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Making the most of ourselves in the 21st century**

**State-of-Science Review: SR-B2
The Influence of Demographic, Social and Physical Factors on Ageing
and the Mental Health of Older People**

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Summary

Depression and dementia are the most pressing public mental health issues for older people and are the focus for this review. For dementia, the most important environmental risk factors (and also, potentially, the most amenable to preventative intervention) are cardiovascular disease and cardiovascular risk factors. Improving the 'vascular health' of a population might have substantial benefits; however, improvements in vascular health will also increase survival and it is not clear what the actual impact on later dementia prevalence will be. Social factors are also important in dementia but primarily in modifying its course and impact after it has developed. Both social isolation and physical ill-health (particularly when associated with disability) are important and preventable risk factors for late-life depression. Depression and dementia are both poorly recognised in general healthcare settings and, if they are recognised, may be associated with reduced quality of healthcare.

1. Introduction: key definitions

'Lifelong mental health' and mental health in older people are increasingly recognised as pressing public health priorities. It is beyond the scope of this review to cover all mental disorders occurring in late life. The focus will rather be on dementia and depression as the two disorders with largest public health and societal impact. It is important at the outset to consider briefly the constructs of old age, depression and dementia:

- **'Old age'** Mental health research in 'older people' most often focuses on people aged 65 years and over – that is, above the most frequent, statutory retirement age in Western nations. This is obviously an arbitrary definition. The 65+ age range itself encompasses very heterogeneous populations. It can refer to people within a decade after retirement who can reasonably expect to be in good physical health with low risk of dementia and cognitive impairment. Or, it can mean those in later decades where physical and mental decline become much more common (although by no means inevitable), and where profound social changes are more likely to have occurred such as the loss of life-partners and friends through bereavement and co-occurring challenges to independent living. The traditional '65+' cut-off is likely to become steadily less relevant as retirement ages become more flexible, so research by necessity may well focus on more variable age ranges. This will present potential challenges for future synthesis.
- **Depression** 'Depression' as a diagnosis applied in clinical settings, generally requires persistent low mood which is accompanied by other symptoms (such as disturbance of sleep and appetite), and which is causing significant distress and/or disablement. However, mood states do not exist naturally in categories, but instead vary across a spectrum of normality to abnormality. As with any 'cut-off' applied to an underlying measure of disturbance (like hypertension, for example), the prevalence of the disorder (i.e. how common it is in a given population) depends substantially on the level set for the cut-off. Severe depressive syndromes have a high individual impact on those affected, but are rare (e.g. 2-3% for the relatively severe syndrome of 'major depression' used frequently in US research). Milder syndromes have a lower individual impact but may have a substantially higher public health impact because they affect many more people. In UK and European epidemiological research, depression in older people is most commonly defined on the basis of 'clinical significance' – i.e. of a sufficient degree to warrant an intervention in a standard clinical setting. This encompasses both moderate and severe forms and its prevalence in older people is generally between 10-20% (Beekman et al., 1999).
- **Dementia** Dementia describes a progressive decline in cognitive function (i.e. in functions of the brain such as memory, concentration, thinking and reasoning). The most common underlying

disorder is Alzheimer's disease, but dementia can also be caused by strokes ('vascular dementia') and can accompany other brain disorders such as Parkinson's disease. There are a wide variety of more rare causes. As with depression, there is no absolute distinction between cognitive function which is normal or abnormal. Dementia is conventionally defined in research settings when cognitive decline has reached the stage of affecting a person's daily activities. There is, however, considerable research interest in 'mild cognitive impairment', on the assumption that interventions may be more effective in earlier disease. It is thought likely that the brain changes underlying Alzheimer's disease have been developing over 10 to 20 years before any symptoms become noticeable. This is an important consideration when considering interventions to delay or prevent dementia.

The influence of demographic, social and physical factors will next be considered for dementia and depression in turn.

2. Demographic, physical and social factors in dementia

The strongest factor associated with risk of dementia is age itself. Estimates of UK dementia prevalence from a recent consensus report were 1% for people aged 65-69, 6% for people aged 75-79, and 20% for people aged 85-89 (Knapp et al., 2007). There is still debate as to whether risk continues to rise in the oldest age groups (e.g. beyond 95 years) with conflicting findings and obvious difficulties in identifying large enough populations for an accurate estimate. Much of the age-associated increase can be accounted for by Alzheimer's disease as the most common cause of dementia in older people, but other causes of cognitive decline such as stroke and Parkinson's also become more common with increasing age. The age structure of a population is the most important determinant of the overall prevalence of dementia.

However, an important unknown is whether risks for a given age group are stable over time. Physical factors, particularly risk factors for vascular disease, are important determinants of dementia risk, but also of mortality (i.e. a person's chances of living long enough to develop dementia). If a population becomes healthier with respect to heart disease and stroke, this may result in lower age-specific incidence of dementia, hence leading to a reduction in overall prevalence. However, if the mortality from cardiovascular disease falls more rapidly than the incidence, then exposure to these important risk factors for dementia could actually increase over time. Increases in survival with dementia would also lead to increases in dementia prevalence.

Current estimates of numbers affected take into account demographic changes in population age structures, but rely on age-specific prevalence estimates principally derived from studies carried out over 10 years ago. There is a pressing need for more up-to-date research and continued surveillance.

Age-specific risk of dementia has not generally been found to differ substantially between men and women. Alzheimer's disease is usually slightly more common in women, particularly among the oldest old, and vascular (stroke-related) dementia more common in men. However, it is still important to bear in mind that the large majority of older people with dementia are women, simply because of their greater longevity. Most studies have found that dementia is less common in people with higher levels of education and/or higher previous socio-economic status (Stern et al., 1994), although these findings are more consistent for cross-sectional compared to longitudinal studies. Several explanations have been proposed for this: in particular the cognitive reserve theory which proposes that people with higher education are able to sustain higher levels of brain damage before manifesting clinical symptoms of dementia. This is supported by some findings to suggest that people with high education, when they do develop dementia, tend to show a more rapid subsequent decline indicative of more severe underlying disease (Stern et al., 1995).

An important consideration arising from this finding is whether cognitive reserve can be influenced later in life. Several studies have found that people who are more active, whether cognitively, socially or physically, have a lower risk of cognitive decline or dementia (Wang et al., 2002). This provides some support for the 'use it or lose it' message, but it is not possible to draw firm conclusions concerning cause and effect from observational research.

Studies of physical factors underlying dementia have focused particularly on 'vascular factors' – both the disorders resulting from arterial disease and risk factors for those disorders. There is a general consensus that the key risk factors for heart disease and stroke are also risk factors for dementia. Stroke has long been recognised to be a risk factor for dementia, and the 'diagnosis' of vascular dementia was coined to reflect dementia caused by stroke and sub-clinical cerebrovascular disease.

However, a growing body of evidence over the last five to 10 years suggests strongly that vascular factors are also important in Alzheimer's disease (Stewart, 1998). This has been particularly the case for vascular risk factors such as high blood pressure, high cholesterol and obesity measured in mid-life, at least a decade before the onset of dementia (Launer et al., 1995; Kivipelto et al., 2001; Gustafson et al., 2003).

Shorter-term follow-up studies have tended to report more variable findings or even reverse associations. This appears to be because dementia itself is accompanied by physical changes which mask these associations – in particular weight loss and a decline in blood pressure and cholesterol (Qiu et al., 2004; Stewart et al., 2005; Stewart et al., 2006). An exception to this is diabetes where associations with increased risk of dementia are most often found in studies with shorter (e.g. three- to five-year) follow-up (Ott et al., 1999). This may be because cognitive decline in diabetes is associated with more severe disease and higher mortality once dementia has developed, reducing the likelihood of the two being observed together in studies with long follow-up periods. Of other recognised vascular risk factors, most have at least some support as risk factors for dementia, such as smoking (Ott et al., 1998), whereas exercise and a low fat diet are potentially protective (Kalmijn et al., 1997; Laurin et al., 2001).

Several studies have sought to evaluate whether modifying vascular risk factors may prevent dementia. These have principally involved medication trials designed to evaluate benefits for heart disease or stroke as outcomes but with cognitive function and/or dementia included as secondary measures. Of these, one trial of antihypertensive agents has reported a protective effect on dementia (Forette et al., 1998), but four others did not find effects on cognitive function in primary analyses (Prince et al., 1996; Starr et al., 1996; Lithell et al., 2003; Tzourio et al., 2003). Three large trials of cholesterol lowering agents have also failed to find effects on cognitive function (Santanello et al., 1997; Heart Protection Study Collaborative Group, 2002).

However, there are a number of reasons why results may be negative: i) vascular factors may exert their risk effect on dementia over a decade or more – far longer than is feasible as a trial duration; ii) participants in many clinical trials are at very low risk of developing dementia or cognitive impairment because of their relatively young age and good health; iii) the measures of cognitive function used in cognitive 'add-on' trials (which tend to be brief global screens) may be inadequate to detect the subtle changes occurring in early dementia; iv) once a trial has shown a benefit on outcomes such as stroke or heart disease it has to be discontinued for ethical reasons – agents are likely to show these benefits before dementia has time to develop. These issues create a dilemma where trials are necessary to prove the effectiveness of interventions, but very difficult in practice to carry out in many circumstances for dementia as an outcome. Other physical and social factors may be important in dementia, but have received less attention. 'Reserve' theory may extend beyond education and earlier cognitive function. A person with early Alzheimer's disease may be more likely to show signs of dementia if they have physical impairments or higher levels of general frailty. Social environment may also be important, with more isolated people presenting at later stages of dementia because the early symptoms have gone unnoticed. Physical health and the quality of a person's social environment will also have a high impact on outcomes of dementia such as a requirement for institutional care.

3. Demographic, physical and social factors in depression

Across the adult age range, the prevalence of depressive disorders increases from young to mid-adult age groups, followed by a fall in prevalence for older people within a decade of the retirement age (Evans et al., 2003). However, studies that have focused upon depressive symptoms and broader depressive syndromes indicate either an increase in their frequency or stability with increasing age (Tannock and Katona, 1995). The high prevalence of physical and social stressors (described below) in these more advanced age groups is most likely to be responsible. The exclusion, in some diagnostic criteria, of symptoms considered to be primarily attributable to bereavement and physical illness may account in part for the apparent lower prevalence of depressive disorders in older people in studies using these criteria.

Higher prevalence of depression is usually found in women compared to men, but this gender difference is generally substantially less than that found in younger age groups. The EURODEP consortium (Prince et al., 1999) reported a clear excess of depression symptoms in older women in population-based studies from 13 out of 14 European centres. Interestingly, this association was consistently modified by marital status, with marriage being protective for men but associated with higher risk among women. In older people, these findings are consistent with the observation from several studies that married older men cite their wife as their main confidant, whereas women more often cite a friend outside the home. Marriage is associated with relatively low mortality and good health, although this protective effect also seems to be stronger for men than for women.

3.1 *Social support and the buffer hypothesis*

One of the more consistent findings from previous research is the apparent bolstering of mood and morale in older people provided by contact with friends, in particular intimate, confiding relationships. While older people typically receive instrumental support from spouses and relatives, they value friends for the companionship and emotional support which they can provide. In the longitudinal Gospel Oak study, no contact with friends was the only social support variable prospectively associated with the onset of depression (Prince et al., 1998). In this study, lack of social support and social participation were associated with the maintenance, rather than with the onset, of depression. Physical health status, age and gender may modify or explain to some extent the association between social support and late-life depression.

There are large gender differences between the social support networks of older people, with women typically having more supportive and extensive networks of friends than men. Social networks deteriorate with increasing age consequent upon bereavement. Social engagement, such as visiting friends, is impaired in those with disability. In younger people, negative self-esteem and lack of social support are believed to act as vulnerability factors, increasing the risk of depression in the presence of a life event. While both life events and lack of social support are consistent risk factors for depression in older people, this interaction has not generally been replicated.

3.2 *Social class, income and education*

There have been many reports from cross-sectional, community surveys from a variety of cultures of associations between late-life depression and relative disadvantage in income. These are, of course, highly correlated variables, and it will always be difficult to determine the effect of one independent of the others. Much of the effect may be explained by physical health. The possibility of reverse causality also needs to be considered because of the well-recognised phenomenon of social drift: people whose adult life has been scarred by depression may experience lifelong occupational and economic disadvantage.

4. Inter-relationship between depression and chronic, non-communicable diseases

There is a substantial excess all-cause mortality risk independently associated with mental disorder. Depression has been studied most extensively, being associated with an approximately 70% increased risk (Saz and Dewey, 2001). The association may be mediated partly through disability, but not apparently through cardiovascular disease, cardiovascular risk factors, or antidepressant use. Evidence is strong from population-based research for substantial prospective associations between depression and outcomes such as angina, non-fatal and fatal myocardial infarction (Hemingway and Marmot, 1999). There is also strong evidence that depression is an independent risk factor for stroke (Larson et al., 2001). Many studies have involved follow-up periods of ten years or more, so that depression induced by pre-clinical cardiovascular disease is an unlikely explanation. The associations are, surprisingly, independent of vascular risk factors such as obesity, smoking and hypertension.

Depression is also an important consequence of cardiovascular disease, complicates its management, and is associated with worse outcomes. Incidence of depression is increased after myocardial infarction (to 15-30% for major depression): principally in the first month after the event (Strik et al., 2004). Comorbid depression is also a consistent and independent predictor of adverse outcomes after non-fatal myocardial infarction such as recurrent CHD events, CHD mortality, and all-cause mortality (Hemingway and Marmot, 1999). Poor prognosis may be explained partly by poor adherence to behaviour and lifestyle changes intended to reduce the risk of subsequent cardiac events. Strong associations are also found between recent stroke and onset of depression, independent of disability (Kim et al., 2006), and post-stroke depression is associated with poor functional outcomes (Parikh et al., 1990) and substantially higher mortality (Morris et al., 1993).

To date, psychological interventions after myocardial infarction have not been found to have effects on total or cardiac mortality, but have shown small reductions in depression (Rees et al., 2004). However, few interventions have specifically targeted affective disorder. SSRI antidepressants have been found to be safe and moderately effective treatments for depression after myocardial infarction, and a large trial of cognitive behavioural therapy and an SSRI antidepressant produced significant improvement in mood and social support, although not with improvement in MI-free or overall survival (Berkman et al., 2003). The evidence base for the effectiveness of antidepressants after stroke is weak, with a lack of findings to date on their effectiveness as a preventive intervention (Anderson et al., 2004). Pharmacological interventions for post-stroke depression show clear evidence for a reduction in symptoms, but not for remission of diagnosable depression or improvement in stroke recovery (Hackett et al., 2005).

Dementia and depression are themselves interrelated disorders in older people. Depression occurs commonly in people with dementia, and late-life depression is also a predictor of dementia (Devenand et al., 1996), although it is not clear whether this is because depression is a risk factor or an early symptom. As with many disorders manifesting in late life, depression and dementia may have common risk factors which operate and interact over a long period. These could include cardiovascular risk factors, cerebrovascular disease and social isolation or deprivation (predisposing to cognitive decline, and impacting negatively on access to health and social care). Recent research strongly supports an overarching model in which it is the disability and restriction in social participation associated with any chronic health condition that most parsimoniously explains the increased risk for late-life depression. This finding, first reported in the UK Gospel Oak study has been subsequently confirmed in several other population-based cohort studies. In Gospel Oak, handicap was overwhelmingly the most important risk factor for onset of late-life depression, with a population-attributable risk fraction of 0.78. Three population-based studies have suggested an interaction between disablement and social support, with the strongest effect of disablement in those with the least social support (Beekman et al., 1997; Schoevers et al., 2000; Prince et al., 1998).

5. Genetic factors and gene–environment interactions in depression and dementia

Gene–environment interactions have been investigated for dementia, although findings to date remain controversial. The apolipoprotein E (APOE) gene has repeatedly been found to modify dementia risk. Some studies have also found associations between ‘environmental’ risk factors and dementia, although findings are inconsistent since some risk factor associations are stronger in the presence of the APOE ϵ 4 allele (Hofman et al., 1997) while others are stronger in its absence (Ott et al., 1998). Gene–environment interactions have attracted increasing interest for depression, with several studies finding that stressful life events are stronger risk factors in the presence of risk forms of the serotonin transporter (5-HTLPR) gene (Caspi et al., 2003). This has recently been replicated in an elderly sample in Korea (Kim et al., 2007), which suggests that gene–environment interactions may persist into later life.

6. Implications: potential impact of current societal changes on mental capital and wellbeing

For dementia, the potential impact of demographic ageing is well-recognised. While changes in population age structure can be predicted with reasonable accuracy, estimates of age-specific prevalence are now potentially out of date, which is a serious knowledge deficit. In a global context, demographic ageing is particularly rapid in many low or middle-income nations. Although these are not UK populations, there may still be substantial implications through the global economy.

Within the UK, the subsections of the population which are ageing most rapidly are minority ethnic groups. Little is known about the risk of dementia in these communities, which is also a major shortfall in our knowledge.

Changes in population physical health (for example, more successful treatment of vascular risk factors) may well have an impact on dementia prevalence, but (as described above) the direction of the effect is difficult to predict because the role of selective intervening mortality is poorly understood.

Societal changes in social fragmentation, disruption of family structures, as well as in expectations of health services and a growing awareness of dementia, are all important factors. But principally these concern the impact of dementia, once this has developed, and pathways through care (which are beyond the scope of this review). These factors, however, are likely to have a substantial impact on prevalence of depression, so often associated with loneliness and social isolation in older people. Similarly, the impact of population ageing depends largely on the extent to which this is comprised of truly healthy ageing, or longevity with chronic and disabling health conditions. An important consideration for dementia is the high volume of current research into underlying neuropathological processes, particularly for Alzheimer’s disease, and into potential pharmacological interventions to halt or delay disease progression. Pharmacological interventions, principally acetylcholinesterase inhibitors, are already available and have been demonstrated to have an effect on dementia progression, although the impact of these agents on quality of life and their cost-effectiveness remain the subjects of debate.

The likely impact of pharmacological and neurobiological research is impossible to predict, although it seems reasonable to assume that significant further breakthroughs will occur and novel interventions will be developed within the next two decades. Any improvements in prevention or disease modification, even if expensive, may well have substantial effects on survival and health, and on social care costs given the high levels of disability associated with this condition.

7. Implications: potential interventions to protect or enhance mental capital in older people

7.1 For depression

- Population-level interventions designed to promote full and active participation of older people in society, consistent with the UN Convention on the Rights of Persons with Disabilities (2006).
- Individual-level interventions in clinical settings to treat impairments, limit disability and maximise function.
- Evaluate, and promote as appropriate, effective models for social network building both within the older age group (e.g. University of the Third Age) and transgenerationally (e.g. schools / youth engagement programmes).
- Ensure that older people are not selectively excluded from evidence-based interventions for depression e.g. cognitive behaviour therapy (CBT), interpersonal therapy (IPT) and antidepressants.

7.2 For dementia

- Promote cardiovascular health.
- Promote and maintain physical activity.
- Promote and maintain mental and social activity.
- Promote and maintain a balanced and healthy diet.
- Address deficiencies in the quality of general healthcare afforded to people with dementia.

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