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Cancer surveillance, obesity, and potential bias

Although Hyuna Sung and colleagues[1] stressed caution in interpreting their ecological study in *The Lancet Public Health* (March, 2019), the naive reader—or the media, as was the case[2]—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[3] 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[1] failed to demonstrate sex or racial specificity, which are hallmarks of the obesity–cancer relationship.[4] 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[3] advocates for "further close epidemiological monitoring". We champion a wider approach, such as that captured by triangulation[5] (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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