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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*Andrew G Renehan, Richard M Martin, D Gareth Evans
andrew.renehan@manchester.ac.uk

Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK (AGR); Manchester Cancer Research Centre, National Institute for Health Research (NIHR) Manchester Biomedical Research Centre, Manchester M20 4BX, UK (AGR, DGE); Department of Population Health Sciences, Bristol Medical School and MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK (RMM); National Institute for Health Research (NIHR) Bristo Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust, Bristol, UK (RMM); and Genomic Medicine, Division of Evolution and Genomic Sciences, Manchester Academic Health Sciences Centre, Manchester Universities Foundation Trust, Manchester, UK (DGE)

1 Sung H, Siegel LR, Rosenberg PS, Jemal A. Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry. *Lancet Public Health* 2019; **4:** e137–47.
2 Laura Donnelly, for The Telegraph. "Shocking" rise in obesity-related cancers among young adults. Feb 4, 2019. https://www.telegraph.co.uk/news/2019/02/04/shocking-rise-obesity-related-cancers-among-young-adults/ (accessed Feb 8, 2019).
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4 Renehan AG, Zwahlen M, Egger M. Adiposity and cancer risk: new mechanistic insights from epidemiology. *Nat Rev Cancer* 2015; **15:** 484–98.
5 Lawlor DA, Tilling K, Davey Smith G. Triangulation in aetiological epidemiology. *Int J Epidemiol* 2016; **45:** 1866–86.