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**Title:** Association between sleep apnoea and cancer incidence. Longitudinal study of a large multicenter Spanish cohort

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**Body:** Background: The role of Sleep Apnoea (SA) in the development of cancer in humans has not yet been assessed. Objective: To investigate whether SA is associated with increased cancer incidence. Methods: We performed a multicenter, clinical cohort study, analyzing 8,961 patients referred to 8 Spanish Sleep Clinics for suspected SA. Subjects with an apnoea-hypopnoea index (AHI)<10 comprised the control group. SA was diagnosed when the AHI was ≥10. We used the log-rank test to compare cancer incidence between groups, and the Cox proportional hazards model to calculate both unadjusted and adjusted HR and 95%CI for incident cancer. Results: 8,542 (95.3%) patients were finally analyzed. The median follow-up of the cohort was 5.1 years (interquartile range 4.0 to 7.5). SA was associated with increased incidence of cancer in unadjusted analyses (HR 1.27, 95%CI 1.04-1.56). The cancer incidence density rate was also significantly higher in patients with SA compared to the control group (14.99 vs. 11.71 per 1,000 person-years; incidence density ratio 1.28 [95%CI 1.04-1.57], p=0.02). However, when these results were adjusted for age and gender, SA was no longer associated with cancer incidence (HR 0.96, 95%CI 0.78-1.18). Further adjustments for body mass index, smoking or alcohol intake did not modify these results. Cancer incidence was not associated with either mild-moderate SA (HR 1.02; 95%CI 0.81 to 1.28), or severe SA (HR 0.85; 95%CI 0.68 to 1.06) in the adjusted models. Conclusions: Sleep Apnoea was

associated with increased cancer incidence, but this association disappeared when the results were adjusted for confounders.