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Supporting Information for

The spectral sensitivity of human circadian phase resetting and melatonin suppression to light changes dynamically with light duration

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Extended competing interests

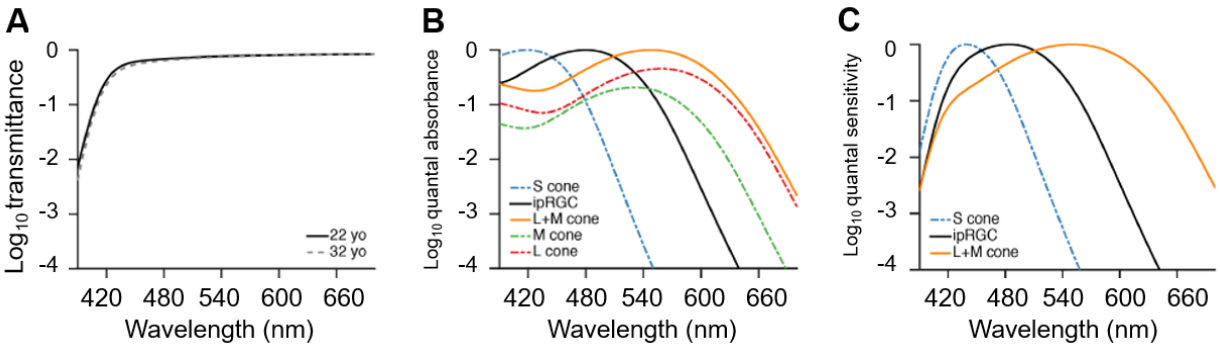

Fig. S1. (**A**) The total lens transmittance of 22- (solid line) and 32-year-old (dashed line) individuals. (**B**) The quantal absorbance spectra of the S cones ($lambda_{max}$ = 419 nm), ipRGCs ($lambda_{max}$ = 480 nm), M cones ($lambda_{max}$ = 531 nm), L cones ($lambda_{max}$ = 558 nm) and L+M cones ($lambda_{max}$ = 548 nm). (**C**) The relative quantal spectral sensitivity of S-cones, ipRGCs and L+M cones accounting for lens transmittance with maximum sensitivity of 439 nm, 484 nm, and 551 nm, respectively.

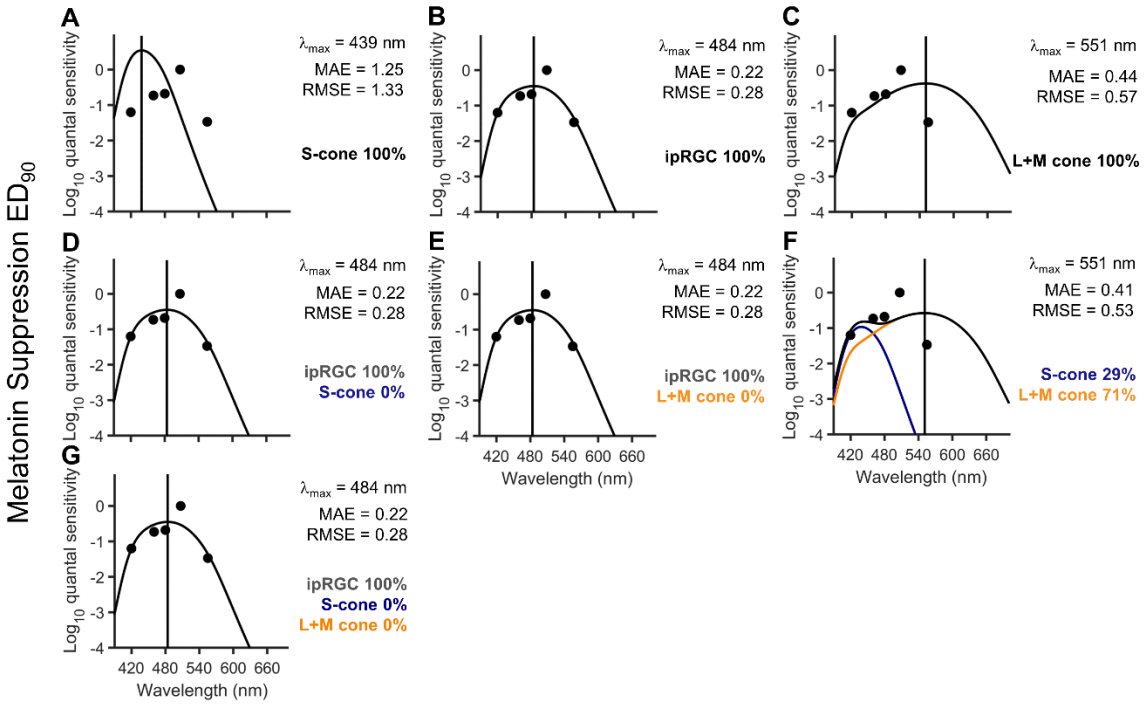

Fig. S2: (**A-C**) The S cone (**A**), ipRGC (**B**), and L+M cone (**C**) single-opsin templates plotted against the relative quantum sensitivities derived from the $\log_{10}ED_{90}$ values for the overall 6.5-hour light exposure for melatonin suppression. (**D-G**) The best-fit linear combination of ipRGCs and S cones (**D**), ipRGC and L+M cones (**E**), S cones and L+M cones (**F**) and ipRGCs, S cones, and L+M cones (**G**). The $lambda_{max}$ reported in each panel indicates the peak sensitivity of the best-fit sensitivity curve. The percentages represent the relative contribution of each spectral sensitivity curve to the overall sensitivity. The MAE and RMSE of the best fits are reported for each model.

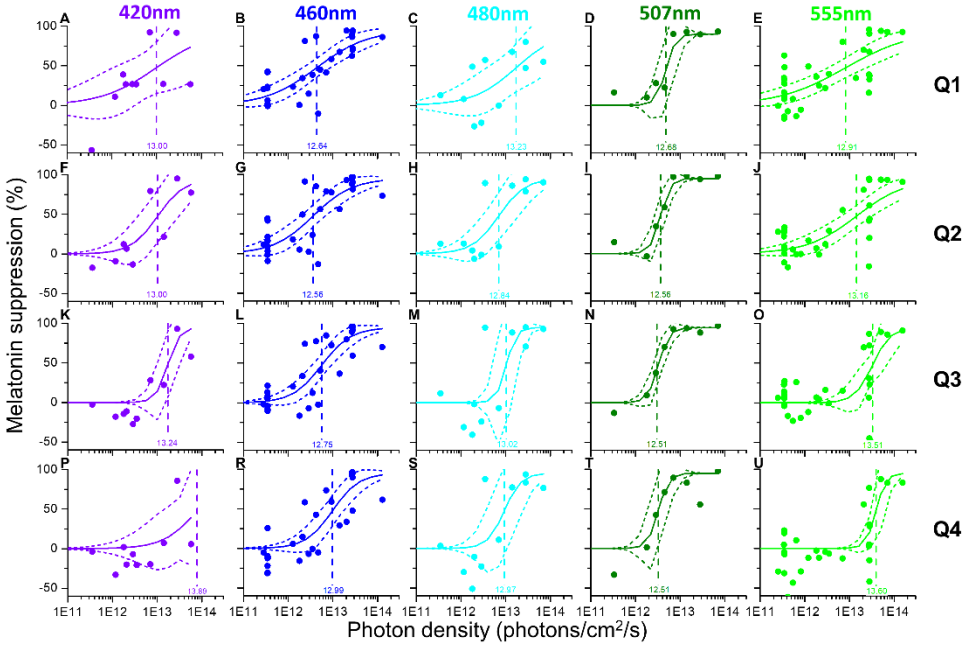

Fig. S3. The best-fit dose response curves for each quarter (Q1-4) of a 6.5-hour light exposure for melatonin suppression as a function of photon density for monochromatic wavelengths of 420 (n=9; **A**, **F**, **K**, **P**), 460 (n=30; **B**, **G**, **L**, **R**), 480 (n=11; **C**, **H**, **M**, **S**), 507 (n=8; **D**, **I**, **N**, **T**), and 555 nm (n = 33; **E**, **J**, **O**, **U**). The minimal and maximal responses were fixed at 0% and 95%, respectively; the ED_{50} and slope were allowed to vary. The $\log_{10}ED_{50}$ values (vertical dashed line) ranged from 12.51 to 13.89 photons/cm^2/sec and the slopes ranged from 0.47-3.76. The adjusted R^2 values for the fits ranged from 0.02 to 0.95.

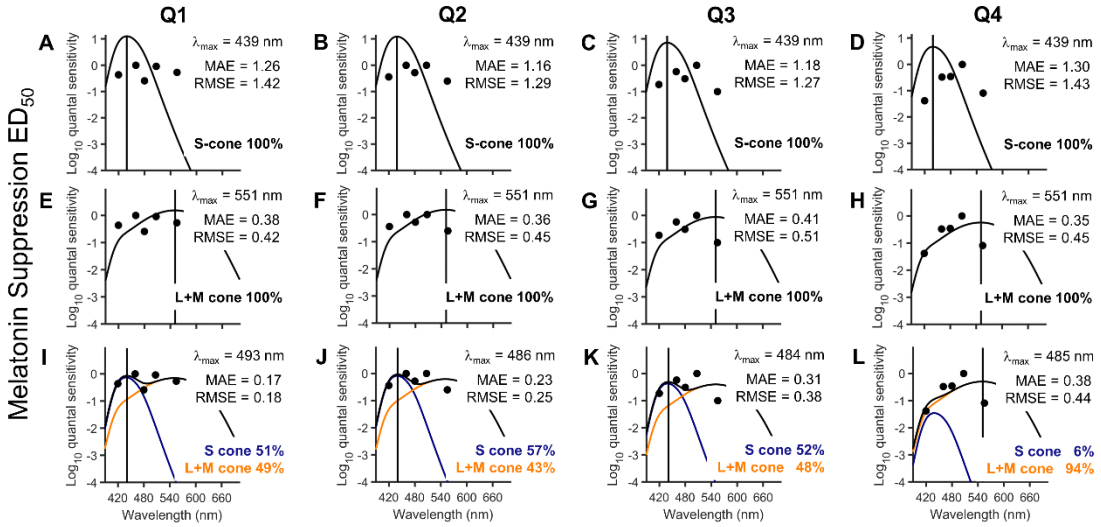

Fig. S4: (**A-D**) The S-cone opsin template and (**E-H**) L+M cone opsin template plotted against the relative quantum sensitivities derived from the $\log_{10}ED_{50}$ values for each quarter (Q1-4 from left to right) of a 6.5-hour light exposure for melatonin suppression. (**I-L**) The best-fit linear combination of S cones and L+M cones. In each panel, the gray solid line represents the ipRGC sensitivity curve, the blue solid line represents the S cone sensitivity curve, and the orange solid line represents the L+M cone sensitivity curve, whereas the black solid line shows the sum of the sensitivity curves, i.e., the best fit through the data points. The $lambda_{max}$ reported in each panel indicates the peak sensitivity of the best-fit sensitivity curve. The MAE and RMSE of the best fits are reported for each model.

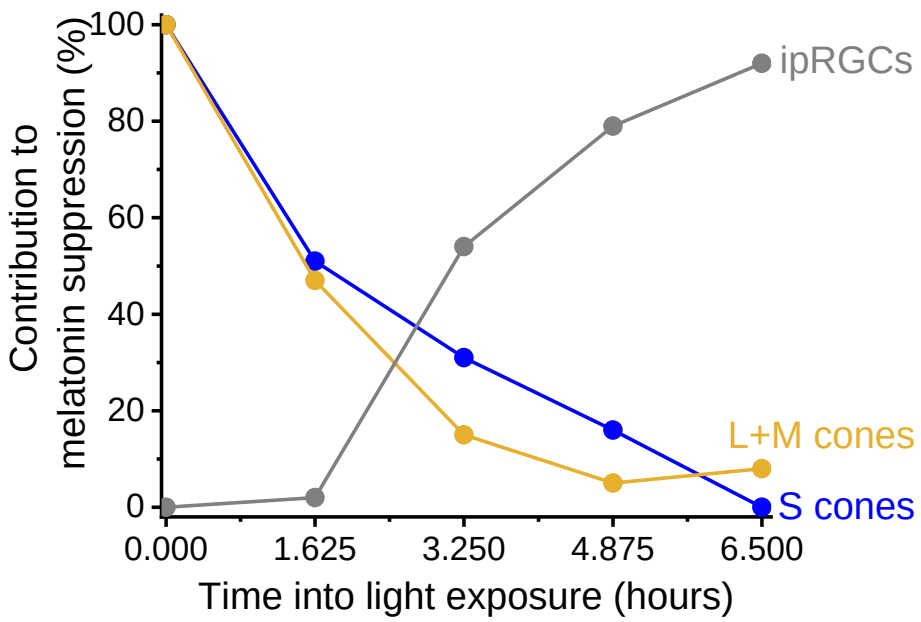

Fig. S5: The time course of the contributions from the ipRGCs (gray symbols and line), the S cones (blue symbols and line), and the L+M cones (orange symbols and line) based on the fits presented in Fig. 3M-P.

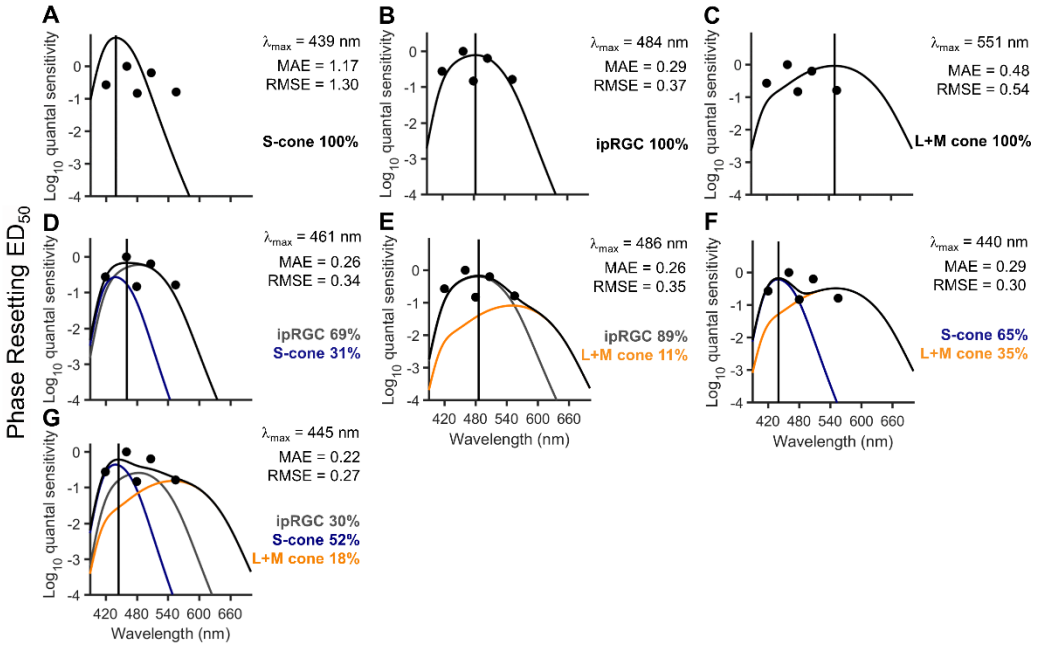

Fig. S6: (**A-C**) The S cone (**A**), ipRGC (**B**), and L+M cone (**C**) single-opsin templates plotted against the relative quantum sensitivities derived from the $log_{10}ED_{50}$ values for the overall 6.5-hour light exposure for circadian phase resetting without the data at 620 nm included in the fits. (**D-G**) The best-fit linear combination of ipRGCs and S cones (**D**), ipRGC and L+M cones (**E**), S cones and L+M cones (**F**) and ipRGCs, S cones, and L+M cones (**G**). The $lambda_{max}$ reported in each panel indicates the peak sensitivity of the best-fit sensitivity curve. The percentages represent the relative contribution of each spectral sensitivity curve to the overall sensitivity. The MAE and RMSE of the best fits are reported for each model.

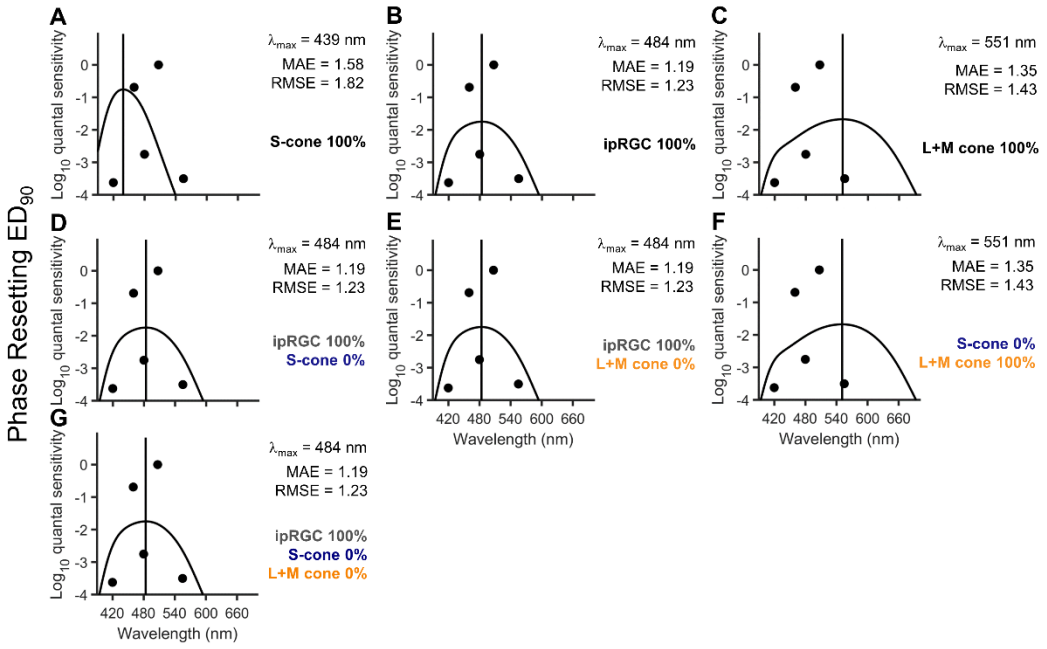

Fig. S7: (**A-C**) The S cone (**A**), ipRGC (**B**), and L+M cone (**C**) single-opsin templates plotted against the relative quantum sensitivities derived from the $log_{10}ED_{90}$ values for the overall 6.5-hour light exposure for circadian phase resetting without the 620nm data. (**D-G**) The best-fit linear combination of ipRGCs and S cones (**D**), ipRGC and L+M cones (**E**), S cones and L+M cones (**F**) and ipRGCs, S cones, and L+M cones (**G**). The $lambda_{max}$ reported in each panel indicates the peak sensitivity of the best-fit sensitivity curve. The percentages represent the relative contribution of each spectral sensitivity curve to the overall sensitivity. The MAE and RMSE of the best fits are reported for each model.

Extended Competing Interests:

The authors declare no conflicts of interest directly related to the work presented in this manuscript. In the interest of full disclosure, the authors have listed all potential conflicts of interest:

M.S.H.: Paid limited consulting to The MathWorks, Inc; honoraria and travel funds as an invited speaker from the Providence Sleep Research Interest Group and the Mayo Clinic Metabolomics Resource Core; honoraria as a reviewer for the Fonds de la Recherche Scientifique.

M.L.A.: No competing interests.

S.A.R.: Holds patents for Prevention of Circadian Rhythm Disruption by Using Optical Filters and Improving sleep performance in subject exposed to light at night; S.A.R. owns equity in Melcort Inc.; has provided paid consulting services to Sultan & Knight Limited, Bambu Vault LLC, Lucidity Lighting Inc.; and has received honoraria as an invited speaker and travel funds from Starry Skies Lake Superior, PennWell Corp., and Seoul Semiconductor Co. Ltd. These interests were reviewed and managed by Brigham and Women's Hospital and Partners HealthCare in accordance with their conflict of interest policies.

S.M.R.: Research funding from Philips Lighting; Vanda Pharmaceuticals; ResMed Foundation; Respironics Sleep and Respiratory Research Foundation; Cephalon Inc.; and Takeda Pharmaceuticals North America.

M.R.: No competing interests.
G.C.B.: Research funding from Philips Lighting BV; OSRM/Sylvania; Apollo Health; process patents for use of short-wavelength light for resetting the human circadian pacemaker and improving alertness and performance, assigned to Thomas Jefferson University and Brigham and Women's Hospital.

C.A.C.: Funding: NASA, NIH, National Institute for Occupational Safety and Health–Centers for Disease Control and Prevention, National Space Biomedical Research Institute, and Department of Homeland Security's Federal Emergency Management Agency; Financial relationships: consulting fees from or served as a paid member of scientific advisory boards for Actelion Ltd., Bombardier Inc., Cephalon Inc., Delta Airlines, Eli Lilly and Co., Fedex Kinko's, Federal Motor Carrier Safety Administration, U.S. Department of Transportation; Fusion Medical Education LLC, Garda Síochána Inspectorate (Dublin, Ireland), Hypnion Inc. (acquired by Eli Lilly and Co. in April 2007), Global Ground Support, Johnson & Johnson, Koninklijke Philips Electronics, N.V., Morgan Stanley, Sanofi-Aventis Groupe, Portland Trail Blazers, Respironics Inc., Sepracor Inc., Sleep Multimedia Inc., Sleep Research Society (for which he served as president), Somnus Therapeutics Inc., Takeda Pharmaceuticals, Vanda Pharmaceuticals Inc., Vital Issues in Medicine, Warburg-Pincus, and Zeo Inc. He owns an equity interest in Lifetrac Inc.; Somnus Therapeutics Inc.; Vanda Pharmaceuticals Inc.; and Zeo Inc. and received royalties from McGraw Hill, the New York Times, and Penguin Press. He has received lecture fees from the Accreditation Council of Graduate Medical Education; Alfresa; the American Academy of Allergy, Asthma and Immunology Program Directors; American Physiological Society; Association of University Anesthesiologists; Baylor College of Medicine; Beth Israel Deaconess Medical Center; Brown Medical School–Rhode Island Hospital; Cephalon Inc.; Clinical Excellence Commission (Australia); Dalhousie University; Duke University Medical Center; Harvard School of Public Health, Harvard University; Institute of Sleep Health Promotion; London Deanery; Morehouse School of Medicine; Mount Sinai School of Medicine; National Emergency Training Center Federal Emergency Management Agency; NIH; North East Sleep Society; Osaka University School of Medicine; Partners HealthCare Inc.; Sanofi-Aventis Inc.; St. Lukes Roosevelt Hospital; Takeda; Tanabe Seiyaku Co. Ltd.; Tokyo Electric Power Company; University of Michigan; University of Pennsylvania; University of Pittsburgh; University of Tsukuba; University of Virginia Medical School; University of Washington Medical Center; University of Wisconsin Medical

School; and World Federation of Sleep Research and Sleep Medicine Societies. He has also received research prizes with monetary awards from the American Academy of Sleep Medicine, American Clinical and Climatological Association, Association for Patient-Oriented Research, National Institute for Occupational Safety and Health, National Sleep Foundation, and Sleep Research Society; clinical trial research contracts from Cephalon Inc., Merck & Co. Inc., and Pfizer Inc.; and an investigator-initiated research grant from Cephalon Inc. His research laboratory at the Brigham and Women's Hospital has received unrestricted research and education funds and/or support for research expenses from Cephalon Inc.; Koninklijke Philips Electronics, N.V.; ResMed; and the Brigham and Women's Hospital. The Harvard Medical School Division of Sleep Medicine (HMS/DSM), which he directs, has received unrestricted research and educational gifts and endowment funds from Boehringer Ingelheim Pharmaceuticals Inc.; Cephalon Inc.; George H. Kidder, Esq.; Gerald McGinnis; GlaxoSmithKline; Herbert Lee; Hypnion; Jazz Pharmaceuticals; Jordan's Furniture; Merck & Co. Inc.; Peter C. Farrell, Ph.D.; Pfizer; ResMed; Respironics Inc.; Sanofi-Aventis Inc.; Sealy Inc.; Sepracor Inc.; Simmons; Sleep Health Centers LLC; Spring Aire; Takeda Pharmaceuticals; and Tempur-Pedic. The HMS/DSM has received gifts from many outside organizations and individuals, including Axon Sleep Research Laboratories Inc.; Boehringer Ingelheim Pharmaceuticals Inc.; Catalyst Group; Cephalon Inc.; Clarus Ventures; Eli Lilly and Co.; Farrell Family Foundation; Fisher & Paykel Healthcare Corporation; George H. Kidder, Esq.; GlaxoSmithKline; Hypnion Inc.; Jordan's Furniture; Merck Research Laboratories; Park Place Corporation; Respironics Inc.; Sanofi-Aventis Inc.; Select Comfort Corporation; Sepracor Inc.; Sleep Health Centers LLC; Takeda Pharmaceuticals; Tempur-Pedic Medical Division; Total Sleep Holdings; and Vanda Pharmaceuticals Inc. The HMS/DSM Sleep and Health Education Program has received Educational Grant funding from Cephalon Inc.; Takeda Pharmaceuticals; Sanofi-Aventis Inc.; and Sepracor Inc. He is the incumbent of an endowed professorship provided to Harvard University by Cephalon Inc. and holds a number of process patents in the field of sleep or circadian rhythms (for example, photic resetting of the human circadian pacemaker). Since 1985, he has also served as an expert witness on various legal cases related to sleep and/or circadian rhythms. Patents: inventor on several patents related to assessment and modification of the phase and amplitude of the endogenous circadian rhythm, apparatus for delivering high-intensity light to modify circadian rhythms, a method to modify circadian rhythms and enhance alertness and performance with short wavelength light, and a test for evaluating visual function in visually impaired people, which are assigned to Brigham and Women's Hospital; and a patent on a wrist-worn activity monitor that monitors exposure to light of different wavelengths, which is assigned to Philips Respironics.

M.A.: No competing interests.

J.J.G.: Conference travel support, Apollo Lighting.

S.W.L.: Reports commercial interests from the last 3 years (2018-2021). His interests are reviewed and managed by Brigham and Women's Hospital and Partners HealthCare in accordance with their conflict of interest policies. No interests are directly related to the research or topic reported in this paper but, in the interests of full disclosure, are outlined below. He has received consulting fees from the BHP Billiton, EyeJust Inc., Noble Insights, Rec Room, Six Senses, Stantec and Team C Racing; and has current consulting contracts with Akili Interactive; Apex 2100 Ltd.; Consumer Sleep Solutions; Headwaters Inc.; Hintsa Performance AG; KBR Wyle Services, Light Cognitive; Lighting Science Group corporation/HealthE; Mental Workout/Timeshifter and View Inc. He has received honoraria and travel or accommodation expenses from Bloxhub, Emory University, Estée Lauder, Ineos, MIT, Roxbury Latin School, and University of Toronto, and travel or accommodation expenses (no honoraria) from IES, Mental Workout, Solemma, and Wiley; and royalties from Oxford University Press. He holds equity in iSleep pty. He has received an unrestricted equipment gift from F. Lux Software LLC, a fellowship gift from Stockgrand Ltd and holds an investigator-initiated grant from F. Lux Software LLC and a Clinical Research Support Agreement and Clinical Trial Agreement with Vanda Pharmaceuticals Inc. He is an unpaid Board Member of the Midwest Lighting Institute (non-profit). He was a

Program Leader for the CRC for Alertness, Safety and Productivity, Australia, through an adjunct professor position at Monash University (2015-2019). He is part-time adjunct professor at the University of Surrey, UK. He holds a pending patent for a ‘Method and system for generating and providing notifications for a circadian shift protocol’ (US20190366032A1). He has served as a paid expert in legal proceedings related to light, sleep and health.