

the predictability of the IMPACT-R test and the PFA COL/ADP; however, with the corrected cutoff values, the Innovance PFA P2Y predicted the primary end point (where it did not with the incorrectly calculated cutoff in the original article).

In addition, we observed an error in Figure 2 concerning the PFA-100 system. The closure times of the PFA COL/ADP are correct, but for the Innovance P2Y the lower line indicates patients with an end point and should not be dotted.

A correction appears in this issue of *JAMA*, and the article has been corrected online. We sincerely regret the errors in the initially calculated cutoff values and subsequent interpretation of the data and apologize for the confusion caused by publication of this incorrect information.

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Conflict of Interest Disclosures: The authors has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr ten Berg reported receipt of speakers' bureau fees from sanofi-aventis, Eli Lilly, Bristol-Myers Squibb, and Merck and providing consultancy services for sanofi-aventis, Eli Lilly, Schering-Plough, and GlaxoSmithKline.

Independent Statistical Analysis: At the request of the authors, Jan G. P. Tijssen, PhD, Clinical Epidemiology and Biostatistics, Academic Medical Centre, University of Amsterdam, was asked to conduct an independent statistical analysis of the correction. Dr Tijssen reviewed the original article, the description of the errors, and the proposed corrections. He received copies of the original dataset and verified that the authors made an error in their reliance on and interpretation of the ROC curve generated by the automated algorithm for calculating the optimal cut-off values of the test variable. Dr Tijssen reported that he checked all of the calculations, visually inspected the ROC curves, and verified that the cut-off values in the corrected article are the optimal values and that the sensitivity and specificity are correctly presented in the corrected article. Dr Tijssen did not request and did not receive financial compensation for his efforts.

1. Breet NJ, van Werkum JW, Bouman HJ, et al. Comparison of platelet function tests in predicting clinical outcome in patients undergoing coronary stent implantation. *JAMA*. 2010;303(8):754-762.

RESEARCH LETTER

Effect of 1 Week of Sleep Restriction on Testosterone Levels in Young Healthy Men

To the Editor: Chronic sleep curtailment is endemic in modern societies. The majority of the daily testosterone release in men occurs during sleep.¹ Sleep fragmentation and obstructive sleep apnea are associated with reduced testosterone levels.² In older men, morning testosterone levels are partly predicted by total sleep time.³ Testosterone is critical in male sexual behavior and reproduction, but also has important beneficial effects on muscle mass and strength, adiposity, bone density, and vigor and well-being.⁴ We investigated the effect of 1 week of sleep restriction on testosterone levels in young healthy men.

Methods. The protocol was approved by the University of Chicago institutional review board. Volunteers responded to flyers posted around campus. Exclusion crite-

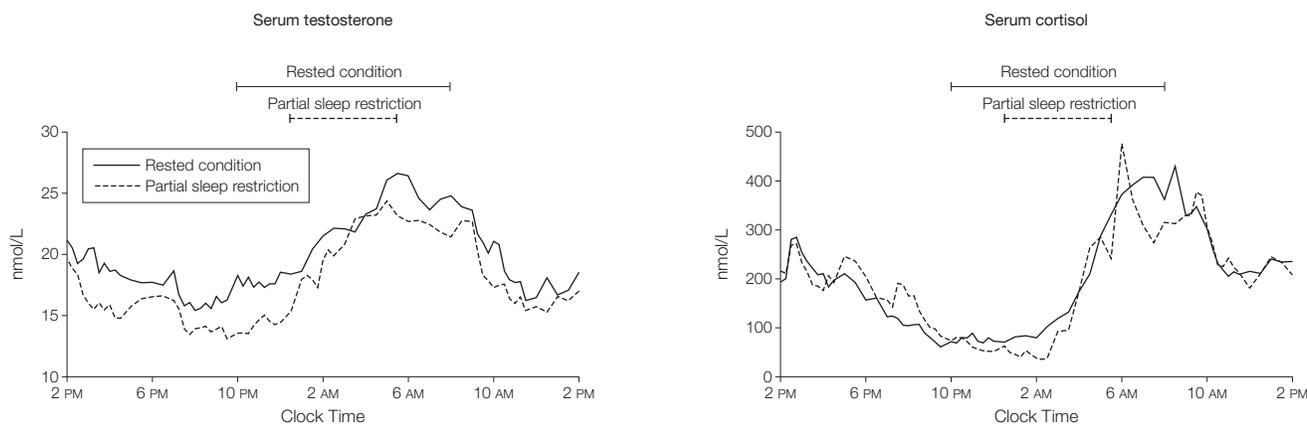
ria included a history of endocrine or psychiatric disorders, irregular bedtimes, and sleep complaints. Written informed consent was obtained from 28 persons. Ten men passed all screening tests and completed the study, which was performed between January 2003 and September 2009. The sample size was estimated using data from previous work on the hormonal impact of sleep restriction.

After 1 week of 8-hour bedtimes (from 11 PM to 7 AM) at home, the participants spent 11 days in the laboratory for 3 nights of 10-hour bedtimes (from 10 PM to 8 AM; rested condition) followed by 8 nights of 5-hour bedtimes (from 12:30 AM to 5:30 AM; sleep restriction). Sleep was recorded each night and visually scored in stages 1, 2, 3, 4, and rapid eye movement (REM). Blood sampling every 15 to 30 minutes for 24 hours was initiated after the second 10-hour night and after the seventh 5-hour night. Samples were assayed for total testosterone and cortisol using an immunochemiluminescent assay (Immulite, Los Angeles, California). (To convert serum testosterone to ng/dL, divide by 0.0347; to convert serum cortisol to µg/dL, divide by 27.588.) Participants completed the visual analog scales for global vigor and global affect at 2-hour intervals each day.⁵ Comparisons between conditions were performed using 2-sided nonparametric Wilcoxon tests with a significance level of .05 (JMP7; SAS Institute, Cary, North Carolina).

Results. The 10 healthy men had a mean (SD) age of 24.3 (4.3) years and a mean (SD) body mass index of 23.5 (2.4) (calculated as weight in kilograms divided by height in meters squared). Total (SD) sleep time decreased from 8 hours 55 minutes (35 min) to 4 hours 48 minutes (6 min) with sleep restriction ($P=.002$). Relative to the rested condition, during each restricted night, participants lost a total (SD) of 2 hours 45 minutes (29 min) of stage-2 sleep ($P=.002$) and 1 hour 3 minutes (18 min) of REM sleep ($P=.002$) and gained 9 minutes (8 min) of sleep in stages 3 + 4 ($P=.01$).

During waking hours common to both conditions (8 AM-10 PM), testosterone levels were lower after sleep restriction than in the rested condition (16.5 [2.8] nmol/L vs 18.4 [3.8] nmol/L; $P=.049$). The effect of restricted sleep was especially apparent between 2 PM and 10 PM (15.5 [3.1] nmol/L vs 17.9 [4.0] nmol/L; $P=.02$). Daytime cortisol profiles were similar under both conditions (FIGURE). Daily sleep restriction was associated with a progressive decrease in mean (SD) vigor scores from 28 (5) after the first night to 19 (7) after the seventh night ($P=.002$).

Comment. Daytime testosterone levels were decreased by 10% to 15% in this small convenience sample of young healthy men who underwent 1 week of sleep restriction to 5 hours per night, a condition experienced by at least 15% of the US working population. By comparison, normal aging is associated with a decrease of testosterone levels by 1% to 2% per year.⁶ This testosterone decline was associated with lower vigor scores but not with increased levels of cortisol, a stress-responsive hormone that can inhibit gonadal function. Symptoms and

Figure. 24-Hour Profiles of Serum Testosterone and Serum Cortisol According to Bedtime Condition

Shown are mean values. In the rested condition, bedtimes were from 10 PM to 8 AM. Values for partial sleep restriction were taken after 1 week of restriction, for which bedtimes were from 12:30 AM to 5:30 AM. On average over the 68 time points, the SD of testosterone levels at each time point was 5.01 nmol/L (range, 2.98-7.53 nmol/L) in the rested condition and 4.26 nmol/L (range, 2.82-6.92 nmol/L) in the restricted condition. On average over the 68 time points, the SD of cortisol levels at each time point was 67.1 nmol/L (range, 15.2-142.7 nmol/L) in the rested condition and 54.0 nmol/L (range, 7.7-162.3 nmol/L) in the restricted condition.

signs of androgen deficiency include low energy, reduced libido, poor concentration, and increased sleepiness, all of which may be produced by sleep deprivation in healthy individuals. Additional investigations of the links between sleep and testosterone are needed to determine whether sleep duration should be integrated in the evaluation of androgen deficiency.

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Author Contributions: Dr Leproult had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Leproult, Van Cauter.

Acquisition of data: Leproult, Van Cauter.

Analysis and interpretation of data: Leproult, Van Cauter.

Drafting of the manuscript: Leproult, Van Cauter.

Critical revision of the manuscript for important intellectual content: Leproult, Van Cauter.

Statistical analysis: Leproult, Van Cauter.

Obtained funding: Van Cauter.

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1. Axelsson J, Ingre M, Akerstedt T, Holmbäck U. Effects of acutely displaced sleep on testosterone. *J Clin Endocrinol Metab.* 2005;90(8):4530-4535.

- Andersen ML, Tufik S. The effects of testosterone on sleep and sleep-disordered breathing in men: its bidirectional interaction with erectile function. *Sleep Med Rev.* 2008;12(5):365-379.
- Penev PD. Association between sleep and morning testosterone levels in older men. *Sleep.* 2007;30(4):427-432.
- Bremner WJ. Testosterone deficiency and replacement in older men. *N Engl J Med.* 2010;363(2):189-191.
- Monk TH. A visual analogue scale technique to measure global vigor and affect. *Psychiatry Res.* 1989;27(1):89-99.
- Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR; Baltimore Longitudinal Study of Aging. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. *J Clin Endocrinol Metab.* 2001;86(2):724-731.

CORRECTIONS

Errors: In the Original Contribution entitled "Standard- vs High-Dose Clopidogrel Based on Platelet Function Testing After Percutaneous Coronary Intervention," published in the March 16, 2011, issue of *JAMA* (2011;305[11]:1097-1105), data in a figure were misplaced, a conflict of interest statement was omitted, and Dr Stillabower's name was misspelled.

The hazard ratios in Figure 2 were placed in the wrong panels. Dr Topol's conflict of interest statement should have read: "Dr Topol reported receiving consulting fees from Bristol-Myers Squibb/sanofi-aventis and Daiichi Sankyo/Lilly & Co."

Error in Calculation of Cutoff Values: In the Original Contribution entitled "Comparison of Platelet Function Tests in Predicting Clinical Outcome in Patients Undergoing Coronary Stent Implantation," published in the February 24, 2010, issue of *JAMA* (2010;303[8]:754-762), an error in the calculation of cutoff values occurred. Due to the negative concordance of 3 of the 8 tests evaluated in the Popular study, the initially calculated ROC curves were mirrored, leading to incorrect cutoff values being reported for these 3 tests. This specific error affects multiple numbers, percentages, and associated odds ratios with confidence intervals in several paragraphs, tables, and figures. The correctly calculated cutoff values do not have any effect on the predictability of the IMPACT-R test and the PFA-100 Collagen/ADP; however, with the corrected cutoff values, the Innovance PFA P2Y predicted the primary end point. In addition, in Figure 2 the lower line for Innovance P2Y indicates patients with an end point and should not have been dashed. The corrected article and supplemental materials were replaced on May 11, 2011. An accompanying letter describes the discovery of this error and correction of this misclassification fully.