Project Details	
Project Code	MRC21NMHBr Mahedy
Title	Using a life course approach to disentangle the association between sleep and dementia
Research Theme	Neuroscience & Mental Health
Summary	Although individuals with dementia experience sleep disruption, it is unclear whether sleep disruption is a risk factor for dementia, or whether sleep disruption is a result of dementia pathology. The aim of this project is to use causal methods applied to a life course epidemiology approach to investigate whether sleep quantity or quality across the life course is a risk factor for dementia progression, or vice versa.
Description	Dementia has been estimated to affect 47 million people worldwide and the prevalence is expected to double in the next 20 years. As there is no known treatment that prevents the progression of dementia, there is an emphasis to focus on prevention as the best strategy to reduce incidence and prevalence. Identifying risk factors many years before the symptoms of dementia appear is crucial to understanding the disorder, as the pre-clinical stage can occur up to 20 years before cognitive symptoms of dementia appear. Although individuals with dementia experience sleep disruption (i.e., duration, quality, and timing), it is unclear whether sleep disruption is a risk factor for dementia, or whether it is a result of dementia pathology. Previous research has been hampered by a number of limitations (i.e., selection bias, small sample size, cross sectional study designs, misclassification of exposure and outcome, lack of control for potentially confounding variables, and different follow-up periods). An approach that examines risk factors many years before the pre-clinical stage of dementia is necessary to help gain a better understanding of the direction of relationship. The primary research question will examine whether sleep disruption is a risk factor for dementia, and the alternative, whether dementia symptomatology is a risk factor for sleep disruption. Once, the direction is established, the secondary research question will examine whether critical or sensitive periods can be identified when sleep disruption may have a greater impact on dementia progression many years before the symptoms are present, or vice versa. In an effort to strengthen the evidence, this project will use a triangulation approach by combining observational and genetic information to better understand the relationship between sleep patterns and dementia. This project will use secondary data sources from Dementias Platform UK, containing rich questionnaire and genetic information on almost 50 cohorts comprising over 3 million individuals (e.g., the Avon Longitudinal Study of Parents and Children, Generation Scotland, English Longitudinal Study of Aging, and UK Biobank). Other potential data sources include The Hunt Study - a longitudinal population-based health study in Norway containing rich questionnaire and genetic information on young to old aged adults, and the International Genomics of Alzheimer's Project. The project consists of 3 work streams (WS). WS 1 will establish the direction of association between sleep patterns and cognitive functioning, assessed in young to mid adulthood, using rich longitudinal data. WS 2 will establish the nature of the longitudinal association between sleep

	patterns, assessed in mid to late adulthood, and dementia. WS 3 will examine whether there are sensitive or critical periods when sleep patterns may have a greater impact on dementia, or vice versa. Combining observational and genetic techniques is essential for testing whether there are critical or sensitive periods at which sleep patterns may have an influence on dementia progression and thereby representing modifiable targets for prevention. It may then be possible that precision medicine will include some applications to dementia directly through risk stratification for targeted prevention or intervention strategies.
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