

New Evidence for an Alzheimer’s Disease – Cancer Trade-off: Adult Infections are Associated With a Higher Risk of AD but a Lower Risk of Cancer

Developing Topics

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Take-Home Message: History of infectious diseases may antagonistically influence risks of AD and cancer (all sites combined) in older adults. Relative contribution of specific cancer sites to this trade-off needs to be determined. Understanding such trade-offs is important for optimizing both AD and cancer prevention and for avoiding situations in which measures aimed at preventing one major disease inadvertently increase the risk of another or negatively affect overall survival.

INTRODUCTION	METHODS	RESULTS	RESULTS	CONCLUSIONS																																																				
Growing evidence suggests that infections are important contributors to late-onset Alzheimer’s disease (AD) risk Some infections have also been linked to cancer risk. However, certain infections have historically been explored as potential cancer treatments, based on the idea that they could stimulate immune responses that, in turn, would help eliminate transformed cells. This suggests that infections may play an ambivalent role in the development of AD and cancer, potentially resulting in trade-off–like effects on the risks of AD and cancer.	We examined associations between history of infections and risks of AD and cancer (all sites) in a subsample of 320,646 UK Biobank (UKB) participants (Table). The risks in each group were estimated using confidence intervals for binomial probabilities, Wilson score interval, confidence intervals for difference of two binomial proportions, Wald interval. The risks were compared by employing Fisher's exact test and Wald risk ratio (RR) estimate. The difference by age between groups was estimated using the Welch test. The logistic regression models were evaluated using the Akaike information criterion.	A history of infections (by ICD-10 codes) was associated with 42% and 67% <u>higher</u> risk of AD in women and men, respectively. Infections were associated with 56% and 54% <u>lower</u> risk of cancer (all sites) in women and men, respectively, compared to individuals without a history of infection. The results are also summarized in Figure. Table. Characteristics of the UKB sample <table><tr><th>Group</th><th>Females</th><th>Males</th><th>Females&Males</th></tr><tr><td>AD</td><td></td><td></td><td></td></tr><tr><td><i>Inf</i>s AD</td><td>416</td><td>428</td><td>844</td></tr><tr><td><i>Inf</i>s noAD</td><td>42550</td><td>39916</td><td>82466</td></tr><tr><td><i>noInf</i>s AD</td><td>1028</td><td>751</td><td>1779</td></tr><tr><td><i>noInf</i>s noAD</td><td>149963</td><td>117165</td><td>267128</td></tr><tr><td>All</td><td>193957</td><td>158260</td><td>352217</td></tr><tr><td>Cancer</td><td></td><td></td><td></td></tr><tr><td><i>Inf</i>s Cancer</td><td>1470</td><td>1819</td><td>3289</td></tr><tr><td><i>Inf</i>s noCancer</td><td>32237</td><td>30730</td><td>62967</td></tr><tr><td><i>noInf</i>s Cancer</td><td>13723</td><td>14044</td><td>27767</td></tr><tr><td><i>noInf</i>s noCancer</td><td>125199</td><td>101424</td><td>226623</td></tr><tr><td>All</td><td>172629</td><td>148017</td><td>320646</td></tr></table> Notes: AD: Alzheimer’s disease. <i>Cancer</i>: all cancers but skin and glioblastoma. <i>Inf</i>s and <i>noInf</i>s: UKB participants <i>with</i> and <i>without</i> history of one or more infectious diseases, based on ICD-10 codes (A00-B99, I30, I33, I40, J09-J18, J20-J22, K35, K85, L04).	Group	Females	Males	Females&Males	AD				<i>Inf</i> s AD	416	428	844	<i>Inf</i> s noAD	42550	39916	82466	<i>noInf</i> s AD	1028	751	1779	<i>noInf</i> s noAD	149963	117165	267128	All	193957	158260	352217	Cancer				<i>Inf</i> s Cancer	1470	1819	3289	<i>Inf</i> s noCancer	32237	30730	62967	<i>noInf</i> s Cancer	13723	14044	27767	<i>noInf</i> s noCancer	125199	101424	226623	All	172629	148017	320646	Figure. Risks of AD and cancer in men and women with (<i>Inf</i>s) and without (<i>noInf</i>s) history of diagnosed infectious diseases. (A) risk of AD, females. <i>Inf</i>s (risk: mean (m) = 0.0097, confidence interval (CI)=[0.0088,0.0107]), <i>noInf</i>s (risk: m=0.007, CI=[0.0064,0.0072]) (B) risk of cancer, females. <i>Inf</i>s (risk: m=0.044, CI=[0.4148,0.0458]), <i>noInf</i>s (risk: m=0.0988, CI=[0.0972,0.1004]) (C) risk of AD, males. <i>Inf</i>s (risk: m=0.011, CI=[0.0097,0.0117]); <i>noInf</i>s (risk: m=0.006, CI=[0.0059,0.0068]) (D) risk of cancer, males. <i>Inf</i>s (risk: m=0.056, CI=[0.0534,0.0584]); <i>noInf</i>s (risk: m=0.122, CI=[0.1198,0.1235])	Our findings support <u>trade-offs between AD and cancer (all sites) influenced by infections</u>. The relative contribution of specific cancer sites to this trade-off remains to be determined. Understanding such trade-offs is important for optimizing AD and cancer prevention and for avoiding situations in which measures aimed at preventing one major disease inadvertently increase the risk of another or negatively affect survival. Acknowledgements This research was supported by the National Institutes of Health's National Institute on Aging (NIA/NIH) grant R01AG076019. This content is solely the responsibility of the authors and does not necessarily represent the official views of the NIA/NIH. This research has been conducted using the UK Biobank Resource, application # 82705. Duke University BARU team: Vladimir Popov, Hongzhe Duan, Igor Akushevich, Arseniy Yashkin, Konstantin Arbeev, Anatoliy Yashin ALZHEIMER'S ASSOCIATION AAIC 26
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