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Plenaries

PO1.1

The rising tide of world-wide, late life dementias: Prospects and evidence for prevention

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During the last quarter of the 20th century, late life cognitive impairment has emerged as an important source of disability. First, in wealthy nations as more people lived to advanced old age and, more recently, in low and middle income countries as their populations become older. The public health burden of the late life dementias, principally Alzheimer's disease, vascular and mixed dementias, the ineffectiveness of available treatments and public expectations that late life be a reward for long life, not experienced as punishment, create a rationale, some would say a mandate, to seek ways to prevent late life dementias.

What are the prospects for prevention? While genetic factors affect longevity and risk for Alzheimer's disease, other environmental factors also affect risk. Like coronary artery disease in young soldiers dying in the Korean War, pathologic changes are evident years before cognitive impairment is. We now know that mixed dementias are more common in older populations and that so called vascular risk factors probably play a role in Alzheimer's disease and mixed dementias. Efforts to find simple prevention remedies like supplements (e.g. antioxidant vitamins) or commonly used drugs (e.g. NSAIDs) or to develop specific neurotransmitter enhancers (e.g. cholinesterase inhibitors) have been disappointing to date. Searches for such remedies continue as we learn more about the pathogenetic processes culminating in neurodegeneration (plaques, tangles, amyloid angiopathy, and microvascular infarcts). Investigation of lifestyle risk factors have shown more promise, identifying education, socioeconomic status, habitual physical activity and possibly higher levels of leisure time activity and social networks as protective. Cognitive training has been shown to have durable effects as well. Other currently promising prevention strategies involving better control of vascular risk, probably throughout life and reducing abnormal insulin resistance.

Recent evidence using U.S. population surveys suggest that while absolute numbers of persons with dementia are increasing, rates of cognitive impairment in persons over 70 years old may have declined between 1993 and 2002. That decline was associated with higher levels of education, greater wealth and better general medical care.

Overall current evidence suggests that absolute prevention of dementia in late life is not likely. Rather a delay in onset and a shorter duration after onset until death, a so called "compression of cognitive morbidity", is an achievable goal. While it is unlikely that the complex neurodegenerative disease processes causing late life dementias can be eliminated in societies where the numbers of old-old are growing rapidly, a prevention strategy designed to delay onset would greatly reduce the burden caused by late life dementias since competing causes of mortality (even in late life) could cause death to occur before onset of disability or by dramatically shortening the duration after disability and dependency appear.

As society has become more knowledge-based, cognitive health throughout life and especially in late life will become an increasingly important determinant of wellbeing and survival. Preventive efforts aimed to preserve cognitive function deserve high priority in today's and tomorrow's increasingly aging societies.

PO1.2

Preventing depression in old age

Charles Reynolds

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Preventing depression in old age is important because depression contributes substantially to the global burden of illness-related disability; and because available treatments are only partially successful in bringing about and sustaining recovery. In addition, the availability of evidence-based treatments is limited, especially to economically disadvantaged and older minority adults. Finally, preventive interventions may well be less costly than treatment of established illness.

The concept of depression prevention in old age encompasses three major objectives: (1) delaying or preventing depression in those at high risk (e.g., "selective" or "indicated" prevention, to borrow IOM terminology [Mrazek and Haggerty, 1994]) and (2) treating to full recovery those

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with established illness ("secondary prevention"), in the hope of (3) preventing further complications, or bad outcomes of depression in old age, such as recurrent/chronic illness, disability, cognitive impairment, non-adherence with treatment for co-existing medical disorders, caregiver burden, and suicide ("tertiary" prevention).

The edidemiology of depression in old age has now established several risk factors (Smit *et al.*, 2006), including but not limited to disability, depletion of psychosocial resources, and low levels of depressive symptoms (arising in response to life events such as bereavement and social role transitions, or ongoing stressors). Data support the value of both simple structured psychosocial interventions, such as problem-solving therapy, for delaying or preventing depression in high-risk people (e.g., with age-dependent macular degeneration [Rovner *et al.*, 2007]). Antidepressive pharmacotherapy may also prevent depression in high-risk people (e.g., post-stroke [Robinson *et al.*, 2008]).

Incomplete response to antidepressant treatment, extremely common in old age, poses the challenge of secondary prevention, to help people fully recover and avoid further "down-stream" problems. Recent work using decision-tree analysis (Andreescu *et al.*, 2008) may point the way for personalized medicine, that is, identifying people at risk for incomplete response and therefore in need of alternative interventions to recover fully.

Finally, opportunities for tertiary prevention are illustrated by maintenance therapy trials showing the ability of psychosocial and pharmacologic interventions to impact the long-term course of illness, and thereby to reduce adverse outcomes like recurrence, progression of cognitive impairment, and suicide (Reynolds *et al.*, 1999; 2006; Bruce *et al.*, 2004).

Going forward, the research agenda should more fully embrace the testing of psychosocial, clinical, and biological predictors and moderators of prevention effectiveness, in order to maximize impact and efficiency of preventive interventions.

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PO2.1

Can depression in later life be prevented?

Robert Baldwin

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Depression in later life has a major negative impact on health and wellbeing, so its prevention ought to be high priority. Rates of incident cases range between 12 and 44 person-years, with a recent average of 28 (Smit *et al.* 2006). Modelling has suggested substantial cost savings through prevention. Risk factors are well known and include prior depression, current depressive symptoms, chronic medical illness, vascular disease, functional limitation, female gender, insomnia and a small social network (Cole & Dendukuri, 2003). Other factors are likely to be elucidated, including genetic risk, early development, diet or metabolism. Some of these are modifiable. Prevention as a public health strategy is only realistic if there is a convenient way of detecting depression, a clear at-risk group and an effective intervention. This presentation will consider whom to target (those at high risk and those with prodromal symptoms) and with what interventions (medication, psychological or psychosocial interventions). Some examples of recent research on prevention will be discussed.

References: Cole, MG, Dendukuri, N (2003) Risk factors for depression among elderly community subjects Am J Psychiatry 160:1147–1156

Smit, FR, Ederveen, A, Cuijpers, P *et al.* (2006) Archives of General Psychiatry 63:290–296

PO2.2

Delay and prevention of dementia: How early must we start interventions?

Steven DeKosky

University of Virginia, Charlottesville, VA, United States

Early diagnosis and treatment, delay of progression, and prevention of Alzheimer's disease (AD) are all interrelated to some extent. Medications directed at treatment, and certainly those for slowing the progression of disease, are candidates for prevention as well. As we have learned more about AD over the past two decades, experienced clinicians have become more and more skilled at diagnosing AD at earlier times and with milder symptoms. An isolated symptom of memory loss, termed mild cognitive impairment or MCI, appears to be one of the earliest ways that AD is manifested, and CSF and neuroimaging biomarkers hold promise for extending diagnostic certainty even in cases of mild cognitive symptoms. Researchers all over the world are working to determine two primary objectives: first, how early can we detect AD—and can we predict who will get the disease before any symptoms are seen? Second, are there treatments or changes in lifestyle (for example, diet, exercise, mental activity etc.) that would decrease the risk of developing AD?

To answer these questions we must know how early the brain changes start before symptoms emerge. We will then be able to devise appropriate

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therapies for each stage of the disease. While different models for prevention trials are evolving, prospective studies aimed at determining whether certain medications can prevent or delay the onset of AD require large numbers of subjects and long duration, and are very expensive. However, the initiation of intervention trials in MCI and delay/prevention trials represent a great advance for the field and hold the potential to tell us much about how to battle AD. Lessons learned from other such prevention efforts—controlling vascular or lipid risks, will be discussed.

PO2.3

Laura Fratiglioni
Karolinska Instituet, Stockholm, Sweden

PO3.1

Can depression in later life be prevented?

Aartjan Beekman
Vrije Universiteit, Amsterdam, Netherlands

The statistics for cardiovascular morbidity and mortality are a reminder that psychiatry has a long way to go. Integrating prevention more systematically into our armory is probably not only the best, but also the only way to go if we want to seriously change the morbidity statistics surrounding major mental health problems in later life. Late life depression is a prime example. No health system, no matter how well endowed, will ever be equipped to treat all the older patients who are eligible for the treatment of affective disorders. If the money were available, the skilled personnel required would not be. That being so, the urgency to do something to diminish the public health effects of late life depression remains.

Prevention may be an attractive option; but is it also realistic? In this presentation the different opportunities for prevention will first be explored. The aim is to identify our focus of attention. Which older people, living under what circumstances, should be contacted at which point in their development toward an affective disorder? Using data from longitudinal epidemiological studies, a fruitful agenda for effective prevention can be drawn up. From there, different interventions can be tested as to their effectiveness. The second aim of this presentation is to identify which sort of interventions may be helpful in preventing depression in older people. To this end, the available literature as to which interventions may be effectively employed will be reviewed. Combining the above, a real-life prevention program can be devised and tested. The third aim of this presentation is to present data from a randomized controlled trial of a stepped-care, indicated prevention program for older (75+) adults in the community in the Netherlands. Both at one and at two year follow-up, the program resulted in a 50% reduction in the onset of major depressive disorder and anxiety disorders. This intervention was far from totally effective and not all older people were able and willing to participate. However, employing self-help strategies, supplemented with locally available nursing personnel, resulted in a user friendly and low-cost program, that may be a valuable aid in our attempts to combat depression in later life. Available studies, such as the one presented, suggest that indeed prevention of depression is possible.

PO3.2

Prevention of depression following stroke and 6 month follow-up

Robert G. Robinson
The University of Iowa, Iowa City, IA, United States

The Institute of Medicine Committee on Prevention of Mental Disorders recommended in 1995 that prevention in psychiatry should be referred to as "preventive intervention," defined as an intervention before the patient receives a diagnosis. Preventive interventions, furthermore, were categorized as "indicated" (i.e. treating high-risk individuals with premorbid signs or symptoms), "selective" (i.e. treating individuals with demonstrated increased risk of developing illness) and "universal" (i.e. treating whole populations including all levels of risk). There are approximately 700,000 new cases of cerebral infarction annually in the United States. Previous research has demonstrated that approximately 37% of stroke survivors develop depression after the acute stroke period, and therefore, represent a reasonable population in which to assess a selective preventive intervention strategy.

Patients were enrolled at 3 sites within 3 months following acute stroke. During the period from 7/9/03 to 10/1/07, 176 nondepressed patients were randomized to double-blind placebo controlled comparison of escitalopram (n = 59) or placebo (n = 58) and a non-blinded Problem Solving Therapy (PST) arm (n = 59). At 3, 6, 9, and 12 months all patients were examined using the Structured Clinical Interview for DSM-IV (SCID) and diagnostic criteria from DSM-IV-TR to assess the development of major or minor (i.e. research criteria) depression. Patients were also assessed for severity of depressive symptoms (Hamilton Depression Scale), functional impairment (Functional Independence Measure) and cognitive impairment (Repeatable Battery for Assessment of Neuropsychological Status (RBANS).

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Patients who received placebo were significantly more likely to develop depression (11 major, 2 minor depressions, 22.4%) than those who received escitalopram (3 major, 2 minor depressions, 8.5%). Time to depression was assessed using a Cox regression proportional Hazard's model. Patients who received placebo were 4.5 times more likely to develop depression compared with escitalopram (adjusted HR = 4.5, 95% CI = 2.4–8.2, p<.001). Patients who received PST (5 major and 2 minor depressions, 11.9%) compared with patients who received placebo (adjusted to HR = 2.2, 95% CI = 1.4–3.5, p<.001) also had fewer depressions and later onset. Analyses were adjusted for all possible confounders. There were no effects of treatment on recovery from impairment. Following 12 months of treatment, 18 month follow-up data on development of depression and recovery of activities of daily living or cognitive function will be presented.

Previous studies have demonstrated that post-stroke depression is associated with increased mortality compared with comparable stroke patients without depression. Similarly, poststroke depression has been associated with impaired recovery of activities of daily living and greater cognitive impairment. Whether prevention of post-stroke depression might lead to increased survival or improved long term recovery is an intriguing issue for further investigation. We will assess these outcome variables at 18 months follow-up.

PO3.3

Preventing depression in age-related macular degeneration

Barry Rovner[1]; Robin Casten[2]

[1]*Jefferson Hospital for Neuroscience, Philadelphia, PA, United States;* [2]*Jefferson Medical College, Philadelphia, PA, United States*

This presentation will describe the results of a behavioral intervention to prevent depression in older persons with vision loss.

PO4.1

Exploring measures to prevent caregiver burden: The effects of the National Long-term Care insurance scheme in Japan

Yumiko Arai

National Center for Gerontology and Geriatrics (NCGG), Obu-shi, Japan

The ever-increasing population of older people with disabilities, including dementia, has been accompanied by a corresponding increase in the number of family caregivers, who are themselves at risk of developing mental and physical health problems. The need for practical and effective approaches for alleviating caregiver burden has been a major concern for some time. One approach involves the development of public policy initiatives to allow the caregiver burden to be borne by society as a whole, rather than by individuals. In 2000, Japan introduced a National Long-term Care (LTC) insurance scheme that requires adults over the age of 40 to pay compulsory monthly premiums, with the aim of sharing caregiver burden.

This presentation will review the effects of this scheme on caregivers' and the general public's perception of caregiver burden, and will assess what other measures are needed to further reduce and/or prevent burden. Drawing on recent studies conducted by my research group, I will address four questions: 1) Have caregivers' attitudes towards caregiving changed since the implementation of the scheme? 2) Do services provided under the scheme alleviate caregiver burden? 3) What are the general public's attitudes to and understanding of family caregiving? 4) What is the general public's level of understanding of dementia?

Results from these studies suggest that caregivers' attitudes have changed since the introduction of the scheme, and more caregivers now believe that the care of older people should be borne by society as a whole, rather than by individuals or families. A community-based observational study indicated that the insurance scheme had successfully reduced the burden felt by caregivers who cared for those receiving LTC services. A recent survey revealed that the majority of the general public did not know how to use the LTC insurance scheme, especially the younger generations who were not required to pay the compulsory monthly premiums. It is possible that concern could be alleviated by making the public, especially those under 40, more aware of the scheme. It was also evident that many members of the general public, particularly men and non-middle aged women, had little understanding of dementia. It is possible that this lack of understanding might contribute to the public's apprehension about potential caregiver burden.

Thus, the LTC insurance scheme in Japan appears to be an effective measure for alleviating the burden of caregiving among current family caregivers. The LTC scheme has involved the general public in sharing the burden of caregiving through compulsory monthly payments. These results have implications for other countries, and suggest that such a system, where the burden of caregiving is shared by society as a whole, can have a positive effect on reducing and possibly

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preventing the burden on current caregivers. More importantly, such a system can accustom the general public to the idea of sharing the burden of caregiving before any individual actually needs assistance. Such a system can thus help to prevent caregiver burden at the societal level by preparing people to become family caregivers.

PO4.2

Psychosocial intervention can prevent family caregivers' burden

Sölve Emstahl

Department of Health Sciences, Malmö, Sweden

In Sweden, the municipalities have the main responsibility for the care of elderly according to the Social Service Act, and local government programs for e.g. the dementia care offer guidelines on settings for special accommodations, staff education, caregiver support and medical investigation.

Previous studies have shown the importance of the next of kin as informant to the staff for subjects suffering from dementia. The relatives' involvement in the care of severely ill persons and the attitude of the staff can support the relatives' sense of coherence.

The concept of caregiver includes both a caring component and a caregiving component (Pearlin *et al.*), and several definitions are used depending on relationship, type of care or living arrangements. Several studies have focused on caregiver burden including the caregivers experienced feelings, attitudes and emotional reactions (George & Gwyther), and instruments like the Caregiver Burden Scale (CBS) have been developed to measure caregiver burden (Elmståhl *et al*). Predictors of burden of family caregiving of demented subjects include caregiver dependent factors (household, age, gender, relationship, income, health status, and sense of coherence) and patient dependent factors (type of dementia, behavioural problems, severity of illness and care settings).

A number of meta-analyses on the effect of psychosocial interventions for caregivers of patients with dementia have been published in the past years. Different diagnosis and definitions of caregiver, small and convenient samples, short follow-up, and measures with limited reliability might explain conflicting results, but several studies reported effects on caregiver burden and subjective well-being.

A previous Swedish controlled psychosocial intervention study on 308 family caregivers with follow-up every sixth month reported lower strain and disappointment after 6 months which remained after 12 months and increased satisfaction in the intervention group (Andrén & Elmståhl). The intervention also delayed time for nursing home placement 6 months for persons with dementia with adult children as caregivers during a five-year follow up.

The findings support the importance of municipalities to provide specific action programs for family caregivers to relatives with dementia in order to reduce burden and suffering and also to delay nursing home placement.

PO4.3

Psychiatric and physical health effects of family caregiving: Treatment and prevention

Richard Schulz

University of Pittsburgh, Pittsburgh, PA, United States

Family members are an essential resource to older individuals with chronic illness and disability. Without the care and support provided by relatives, it would be difficult and often impossible for persons with disability to remain in the community. There is strong consensus that caring for an individual with disability is burdensome and stressful to most family members and contributes to physical health problems and psychiatric morbidity in the form of elevated rates of depression and anxiety and, in extreme cases, murder-suicide. In this presentation we describe the burden and health effects of caregiving, the causes of caregiver burnout, and existing treatments for relieving caregiver stress. Effective caregiver burnout strategies have several common features including (a) risk appraisals to assess unique circumstances of the caregiver; (b) multicomponent treatments at high doses that address a variety of caregiver needs; and (c) some degree of tailoring based on caregiver input. Concluding observations are made about the future demography of caregiving and the challenges this poses for the next generation of caregivers and care recipients.

PO5.1

Suicide prevention in older people: An Asian perspective

Helen Fung-kum Chiu

The Chinese University of Hong Kong, Hong Kong, SAR PR China

Suicide in older people is a major challenge in many countries in Asia despite the traditional veneration of older people in Asian culture. In particular, the suicide rates of older people in rural China and rural India are very high. Another feature is the high suicide rate in older females in many

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Asian countries. Unfortunately very few countries in Asia have a national strategy on suicide prevention. Suicide prevention programs are beginning to be established in some countries in Asia in recent years. This presentation will describe some of these suicide prevention programs. In Hong Kong, the Elderly Suicide Prevention project was established in 2002. The experience of this territory-wide program in Hong Kong will be presented as well as the preliminary findings of the evaluation of the project, together with the lessons obtained. The challenges of suicide prevention in older people in Asia will be discussed in light of the research findings and experience of suicide prevention in Asia, with recommendations on the way forward.

PO5.2

Late-life suicide prevention: A person-centered complement to the prevailing population-focused and patient-oriented paradigms

Paul Duberstein

University of Rochester, Rochester, NY, United States

In this talk, I will review the latest research on risk for suicide mortality in older adults, and the two prevailing models of prevention. One is population-based and public health oriented, the other is patient-based and biomedically oriented. I will then present a third, "person-centered" prevention model that emphasizes personality traits, interpersonal patterns, treatment attitudes, and health-care decision-making. This person-centered model was initially derived to explain the findings, repeatedly replicated, that many older adults who take their own lives had been seen by a primary care provider in the weeks or months prior to death, that most had not received any mental health treatment, and that many of those who did receive treatment did not derive full benefit due to nonadherence or because the treatment was insufficiently potent. The person-centered model of late life suicide posits that some at-risk older adults' longstanding personality traits (e.g., low Openness, low or high Extraversion) and interpersonal patterns make it difficult for health-care providers, family members, and friends to see them as "at risk." Health care providers and network members do not broach the topic of suicide or probe beneath the surface. The patients themselves do not disclose their thoughts of suicide or reveal their plans. Reasons for non-disclosure or incomplete disclosure remain to be elucidated, but probably also include deeply personal beliefs about the causes of mental disorders and attitudes about mental health treatment and treatment providers. These beliefs create significant barriers to effective treatment up-take and adherence, and are exacerbated by sociocultural pathogens (ageism, racism, stigma) and economic barriers. More potent treatments and significant structural changes in the delivery of health care could decrease risk. Beyond these advances, a truly person-centered health care delivery system would be responsive to individual differences and accommodate individual traits, health care preferences, treatment attitudes, and decision-making styles, all of which have been shown to influence health outcomes but are ignored by the two prevailing prevention models. Only by accounting for and examining individual differences will we be able to develop tailored, person-centered intervention strategies. I will conclude by providing an example of how personology can inform social marketing campaigns and primary care based initiatives to enhance the appeal of mental health treatment.

PO5.3

Late-life suicide: New insights from clinical and translational research

Katalin Szanto

University of Pittsburgh, Pittsburgh, PA, United States

Despite the huge progress in psychopharmacology, so far we have had very limited progress in preventing suicide. One of the most intriguing questions is why the elderly have the highest suicide rate in almost all countries in the world where data are available. It is also not clear why certain countries follow the so called "Hungarian model," that is, the elderly in both sexes have the highest suicide rates, while in the U.S. the suicide rate increases only in men, more specifically in elderly Caucasian men (in 2005, the suicide rate of Caucasian males aged 85 and older was almost six times the nation's rate). It cannot be assumed that risk and protective factors are the same in the elderly as in middle age and younger adults. Based on evidence from the literature, as well as from recent clinical and cognitive data from our studies, the first part of the presentation will discuss a newly developed stress/diathesis model of suicidal behavior in late-life that may help to identify potentially modifiable risk factors. In the second part of the presentation, I will review data from our treatment studies of high suicide risk elderly.

Our studies showed that elderly suicide attempters, particularly men over 70, carry out high lethality suicide attempts. About two-thirds of elderly suicide victims have major or minor depression. Fortunately, most depressed elderly

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never manifest suicidal behavior. What is different about those who do? While the severity of the current depressive episode does not differentiate suicidal elderly, our studies show that there is a subgroup of depressed elderly who present with suicide ideation and attempts in consecutive depressive episodes. These patients exhibit early onset, recurrent depressive episodes, high levels of anxiety and hopelessness, low self-esteem, often suffer from complicated grief, and have poor treatment response. Suicidal older adults needed twice as much time to get well (median time to response was six weeks in patients who endorsed suicidal ideation at baseline vs. three weeks in non-suicidal patients). High levels of hopelessness persist in suicide attempters even after remission of depression, but not in suicide ideators or non-suicidal patients. Beyond clinical risk factors we have preliminary evidence that low SES is associated with suicidal ideation in late-life. Our data indicate that depressed suicide attempters, even those who have intact global cognition, have impairment in cognitive control (executive function). More interestingly, only suicide attempters, but not suicide ideators, are impaired in specific aspects of cognitive control related to key aspects of decision-making, but are unimpaired in "cold" cognitive control functions such as working memory and planning. Age-related decline in decision-making abilities may precede other forms of cognitive impairment, as the ventral prefrontal cortex that is thought to subserve decision-making may be disproportionately affected by aging. These deficits may undermine the older person's ability to adapt and problem-solve in this stage of life when it is most needed to face dramatic life changes. Once suicidal thoughts arise in this context, impaired decision-making may lead one to choose suicide to the exclusion of more adaptive strategies.

PO7.1

Can dementia be prevented? A call for possible treatments

Charles DeCarli

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Dementia is a clinical state of severe cognitive impairment that likely reflects the summed effects of multiple pathological processes. Alzheimer's disease (AD) and cerebrovascular disease (CVD) are two very common diseases associated with advancing age. It is not surprising, therefore, that these two processes commonly occur in the same individual. Clinical, epidemiological and basic science research suggests a number of ways by which CVD may interact synergistically with AD to increase the likelihood of clinically expressed dementia that deserve further study. Current limitations to understanding the interaction between CVD and AD include a limited understanding of the full spectrum and time course of CVD. Recent behavioral, neuroimaging and pathological evidence strongly supports the notion that CVD occurs commonly in dementia, even among individuals diagnosed with AD. If fact, it is likely that "mixed" dementias (dementia with multiple etiologies) are the most common form of last life cognitive impairment. In this presentation, I will elucidate the notion of mixed dementia, focusing mostly on CVD and AD pathologies, but also including other risk factors as necessary to elucidate this concept. Given that CVD is potentially preventable, a more thorough understanding of the impact of CVD on the brain structure and function during normal aging and in the setting of AD may result in substantially improved health for our aging population. I will, therefore, introduce the possibility for preventative therapeutic trials focusing on the potential effects of treating vascular risk factors.

PO7.2

Modifiable risk factors and recommendations for dementia prevention

Lutz Frölich

Central Institute for Mental Health, Mannheim, Germany

Several potentially modifiable risk factors are known for dementia and Alzheimer's disease (AD), e.g. cardiovascular (hypertension, cholesterol, diabetes + metabolic syndrome, overweight + obesity), environmental/nutritional (antioxidants/vitamins, fat + fish intake, alcohol, smoking) and behavioural factors (physical activity, cognitive + psychosocial activity, depression). Blood pressure monitoring in middle age reduces the risk of developing dementia in later life. However, a specific target systolic blood pressure cannot be proven for reducing the risk of dementia as yet. Cross-sectional studies consistently showed a reduced occurrence of dementia among statin users. Results of ongoing interventional statin trials need to be positive before statin use for dementia prevention can be recommended. Although there are many reasons for treating type 2 diabetes mellitus, hyperlipidemia and hyperhomocysteinemia, there is insufficient evidence to recommend for or against treatment of these conditions for the specific purpose of reducing the risk of dementia.

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Although obesity and especially central obesity in midlife increases the risk of dementia independent of diabetes and cardiovascular co-morbidities, there is no interventional study on reduced dementia risk after weight reduction. There is some evidence that natural or high intake of vitamins B, C and E from food decreases dementia risk. There is insufficient evidence to recommend for or against supplementation with vitamins B, C and E for the prevention of dementia. Adherence to a Mediterranean diet (MeDi) may affect not only risk for AD but also subsequent disease course: Higher adherence to the MeDi is associated with lower mortality in AD. Because of a complete lack of interventional studies, clear recommendations on nutrition cannot be given. Frequent consumption of fruits and vegetables, fish, and omega-3 rich oils may decrease the risk of dementia and AD. There are potential advantages of moderate consumption of wine (specific doses cannot be stated). Regular exercise, both physical and mental and social, may reduce the risk of dementia, and can therefore be recommended in midlife and later age groups. Recent studies have found that AD in particular is negatively associated with diversity of activities and intensity of intellectual activities and positively associated with psychosocial inactivity and unproductive working style. Therefore, a more demanding work and social activity can be recommended. A potential protective effect of the psychosocial network on dementia can be demonstrated in several studies. The interaction of depression with dementia is complicated. Depression can be a prodromal symptom, a first sign of dementia, or it can be the result of dementia and can be an independent risk factor. There is robust evidence that persons with history of depression have a higher risk of dementia in later life. Although depression may be modifiable, there is no evidence that interventions on depression reduce the elevated risk for dementia. In conclusion, a healthy, active socially-integrated life-style with balanced nutrition in combination with monitoring metabolic and cardiovascular risk factors is recommended for reducing the risk of dementia. Diverse factors influence the development of AD and dementia. Therefore, a multi-component-integral approach for preventive strategies is more likely to exert beneficial effects than a single risk-factor directed intervention. A possible synergy between moderate exercise, cognitive and social activity and healthy diet on cognition and dementia incidence in the elderly needs to be further investigated. There is need for health programs to increase awareness for dementia development in old age and particular attention should be paid to high-risk groups in mid life to prevent dementia or delay its onset and to high risk groups already on the edge of dementia, e.g. socially isolated elderly subjects after retirement age.

PO7.3

Dementia prevention: Lessons from randomized clinical trials

Mary Sano

Mount Sinai Medical Center, New York, NY, United States

Cognitive loss and dementia affect millions of older people worldwide and represent one of the fastest growing public health threats of modern time, attenuating any quality of life benefit gained by improved longevity. Treatment of dementia has been only mildly effective and there are many reasons to believe that prevention of dementia and cognitive loss may be more effective in reducing the impact of this group of diseases. Several clinical trials of dementia prevention have been unable to demonstrate efficacy, but have informed us of important aspects of trial design and strategies for assessing interventions. Recent observational studies have suggested lifestyle factors that may maximize cognitive health in aging. Clinical trials, designed to assess these factors, have provided hopeful results. Further, several epidemiological reports have indicated overall reduced incidence of dementia over the past decade, suggesting that global efforts to raise awareness and address known risk factors may have a benefit. In the area of Alzheimer's disease, the most common form of dementia, growing knowledge of pathogenic mechanisms and methods of manipulation of these mechanisms have been used to develop experimental approaches to both pharmacological and non-pharmacological therapeutic interventions. This data will be reviewed and evaluated as a powerful model for a method to approach dementia prevention goals.

PO8.1

Can behavioral disturbances associated with dementia be prevented?

Akira Homma

Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

Behavioral disturbances associated with dementia are modified by various factors including physical, psychological and environmental factors. Early intervention including pharmacotherapy will delay the manifestation of behavioral disturbances.

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Although empirical reports are quite poor, some practical issues in the community under the long-term care insurance to support persons with dementia will be described.

Up to now, many studies have been reported regarding the risk/protective factors on the manifestation of behavioral disturbances associated with dementia. There is no doubt that the prevention of such disturbances is quite essential, if it can be possible, since they are closely related to the quality of life of patients with dementia and their caregivers. However, as far as I know, no reports have been reported regarding the prospective intervention studies focusing on the specific behavioral disturbances associated with dementia. This is probably due to the difficulty of methodological issues to clarify the effect of the prospective intervention. Also, there is no report on the natural history of behavioral disturbances in patients with dementia from very mild stage to very severe stage, including modifying variables related to specific behavioral disturbances appearing in each stage. Apart from the operational definition of behavioral disturbances, even if a sufficient number of patients with dementia without any behavioral disturbances can be recruited, it may be quite difficult to control a lot of possible variables related to the manifestation of such disturbances, including physical, psychological and environmental conditions, especially for patients with dementia living at home. In particular, there is no standardized methodology to quantify the environmental conditions including care. Actually, some acetylcholine esterase inhibitors are indicated or recommended for the treatment of behavioral disturbances in patients with DLB in a few clinical practice guidelines. However, any preventive administration of them is not described in the guidelines. In the presentation, I would like to describe some personal experiences in my out-patient clinic. It seems that critical issues that have to be solved in the management of dementia are included in the context of how to prevent behavioral disturbances associated with dementia in order to support the lives of persons with dementia.

PO8.2

Serotonergic antidepressants and cognitive enhancers for patients with BPSD

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Given the frequency and distress caused by behavioral and psychotic symptoms in patients with dementia (BPSD) there remains an urgent need for improved treatment approaches. Pharmacotherapy should be reserved for severe, persistent or recurrent BPSD that is unresponsive to nonpharmacologic interventions. Although second generation anti-psychotics are most commonly used, they are associated with increased mortality. This lecture will review double-blind trials conducted with donepezil, galantamine, rivastigmine, memantine, trazodone, sertraline, and citalopram. Although these medications may reduce symptoms of BPSD, overall results are inconsistent and small numbers or trial design, including variation in the type and severity of symptomatology, limit available data. Neuropsychiatric symptoms in Alzheimer's disease (AD) are fundamental expressions of the degenerative disorder. Despite the high risk of delirium, our work has revealed significant levels of serum anticholinergic activity in AD patients in the face of diminished cholinergic function. Although there is evidence that randomized withdrawal of donepezil was associated with significant worsening of neuropsychiatric symptoms, there was no short-term benefit for treatment of clinically significant agitation in a large randomized control trial (RCT). Cholinesterase inhibitors (ChEI) may have their greatest effects on depression/dysphoria, anxiety or apathy/indifference. Similarly, the neuropharmacologic rationale for using dopamine antagonists in elders with dopaminergic deficits is questionable. Agitation in AD is commonly derived from anxious, impulsive and compulsive symptoms, which may be responsive to serotonergic agents. Nyth and Gottfries provided placebo-controlled evidence that citalopram reduced symptoms of irritability, restlessness, anxiety, and depressed mood in AD subjects with mild to moderate behavioral symptoms. In our initial NIH-sponsored RCT, citalopram was found to be more efficacious than placebo, and as efficacious but better tolerated than perphenazine, in the acute treatment of patients with AD hospitalized to treat behavioral disturbances. Our more recent NIH RCT compared citalopram and risperidone. At the time this study was approved, risperidone was believed to have demonstrated efficacy and reviewers considered it unethical to have a placebo arm. A total of 103 non-depressed subjects with moderate to severe BPSD were randomized. Following acute treatment on a geriatric psychiatry inpatient unit, patients were followed for up to 12 weeks as they returned to nursing homes for continued care. Citalopram was found to be comparable in efficacy to risperidone and differentiated by its significant effect on agitation symptoms, and superior tolerability. Nonetheless, the absence of a placebo control reinforces the

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rationale for the new multisite trial, CITAD, which will focus on treating symptoms of agitation.

PO8.3

Physical activity and cognition in cognitively intact and impaired older persons

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Epidemiological studies show less prevalence of dementia among older persons who were physically active during childhood and adolescence. In addition, physical activity throughout life may decrease the risk for dementia. This positive relationship between physical activity and cognition does not automatically imply a causal relationship. To examine whether an increase in physical activity improves cognitive functioning in older persons with and without dementia, randomized controlled trials are essential. Results of those studies show that in older persons without dementia particularly executive functions (prefrontal cortex) respond positively to brisk walking. Positive effects of walking on executive functions have also been observed in older persons with very early signs of dementia. Results of recent studies show that walking does not improve cognition in a more advanced stage of dementia. The presentation will also address possible effects on cognition of other types of physical activity such as hand motor activity and mastication. Furthermore, some preliminary findings indicate that people who are ambulatory but do not take the initiative to walk anymore may benefit from watching the walking of other people on video. Finally, suggestions for future studies on the relationship between physical activity and cognition in older persons with dementia will be made.

PO9.1

Can epidemiological data be used to design a preventative intervention?

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In recent years, tee-shirts and bumper stickers have proclaimed that "Epidemiologists Count!" and "Epidemiologists are Broken Down by Age and Sex!". Certainly the major task of epidemiology is counting. Epidemiologists estimate prevalence rates of health problems by counting (the number of cases compared to the number in the total population). And they estimate the incidence of disease by counting (the number of cases that emerge over time from the population of individuals who are disease-free in the beginning). By comparing incidence rates across sociodemographic groups ("broken down by age and sex"), epidemiologists can identify populations that carry the greatest burden of disease. But can epidemiological data be used to design a preventative intervention? This talk uses examples from community-based studies of depression and disability in older adults to explore the use of epidemiologic data to identify: 1. settings and populations that might benefit most from preventive interventions, and 2. biopsychosocial factors that may be suitable targets for preventive interventions that aim to either eradicate the risk factor or change its impact on outcome. Finally, the limits of epidemiology are discussed and, although their tee-shirts are silent on the subject, the importance of collaborating with medical and social sciences disciplines in the design process.

PO9.2

The contribution of epidemiology to mental health promotion and disease prevention in low and middle income countries

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Mental health and wellbeing among older people is indivisible from their general health and functioning, and their social welfare. It follows that mental health promotion actions will be somewhat generic in their focus. There is no specific evidence-base to inform mental health promotion in low and middle income countries. Recent evidence from the 10/66 Dementia Research Group's studies in 11 sites in China, India and Latin America, taken together with that gleaned from developed country studies, does provide some clues to guide future strategies. Initiatives to enhance social protection, promote general health, prevent chronic diseases, limit disability and increase participation, and to improve the quality and accessibility of general healthcare should all be highly salient to improvements in mental health among older people in those regions. Many of these measures are already promoted in the Madrid International Plan for Action on Ageing, and the UN Convention on the Rights of People with Disabilities. Aside from prevention of disease and promotion of healthy functioning, there is an urgent

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need to strengthen the ability of community health services to deliver evidence-based mental health care for older people. This should be done in an integrated way, within an overarching chronic disease management framework. More research is needed, into the epidemiology of late-life mental disorders (particularly their aetiology), into the effectiveness of high risk prevention strategies for late-life depression and of interventions for depression and dementia. True mental health promotion (as opposed to disease prevention or control) activities will need to be carefully culturally nuanced—more research is required to inform their development.

P09.3

Translating epidemiological risk factors into public health practice: The example of anticholinergic load reduction in reducing dementia risk

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Longitudinal population studies have pointed to a number of potential risk factors for dementia that are potentially reversible. The implementation of public health intervention measures are, however, costly and require substantial proof of likely cost-benefit. The principal problem in translating results from epidemiological findings to public health practice is that causality cannot be proved. On the other hand a number of criteria exist that indicate the probability of causality. Data from a longitudinal population study of community-dwelling elderly observed that use of drugs with high anticholinergic activity was associated with poorer performance on reaction time, attention, delayed non-verbal memory, narrative recall, visuospatial construction and language tasks. Eighty percent of users were classified as MCI after one year of anticholinergic drug use compared to 35.3% of non-ACM users. Anticholinergic medication use was a strong predictor of MCI classification ($OR = 5.12$, $p = 0.001$). In a subsequent study on a larger cohort, anticholinergic drug users were found to be at significantly increased risk of dementia. The risk of incident dementia over four years was increased in continuous users ($HR = 1.71$, $CI = 1.04–2.82$) but not in those having discontinued ($HR = 1.27$, $CI = 0.59–2.74$). Validation criteria are applied to the results in order to assess probability of causality and the likely effect on dementia incidence of a public health campaign to reduce anticholinergic burden.

P10.1

Prevention of late-life mental disorders: What is possible?

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This presentation will summarize the information presented during the Congress and, based on this information, discuss what is currently possible in terms of universal, selective, and indicated prevention of late-life mental disorders.

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