

Don't take their word for it — moving towards objective measures in sleep epidemiology

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The use of objective measures in epidemiological research may be limited by the cost or inconvenience of obtaining objective measures, which can provide greater insight into links between sleep and health. The importance of sleep and chronobiology for human health has been fully recognized only relatively recently (i.e. within the past two decades). This has delayed the inclusion of related measures in large prospective studies. At its inception in 2006, the UK Biobank study included a number of brief questions related to sleep — sleep duration, ease of getting up in the morning, chronotype, daytime napping, frequency of sleep disturbances, snoring, and daytime napping. Some self-report measures are remarkably accurate. Chronotype, for example, has been shown to correlate strongly with physiological measures¹ and even the single chronotype question used by the UK Biobank encompasses a heritability which overlaps with and is comparable in magnitude to that of the full questionnaire². By contrast, self-reported sleep duration is notoriously unreliable^{3,4} and inconsistently assessed among studies. This makes the addition of accelerometry data for approximately 100,000 UK Biobank participants so valuable, even though it occurred five years after baseline. This subsample has previously provided crucial confirmation for GWAS of sleep duration^{5,6}. The UK Biobank dataset has been used in an article published in the present issue⁷ to probe associations between mortality (all-cause and cause-specific) and several sleep characteristics, including duration, continuity, and timing of sleep, with an average follow-up time of 6.8 years. This complements a number of previously performed studies with smaller participant numbers⁸⁻¹⁰. The relationship between sleep duration and mortality had previously been analysed in the UK Biobank sample^{11,12}. The UK Biobank data confirm a J-shaped curve of mortality versus sleep duration, indicating significantly increased risk of mortality among short sleepers (<7 hours). This finding first emerged from self-reported data and has been confirmed with the new objective measures in a way which fits with what we know about sleep being imperative to health. Previous research, predominantly based on self-reported sleep duration, observed increased mortality among longer sleepers as well, which has always been controversial since an underlying mechanism

remained to be identified. A prior review³ found that the “U-shape” was only present in studies that assess sleep duration based on questions asking respondents to report amount of sleep but studies that used time in bed (i.e. habitual bedtime to habitual wake) did not observe a U-shape. The current study, which used objectively estimated sleep duration, observed no significant associations between long sleep and all-cause or cause-specific mortality, suggesting that self-reported sleep duration may be biased.

Another strength of the new article by Saint-Maurice and colleagues⁷ is that it includes more than sleep duration, such as sleep timing. They observed significant associations between sleep timing and mortality risk, which is consistent with prior studies demonstrating the importance of chronotype and health. The paper reports a tendency towards a U-shaped mortality curve for the midpoint of L5, the non-parametric value representing the five hours of lowest activity over the 24-hour period¹³. It appears that both very early and very late sleepers have increased mortality. Does that contradict our previous report¹⁴ (also from UK Biobank data) that later chronotype is associated with elevated mortality, but earlier chronotype is not? Our interpretation is that it does not, and that what it reflects that a sleeping schedule adjusted to our natural chronotype (which, for the majority of us, is intermediate) is optimal for good health. Further, the clock is circular and therefore “very early” could also be very, very late.

One could argue that the greatest increase in quality from self-reported to objective measure pertains to the question “Do you have trouble falling asleep at night or do you wake up in the middle of the night?” which was asked at baseline in the UK Biobank. Although the answers to this question may reflect a multitude of intrinsic sleep disorders and extrinsic sleep disturbances, it was successfully applied to GWAS analysis^{15,16} and we reported that frequent sleep disturbances were associated with increased

mortality.¹⁷⁴ Interestingly, however, none of the objective measures of sleep continuity (wake after sleep onset or WASO, sleep efficiency, number of 5-minute awakenings, and number of nights within the one-week measurement period with WASO >30 min) showed significant associations with mortality, except for an association between the latter measure and cancer mortality. This is a surprising finding, but perhaps also a reassuring one. It seems to suggest that, for the ultimate health outcome, the most important factor is how much sleep we get — not whether it is fragmented or not. In the absence of concrete evidence as to whether or not consolidated sleep is an ancestral or acquired feature of our species, this evidence seems to suggest that it does not increase the odds of survival.

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