Letter to the editor on 'Body mass index and 20-specific cancers—re-analyses of dose-response meta-analyses of observational studies'

In a recently published paper in the *Annals of Oncology* [1], Choi et al. evaluated the strength of the evidence in the literature for the association between body mass index and 20 cancers in a manner that resembles our umbrella review on the same topic [2]. We were surprised to see that there were many discrepancies between the two assessments. The current paper used a grading scheme consisting of similar criteria used in our umbrella review, but structured the grading differently without providing a justification for this choice. Our umbrella review used a grading scheme that has been extensively applied and justified in previous studies [3], and the results for adiposity and cancer in our study were consistent with previous assessments by the World Cancer Research Fund (WCRF) and the International Agency for Research on Cancer (IARC) (Table 1) [4, 5]. We feel that the authors' choice of grading scheme fails to correctly classify the evidence. Associations between adiposity and risk of postmenopausal breast, colon, gallbladder, gastric, liver, ovarian and thyroid cancers received weak or not significant evidence grades in the current paper in contrast to convincing evidence grades received in the previous reports [2, 4, 5].

There are also a number of other methodological concerns that may affect the validity of the evidence grading in the current paper. First, the authors pooled studies from several meta-analyses on the same topic (e.g. for prostate and pancreatic cancer) without acknowledging/correcting for study overlap across meta-analyses, which is substantial. Second, the authors updated existing meta-analyses by selectively adding only one newly published study without conducting a systematic literature search. Third, the authors do not report or differentiate their analysis by study design (e.g. cohort versus case–control), which may have important implications in the quality of the evidence. Fourth, several associations by cancer subsite or according to modifying factors have been omitted from the current paper (e.g. by menopausal status or hormone replacement therapy use for gynaecological malignancies). Fifth, the authors used a *P*-value threshold of 0.05 for Egger's regression asymmetry test as evidence for small-study effects, but this test is known to be underpowered and 0.10 is the widely accepted threshold.

In summary, IARC, WCRF and our umbrella review have rated the quality of evidence in the field of adiposity and cancer by using different methodologies, but reached similar conclusions. In contrast, we are afraid that the current paper fails to correctly classify this evidence.

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Table 1. Strength of the evidence for the association of adiposity and cancer as evaluated by different organizations/investigators

Type	Choi et al.	IARC	WCRF 2017	Kyrgiou et al.
Breast cancer, premenopausal	Weak	NA	Probable decreased risk	Suggestive
Breast cancer, postmenopausal	Weak	Sufficient	Convincing increased risk	Strong (never HRT use)
Colon cancer	Weak	Sufficient	Convincing increased risk[a]	Strong (men)
Rectal cancer	Convincing	Sufficient	Convincing increased risk[a]	Strong (men)
Endometrial cancer	Convincing	Sufficient	Convincing increased risk	Strong
Gallbladder cancer	Weak	Sufficient	Probable increased risk	Strong
Gastric cancer	Non-significant	Sufficient	Probable increased risk (cardia only)	Strong (cardia)
Leukemia	Convincing	NR	NR	Highly suggestive
Liver cancer	Weak	Sufficient	Convincing increased risk	Highly suggestive
Lung cancer	Weak	Inadequate	Limited-no conclusion	Suggestive (smokers)
Melanoma	NR	Inadequate	NR	Weak
Multiple myeloma	Convincing	Sufficient	NR	Strong
Non-Hodgkin's lymphoma	Suggestive	Limited	NR	Suggestive
Esophageal adenocarcinoma	Convincing (men)	Sufficient	Convincing increased risk	Strong
Ovarian cancer	Weak	Sufficient	Probable increased risk	Strong
Pancreatic cancer	Convincing	Sufficient	Convincing increased risk	Strong
Prostate cancer	Non-significant	Limited	Probable increased risk (advanced)	Highly suggestive (mortality)
Renal cell carcinoma	Convincing	Sufficient	Convincing increased risk	Strong
Thyroid cancer	Weak	Sufficient	NR	Suggestive

[a]Evaluated as colorectal.

NR, not reported; HRT, hormone replacement therapy; WCRF, World Cancer Research Fund; IARC, International Agency for Research on Cancer.

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Disclosure

The authors have declared no conflicts of interest.

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