Appendix

**Nonalcoholic fatty liver disease, sleep behaviors, and incident type 2 diabetes**

**Supplemental Table 1** Sleep questionnaire

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**Supplemental Table 7** Multivariable-adjusted relative risks (95% CIs) for type 2 diabetes by NAFLD and low-risk sleep factors (further adjusted for waist circumference, anti-obesity medications and psychotropic medications)

Supplemental Table 1 Sleep questionnaire

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Sleep behavior | Questions | Field ID | Categories | Low risk behavior |
| Sleep duration | About how many hours sleep do you get in every 24 hours? | 1160 | Normal (7–8 h), Short (<7 h), Long (>8 h) | Normal (7–8 h) |
| Chronotype | Do you consider yourself to be (1) definitely a “morning” person, (2) more a “morning” than “evening” person, (3) more an “evening” than “morning” person, or (4) definitely an “evening” person? | 1180 | Morningness, Morningness than eveningness, Eveningness than morningness, Eveningness | Morningness, Morningness than eveningness |
| Insomnia | Do you have trouble falling asleep at night or do you wake up in the middle of the night? If this varies a lot, answer this question in relation to the last 4 weeks. | 1200 | Never/rarely, Sometimes, Usually | Never/rarely |
| Snoring | Does your partner or a close relative or friend complain about your snoring? | 1210 | No, Yes | No |
| Daytime sleepiness | How likely are you to doze off or fall asleep during the daytime when you don’t mean to (e.g. when working, reading or driving)? | 1220 | Never/rarely, Sometimes, Often/Always | Never/rarely, Sometimes |

Supplemental Table 2 Multivariable-adjusted RRs (95% CIs) for incident diabetes by sleep factors among 363,834 participants

|  | **N** | **Cases** | **Model 1** | **Model 2** | **Model 3** |
| --- | --- | --- | --- | --- | --- |
| **Chronotype** |  |  |  |  |  |
| Morningness | 97595 | 2208 | 1.00 | 1.00 | 1.00 |
| Morningness than eveningness | 130529 | 2417 | **0.82(0.77,0.86)** | **0.90(0.85,0.95)** | 0.94(0.89,1.00) |
| Eveningness than morningness | 103137 | 2030 | **0.87(0.82,0.92)** | **0.92(0.87,0.98)** | 0.95(0.89,1.01) |
| Eveningness | 31573 | 739 | 1.04(0.95,1.13) | 1.04(0.96,1.12) | 1.07(0.98,1.17) |
| **Sleep duration** |  |  |  |  |  |
| Normal (7–8 h) | 249411 | 4303 | 1.00 | 1.00 | 1.00 |
| Short (<7 h) | 86816 | 2253 | **1.52(1.44,1.60)** | **1.23(1.17,1.29)** | **1.16(1.10,1.23)** |
| Long (>8 h) | 26607 | 838 | **1.85(1.72,2.00)** | **1.46(1.36,1.57)** | **1.38(1.28,1.49)** |
| **Insomnia** |  |  |  |  |  |
| Never/rarely | 89137 | 1452 | 1.00 | 1.00 | 1.00 |
| Sometimes | 174413 | 3363 | **1.19(1.12,1.26)** | **1.18(1.11,1.25)** | **1.18(1.11,1.25)** |
| Usually | 99284 | 2579 | **1.61(1.51,1.72)** | **1.42(1.33,1.51)** | **1.39(1.30,1.49)** |
| **Snoring** |  |  |  |  |  |
| No | 229912 | 3637 | 1.00 | 1.00 | 1.00 |
| Yes | 132922 | 3757 | **1.81(1.73,1.90)** | **1.54(1.47,1.61)** | **1.23(1.18,1.29)** |
| **Excessive daytime sleepiness** |  |  |  |  |  |
| Never/rarely | 279579 | 4833 | 1.00 | 1.00 | 1.00 |
| Sometimes | 74152 | 2141 | **1.69(1.61,1.78)** | **1.30(1.24,1.36)** | **1.21(1.15,1.27)** |
| Often/Always | 9103 | 420 | **2.75(2.48,3.05)** | **1.72(1.56,1.90)** | **1.53(1.38,1.70)** |

Model 1 was unadjusted.

Model 2 was adjusted for age, sex, ethnicity (White/others), education (university or college degree/others), family history of diabetes (yes/no), the Townsend index (continuous), smoking status (current, ever, never), drinking status (drinks, continuous variable), physical activity (MET minutes per week, continuous), and dietary score ≥4.

Model 3 was adjusted for terms in model 2 and overweight and obesity (BMI ≥25kg/m2), HbA1c, systolic blood pressure, total cholesterol, use of blood pressure-lowering medications (yes/no) and cholesterol-lowering medications (yes/no), alanine aminotransferase-to-aspartate aminotransferase ratio.

Supplemental Table 3 Multivariable-adjusted HRs (95% CIs) for type 2 diabetes by non-alcoholic fatty liver disease and low-risk sleep factors using Cox regression model

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | % of 363,834 participants | Model 1 | Model 2 | Model 3 |
| NAFLD\* | 24.6 | 3.89(3.71,4.07) | 3.59(3.41,3.77) | 1.77(1.67,1.87) |
| Sleep 7-8h/day | 68.7 | 0.71(0.68,0.75) | 0.78(0.74,0.81) | 0.82(0.78,0.86) |
| Early chronotype | 62.9 | 0.99(0.95,1.04) | 0.98(0.93,1.03) | 0.96(0.92,1.01) |
| Never/rarely insomnia | 24.6 | 0.76(0.72,0.80) | 0.80(0.76,0.85) | 0.82(0.78,0.87) |
| No self-reported snoring | 63.4 | 0.69(0.66,0.72) | 0.73(0.70,0.76) | 0.87(0.83,0.91) |
| No frequent daytime sleepiness | 97.5 | 0.55(0.50,0.61) | 0.64(0.58,0.71) | 0.73(0.66,0.81) |
| NAFLD | 24.6 | 4.21(4.02,4.41) | 3.78(3.59,3.97) | 1.80(1.70,1.90) |
| Five healthy behaviors | 7.2 | 0.54(0.48,0.61) | 0.61(0.54,0.69) | 0.69(0.61,0.78) |

NAFLD, non-alcoholic fatty liver disease

Model 1 was unadjusted.

Model 2 was adjusted for age, sex, ethnicity (White/others), education (university or college degree/others), family history of diabetes (yes/no), the Townsend index (continuous), smoking status (current, ever, never), drinking status (drinks, continuous variable), physical activity (MET minutes per week, continuous), and dietary score ≥4.

Model 3 was adjusted for terms in model 2 and overweight and obesity (BMI ≥25kg/m2), HbA1c, systolic blood pressure, total cholesterol, use of blood pressure-lowering medications (yes/no) and cholesterol-lowering medications (yes/no), alanine aminotransferase-to-aspartate aminotransferase ratio.

\* results from the model when NAFLD (yes/no) and five separate sleep behaviors were included simultaneously in the model.

Supplemental Table 4 Multivariable-adjusted HRs (95% CIs) for non-alcoholic fatty liver disease with type 2 diabetes, stratified by sleep behaviors using Cox regression model

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Case/subjects | HR (95%CI) | P for interaction |
| Sleep duration | Low risk | 4303/249411 | 1.74(1.61,1.87) | 0.109 |
|  | High risk | 3091/113423 | 1.84(1.70,2.00) |  |
| Chronotype | Low risk | 4625/228124 | 1.89(1.77,2.02) | 0.393 |
|  | High risk | 2769/134710 | 1.64(1.50,1.80) |  |
| Insomnia | Low risk | 1452/89137 | 1.55(1.37,1.74) | 0.033 |
|  | High risk | 5942/273697 | 1.88(1.77,2.01) |  |
| Snoring | Low risk | 3637/229912 | 1.78(1.64,1.93) | 0.072 |
|  | High risk | 3757/132922 | 1.74(1.62,1.87) |  |
| Daytime sleepiness | Low risk | 6974/353731 | 1.80(1.70,1.91) | 0.972 |
|  | High risk | 420/9103 | 1.80(1.43,2.27) |  |
| Five healthy sleep behaviors | Yes | 268/26263 | 1.44(1.07,1.94) | 0.057 |
| No | 7126/336571 | 1.81(1.71,1.91) |  |

Model was adjusted for age, sex, ethnicity (White/others), education (university or college degree/others), family history of diabetes (yes/no) and the Townsend index (continuous), smoking status (current, ever, never), drinking status (drinks, continuous variable), physical activity (MET minutes per week, continuous), dietary score ≥4, overweight and obesity (BMI ≥25kg/m2), HbA1c, systolic blood pressure, total cholesterol, use of blood pressure-lowering medications (yes/no), cholesterol-lowering medications (yes/no) and alanine aminotransferase-to-aspartate aminotransferase ratio.

Supplemental Table 5 Multivariable-adjusted RRs (95% CIs) for type 2 diabetes by non-alcoholic fatty liver disease and low-risk sleep factors, limiting participants with a follow-up time of > 1 year

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | % of 363,834 participants | Model 1 | Model 2 | Model 3 |
| NAFLD\* | 24.6 | 3.99(3.80,4.19) | 3.80(3.60,4.01) | 1.81(1.70,1.93) |
| Sleep 7-8h/day | 68.7 | 0.71(0.67,0.74) | 0.77(0.73,0.81) | 0.81(0.77,0.85) |
| Early chronotype | 62.9 | 1.00(0.95,1.05) | 0.96(0.94,1.04) | 0.98(0.93,1.03) |
| Never/rarely insomnia | 24.6 | 0.76(0.71,0.80) | 0.81(0.76,0.86) | 0.81(0.76,0.87) |
| No self-reported snoring | 63.4 | 0.68(0.65,0.72) | 0.72(0.69,0.76) | 0.86(0.82,0.91) |
| No frequent daytime sleepiness | 97.5 | 0.56(0.50,0.62) | 0.64(0.58,0.71) | 0.72(0.65,0.81) |
| NAFLD | 24.6 | 4.32(4.12,4.53) | 4.00(3.79,4.22) | 1.84(1.73,1.96) |
| Five healthy behaviors | 7.2 | 0.54(0.47,0.61) | 0.61(0.54,0.69) | 0.69(0.61,0.79) |

NAFLD, non-alcoholic fatty liver disease

Model 1 was unadjusted.

Model 2 was adjusted for age, sex, ethnicity (White/others), education (university or college degree/others), family history of diabetes (yes/no), the Townsend index (continuous), smoking status (current, ever, never), drinking status (drinks, continuous variable), physical activity (MET minutes per week, continuous), and dietary score ≥4.

Model 3 was adjusted for terms in model 2 and overweight and obesity (BMI ≥25kg/m2), HbA1c, systolic blood pressure, total cholesterol, use of blood pressure-lowering medications (yes/no) and cholesterol-lowering medications (yes/no), alanine aminotransferase-to-aspartate aminotransferase ratio.

\* results from the model when NAFLD (yes/no) and five sleep behaviors were included simultaneously in the model.

Supplemental Table 6 Multivariable-adjusted RRs (95% CIs) for non-alcoholic fatty liver disease with type 2 diabetes, stratified by sleep behaviors, limiting participants with a follow-up time of > 1 year

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Case/subjects | RR (95%CI) | P for interaction |
| Sleep duration | Low risk | 4130/249411 | 1.74(1.61,1.89) | 0.015 |
|  | High risk | 2980/113423 | 1.96(1.79,2.16) |  |
| Chronotype | Low risk | 4456/228124 | 1.95(1.81,2.11) | 0.407 |
|  | High risk | 2654/134710 | 1.70(1.54,1.88) |  |
| Insomnia | Low risk | 1396/89137 | 1.64(1.44,1.87) | 0.029 |
|  | High risk | 5714/273697 | 1.91(1.78,2.04) |  |
| Snoring | Low risk | 3490/229912 | 1.86(1.71,2.03) | 0.063 |
|  | High risk | 3620/132922 | 1.80(1.65,1.97) |  |
| Daytime sleepiness | Low risk | 6712/353731 | 1.84(1.73,1.96) | 0.949 |
|  | High risk | 398/9103 | 1.87(1.44,2.43) |  |
| Five healthy sleep behaviors | Yes | 258/26263 | 1.52(1.11,2.10) | 0.057 |
| No | 6852/336571 | 1.86(1.75,1.98) |  |

Model was adjusted for age, sex, ethnicity (White/others), education (university or college degree/others), family history of diabetes (yes/no) and the Townsend index (continuous), smoking status (current, ever, never), drinking status (drinks, continuous variable), physical activity (MET minutes per week, continuous), dietary score ≥4, overweight and obesity (BMI ≥25kg/m2), HbA1c, systolic blood pressure, total cholesterol, use of blood pressure-lowering medications (yes/no), cholesterol-lowering medications (yes/no) and alanine aminotransferase-to-aspartate aminotransferase ratio.

Supplemental Table 7 Multivariable-adjusted relative risks (95% CIs) for type 2 diabetes by NAFLD and low-risk sleep factors (further adjusted for waist circumference, anti-obesity medications, psychotropic medications, aspartate aminotransferase and C-reactive protein)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | % of 363,834 participants | Model 1 | Model 2 | Model 3 |
| NAFLD\* | 24.6 | 3.96(3.78, 4.15) | 3.78(3.58, 3.99) | 1.43(1.34,1.52) |
| Sleep 7-8h/day | 68.7 | 0.71(0.68, 0.74) | 0.77(0.73, 0.81) | 0.83(0.79,0.87) |
| Early chronotype | 62.9 | 0.99(0.95, 1.04) | 0.98(0.93, 1.03) | 0.99(0.94,1.04) |
| Never/rarely insomnia | 24.6 | 0.76(0.71, 0.80) | 0.81(0.76, 0.85) | 0.82(0.77,0.88) |
| No self-reported snoring | 63.4 | 0.68(0.65, 0.72) | 0.72(0.69, 0.76) | 0.91(0.86,0.95) |
| No frequent daytime sleepiness | 97.5 | 0.54(0.49, 0.60) | 0.63(0.57, 0.70) | 0.76(0.68,0.85) |
| NAFLD | 24.6 | 4.29(4.09, 4.49) | 3.98(3.78, 4.20) | 1.43(1.34,1.53) |
| Five healthy behaviors | 7.2 | 0.53(0.47, 0.60) | 0.61(0.54, 0.69) | 0.72(0.63,0.81) |

NAFLD, non-alcoholic fatty liver disease NAFLD, non-alcoholic fatty liver disease

Model 1 was unadjusted.

Model 2 was adjusted for age, sex, ethnicity (White/others), education (university or college degree/others), family history of diabetes (yes/no), the Townsend index (continuous), smoking status (current, ever, never), drinking status (drinks, continuous variable), physical activity (MET minutes per week, continuous), and dietary score ≥4.

Model 3 was adjusted for terms in model 2 and waist circumference, HbA1c, systolic blood pressure, C-reactive protein, total cholesterol, fat mass, use of blood pressure-lowering medications (yes/no), cholesterol-lowering medications (yes/no), anti-obesity medications (yes/no), psychotropic medications (yes/no) and alanine aminotransferase-to-aspartate aminotransferase ratio.

\* results from the model when NAFLD (yes/no) and five sleep behaviors were included simultaneously in the model.