting the retinal pigment epithelium (RPE) from photochemical damage^[14-15]. However, present studies report conflicting findings about the effect comparison of the two types of IOLs on the prognosis, including sleep quality^[3,5-8,16-17].

To our best knowledge, the data regarding the effect of cataract surgery involving UVB-IOLs or/and BF-IOLs on sleep quality have not yet been systematically evaluated and reported. We therefore conducted a systematic review and Meta-analysis to evaluate the effect of cataract surgery on sleep quality and compare the difference between UVB-IOL and BF-IOL implantation.

MATERIALS AND METHODS

Search Strategy and Study Eligibility This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines^[18] for reporting systematic reviews and Meta-analyses. We performed a literature search of the electronic databases PubMed, Embase, and the Cochrane Library up to January 2016. We also

manually checked the reference lists of all retrieved studies, review articles, and conference abstracts using electronic searches. In our literature search, we included a combination of keywords, such as (cataract OR age-related cataract), (sleep OR circadian rhythm) and (IOL), in the form of title words or medical subject headings. Two reviewers (Zheng L and Wu XH) completed the literature search independently. In addition, these two reviewers further cross-checked the reference lists of all selected articles to identify other relevant studies. When screening discrepancies occurred, consensus was achieved after further discussion.

Inclusion and Exclusion Criteria We included studies that met the following inclusion criteria: 1) randomized or non-randomized trials focusing on the effect of cataract surgery on sleep quality; 2) the included patients received either an UVB-IOL or a BF-IOL followed by phacoemulsification in surgery; 3) the included patients were at least sixty years of age; 4) the subjects were diagnosed with age-related cataract with nuclear opacification grades of ≥ 2 according to Lens Opacities Classification System II; 5) the sleep quality of the participants was evaluated using the Pittsburgh sleep quality index (PSQI). The studies were excluded if they were 1) abstracts from conferences, full texts without raw data, duplicate publications, letters, or reviews; 2) the subjects' conditions were in combination with the following (but not restricted to) cardiovascular or cerebrovascular diseases, severe corneal lesions, vitreous hemorrhage, macular edema, age-related macular degeneration (AMD) or glaucoma.

Data Extraction and Outcomes of Interest Two authors (Zheng L and Wu XH) extracted the data and compared the results; discrepancies were resolved by discussion. We did not contact the authors of the eligible studies for additional data. The primary outcome was defined as a change in sleep quality before and after surgery, as evaluated by the PSQI. The change in the ratio of poor sleepers before and after surgery was analyzed as the secondary outcome.

Assessment of the Risk of Bias The risk of bias of each trial was assessed according to Cochrane methodology^[19], considering six aspects: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of the outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias). Each domain was graded as low, unclear, and high risk of bias according to the criteria outlined in the Cochrane Handbook for Systematic Review of Interventions. Two authors (Zheng L and Wu XH) assessed each trial independently and resolved disagreements *via* consensus.

Data Synthesis and Statistical Analysis The change estimate of the sleep quality (PSQI scores) and ratio of poor sleepers (PSQI score > 5.5) were calculated by a Meta-analysis based on

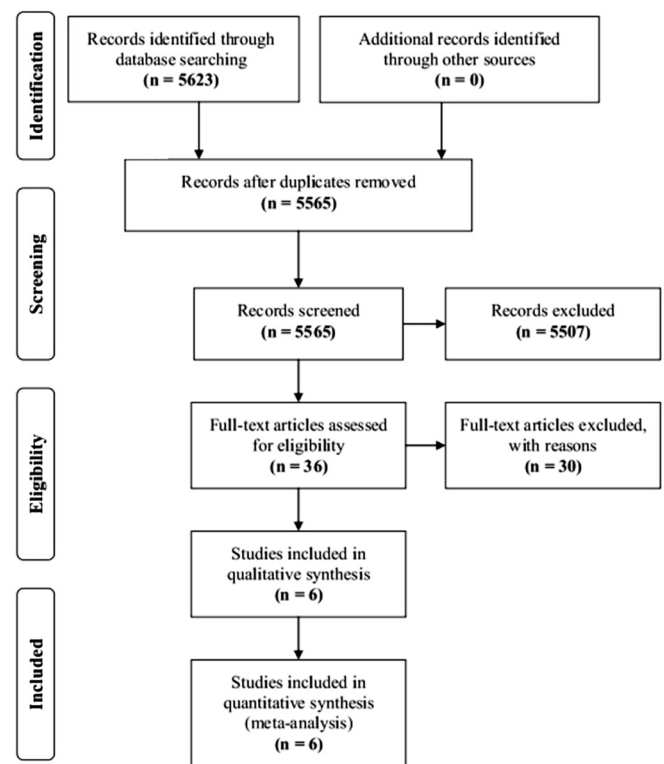


Figure 1 Flowchart of the study selection process.

the weighted mean differences (WMDs) and odds ratio (OR), respectively. Between-study heterogeneity was assessed using standard χ^2 tests and the I^2 statistic. I^2 values of 50% or more were considered to indicate substantial heterogeneity, and the random-effects model was then used; otherwise, the fixed-effects model was used^[20]. All analyses were performed using Review Manager (Version 5.3; The Cochrane Collaboration, 2014, the Nordic Cochrane Centre, Copenhagen, Denmark). Statistical tests were 2-sided and used a significance threshold of $P < 0.05$.

RESULTS

Literature Search and Study Characteristics In total, 5623 articles were initially identified. After duplicates and nonrelevant studies were removed, the abstracts of the remaining 5565 studies were reviewed, and 36 articles with potentially relevant studies were further identified in full text. Finally, 6 published studies were determined to be eligible and were included in this Meta-analysis. For details, please refer to Figure 1.

Among the 6 eligible studies published from 2013 to 2015, three studies were from Japan, 1 from Denmark, 1 from the UK, and 1 from China. One of the included studies was a randomized trial, whereas the other five were nonrandomized trials. The sample sizes of the included studies ranged from 40 to 961 subjects, with a combined total of 1509 patients in the pooled estimate. The extracted mean age of the subjects ranged from 73.7 to 76.9 years of age. For more details, refer to Table 1.

Quality of Evidence According to the Cochrane methodology, the risk of bias of the included studies was assessed by considering adequate sequence generation, allocation

Table 1 Characteristics of 6 included studies in the systematic review and Meta-analysis

Study	Country	Study type	Participants	Age (a)	M/F	IOL implant	Outcome
Brondsted <i>et al</i> , 2015 ^[8]	Denmark	Randomized	76	Mean 73.7 (range 50-94)	35/41	UVB BF	PSQI
Ayaki <i>et al</i> , 2015 ^[6]	Japan	Nonrandomized	206	Mean 74.1	83/123	UVB BF	PSQI
Alexander <i>et al</i> , 2014 ^[3]	UK	Nonrandomized	961	76.94 (5.35)	412/549	UVB BF	PSQI
Ayaki <i>et al</i> , 2014 ^[7]	Japan	Nonrandomized	71	74.1 (8.8)	30/41	UVB	PSQI
Wei <i>et al</i> , 2013 ^[13]	China	Nonrandomized	40	Median 74 (range 70-78)	14/26	BF	PSQI
Ayaki <i>et al</i> , 2013 ^[5]	Japan	Nonrandomized	155	74.8 (8.0)	62/93	BF	PSQI

PSQI: Pittsburgh sleep quality index; UVB: Ultraviolet-blocking clear intraocular lens; BF: Blue-filtering intraocular lens; SD: Standard deviation.

concealment, blinding, the evaluation of incomplete outcome data, lack of selective reporting, and lack of other biases (Figure 2A; Table 2).

Cumulatively, for the six included studies regarding the respective cochrane factors, the studies with a low risk of bias had values (a quantitative index of the risk of bias, range 0-100%) of 16.7%, 16.7%, 16.7%, 33.3%, 100%, 83.3%, and 33.3%; the studies with unreported features and a moderate risk of bias had values of 83.3%, 50.0%, 83.3%, 50.0%, 0, 16.7%, and 66.7%; and the studies at a high risk of bias had values of 0, 33.3%, 0, 13.3%, 0, 0, and 0 (Figure 2B).

Overall Effect of Cataract Surgery on Sleep Quality Six studies reported the change in sleep quality (PSQI) before and after surgery as the mean difference (MD) at different time points of follow-up. Examination of the forest plots revealed a significant PSQI reduction, namely, the sleep quality improvements during the 0-3mo (MD=-0.62, 95%CI: -1.14 to -0.11, $P=0.02$, $I^2=66\%$) and 3-12mo (MD=-0.32, 95%CI: -0.62 to -0.02, $P=0.04$, $I^2=0$) follow-up after surgery (Figure 3).

Effect of Ultraviolet-blocking Clear Intraocular Lens on Sleep Quality Four studies reported the change in sleep quality (PSQI) before and after surgery as the MD at different time points of follow-up. The Meta-analysis of the fixed-effect model was used for calculating the pooled effect regarding the insignificant heterogeneity ($I^2<50\%$). Examination of the forest plots revealed significant PSQI reduction, namely, the sleep quality improvements during the 0-3mo (MD=-0.51, 95%CI: -0.90 to -0.12, $P=0.01$, $I^2=0$) and 3-12mo (MD=-0.43, 95%CI: -0.86 to -0.01, $P=0.05$, $I^2=0$) follow-up after surgery (Figure 4A).

Effect of Blue-filtering Intraocular Lens on Sleep Quality Five studies reported the change in sleep quality (PSQI) before and after surgery as the MD at different time points of follow-up. Meta-analysis of the random effect model (0-3mo after surgery)/fixed-effect model (3-12mo after surgery) was used for calculating the pooled effect regarding the heterogeneity. Examination of the forest plots revealed relative PSQI reductions during the 0-3mo (MD=-0.75, 95%CI: -1.71 to 0.20, $P=0.12$, $I^2=82\%$) and 3-12mo (MD=-0.20, 95%CI: -0.62 to 0.21, $P=0.34$, $I^2=0$) follow-up after

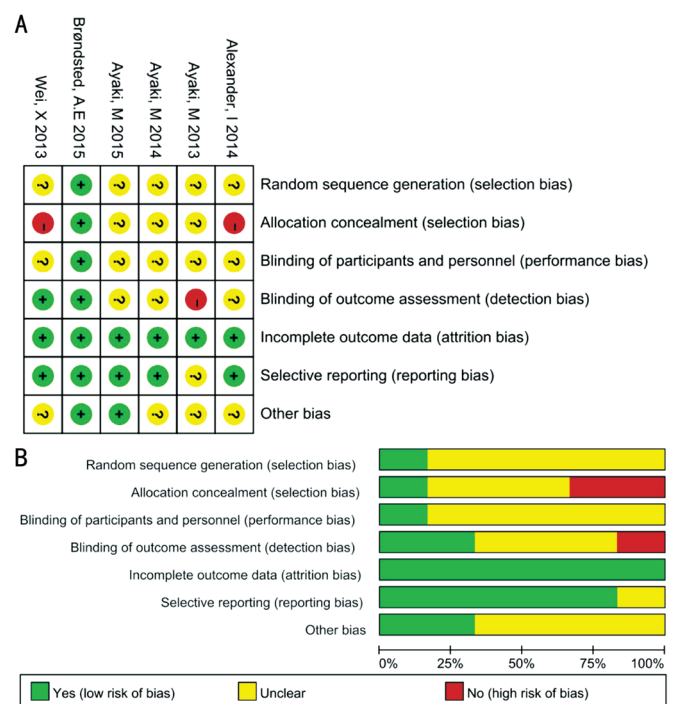


Figure 2 Risk of bias evaluation of the included studies A: Risk of bias summary; B: Risk of bias graph. The green bar: Reported and a low risk of bias; The yellow bar: Unreported and a moderate risk of bias; The red bar: Unreported and a high risk of bias.

surgery, but the differences were not statistically significant (Figure 4B).

Effect of Ultraviolet-blocking Clear Intraocular Lens vs Blue-filtering Intraocular Lens on Sleep Quality Three studies provided the results comparing the effect of the two types of IOLs on sleep quality (PSQI) before and after surgery as the MD at different time points of follow-up. Meta-analysis of the random effect model (0-3mo after surgery)/ fixed-effect model (3-12mo after surgery) was used for calculating the pooled effect regarding the heterogeneity. Examination of the forest plots revealed a larger amplitude of PSQI reductions for UVB-IOL compared with BF-IOL during the 0-3mo (MD=-0.27, 95%CI: -1.05 to 0.51, $P=0.50$, $I^2=53\%$) and 3-12mo (MD=-0.20, 95%CI: -0.64 to 0.24, $P=0.37$, $I^2=0$) follow-up after surgery, but the differences were not statistically significant (Figure 4C).

Table 2 Risk of bias assessment of included studies

Studies	Bias	Authors' judgement	Support for judgment
Brøndsted <i>et al</i> , 2015 ^[8]	Random sequence generation (selection bias)	Low risk	Randomization was performed on the day of the surgery using automated, computerized block-randomization lists with a 1:1 allocation ratio and a block size of 9
	Allocation concealment (selection bias)	Low risk	The participants were masked to IOL type
	Blinding of participants and personnel (performance bias)	Low risk	The IOL type was masked to the participants, but impossible to the investigator
	Blinding of outcome assessment (detection bias)	Low risk	Statistical analyses were performed after a complete re-masking of the data post hoc. Masking was not broken before all statistical analyses had been performed
	Incomplete outcome data (attrition bias)	Low risk	72/73 included participants completed the 3-week postoperative visit
	Selective reporting (reporting bias)	Low risk	Important outcomes were reported
	Other bias	Low risk	Not likely
Ayaki <i>et al</i> , 2015 ^[6]	Random sequence generation (selection bias)	Unclear risk	Nonrandomized trial with consecutive patients enrolled
	Allocation concealment (selection bias)	Unclear risk	Not reported
	Blinding of participants and personnel (performance bias)	Unclear risk	Not reported
	Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
	Incomplete outcome data (attrition bias)	Low risk	All included patients completed the 2mo and 7mo postoperative follow-up visit
	Selective reporting (reporting bias)	Low risk	Important outcomes were reported
	Other bias	Low risk	Not likely
Alexander <i>et al</i> , 2014 ^[3]	Random sequence generation (selection bias)	Unclear risk	Dual-site study. Patients operated on in Oxford received UVF-IOL (SA60AT); those operated on in Windsor received BF-IOL (SN60AT)
	Allocation concealment (selection bias)	High risk	Neither investigators nor patients were masked to IOL allocation
	Blinding of participants and personnel (performance bias)	Unclear risk	Not likely to blind patients or personnel
	Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
	Incomplete outcome data (attrition bias)	Low risk	1482 recruited, 961 completed study; in UVF IOL group, 44 patients (9%) dropped out and in BF-IOL group, 100 patients (22%) dropped out before 1mo postoperation
	Selective reporting (reporting bias)	Low risk	Important outcomes were reported
	Other bias	Unclear risk	Not reported
Ayaki <i>et al</i> , 2014 ^[7]	Random sequence generation (selection bias)	Unclear risk	Nonrandomized trial, consecutive patients enrolled
	Allocation concealment (selection bias)	Unclear risk	Not likely
	Blinding of participants and personnel (performance bias)	Unclear risk	Not likely
	Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
	Incomplete outcome data (attrition bias)	Low risk	All included patients completed the 7mo postoperative follow-up visit
	Selective reporting (reporting bias)	Low risk	Important outcomes were reported
	Other bias	Unclear risk	Not reported

Table 2 (Continued) Risk of bias assessment of included studies

Studies	Bias	Authors' judgement	Support for judgment
Wei <i>et al</i> , 2013 ^[13]	Random sequence generation (selection bias)	Unclear risk	Nonrandomized, pre-test/post-test experiment
	Allocation concealment (selection bias)	High risk	Not likely
	Blinding of participants and personnel (performance bias)	Unclear risk	Not reported
	Blinding of outcome assessment (detection bias)	Low risk	Investigators did not tell subjects supposed relationship between IOL and sleep quality
	Incomplete outcome data (attrition bias)	Low risk	All included patients completed the 1mo postoperative follow-up visit
	Selective reporting (reporting bias)	Low risk	Important outcomes were reported
	Other bias	Unclear risk	Not reported
Ayaki <i>et al</i> , 2013 ^[5]	Random sequence generation (selection bias)	Unclear risk	Nonrandomized trial, consecutive patients enrolled
	Allocation concealment (selection bias)	Unclear risk	Not likely
	Blinding of participants and personnel (performance bias)	Unclear risk	Not reported
	Blinding of outcome assessment (detection bias)	High risk	Not likely
	Incomplete outcome data (attrition bias)	Low risk	All included patients completed the 2mo postoperative follow-up visit
	Selective reporting (reporting bias)	Unclear risk	Most important outcomes were reported
	Other bias	Unclear risk	Not reported

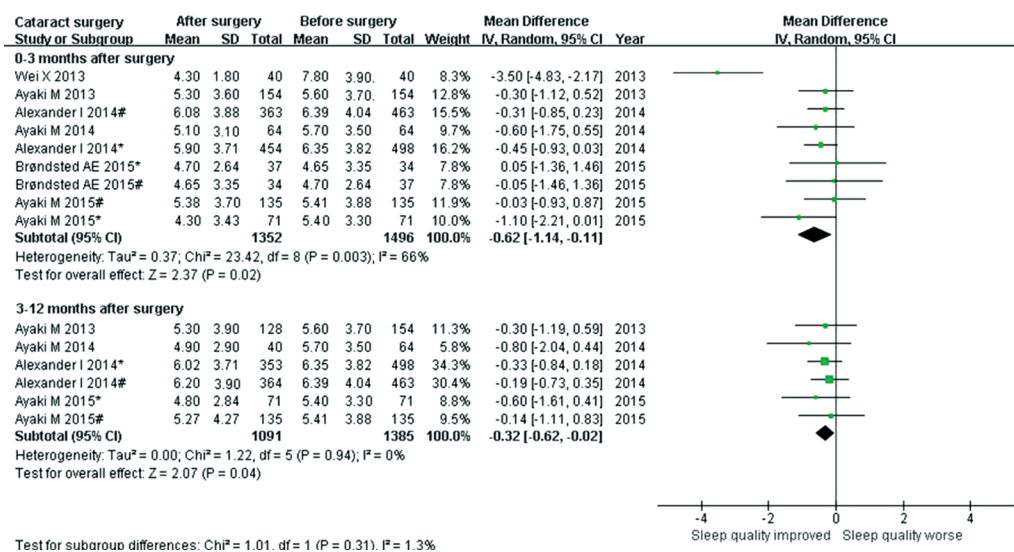


Figure 3 Forest plot estimating the pooled effect of cataract surgery on sleep quality.

Effect of Cataract Surgery (Blue-filtering Intraocular Lens) on the Poor-sleepers Ratio Two studies compared the change in the poor-sleepers (PSQI >5.5) ratio before and after cataract surgery as the OR at the 0-3mo follow-up after surgery. Meta-analysis of the random effect model was used for calculating the pooled effect regarding the substantial heterogeneity. Examination of the forest plots revealed relative reductions in the poor-sleepers ratio during the 0-3mo (MD=0.34, 95%CI: 0.08 to 1.51, P=0.16, I²=79%) after surgery, but the differences were not statistically significant (Figure 5).

DISCUSSION

In this systematic review and Meta-analysis, we evaluated the effect of cataract surgery on sleep quality and compared the difference between the UVB-IOL or BF-IOL implantation. Cataract surgery was found to significantly improve the PSQI score-derived, subjective sleep quality. However, no significant difference was found between the effect of UVB-IOLs and BF-IOLs. The results were in accordance with the theory that replacing the aging lens with an artificial IOL restores the transmitted light reaching the retina and thereby

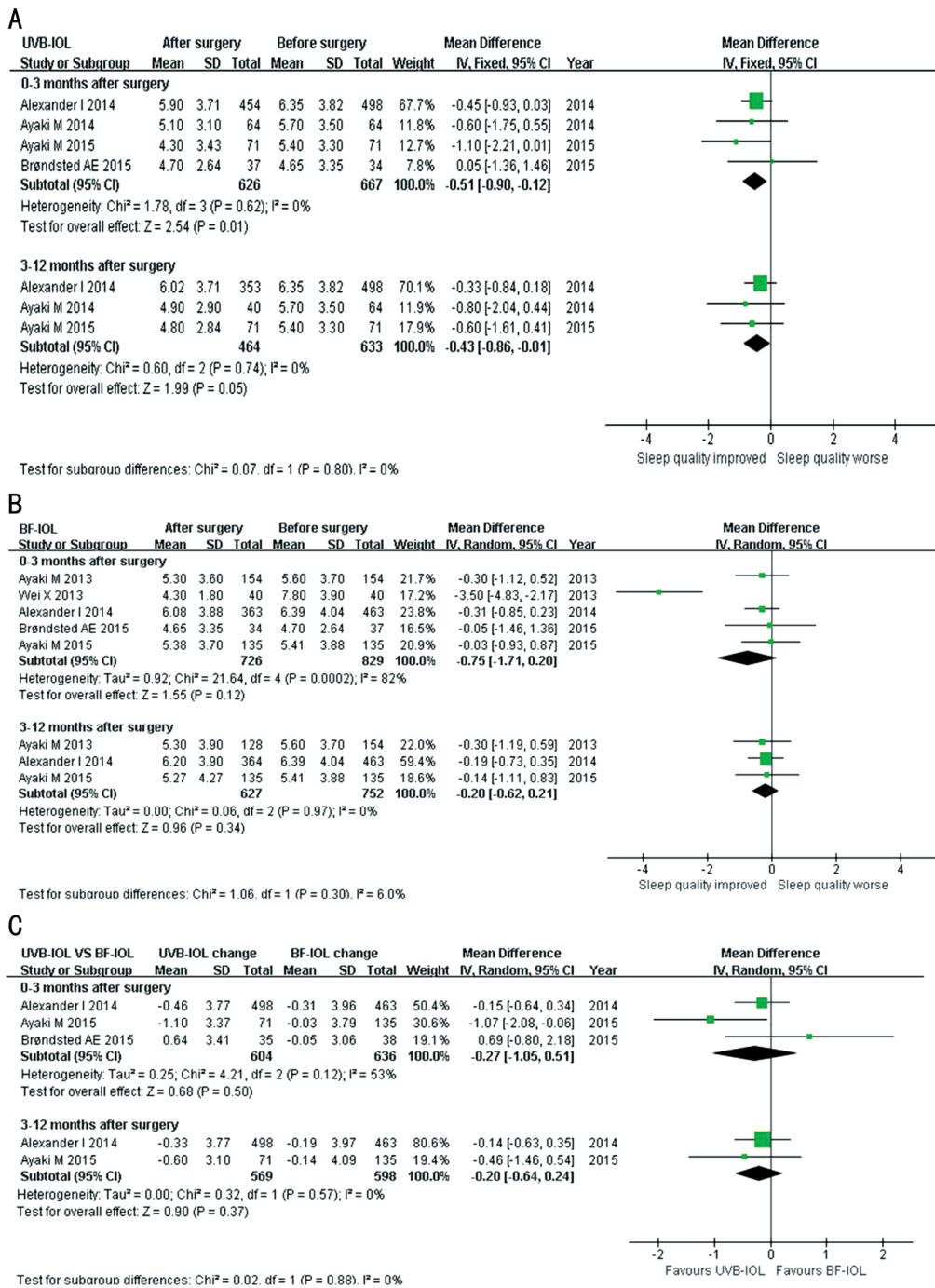


Figure 4 Forest plot estimating the pooled effect of cataract surgery on sleep quality, considering different IOL types A: Forest plot estimating the pooled effect of cataract surgery with UVB-IOL implantation on sleep quality; B: Forest plot estimating the pooled effect of cataract surgery with BF-IOL implantation on sleep quality; C: Forest plot comparing the pooled effect of cataract surgery with UVB-IOL vs BF-IOL implantation on sleep quality.

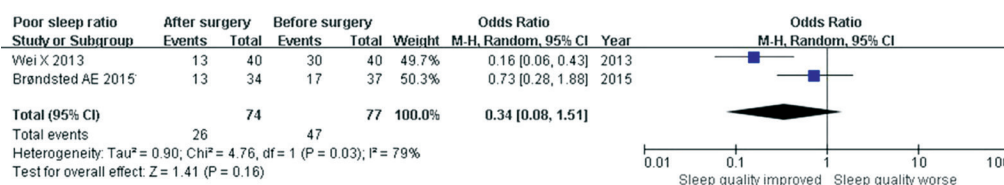


Figure 5 Forest plots showing the effect of cataract surgery (BF-IOL) on the poor-sleepers ratio.

stimulates the activity of all photoreceptors, rods, cones, and the directly photosensitive retinal ganglion cells (pRGCs) and, consequently, the responses to the environmental irradiance,

including the sleep systems^[21-23]. Yet, it remains controversial which type of IOL is better, considering sleep quality improvements for the elderly. Some

researchers have argued that it is beneficial to implant the BF-IOL for improving sleep quality based on the theory that the BF-IOL blocks the short wavelength spectrum blue light more efficiently than the UVB-IOL does^[15], consequently protecting the RPE from photochemical damage^[24-27]. However, this study, consistent with several previous studies^[3,5-8,16-17], found no significant difference between the UVB-IOL and BF-IOL with respect to sleep quality in senile cataract patients. This finding can be partly explained by the relatively high blue light transmission of 80% and 95%, respectively, compared with 32% in the participants before cataract surgery. Thus, cataract surgery increases the blue light transmission by approximately 250% and 300%, covering the effect of the 15% difference between the UVB-IOL and the BF-IOL^[8].

The difference between the effects of the UVB-IOL and the BF-IOL has long been discussed. Ham *et al*^[28] showed that light-induced retina damage from ultraviolet V is associated with the exposure time-span and light intensity. BF-IOLs can prevent part of this light-induced retinal damage and guards against the initiation and development of AMD^[29-30]. Furthermore, BF-IOLs improve contrast sensitivity, reduce glare under photopic and mesopic conditions^[31], and compromise the disturbance of blue color vision^[32-33]. However, the blue-blocking IOL still maintains a certain amount of blue light transmission to the retina and may improve sleep quality due to the yellow crystal^[21-22]. Adjusting the lighting to 460-480 nm would possibly minimize any retinal injury while still retaining the most effective short wavelengths of light necessary for circadian entrainment^[23].

The findings of the study should be interpreted within the few limitations. First, only a few publications reached our standard. Only one was a semi-randomized trial, and the others were not. The nonrandomized artificial crystal implantation might have caused bias with respect to the study results and might have affected the reliability of the estimate. Second, the participants in the studies came from different areas, even different races, with a varied understanding of and tolerance for sleep disorders when they were asked to complete the PSQI. Additionally, the subjective PSQI method might have produced memorizing bias, interfering with the pooled result. Third, the records of the outcome data among the included studies were not at the same follow-up time point, which possibly affected the reliability of the calculation.

In conclusion, this study found that cataract surgery significantly improved the PSQI score-derived subjective sleep quality irrespective of the intraocular lens type implanted. These findings highlight a substantial benefit of cataract surgery on systemic health with photoreceptive restoration in addition to visual acuity improvements. Further studies with a larger sample size and a randomized study design are expected.

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Conflicts of Interest: Zheng L, None; Wu XH, None; Lin HT, None.

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