Correspondence

EDITED BY MATTHEW HOTOPF

Advising relatives of risk of Alzheimer's disease

Liddell *et al* (2001) reviewed what knowledge we have on the genetic epidemiology of Alzheimer's disease for the purpose of informing relatives of patients about their own risks. We read their review with interest; however, we disagree on several points.

First, in many cases of late-onset dementia, differentiating between the common causes of Alzheimer's disease and vascular dementia is difficult. In everyday clinical practice even differentiating Alzheimer's disease from Lewy-body disease and frontal–temporal dementia is not always feasible. To what extent these distinctions are relevant to genetic counselling with respect to late-onset dementia is not clear.

Second, the very high prevalence of dementia found in centenarians (Asada *et al*, 1996; Blansjaar *et al*, 2000) is not the only argument against a slowing down of the rate of increase in dementia over 85, 90 or 95 years of age. Meta-analyses, not included in the review, did not find evidence for such a slowing down (Gao *et al*, 1998; Jorm & Jolley, 1998). Therefore, the prevalence of dementia almost certainly increases substantially, exceeding 15% from the age of 85.

Most investigations attributed some three-quarters of late-onset dementia to Alzheimer's disease. We agree that the literature indicates a three- to fourfold risk in first-degree relatives of patients with late-onset dementia (seven- to eightfold with two affected first-degree relatives). We can only conclude that this leads to a risk of one in three, if not higher, for those first-degree relatives who reach the age of 85 years. Obfuscating this information by showing graphs to anxious relatives is, in our opinion, not an appropriate reassurance. We feel that better consolation can be effected by proffering the view that most people do not reach the age of 85, and by explaining the slowly progressive course of most cases of late-onset dementia.

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Blansjaar, B. A., Thomassen, R. & van Schaick, H. W. (2000) Prevalence of dementia in centenarians. *International Journal of Geriatric Psychiatry*, **15**, 219–225.

Gao, S., Hendrie, H. C., Hall, K. S., *et al* (1998) The relationships between age, sex, and the incidence of dementia and Alzheimer's disease: a meta-analysis. *Archives of General Psychiatry*, **55**, 809–815.

Jorm, A. F. & Jolley, D. (1998) The incidence of dementia: a meta-analysis. *Neurology*, **51**, 728–733.

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Authors' reply: For the most part, the points of disagreement that Drs Blansjaar and van Schaick raise are differences more of emphasis than of substance.

True, the diagnosis of the type of dementia, particularly in late old age, is not always easy. Dementia in later life is probably best described as a syndrome, the emergence of clinical dementia being dependent upon the interplay of two or more pathologies. The 'Nun Study' by Snowdon *et al* (1997) is probably one of the best demonstrations of this. Yet, it is believed that Alzheimer's disease is a major cause of dementia in later life. Even without having seen the patient, one is going to be correct in a diagnosis of Alzheimer's disease, or Alzheimer's disease and cerebrovascular disease, 75% of the time. Rarer diagnoses, such as frontal–temporal dementia and Lewy-body disease, should suggest themselves if they are kept in mind, a careful history taken and the patient followed-up so that departures from the normal symptom progression for Alzheimer's disease are noted. Of course, mistakes in diagnosis will occur, but we think that this will occur insufficiently frequently to compromise the very broad-brush approach to estimating the familial risk of dementia that we have advocated.

As to whether the rate of increase in the incidence and prevalence of dementia begins to slow or goes on increasing exponentially into extreme old age, this is a controversial area, which is, in fact, also highlighted in the two meta-analyses cited by Drs Blansjaar and van Schaick. Jorm & Jolley (1998) suggest that "the incidence rises exponentially up to the age of 90 years". Gao *et al* (1998) suggest that "the acceleration of incidence rates for AD and dementia slows down with the increase in age, although we find no evidence of a rate decline". Faced with such difficulties of interpretation, we can only commend the clarity of Blansjaar *et al*'s own study (2000), which suggests that the increase in dementia prevalence does not slow down in extreme old age.

We agree that the risk of a first-degree relative of a proband with Alzheimer's disease developing the disorder once they reach the age of 85 may be one in three, if not higher. Perhaps this point could have been made more clearly in our review. The main point we tried to make was that the actual likelihood of surviving to age 85 *and* developing Alzheimer's disease is lower. We disagree that showing graphs to anxious relatives is "obfuscating this information", but we accept that Drs Blansjaar and van Schaick and, indeed, other clinicians may think differently.

In non-Mendelian Alzheimer's disease it is difficult to estimate how much the risk increases as the number of affected first-degree relatives goes up, principally because few studies have addressed this issue. However, the 'conjugal Alzheimer's disease' study of Bird *et al* (1993), which we cited, and the transmission study of Farrer *et al* (1990), which we did not cite, indicate that the risk increases substantially. With such pedigrees showing apparently high genetic loading for Alzheimer's disease, we suggested that a psychiatrist seek the advice of a clinical geneticist.

Finally, we agree that it is often reassuring to point out that the course of dementia in late old age is usually more slowly progressive and more benign than dementia occurring in a younger person.

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