Section A: CPH to complete	
Name:	Adrian Williams
Job title:	Director of Sleep Studies, St Thomas'
Address:	St Thomas' Hospital Westminster Bridge Road London SE1 7EH
Guidance title:	Disability, dementia and frailty in later life - mid-life approaches to prevention
Committee:	PHAC D
Subject of expert testimony:	Sleep and risk of dementia
Evidence gaps or uncertainties:	
The relationship between sleep disturbance and dementia risk	
The evidence on risk reduction through sleep interventions	
Section B: Expert to complete	
Summary testimony:	[Please use the space below to summarise your testimony in 250 – 1000 words – continue over page if necessary]

1. Relationship between sleep disturbance and dementia risk

Background

Sleep complaints are amongst the commonest in medical practice and include **insomnia** that is difficulty getting to sleep, staying asleep or sleep that is unrefreshing which is a complaint of 1 in 3 of the population in any one year and a persistent complaint in 1 in 10; **hypersomnia** or excessive wake-time sleepiness which may affect 5% of the overall population and as may as 10% of the middle aged with other co morbidities; and **parasomnias** or things that happen at night that are unwanted, which include sleepwalking, which are common in childhood with as many as 1 in 6 children having some nocturnal event that is unwanted and 1 in 50 adults.

In the context of dementia risk itshould be noted that the **sleep changes with aging**. It is more difficult to maintain sleep as we get older, with an increase in wake after sleep-onset. This tendency to wake in the early hours of the morning may lead to light exposure which is a drive to a shift to an earlier time in the body clock so that the sleep phase is "advanced". It is well accepted that there would be an increase on other co morbidities with aging which themselves may compromise sleep including of course Obstructive Sleep Apnoea which affects 1 in 4 middle aged man to some degree and the other complaint of Restless Legs Syndrome which on a regular basis probably affects 1 in 20 individuals.

With regard to **dementia,** and in particular Alzheimer's disease, it has been appreciated since the 1990's that this condition is **associated with poor**

sleep, in particular insomnia and circadian problems (that is a tendency to sleep at unusual times something which has been called Sundowning). It has traditionally been thought that sleep disorders are symptoms of the dementia, but is it sleep that is sensitive to dementia pathology, or is sleep disturbance a contribution; and are sleep disorders predictive of the development of dementia?

Evidence for the importance of sleep disorders in dementia

Studying Alzheimer's disease to answer this question is not appropriate because of the prominence of sleep complaints in that condition, but mild cognitive impairment may offer an experiment of nature to explore this possibility. In the Journal SLEEP in 2013 a Spanish study of polysomnography in patients with mild cognitive impairment subjective sleep markers, (reported sleep latency, sleep duration, wake after sleep-onset and sleep quality) were more common in mild cognitive impairment. Objective sleep parameters were also associated with this impairment, specifically reduction in rapid eye movement sleep, (interestingly especially in carries of the ApoE allele) along with increased fragmentation of slow wave sleep.

In SLEEP in 2012 it was noted that excessive daytime sleepiness was predictive of cognitive decline in an elderly French population and sleep quality, as judged by the Pittsburgh Sleep Quality Index, predictive in one year of the development of cognitive impairments (with the odds ratio of 2.6).

There is in addition animal and other experimental evidence for some relationship: sleep restriction in the rat Alzheimer's model produces an increase in Beta amyloid plaques in the brain; better sleep reduces the harmful effects of ApoE 4; reduced sleep led to more Alpha Beta deposits; and protein trafficking in mice was more effective in sleep, with more clearance of Alpha Beta deposits.

Specific Sleep Disorders and dementia

There are also clinical associations which are well known:

REM Sleep Behaviour Disorder is predictive of the development of Lewy Body disorders with 80% of latter having REM Sleep Behaviour Disorder, though many fewer Alzheimer's patients have this condition.

The important condition Obstructive Sleep Apnoea, which I have already indicated as extremely common (1 in 4 adult man have some and 1 in 10 a lot of the disturbance) is associated with cognitive effects such as impaired short-term memory, reduced motor coordination, and reduced ability to maintain attention. It is certain that Obstructive Sleep Apnoea can disturb cerebral vasculature leading to white matter change as reported in SLEEP in 2013. Treatment with CPAP has been shown to improve these cognitive effects making the case yet stronger for sleep apnoea as an important drive to “dementia”.

Other evidence that sleep interventions can make a defence are less clear. It was felt that control of light exposure and use of melatonin might improve the sleep of patients with Alzheimer's, but although there is research evidence for this in practice it has proved difficult to implement

References (if applicable):