Report

Current Biology

A meta-analysis of the associations between insufficient sleep duration and antibody response to vaccination

Highlights

- Insufficient sleep (<6 hours/night) around vaccination reduces the antibody response
- The reduction is similar to the waning of COVID-19 vaccine antibodies over 2 months
- The association seems robust in men, but more data are needed in women
- Optimizing sleep duration around the time of vaccination may boost antibody response

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In brief

Spiegel et al. use a meta-analytic approach to show that insufficient sleep is associated with a reduced antibody response to vaccination. The authors call for large-scale studies to define when optimizing sleep duration is most beneficial, the causes of the sex disparity, and the amount of sleep needed to protect the response.

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A meta-analysis of the associations between insufficient sleep duration and antibody response to vaccination

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SUMMARY

Vaccination is a major strategy to control a viral pandemic. Simple behavioral interventions that might boost vaccine responses have yet to be identified. We conducted meta-analyses to summarize the evidence linking the amount of sleep obtained in the days surrounding vaccination to antibody response in healthy adults. Authors of the included studies provided the information needed to accurately estimate the pooled effect size (ES) and 95% confidence intervals (95% CI) and to examine sex differences.[1-7] The association between self-reported short sleep (<6 h/night) and reduced vaccine response did not reach our pre-defined statistical significant criteria (total n = 504, ages 18–85; overall ES [95% CI] = 0.29 [−0.04, 0.63]). Objectively assessed short sleep was associated with a robust decrease in antibody response (total n = 304, ages 18–60; overall ES [95% CI] = 0.79 [0.40, 1.18]). In men, the pooled ES was large (overall ES [95% CI] = 0.93 [0.54, 1.33]), whereas it did not reach significance in women (overall ES [95% CI] = 0.42 [−0.49, 1.32]). These results provide evidence that insufficient sleep duration substantially decreases the response to anti-viral vaccination and suggests that achieving adequate amount of sleep during the days surrounding vaccination may enhance and prolong the humoral response. Large-scale well-controlled studies are urgently needed to define (1) the window of time around inoculation when optimizing sleep duration is most beneficial, (2) the causes of the sex disparity in the impact of sleep on the response, and (3) the amount of sleep needed to protect the response.

RESULTS

To date, the SARS-CoV-2 pandemic has involved nearly 650 million officially recorded cases and over 6.5 million deaths. Vaccination was widely expected to be effective in controlling the pandemic. Only 63% of adults worldwide have been fully vaccinated and more contagious variants have emerged. Thus, the vaccination effort needs to continue. In parallel, new threats like mpox have emerged and new flu strains are continuously identified, making vaccination a major tool for public health in an increasingly globalized society.

The protection conferred by a given vaccine depends on the magnitude of the individual immune response. Antibody response is a clinically significant biomarker of protection and is an early indicator of immunity.[8] Recent studies have reported a wide variability in antibody response to the same anti-COVID-19 vaccine in healthy adults not previously infected with SARS-CoV-2. Male sex, older age, excess adiposity, history of smoking, and hypertension have been among the demographic and

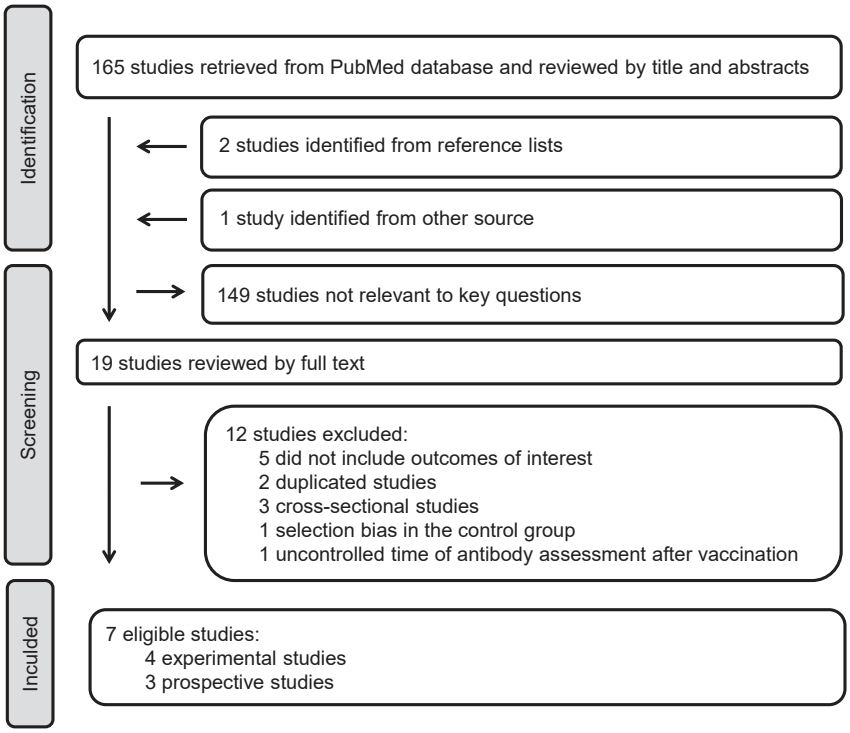

Figure 1. Flowchart of study screening and selection

clinical factors identified as predictors of lower antibody titers post-vaccination.[9,10] None of these risk factors may be targeted by rapid behavioral interventions to optimize the humoral response.

In 2002, an experimental study of sleep restriction in the days surrounding influenza vaccination showed that immunoglobulin (IgG) antibody titers 10 days after inoculation were less than half of those measured in control subjects.[1] The role of insufficient sleep duration in individual differences in responses to influenza and hepatitis vaccination has been examined in subsequent studies with somewhat mixed results, possibly as a consequence of relatively small samples and methodological differences. Recently, several authors have called for a thorough examination of the hypothesis that obtaining healthy amounts of sleep at the time of vaccination might increase and extend the protective effect.[11–13] In order to summarize the existing evidence and estimate the pooled ES across studies, we have used a meta-analytical approach. Our objective is to better inform the scientific community and the public about a relatively easily modifiable behavior that may optimize vaccine response in the context of the current COVID-19 pandemic.

Literature search

The PRISMA flow diagram is presented in Figure 1. A total of 165 human studies were retrieved from PubMed that included both sleep* and vaccin* terms, two studies were identified from reference lists,[14,15] and one 2022 study was obtained from another source.[16] 149 articles were excluded after being reviewed by title and abstracts when the design of the study and/or the variables measured would not allow us to determine whether nocturnal short sleep duration is linked to antibody response after vaccination in healthy adults. Hence, 19 studies underwent full-text review with discussion during consensus meetings (K.S and E.V.C.). Twelve studies were excluded for the following reasons: five did not include assessment of sleep duration or antibody response to vaccine; two duplicated the results included in Prather et al.[7,17,18]; three did not evaluate sleep around the time of vaccination[14,15,19]; one involved a selection bias where subjects were included only if their sleep duration was greater than 7.5 h.[20]; one measured antibody levels after vaccination against COVID-19 in a time interval ranging from as little as 1 week to up to 5 months,[16] in contrast to all other included studies where the timing of assessment of antibody levels relative to vaccination was fixed. Further, more than 90% of the participants of this recent study received a mRNA vaccine (Pfizer-BioNTech or Moderna-NIAID).[16] For both these vaccines, a more than 6-fold waning of the humoral response over a 6-month period has been reported, preventing the reliable detection of sleep around the time of vaccination on antibody levels measured at highly variable times post-inoculation.[21,22] Four experimental studies and three prospective cohorts were included in the meta-analysis.[1–7] Tables 1 and 2 summarize the characteristics of the included studies. Because self-reported sleep duration is only modestly correlated with objective sleep duration,[23] we built two separate forest plots according to the assessment method of sleep duration.

Association between insufficient sleep and vaccine response

The relationship between self-reported short sleep, i.e. < 6 h /night, and vaccine response did not reach our predefined statistical significant criteria (total n = 504, ages 18–85, effect size and 95% confidence interval (ES [95% CI]) = 0.29 [−0.04, 0.63]; Figure 2A). The overall ES [95% CI] was 0.40 [−0.09, 0.89] for men and 0.21 [−0.29, 0.71] for women. Given that sleep duration and quality are generally reduced in older adults, we conducted an exploratory analysis excluding the study recruiting only adults ≥65 years, an age group not represented in studies that used objective sleep assessment; in the remaining total sample of 299 adults ages 18–60, a significant association emerged (ES [95% CI] = 0.59 [0.12, 1.05]). When analyses were performed for men and women separately, the association between self-reported short sleep and antibody response was significant in men, but not in women (ES [95% CI] = 0.75 [0.16, 1.34] vs. 0.55 [−0.38, 1.47], respectively). ES between 0.50 and 0.80 are typically considered as "medium".

For studies that used objective measures of sleep, a robust adverse impact of short sleep on vaccine response was detected (total n = 304, ages 18–60, ES = 0.79 [0.40, 1.18]; Figure 2B). The

Table 1. Description of studies evaluating response to vaccination as indexed by antibody titers (Ab) and protection status (PS) and sleep duration as experimentally shortened, i.e., total sleep deprivation (TSD) or sleep restriction (partial sleep deprivation, [PSD])

Study	N	Age range	M/W	Manipulation of sleep duration	Vaccine	Nb of inoculations	Ab assessment	Time of Ab assessment	Findings
Spiegel et al., 2002[1]	25	18–27	25/0	4 nights of PSD (4h in bed) before vaccination followed by 2 nights of PSD and 7 nights of 12 h in bed **vs.** 8 h in bed	Influenza, trivalent types A and B	1	Anti-influenza Ab (IgG)	0, 10 and 21–30 days	*t = 10 days and overall
Lange et al., 2003[2]	19	20–35	10/9	1 night TSD after vaccination **vs.** 8 h in bed	hepatitis A	1	Hepatitis A virus Ab (IgM and IgG)	0, daily 5–14 days, 28 days	*t = 28 days and overall
Lange et al., 2011[3]	27	19–36	27/0	1 night TSD after each vaccination **vs.** 7.5 h in bed	hepatitis A	3; wk 0, 8, 16	Hepatitis A virus Ab (IgG1, IgG2, IgG3, and IgG4)	0, 1, 2, and 4 wks after each inoculation (wks 0–20) and 1 year after the first inoculation (wk 52)	* for IgG1 subtype from the 2nd vaccination and overall
Lange et al., 2011[3]	27	19–36	27/0	1 night TSD after each vaccination **vs.** 7.5 h in bed	hepatitis B	3; wk 0, 8, 16	Hepatitis B virus surface antigen Ab (IgG1, IgG2, IgG3, and IgG4) and PS	0, 1, 2, and 4 wks after each inoculation (wks 0–20) and 1 year after the first inoculation (wk 52)	* for IgG1 subtype at wk 20 and 52; NS for PS
Benedict et al., 2012[4]	11	18–25	11/13	1 night TSD before vaccination **vs.** 8 h in bed	influenza A H1N1 (swine flu)	1	Hemagglutination inhibition Ab against the H1N1 virus	5, 10, 17, 52 days	*t = 5 days and overall in M; NS in W

Significant findings indicate an association in the hypothesized direction, i.e., sleep deprivation as PSD or TSD linked with lower Ab or PS. *p < 0.05; #p < 0.10; M: Men; W: Women; NS: no significant; wk: week.

Table 2. Description of studies evaluating response to vaccination as indexed by antibody titers (Ab) and protection status (PS) and sleep duration as assessed in prospective studies

Study	Sample/population	N	Age range	M/W	Vaccine	Nb of inoculations	Ab assessment and timing	Assessment of sleep duration	Findings
Prather et al., 2012[5]	healthy middle-aged adults	125	40–60	55/70	Recombinant hepatitis B	3; mth 0, 1,6	Ab by enzyme-linked immunoassay prior to the 2nd and 3rd vaccination (primary and secondary Ab responses) and at 6 mths (PS)	7 days self-reported (diary-based) surrounding each of the 3 vaccinations	NS Ab response; * PS linked to self-reported sleep duration on the 7 days surrounding the 1st vaccination
id.	id.	id.	id.	id.	id.	id.	id.	7 days objective (actigraphy) surrounding the 1st vaccination	* secondary Ab response and PS
Ayling et al., 2018[6]	community-dwelling older adults	138	65–85	77/61	2014/15 northern hemisphere influenza vaccine (H1N1, H3H2, B)	1	Ab (IgG) via antigen microarray and PS via hemagglutination inhibition assays at 0, 4 and 16 wks post-vaccination.	6 wks self-reported (adapted items from the PSQI, 3 days/wk) for 2 wks prior and 4 wks following vaccination	NS 6 wks sleep duration
Prather et al., 2020[7]	healthy young adults	83	18–25	37/46	Influenza (A/New Caldonia (H1N1) and A/Panama (H3N2) and B/Yamanashi or B/Victoria (H1N1))	1	Ab to the 3 influenza viral strains via hemagglutination inhibition assays at 0, 1, and 4 mths	13 days self-reported (diary-based) for 3 nights prior and 10 nights following vaccination.	* 13 days sleep duration linked to Ab to A/New caledonia (H1N1) at 1 and 4 mths (largely driven by the 2 nights preceding vaccination); # A/Panama viral strain at 1 mth

Significant findings indicate an association in the hypothesized direction, i.e., habitual short sleep linked with lower Ab or PS. *$p < 0.05$; #$p < 0.10$; M: Men; W: Women; NS: no significant; mth: month; PSQI: Pittsburgh Sleep Quality Index Questionnaire.

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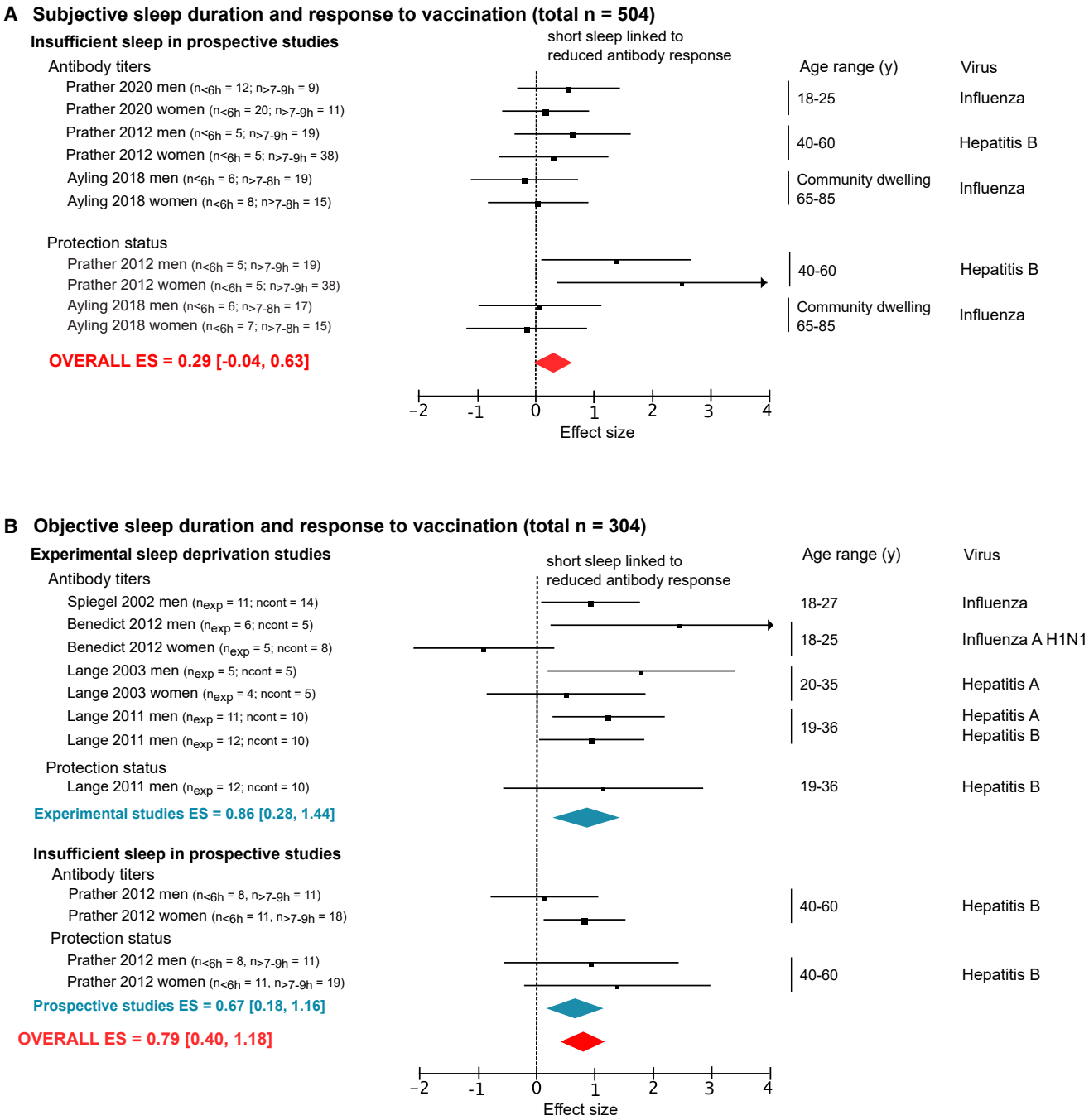

Figure 2. Forest plots of subjectively and objectively measured short sleep associated with reduced response to vaccination

(A) Forest plot of subjectively assessed habitual short sleep associated with reduced response to vaccination as indexed by antibody titers and protection status in prospective studies.

(B) Forest plot of objectively assessed experimentally shortened sleep duration (top) or habitual short sleep (bottom) associated with reduced response to vaccination as indexed by antibody titers and protection status.

Results are expressed as effect sizes and 95% confidence intervals (ES [95% CI]). The area of the block indicates the weight assigned to that study in the meta-analysis while the horizontal line depicts the 95% CI. Positive ES indicate an effect in the hypothesized direction, i.e., short sleep associated with lower level of antibodies or reduced protection status. In experimental studies, sleep duration was shortened by either partial or total sleep deprivation for one night or for multiple nights. In prospective cohort studies, sleep duration was assessed categorically, with short sleep being defined as <6 h and normal sleep being defined by sleep duration of >7 to 9 h per night for people under 65 years and of 7 to 8 h for people ≥65 years; and ES [95% CI] were calculated using the sleep data collected within a window of 7 days around inoculation because recent evidence suggests that antibody levels are mostly affected by insufficient sleep on the closest nights around vaccination.[7] When results were reported for individual strains or for different subtypes of immunoglobulins, the most significant result in the expected direction was used.

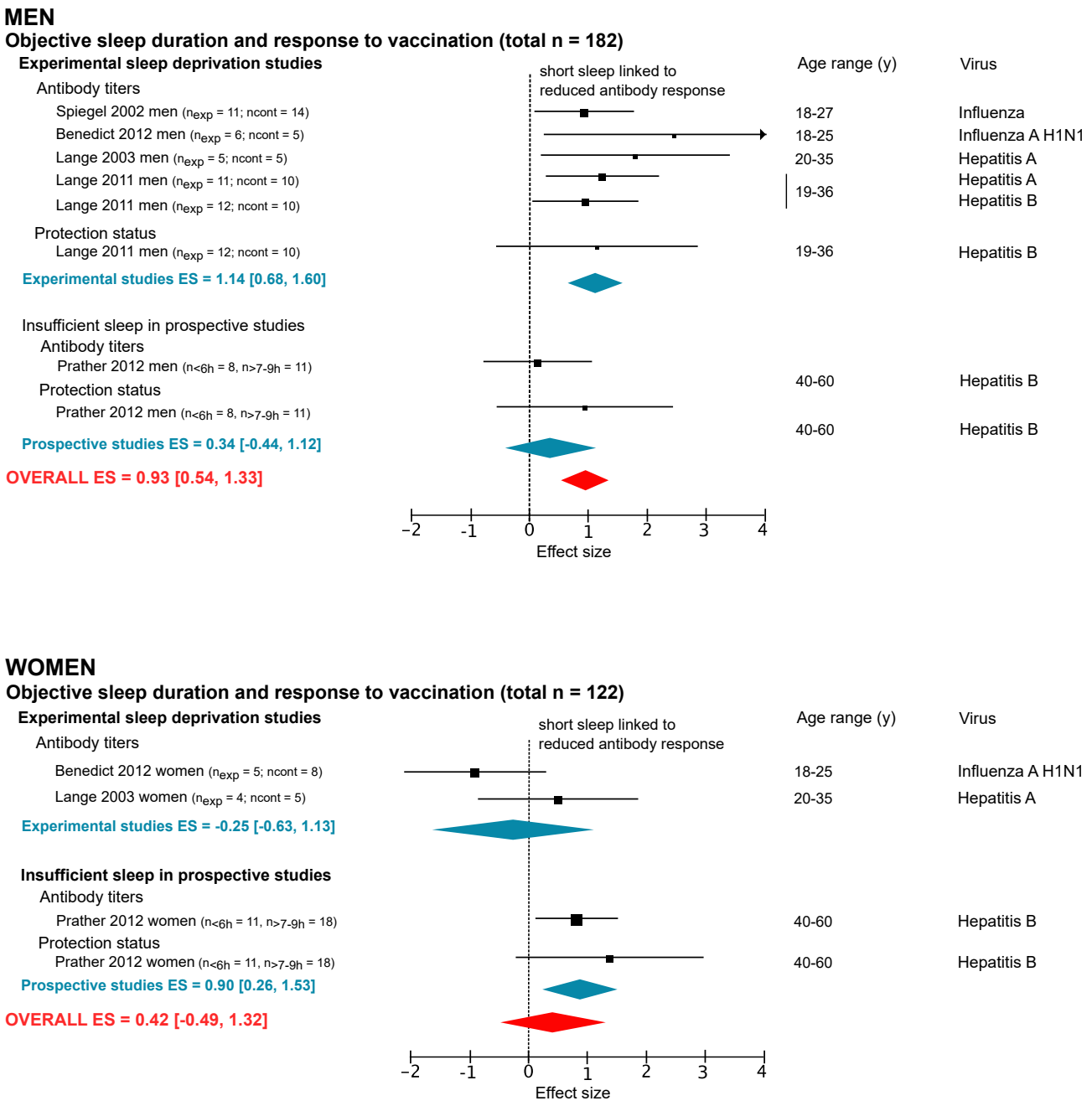

Figure 3. Forest plots of objectively assessed experimentally shortened sleep duration or habitual sleep associated with reduced response to vaccination in men (top) and women (bottom)

Results are expressed as effect sizes and 95% confidence intervals (ES [95% CI]). The area of the block indicates the weight assigned to that study in the meta-analysis while the horizontal line depicts the 95% CI. Positive ES indicates an effect in the hypothesized direction, i.e., short sleep associated with lower level of antibodies or reduced protection status.

pooled ES [95% CI] was 0.86 [0.28, 1.44] for experimental studies (n = 133) and 0.67 [0.18, 1.16] for prospective studies (total n = 171). ES of 0.80 and above are typically considered as "large". In men, short sleep was associated with a reduced antibody titers with an overall large pooled ES [95% CI] of 0.93 [0.54, 1.33] (Figure 3). In women, this association failed to reach significance with an ES [95% CI] of 0.42 [− 0.49, 1.32] (Figure 3).

DISCUSSION

These meta-analyses investigated the association of sleep duration with the response to anti-viral vaccination as assessed by antibody titers and/or seroprotection. The main result is that, when assessed by objective methods, short sleep duration (<6 h/night), in adults aged 18–60 was associated with a decrease in response In

response to vaccination with a medium to large pooled ES. The unequivocal findings from our rigorous meta-analysis are consistent with the conclusion of a recent systematic review.[24]

Given that sex impacts the response to vaccine,[9,25] we calculated separate overall ES for men and women. When sleep was assessed objectively, the pooled ES was large and highly significant for men, whereas it was smaller and not significant for women, likely due to the wide variations in sex hormone levels according to phase of the menstrual cycle, use of hormonal contraception, menopausal status, and use of hormonal replacement in post-menopausal women.[25] None of the studies included in our meta-analysis controlled for these known hormonal modulators of immune function.

While all studies that performed objective sleep assessment were conducted in young and middle-aged subjects, the studies based on self-reported sleep also enrolled 65–85-year-old adults.[6] Given that sleep duration, sleep quality, and vaccination response are generally reduced and more variable in this age range,[26] we performed an exploratory analysis excluding the older age group. The association between self-reported short sleep and reduced vaccine response was stronger, although it remained smaller than when sleep was objectively assessed, consistent with the observation that self-reported and objective sleep are only moderately correlated and that subjective report tends to overestimate actual sleep duration.[23]

The present meta-analyses include data from studies examining associations between sleep duration and antibody responses to the influenza and hepatitis vaccines. At the present time, there are no comparable published data for COVID-19 vaccines. To obtain a comparison relevant to the SARS-CoV-2 pandemic, we estimated the ES of the waning of the humoral immune response to the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine from baseline to an average of 2 months post-injection using published numerical data.[21] The ES for waning over two months was 0.79, essentially identical to the ES estimated for objectively assessed short sleep duration. If, similar to the influenza and hepatitis vaccines, the antibody response to COVID-19 vaccines is adversely affected by insufficient sleep, then insufficient sleep around the time of COVID-19 vaccination may reduce antibody titers in the same range as the waning of the response to the most commonly administered vaccine over 2 months.

Though vaccination remains the most important strategy to control the current pandemic of COVID-19, simple behavioral interventions that might boost vaccine response remain to be identified. As suggested by our meta-analysis, adequate amounts of sleep (at least 6 h/night) during the days surrounding the time of vaccination may enhance the humoral response to diverse strains of viruses. Such recommendation of obtaining adequate sleep duration is realistic as at-home behavioral sleep extension has proven to be feasible, acceptable, and efficient in a variety of populations.[27] The National Sleep Foundation recommends 7 to 9 h of sleep for healthy adults and 7 to 8 h of sleep for adults > 65 years.[28] However, large-scale studies are needed (1) to define the time window before and after vaccination where optimizing sleep duration is most likely beneficial, (2) to delineate the impact of sex hormones in the relationship between sleep duration and antibody response to vaccination in women, and (3) to estimate the amount of sleep debt capable of adversely affecting the response. Therefore, collecting information about sleep duration around the time of vaccination and about sex hormone levels in the millions of people who will receive vaccines and boosters against COVID-19 and other viruses is an unprecedented opportunity to study the role played by sleep duration in vaccine response.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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AUTHOR CONTRIBUTIONS

K.S., E.V.C., and M.R.I designed the meta-analysis. K.S. performed the database search. K.S. and E.V.C. identified relevant articles and extracted data; discussion and consensus meetings with A.E.R. and M.R.I resolved differences. K.S. and A.C. performed the statistical analyses. A.E.R. performed the quantitative analysis in Revman v.5.3. The first authors of the papers identified as relevant for this meta-analysis provided data to calculate effect size consistently (K.S., K.A., C.B., T.L., A.A.P., and D.J.T.). All the authors participated in the revision of the manuscript and vouch for the accuracy of the data. K.S. and E.V.C. have directly accessed and verified the data included in this meta-analysis.

DECLARATION OF INTERESTS

No author has a conflict of interest directly related to the submitted work. Outside of the submitted work, C.B. report grants from Repha GmBH, A.A.P. is the recipient of an investigator-initiated research grant from Eisai Co. Ltd, a sponsor-initiated research grant from Big Health, Inc, and serves as a consultant for NeuroGeneces, E.V.C. is a member of the Scientific Advisory Board of the Sleep Number Corporation (Minneapolis, MN), a consultant for Calibrate Health, Inc (Delaware) and the recipient of an investigator-initiated research grant on "Circadian Misalignment in Adrenal Insufficiency" from the Takeda Pharmaceutical Company.

INCLUSION AND DIVERSITY

We support inclusive, diverse, and equitable conduct of research.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
R software for statistical analyses	The comprehensive R Archive Network (CRAN)	https://cran.r-project.org/
Revman v.5.3	Cochrane Collaboration, 2014, Nordic Cochrane Center, Copenhagen, Denmark	N/A
Formulas Used to calculate SMD and 95%CI	Wilson[34] Formulas Used by the "Practical Meta-Analysis Effect Size Calculator".[29] A companion to the book entitled "Practical meta-analysis" co-authored by Lipsey M.W and Wilson, D.B. and published by Sage in 2001.[30]	https://mason.gmu.edu/~dwilsonb/downloads/esformulas.pdf
Deposited data		
Data used to estimate ES [95% CI]	This paper; Mendeley Data	https://doi.org/10.17632/dp45t6f8s6.1[31]

RESOURCE AVAILABILITY

Lead contact

Further information and requests should be directed to and will be fulfilled by the lead contact, Karine Spiegel (karine.spiegel@univ-lyon1.fr).

Materials availability

This study did not generate new unique materials.

Data and code availability

- For each selected study, sample size of each sleep group, mean, beta or odd ratio and respective dispersion parameters used to estimate ES [95% CI] are publicly available at https://doi.org/10.17632/dp45t6f8s6.1[29] as of the date of publication.
- This study did not generate original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

METHOD DETAILS

This meta-analysis followed the PRISMA guidelines.[30]

Data sources and search strategy

The PubMed database was searched from the first date available to July 19, 2022 to identify studies that examined the relationship between sleep duration and vaccine response. The combination of the terms "sleep*" and "vaccin*" was searched in the text. Filters were applied to select original articles written in English or French and reporting data on human adults (19 + years).

Two researchers (K.S. and E.V.C.) reviewed titles and abstracts of the retrieved papers to identify potentially relevant articles. Reference lists of included articles were searched to identify articles that may have been missed in the database search. One 2022 paper was identified by another source. When eligibility could not be determined based on the abstract, the full article was reviewed. When multiple published reports from the same study were available, we included only the one with the most detailed information.

Study selection

Studies were selected from the initial search if they met the following criteria: (1) were performed on healthy human adults who have nocturnal sleep habit or were case-control studies with a group of healthy controls of substantial size ($N \geq 50$), (2) assessed antibody titers and/or protection status, (3) performed subjective and/or objective measures of sleep duration, (4) were laboratory-conducted studies of sleep duration manipulation over one or more nights or prospective cohort studies, (5) were peer-reviewed original research papers.

Data extraction and quality assessment

Two investigators (K.S. & E.V.C) extracted data; discussion and consensus meetings with two additional investigators (A.E.R. & M.R.I) resolved differences. Relevant data included the first author's surname, title of the article, year of publication, number of participants, participants age and sex, study design (i.e. prospective vs. experimental study), covariates adjusted in the analysis, methods used to evaluate sleep duration (i.e. single survey item, validated questionnaire, sleep diary, actigraphy, or polysomnography), methods used to manipulate experimentally sleep duration (total sleep deprivation or sleep restriction over one or more nights), vaccine response assessed by antibody titers and/or protection status during a specified window of time post-inoculation, and measures of the association.

To optimize the quality of the meta-analysis, we obtained from the authors the information needed to calculate the relevant effect size consistently. We did so for experimental papers that used non-parametric testing to compare the means of antibody titers between sleep manipulation groups to obtain log transformed data. For all prospective studies, we requested the raw data to categorize sleep duration as short, intermediate or normal. We calculated effect sizes and 95% confidence intervals (ES [95% CI]) for the impact of short sleep (<6h) versus normal sleep on the response to vaccination. Normal sleep was defined as a sleep duration of >7h to 9h for participants under 65 years and as a sleep duration of >7h to 8h for participants aged $\geq$ 65 years, consistent with the recommendations proposed by the National Sleep Foundation.[28] Because sex and age influence humoral immune responses to vaccination,[9,25,26] we calculated a separate effect size for men and women and corrected our analyses for age, except when the sample included only young adults with a narrow age range (<10 years). Analyses were controlled for all other covariates used in the original papers. Finally, since a recent study has suggested that antibody levels are mostly affected by insufficient sleep on the closest nights around vaccination,[7] we asked the authors of the selected papers to provide sleep data collected within no more than 7 days around the date of vaccination. All authors provided the requested information.

Whenever available, both antibody titers and protection status were reported. When results were reported for individual strains or for different subtypes of antibodies (e.g., IgG1), the most significant result in the expected direction was used.

The quality of the studies included in the meta-analysis was evaluated by the Downs and Black Quality Index score system,[31] a validated checklist, which consists of five subscales (i.e., reporting, external validity, bias, confounding, and power) with a maximum score of 14 for non-randomized, non-prospective studies. All included studies scored between 14 and 22.

QUANTIFICATION AND STATISTICAL ANALYSIS

In the prospective studies, sleep duration was reported as a continuous variable. The first step of our analysis was to convert sleep duration to a categorical variable with three categories as defined above. We then calculated the impact of short sleep (<6h/night) versus normal sleep on the response to vaccination. Antibody titers were modeled with a linear regression and seroprotection status with a logistic model. All regressions included the sleep category as predictor along with covariates. Regressions and logistic regression models were fitted using the lm() and glm() functions, respectively, in R (version 4.1.1). The sleep contrast (an odds-ratio in the case of logistic models) and the associated 95% CI were calculated using the emmeans package (version 1.7.4.1). For two datasets of seroprotection status (women objective sleep[5] and[3]) models showed quasi-separation, which lead to inappropriate estimate (here, infinite upper limit for the odds-ratio).[32,33] We addressed this issue with Firth's logistic regression using the logistf package (version 1.24.1). This approach uses a penalty likelihood for the point estimates. Although it is recommended to estimate confidence intervals from profile likelihood, we used Wald confidence intervals to ensure symmetry of confidence interval around the point estimate, a required property for quantitative analysis using Revman v.5.3 (Cochrane Collaboration, 2014, Nordic Cochrane Center, Copenhagen, Denmark).

For prospective and experimental studies, we then derived the effect sizes and 95% confidence intervals (ES [95% CI]) for short sleep (<6h) versus normal sleep and for sleep restriction or deprivation versus normal sleep, respectively. ES was calculated as standardized mean difference (SMD aka Cohen's d). To calculate ES [95% CI] from the unstandardized coefficient of regression, we used equations (19) and (20) in Wilson 2017[34] (a companion to Lipsey & Wilson[35]) for the calculation of Cohen's d, equations (2) and (3) for the Hedges' correction for low sample size, and equation (4) for the calculation of the 95% CI. OR and 95%CI of the sleep predictor in logistic regression models were converted to SMD and 95% CI with equation (9) in Wilson 2017.[34] Mean and standard deviation from experimental studies were converted to ES [95% CI]) using Revman v.5.3 (Cochrane Collaboration, 2014, Nordic Cochrane Center, Copenhagen, Denmark).

Quantitative analysis was undertaken in Revman v.5.3 (Cochrane Collaboration, 2014, Nordic Cochrane Center, Copenhagen, Denmark). Overall ES were calculated assuming random effects model[36] and were interpreted as small ($\geq$0.20), medium ($\geq$0.50) or large ($\geq$0.80).[37]

Due to the small number of studies, heterogeneity among studies was not evaluated using the point estimate I^2,[38] but by examining confidence intervals, as recently recommended.[39]