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Cancer surveillance, obesity, and potential bias

Although Hyuna Sung and colleagues stressed caution in interpreting their ecological study in *The Lancet Public Health* (March, 2019), the naive reader—or the media, as was the case—might conclude that obesity is fuelling the reported disproportionate temporal increases in incidence of obesity-related cancers in young adults. However, there are many arguments against obesity as a causal driver.

First, as the accompanying Comment highlighted, the biological mechanisms for many early-onset cancers are distinct from those of late-onset cancers. In colorectal cancer, the malignancy in which increases among young adults are most striking, the molecular phenotype of early-onset cancer is often an aggressive consensus molecular subtype (CMS), such as CMS-1 or CMS-3, whereas obesity-related cancers generally follow a more canonical CMS-2 pathway. Second, the Article by Sung and colleagues failed to demonstrate sex or racial specificity, which are hallmarks of the obesity–cancer relationship. Finally, the fundamental premise in age-period-cohort modelling attributes cohort effects to modifiable lifestyle or environmental factors, at the absolute rejection of short-term changes in population-level genetic susceptibility. This method ignores the contributory role of epigenetic effects (for example, methylation), which can influence short-term trends.

There is a need for a concerted effort from the research community to bring together wide-ranging disciplines to disentangle the causes of this emerging public health problem. The linked Comment advocates for “further close epidemiological monitoring”. We champion a wider approach, such as that captured by triangulation (the combination of evidence from studies that yield causal estimates with different potential sources of bias, but where these biases are independent), and inclusion of the use of non-conventional approaches, such as instrumental variable analyses.

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