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REVIEW OF A SCIENTIFIC CONSULTANT

to the doctoral dissertation by Aiym Kaiyrlykyzy
entitled «Risk factors associated with Alzheimer's disease in Kazakhstan»
submitted for the degree of Doctor of Philosophy (PhD) in Public Health (8D10101)

As the scientific consultant to this doctoral dissertation, I am pleased to provide my assessment of the work carried out by Aiym Kaiyrlykyzy. She is a graduate of the Department of Epidemiology at the University of Pittsburgh, where she earned her Master of Public Health in Epidemiology in 2014.

Overall, this dissertation is ambitious and highly valuable, particularly because it addresses Alzheimer's disease risk factors in Kazakhstan and Central Asia, a region that remains substantially underrepresented in global dementia epidemiology. To my knowledge, it is the first comprehensive, multi-domain characterization of Alzheimer's disease risk factors in this population, and its contribution lies not only in extending established global findings to an understudied setting but also in showing why population-specific evidence is needed. The principal findings are coherent and well supported. The dissertation identifies functional illiteracy as the strongest modifiable correlate of Alzheimer's disease, together with depression and social isolation, and documents the contribution of the APOE ε4, including a regional gradient in its distribution. The biochemical, adiponectin, and inflammatory analyses point to systemic metabolic and immune involvement, while the dietary, microbiome, and genetic analyses are appropriately framed as generating hypotheses for future study. Taken together, they offer a coherent and multifactorial picture of Alzheimer's disease in the Kazakhstani population.

Throughout the consultation process, I raised several methodological points on epidemiological design, its analysis, and the interpretation of the results, and I recommended strengthening the methods section by clearer separation between the robust, hypothesis-driven findings and the exploratory high-dimensional analyses, together with an explicit multiple-testing strategy, and this is now consistently reflected throughout the dissertation. I drew attention to the composition of the control group, in which cerebrovascular and cardiometabolic conditions were comparatively prevalent, and recommended sensitivity analyses that excluded participants with prior stroke and, separately, prior stroke or transient ischemic attack. These were carried out, and the principal associations, such as illiteracy, rural birthplace, and depression, remained robust. The independence the candidate showed in addressing these points is exactly what one hopes to see in a doctoral scientist.

In summary, this dissertation makes an original and substantial contribution to the epidemiology of Alzheimer's disease, and I support it without reservation and recommend it for defense.

Scientific consultant:



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