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# New study reveals that Epstein–Barr virus infection may increase risk of a broad spectrum of cancer types

**Lyon, France, 8 July 2025** – A new study from the International Agency for Research on Cancer (IARC) and its partners explores the link between levels of Epstein–Barr virus (EBV) capsid antigen (VCA-IgA) antibodies, which are produced in response to EBV infection, and cancer risk.

The findings, published in *Nature Communications*,<sup>1</sup> reveal a significant association between the presence of these antibodies and an increased risk of multiple cancer types. Individuals who tested positive for EBV VCA-IgA antibodies were found to have a higher risk of developing cancers such as lung cancer, liver cancer, nasopharyngeal carcinoma, and lymphoma; the association with nasopharyngeal carcinoma was the strongest.

The study evaluated the cancer risk in two large prospective cohorts in Southern China comprising 73 939 adults. During about 8–10 years of follow-up, 964 incident cases of cancer were identified in the Zhongshan cohort and 1026 in the Wuzhou cohort.

## **Risk estimates**

The study found that individuals who tested positive for EBV VCA-IgA antibodies were nearly 5 times as likely to develop cancer compared with individuals who tested negative, with a hazard ratio  $(HR)^2$  of 4.88 (95% confidence interval [CI], 2.84–8.37) for all types of cancer combined.

The results also showed significantly higher risks of developing specific cancer types among seropositive individuals. For lung cancer, individuals with EBV VCA-IgA antibodies were 1.76 times as likely to develop the disease (HR, 1.76; 95% CI, 1.23–2.54), and for liver cancer, seropositive individuals were 1.70 times as likely to develop the disease (HR, 1.70; 95% CI, 1.10–2.63).

<sup>&</sup>lt;sup>1</sup> Ji MF, He YQ, Tang MZ, Xue WQ, Yu X, Diao H, et al. (2025). Epstein Barr virus antibody and cancer risk in two prospective cohorts in Southern China. *Nat Commun*. Published online 1 July 2025; <u>https://doi.org/10.1038/s41467-025-60999-5</u>

<sup>&</sup>lt;sup>2</sup> Hazard ratios measure the risk of developing cancer for seropositive individuals compared with individuals without the antibodies; a higher hazard ratio indicates a stronger association.





The most striking finding was for nasopharyngeal carcinoma; seropositive individuals were found to be 26.05 times as likely to develop the disease (HR, 26.05; 95% CI, 11.77–57.65); this was the highest risk increase among the cancer types studied.

Individuals with EBV VCA-IgA antibodies also had a significantly higher likelihood of developing lymphoma; seropositive individuals were 3.20 times as likely to develop the disease (HR, 3.20; 95% CI, 1.46–6.99).

These results highlight the strong association between EBV seropositivity and various types of cancer. The risk increase was the most pronounced for nasopharyngeal carcinoma.

The study revealed a dose–response relationship, in which higher levels of VCA-IgA antibodies were associated with an increased cancer risk. This elevated risk persisted even up to 10 years before diagnosis, suggesting that EBV infection and seropositivity may play a long-term role in cancer development.

Finally, the study estimated that 7.8% of the total cancer burden in Southern China could be attributed to EBV VCA-IgA seropositivity. This highlights the significant contribution of EBV infection to cancer incidence in the region.

## **EBV** and cancer

EBV is the most common and persistent human virus. It infects approximately 95% of the global population with a lifelong asymptomatic infection. Despite its widespread presence, EBV infection has been linked to a relatively small proportion of diseases, primarily cancers.

EBV was classified as carcinogenic to humans (Group 1) by IARC in 1997. To date, EBV infection has been directly linked to a few specific types of cancer, including certain lymphomas, nasopharyngeal carcinoma, lymphoepithelioma-like carcinoma, and a small proportion (~10%) of stomach cancers, although the link with stomach cancer is still being debated. These cancer types are estimated to account for 239 700–357 900 new cancer cases and 137 900–208 700 cancer deaths globally in 2020.<sup>3,4</sup>

"Although the association of EBV infection with certain cancer types, such as lymphomas and nasopharyngeal carcinoma, is well established, there have been less data on its broader cancer risk," says Dr Zisis Kozlakidis, Head of Laboratory Support, Biobanking, and Services at IARC and a co-author of the new study. "This study not only explores risks of individual cancer types but also assesses overall cancer risks. It aims to evaluate the cancer burden attributable to EBV infection and to better understand the link between EBV VCA-IgA antibodies and the risk of various cancer types."

<sup>&</sup>lt;sup>3</sup> de Martel C, Georges D, Bray F, Ferlay J, Clifford GM (2020). Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*. 8(2):e180–e190. <u>https://doi.org/10.1016/S2214-109X(19)30488-7</u>

<sup>&</sup>lt;sup>4</sup> Wong Y, Meehan MT, Burrows SR, Doolan DL, Miles JJ (2022). Estimating the global burden of Epstein–Barr virusrelated cancers. *J Cancer Res Clin Oncol*. 148(1):31–46. <u>https://doi.org/10.1007/s00432-021-03824-y</u>

# International Agency for Research on Cancer





# Note to the Editors

This study involved collaboration with a wide range of institutions, including the Cancer Research Institute of Zhongshan City and Zhongshan City People's Hospital in Guangdong, China; the State Key Laboratory of Oncology in South China and the Collaborative Innovation Center for Cancer Medicine at Sun Yat-sen University Cancer Center in Guangzhou, China; Wuzhou Red Cross Hospital and Wuzhou Cancer Center in Guangxi, China; the School of Public Health at Sun Yat-sen University; and the School of Public Health at the University of Hong Kong, Hong Kong Special Administrative Region.

## For more information, please contact

Veronique Terrasse, at terrassev@iarc.who.int

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