Evidence-to-Decision Table

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Worldwide ageing of populations is strongly associated with dementia, causing major health, economic and social burdens. In 2015, it has been estimated that there were 50 million people with dementia in the world, and the number is predicted to double every 20 years, reaching 82 million in 2030 and 152 million in 2050.[1] Since no cure is available for Alzheimer's disease, the main cause of dementia, prevention could be crucial in halting the rapid increase in the prevalence of this condition and international experts have called upon world-wide governments to make prevention of dementia one of their key health priorities.	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ● Varies ○ Don't know	There is evidence showing that the treatment with statins does not affect the risk of dementia (low quality) and/or cognitive decline (moderate quality). In the systematic review considered[20] only two RCTs were identified that investigated the effect of statins treatment on dementia and cognitive outcomes. Although both studies benefitted from quite large populations (more than 26000 participants in total), data related to diagnosis of dementia and cognitive performance were not pooled, due to differences in study design. Limitations due to indirectness were identified as the review specifically focused on individuals at high risk of dementia and/or cognitive decline (due to age). However, a large body of observational evidence has linked dyslipidemia to an increased risk of dementia and/or cognitive decline and found an association between control of dyslipidemia and reduction of dementia and/or cognitive decline risk. Indirect evidence suggests that managing dyslipidaemia in mid-life can help reducing the risk of cognitive decline and/or dementia.	Life-course perspective is crucial since there is no evidence of an effect in late-life, but in mid-life. Detecting dyslipidaemia earlier in life could have beneficial effects and that is why the timing of the intervention is particularly important.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	There is moderate quality evidence that the treatment with statins does not increase the incidence of serious adverse events that led to the discontinuation of the trials compared to the placebo. In this case, data from the 2 RCTs were pooled[20] and no difference between the intervention and control (placebo) group was identified.	
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ● Low ○ Moderate ○ High ○ No included studies	The evidence gathered suggest that controlling dyslipidemia through statin treatment in older adults (65-year-old or more) does not seem to have an effect on the incidence of dementia (low quality evidence) and/or cognitive decline (moderate quality evidence). However the studies included suffer from several limitations, the most important being: 1. no clear criteria to define the diagnosis of dementia as outcomes where provided; 2. cognitive performance was not among the primary outcomes; 3. the evidence rated to the incidence of dementia was deemed of low quality due to the very small number of cases identified (3/1000); and 4. both studies were conducted on a selected population of individual at high risk of developing dementia but neither ascertained dementia at baseline in a systematic fashion, although in both cases attempted were made to exclude people with pre-existing dementia or significant cognitive impairment. However, the observational evidence clearly points towards a beneficial effect of reduction of dyslipidemia on the risk of dementia and/or cognitive decline. There is a complex association between blood lipids and risk of cognitive decline and/or dementia especially in relation to age. The evidence are mostly observational and pharmaco-epidemiological.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability	Cognitive impairment and dementia can have a major impact in the life not only of the person affected but also of the close network of family and friends, as well as caregivers and health professional in general.[28,29] Functional ability and dependency are playing are the major component of this effect. Furthermore, dementia, the main cause of disability and institutionalization among older adults[1], therefore reducing or delaying the onset of dementia could results in lower costs for public healthcare services. Patients, caregivers, and policy makers are likely to be the people who will value these recommendations the most.	
Balance of effects		

Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ● Varies ○ Don't know	Based on evidence from both observational and intervention studies the balance of the effect is towards the intervention as statin treatment showed negligible effect on adverse events and observational evidence links dyslipidemia control to reduction of dementia and/or cognitive decline. Complex relationship between blood lipids and risk of cognitive decline and/or dementia. Using statins in midlife to manage dyslipidaemia may have beneficial effects on the risk of cognitive decline and dementia.	
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The main costs of the intervention are related to the medication. Very recently, it has been estimated that about 400 USD is the annual cost for a statin treatment (all fills).[30] Lifestyle interventions to control dyslipidemia generally include weight-loss, healthy diet patterns and physical activity components. These interventions can therefore be cost-intensive depending how much supervision and support is required from healthcare professionals. However, no specific evidence on lifestyle interventions are available.	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ● High ○ No included studies	Statins are the most common medications regularly used for cholesterol lowering therapies. They are well established, and cost are well known.[30]	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	Statin treatment in older adults (75-94 years old) is projected to be cost-effective for primary prevention of cardiovascular disease.[31] No evidence was found directly for the prevention of dementia and/or cognitive decline. If other outcomes, such as cardiovascular disease, are considered, statins treatment is cost-effective.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Lower socioeconomic groups are more likely to have earlier onset of dementia than higher socioeconomic groups. Older people from lower socioeconomic backgrounds are also more likely to experience cognitive dysfunction at earlier stages of cognitive decline and cognitive impairment, and will have fewer resources to cope with the symptoms than their counterparts from higher socioeconomic groups People from lower socioeconomic groups are more likely to live, work and age in physical and economic environments that do not support social connectedness, physical activity or mental stimulation. this can increase the risk of cognitive impairment and dementia in later life.[32] Based on this it is believed that interventions to reduce risk of cognitive decline and dementia will increase equity in health. Furthermore, women are disproportionally affected with AD. The larger proportion of older women who have AD and other dementias is explained primarily by the fact that women live longer, on average, than men.[33] Finally, low socioeconomic position (SEP) was associated with overall and rapidly increasing statin nonadherence among men. Conversely, in women, associations between SEP and nonadherence were weak and inconsistent. Group-based trajectory modelling provided insight into the dynamics of statin adherence and its association with SEP.[34]	
Acceptability Is the intervention acceptable to key stakeholders?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Although relatively safe, statins are known to have adverse events, being headache, altered liver-function tests, paraesthesia, and gastrointestinal effects, including abdominal pain, some of the most commonly reported. No evidence was available for lifestyle interventions. Acceptability could vary among countries and stakeholders. Lifestyle interventions may be more acceptable than statin treatment.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Prescription of statins is common and can be done by GPs in many countries. Cost represent the main barrier. Lifestyle interventions to control dyslipidemia generally include weight-loss, healthy diet patterns and physical activity. The main barriers for these types of intervention are costs, lack of motivation, lack of time, and physical limitations.	