

## COMMENTARY

# Increasing incidence of dementia in the oldest old: evidence and implications

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### Abstract

The oldest old are the fastest growing segment of the US population but accurate estimates of the incidence of dementia in this age group have been elusive. Corrada and colleagues present data on the 5-year age-specific rates of dementia incidence in persons 90 years and older from The 90+ Study. Their findings show a continued exponential increase in dementia incidence after age 90 that mirrors the increase observed in persons aged 65 to 90, with a doubling every 5.5 years. This contrasts with previous smaller studies reporting a slowing of the increase in incidence after age 90. If confirmed, the continued increase, rather than a plateau, in the incidence of dementia in the oldest old has implications for proper healthcare planning. Strategies for prevention and treatment will require more information regarding risk factors and the etiopathogenesis of dementia in the oldest old.

The oldest old, persons living into the 10th and 11th decades of life, are the fastest growing segment of the population, with numbers expected to quadruple to over 8 million by 2050 [1]. Because advancing age is a major risk factor for dementia, this demographic shift may significantly increase the burden of dementia borne by our society. Indeed, the dementia incidence in persons aged 65 to 90 has been reported to double every 5 years [2]. However, few studies have had sufficient numbers of participants older than 90 years of age to provide accurate estimates in the oldest old and some studies have suggested a slowing of the incidence in the oldest old [3,4]. Further work is thus needed to determine the incidence of dementia in the oldest old. The present work not only has important implications for public health

planning, but is also relevant for studies of etiopathogenesis and strategies for prevention and treatment.

In a pivotal study addressing this question, Corrada and colleagues present data showing that the incidence of dementia continues to exponentially rise in the oldest old [5]. The authors studied 330 persons from The 90+ Study, a longitudinal cohort study of dementia in the oldest old. Participants were originally members of an epidemiological study of a retirement community in the 1980s [6]; 950 of the 1,150 persons at least 90 years old in 2003 were enrolled. Analyses for this study included only non-demented persons at baseline, as ascertained by in-person evaluation, who had at least one follow-up over 4 years. The authors found that the incident rate of dementia increased exponentially, from 12.7% per year for 90 to 94 year olds, to 21.2% per year for 95 to 99 year olds, to 40.7% per year for persons aged 100 years and older. The estimated doubling time for incidence rates was 5.5 years and is comparable with that observed for persons aged 65 to 90.

The results of this study contrast with other studies that showed a slowing of dementia incidence after age 90 [7-13]. Importantly, the study has a number of strengths that strongly support the validity of the estimate. Having a much larger sample size, particularly for the 95 to 100 year olds and centenarians, allows for more stable estimates of incidence rates. Additionally, 6-month intervals between assessments and high follow-up rates (96%) make it unlikely that loss to follow-up could erroneously result in an underestimate of incidence. There were some limitations, including the selective nature of the cohort, raising questions about selection bias and generalizability. The authors note that their study population – predominantly female, white, with high education and socioeconomic status – is representative of individuals aged 90+ in the US. Nonetheless, participants were originally recruited from one retirement community and agreed to participate in not one but two cohort studies, making selection bias still a potential issue. Epidemiologic studies with more racially and ethnically diverse cohorts will be important to confirm and extend these findings.

If confirmed, these data suggest a looming public health crisis. How can we prevent, delay, or treat dementia

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in the oldest old? To better address these questions, it will be important to determine the pathogenesis of dementia in the oldest old. Longitudinal clinicopathologic epidemiologic studies suggest that dementia in older persons is most commonly the result of mixed pathologies; most commonly Alzheimer's disease and vascular pathology [14-16]. While there are few pathologic data on the oldest old, a recent autopsy study in this group showed that mixed Alzheimer's disease and vascular pathology continues to increase with age [17]. Meanwhile, it has been suggested that the relationship between Alzheimer's disease pathology and dementia is attenuated in the oldest old [18]. This hypothesis may suggest a greater role for vascular factors or even suggest additional unrecognized pathologies. Further study of aging, dementia, and pathology in longitudinal community-based cohorts will be needed to address these important questions.

As the first major study to report that dementia incidence continues to rise exponentially in the oldest old, the present study has implications for how we conceive of the relationship between aging and dementia. It has been argued that a plateau in incidence in the oldest old indicates that dementia is not an 'aging-related' process – that is, an inevitable part of aging [19] – but rather an 'age-related' process, due to potentially preventable age-related risk factors [4,12,13]. Yet the distinction between these two concepts may be artificial. Indeed, the continued rise in incidence could result from the continued accumulation of age-related risk factors eventually surpassing the brain's compensatory facilities (that is, reserve capacity). In addition, even if some components of the pathologic process are inevitable, given the possible continued accumulation of Alzheimer's disease and mixed pathologies, it remains quite feasible that targeted strategies could prevent, delay, or treat at least part of the dementing process in the oldest old. After all, public health initiatives have dramatically pushed back the average age of death, the most inevitable consequence of aging.

#### Competing interests

JAS is a neuropathology consultant for AVID Radiopharmaceuticals, Inc. and is on the Alzheimer's Medical Advisory Board for GE Healthcare. The authors declare no other competing interests.

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