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Relative risk for Alzheimer disease based on complete family history

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Study objective and summary result

This study used a large population data base and family history of Alzheimer disease (AD) extending beyond the immediate family to provide accurate and individualized risk predictions for AD.

What is known and what this paper adds

Family history is a recognized risk factor for AD, but most clinicians consider only immediate family members. This study provides evidence for the utility of medical history in the extended family, as well as specific and useful risk predictions for many family history constellations.

Participants and setting

This study analyzed data for 270,818 decedents listed in the Utah Population Database (UPDB), a genealogy database listing 19th century Utah pioneers and their descendants through to the present. For each decedent, this study obtained a Utah death certificate and genealogy data covering both parents, all 4 grandparents, and ≥6 great-grandparents. Of the decedents, 149,303 died in or after 1979, the year in which AD started being listed as a cause of death on Utah death certificates.

Design, size, and duration

This study reviewed the post-1978 death certificates to identify cases of AD-related death. For each AD family history pattern, this study identified all individuals with the given pattern (i.e., the probands) and then determined the relative risk for AD associated with that pattern by dividing the number of probands with AD by the number that would be expected from chance.

Primary outcome measures

The primary outcomes were specific relative risk estimates for AD associated with different family history patterns.

Main results and the role of chance

This study identified 4,436 AD-related deaths. The risk of AD increased with the presence of affected first-degree relatives (FDRs), second-degree relatives (SDRs), and was even elevated with only a family history in third-degree relatives (TDRs). In addition, higher risks for males than females with equivalent family history were observed.

Table Associations between family history patterns and risks of AD

AD family history pattern	Relative risk (95% confidence interval) for AD
≥2 FDRs	3.98 (3.26–4.82)
≥4 FDRs	14.77 (5.42–32.15)
0 FDRs and ≥3 SDRs	2.46 (1.13–4.68)
1 FDR and 2 SDRs	21.29 (5.80–54.52)
0 FDRs, 0 SDRs, and ≥3 TDRs	1.43 (1.21–1.68)

Bias, confounding, and other reasons for caution

Reliance on death certificates is known to cause underestimation of AD prevalences. The reliance on UPDB data might have introduced selection bias.

Generalizability to other populations

The reliance on data from descendants of Utah pioneers may limit the generalizability of this study's results.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.