

Improvement in Sleep Duration and Maintenance with Ion-Powered Continuous Release and Absorption Melatonin in a Cohort of Patients with Chronic Short Sleep Duration: Results from a Patient-Reported Outcomes Study

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Introduction

The long-term cumulative effects of sleep loss and sleep disorders has negative health consequences, including increased risk of hypertension, diabetes, obesity, depression, heart attack, and stroke.¹

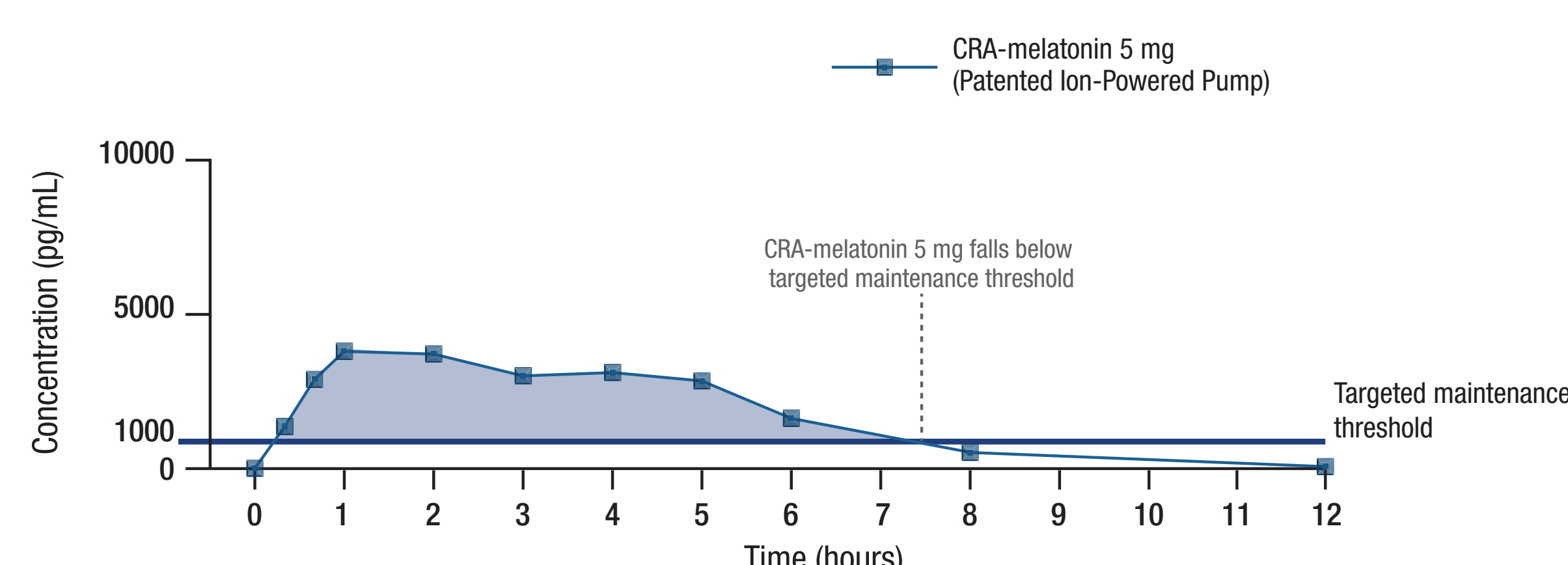
At least 35 epidemiologic studies have been published, which observe an association between sleep duration and health outcomes.² In some of these studies, and others, short-sleep durations were associated with increased morbidity or mortality risk.³ The AASM/SRS consensus statement recommends that 7 hours or more/night is optimal to promote good health.⁴

A study looking at the association of suboptimal sleep and greater burden of disease found that patients who typically slept the least—5 hours or less—had a QALY (Quality-Adjusted Life Years) that was nearly one-third lower than those patients who slept 7 hours/night.⁵ Additionally, short-sleep duration lowers productivity levels and increases the risk of mortality, leading to a loss of roughly 1.2 million working days and a cost of up to \$411 billion per year—which translates to 2.28% of the United States GDP.⁶

Further, morbid or extreme short sleep duration of 4 hours or less, was associated with increased mortality from cardiovascular disease (CVD), non-CVD/non-cancer causes, and all-cause mortality for both men and women.⁷ People are searching for non-drug alternatives to aid their sleep efforts, as evidenced by the over 3 million US adult melatonin users.⁸

Continuous Release and Absorption melatonin (CRA-melatonin) with its IPP (Ion-Powered Pump) delivery technology demonstrated the desired 7-hour pharmacokinetic (PK) profile in the REMfresh Absorption Kinetics Trial (REMAKT).⁹

Figure 1. Median Concentrations of Plasma Melatonin after 5 mg CRA-melatonin



REMAKT was a randomized, crossover, clinical PK evaluation in 10 healthy non-smoking adults. The median time it took plasma melatonin levels to exceed the initial threshold level of 100 pg/mL was 0.131 hours for CRA-melatonin. Melatonin levels showed a median plateau time of 6.7 hours with CRA-melatonin. There were no TEAEs seen with CRA-melatonin.

Methods

The REMfresh Short Sleep Cohort Assessment (REMSS) analyzed a cohort of 311 patients who reported sleeping 4 hours or less nightly from REMfresh Duration Validation (REMVAl) study, a 1,116 self-reported patient-outcomes study. This cohort analysis was designed to obtain clinically relevant information from patients experiencing morbid short sleep disturbances, including sleep patterns and melatonin usage before taking CRA-melatonin, sleep duration before and after taking CRA-melatonin, improvement in sleep latency, maintenance

and quality after taking CRA-melatonin, and overall product satisfaction.

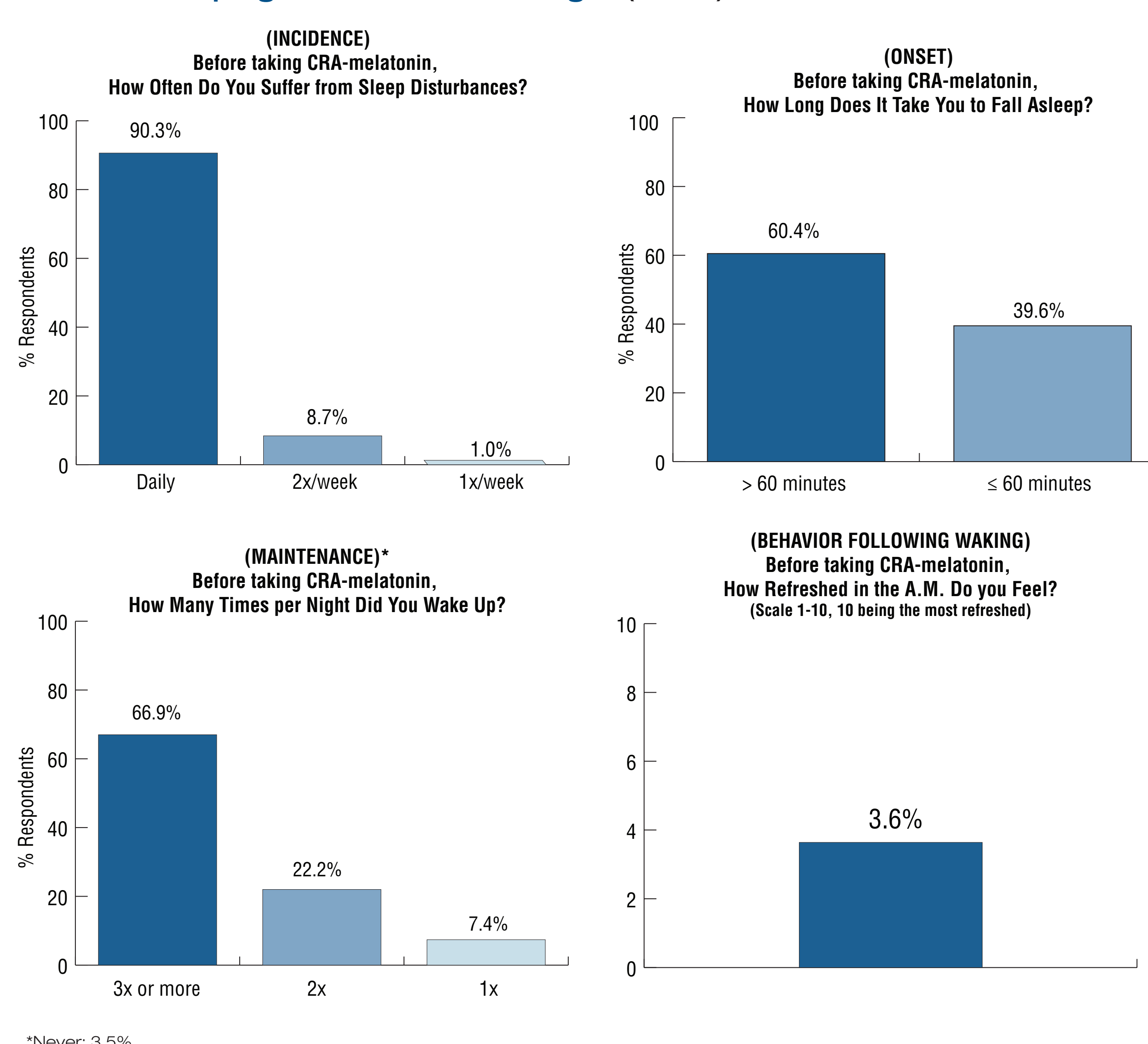
Patients with sleep disturbances in the general population, who received a sample of CRA-melatonin (REMfresh) from their physicians, were invited to complete a 13-question online survey through Survey Monkey. The authors note that there may be inherent bias in these types of open-label studies.

Survey Questions

1. Prior to taking CRA-melatonin, how often did you suffer from sleep disturbances?
2. Prior to taking CRA-melatonin, on average, how long did it take you to fall asleep?
3. Prior to taking CRA-melatonin, on average, how many times a night did you wake up?
4. Prior to taking CRA-melatonin, how refreshed did you feel when you woke in the morning? (Scale 1-10, with 10 being the most refreshed)
5. Prior to taking CRA-melatonin, how many hours of sleep per night did you get?
6. Since taking CRA-melatonin, how many hours of sleep per night do you get? Overall, how would you rate the improvement in your sleep onset (time it takes to fall asleep) while taking CRA-melatonin?
7. Overall, how would rate your improvement in your sleep maintenance (staying asleep) while taking CRA-melatonin?
8. Overall, how would rate the improvement in your total sleep quality while taking CRA-melatonin?
9. Have you taken other brands of melatonin in the past?

Results

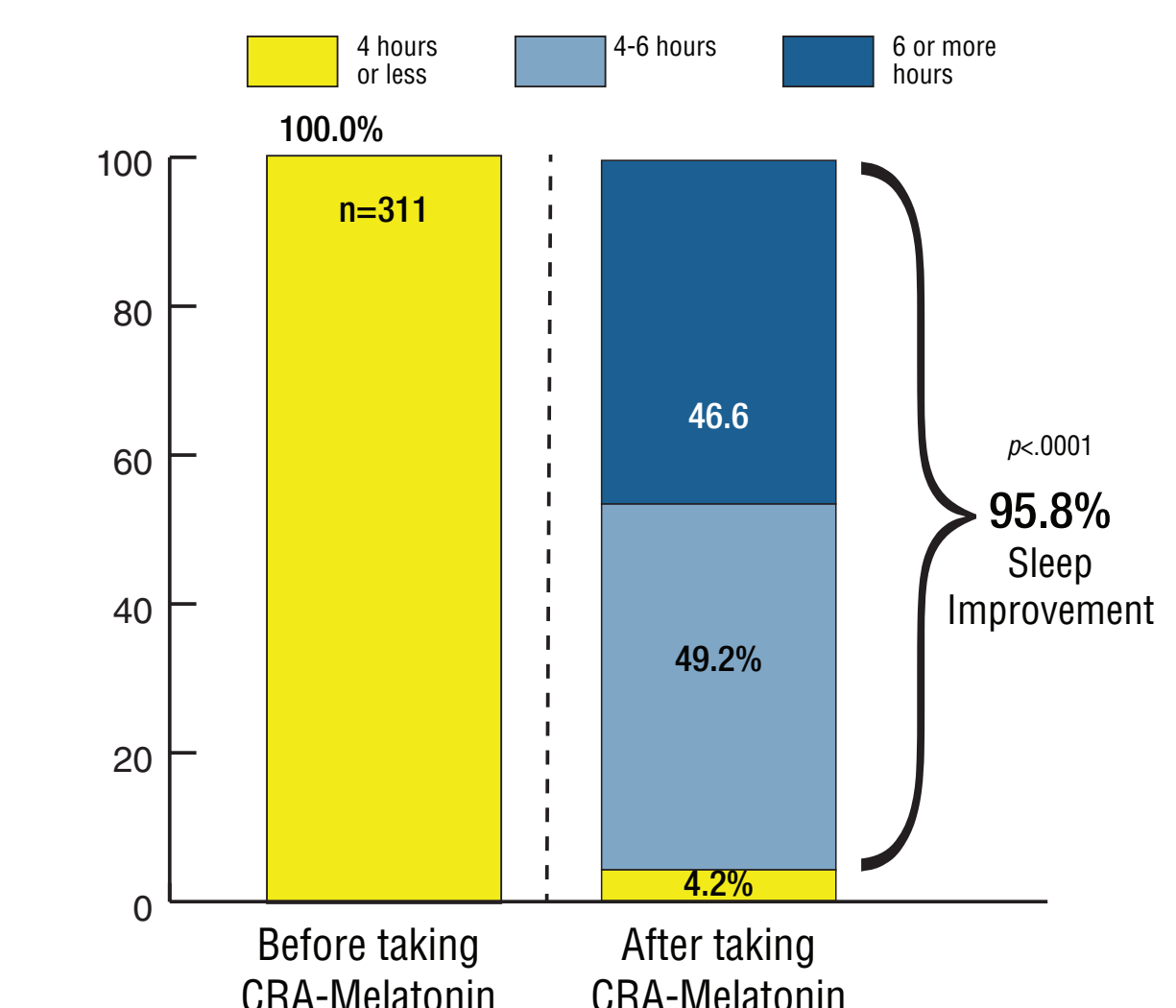
Figure 2. Patient Key Sleep Parameters Before Taking CRA-melatonin in Patients Sleeping 4 Hours or Less/Night (n=311)



*Never: 3.5%

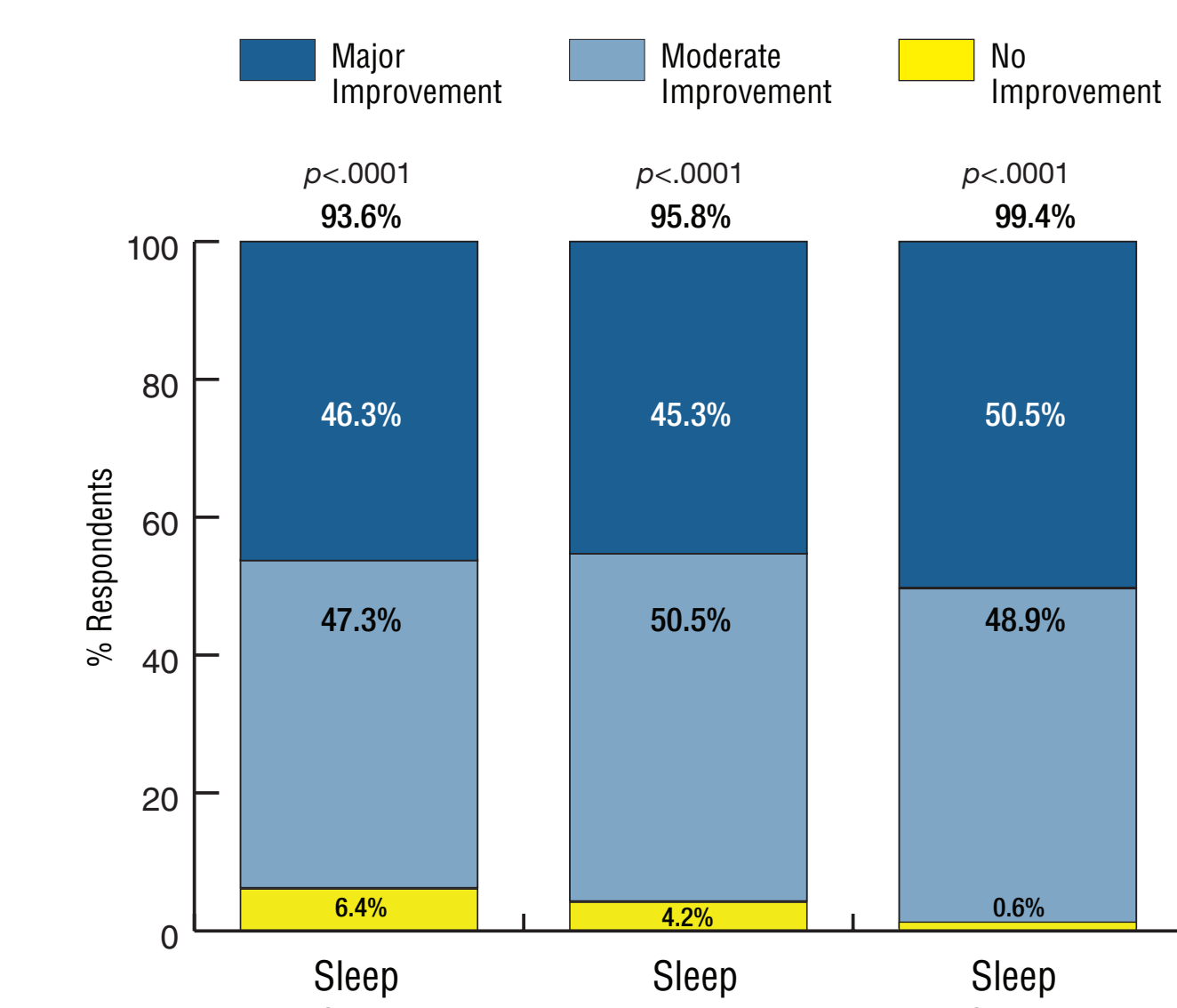
Responses to questions 1-4, prior to taking CRA-melatonin: 1) Over 90% of these patients responded that they suffered nightly. 2) More than 60% of these patients required an hour or more to fall asleep. 3) More than 66% of these patients experienced 3 or more awakenings/night and 4) On a scale of 1-10, 10 being the most refreshed, patient's qualitative assessment of how refreshed they felt upon awakening was a 3.6.

Figure 3. Hours of Sleep Reported by Patients Sleeping 4 Hours or Less/Night Before and After Taking CRA-melatonin (n=311)



When asked 'since taking CRA-melatonin how many hours did you sleep?', 95.8% of patients reported an improvement in their sleep duration ($p < .0001$). 49.2% of those patients achieved a sleep duration of 4-6 hours while 46.6% of patients achieved a sleep duration of 6 hours or more ($p < .0001$). 4.2% of patients experienced no improvement.

Figure 4. Improvement in Key Sleep Parameters after Taking CRA-melatonin (n=311)



When asked 'how they would rate their improvement in sleep onset, sleep maintenance and sleep quality after taking CRA-melatonin' more than 93% of patients reported a major/moderate improvement for each of three sleep parameters measured, as compared to no improvement ($p < .0001$).

Conclusions

95.8% of patients who previously experienced daily, morbid short sleep duration of ≤ 4 hours reported an improvement in sleep duration ($p < .0001$), including more than 46% who achieved a sleep duration of ≥ 6 hours.

More than 93% of patients reported a major/moderate improvement in sleep latency, maintenance and sleep quality ($p < .0001$ for each parameter).

99% of the patients suffering with morbid short sleep (27.2% of whom had never previously tried a melatonin brand), reported that they were very likely or likely to continue using CRA-melatonin.

These results provide real-world evidence that CRA-melatonin with its extended 7-hour PK plateau time and benign safety-profile may be a practical baseline therapy to improve sleep duration and other key sleep parameters, including, sleep maintenance and quality in these high risk patients for all cause mortality.

References

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DISCLOSURES

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