Distinguishing sedentary from inactive: implications for meta-analyses

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We read with great interest the meta-analysis by Cong et al (2014) recently published in British Journal of Cancer. As the authors acknowledge, sedentary behaviour is distinct from the lack of moderate-to-vigorous-intensity physical activity. As the first quantitative review of the studies examining associations of sedentary behaviour on colon and rectal cancer risk, this article makes a timely and novel contribution to the literature. However, we are concerned that the combined risk estimates generated by this meta-analysis may not be accurately reflect the effect that can be attributed to sedentary behaviour.

Many of the risk estimates included in the meta-analysis are from studies that investigated the association between occupational physical activity and the risk of colon and/or rectal cancers. As noted by Yates et al (2011), the ordinal scales commonly used to assess occupational physical activity (e.g., ‘sedentary’, ‘moderate’, ‘high’) are not necessarily ordinal scales of sedentary behaviour. As high levels of sedentary behaviour can co-exist with high levels of physical activity, even within specific occupations, using these estimates of occupational physical activity to infer sedentary behaviour is likely to introduce substantial misclassification bias.

A related issue is the inclusion of studies that have classified sedentary behaviour based on job title. While we do not believe it is necessarily wrong to include estimates of sedentary behaviour that are job title based, it is important to note that this method does not take into account within-job variation, seasonal changes or changes in job requirements over time (LaPorte et al, 1985), and may not reflect the actual activities performed on the job (Ainsworth et al, 1999). We would recommend that in future meta-analyses and reviews, these studies be given a lower exposure assessment quality rating than studies using self-reported or objectively assessed measures of sedentary behaviour. In addition, we suggest that subgroup analyses are conducted to investigate whether the results of studies relying on job title-based measures of sedentary behaviour differ from the results of studies with self-reported or objectively assessed measures of sedentary behaviour.

Another issue that arises when using ordinal scales of occupational physical activity (job title-based or self-reported) in a sedentary behaviour context is the selection of the appropriate referent category. The most suitable referent group to compare jobs with high amounts of sedentary behaviour with are jobs that involve ‘mostly standing’ or ‘light’ activity. Within the meta-analysis performed by Cong et al (2014), there are several instances where the authors selected the most physically active category as the referent group (Garabrant et al, 1984; Fraser and Pearce, 1993; Weiderpass et al, 2003; Moradi et al, 2008). The relative risks generated by comparing the sedentary category with the most physically active category will not solely reflect the effect of sedentary behaviour on colorectal cancer risk, part of the risk estimate will be attributed to the (inverse) of the risk reduction associated with physical activity. A similar error was made with the inclusion of data from two studies that compared recreational sedentary behaviour with recreational physical activity (Thune and Lund, 1996; Colbert et al, 2001).

There are two final points that we would like to raise. First, the risk estimates included in the meta-analysis from the Campbell et al (2013) study pertain to colorectal cancer-specific survival rather than colorectal cancer risk. Second, there are three studies for which the authors have included risk estimates for two different measures of sedentary behaviour (e.g., recreational and occupational sedentary behaviour) in the primary meta-analysis (Thune and Lund, 1996; Colbert et al, 2001; Howard et al, 2008). This is effectively including the same behaviour.
study population twice, so these studies are arguably contributing more weight to the overall effect size than appropriate.

Despite the concerns raised, we acknowledge that the meta-analysis presented by Cong et al (2014) has drawn attention to the potential role of sedentary behaviour in colon and rectal cancer aetiology. Clearly further studies, using well-designed and tested measures of sedentary behaviour, are required in this field.

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Letters to the Editor

Reply: Comment on ‘Association of sedentary behaviour with colon and rectal cancer: a meta-analysis of observational studies’

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We would like to thank Dr. Lynch and Boyle (2014) for their valuable comments and suggestions on our meta-analysis ‘Association of sedentary behaviour with colon and rectal cancer: a meta-analysis of observational studies’ (Cong et al, 2014). This meta-analysis made a timely and novel contribution to the literature about associations of sedentary behaviour on colon and rectal cancer risk. Although some imperfection may exist, they did not materially influence our result. Now, we are replying to the main comments mentioned by Lynch and Boyle.

Indeed, sedentary behaviour is distinctly different from occupational sedentariness and the lack of moderate- to vigorous-intensity physical activity. But in the included original studies, these exposures are difficult to be strictly differentiated. In our initial manuscript, we only focused on self-reported sedentary behaviours. On the basis of the suggestion of one of the reviewers, in order to avoid missing more relevant studies, we took into account the sedentary behaviour that is measured by job title-based response in the revised manuscript. Now, we did a subgroup analysis by types of assessment of sedentary behaviour, and the result showed that there was no substantial difference in the two types of measures of sedentary behaviour. For colon cancer, the pooled OR of sedentary behaviour measured by job title-based response was 1.39 (95% CI, 1.20–1.60, I² = 63.7%), whereas the pooled OR of self-reported sedentary behaviour was 1.27 (95% CI, 1.18–1.36, I² = 26.7%).

The difference between them was insignificant (P for interaction = 0.289). For rectal cancer, the pooled OR of sedentary behaviour measured by job title-based response was 1.11 (95% CI, 1.03–1.20, I² = 42.5%), whereas the pooled OR of self-reported sedentary behaviour was 1.01 (95% CI, 0.92–1.11, I² = 19.7%). The difference between them was insignificant too (P for interaction = 0.156).

There are three studies that we included twice because the authors reported the risk estimates for two different measures of sedentary behaviour. Indeed, this may be contributing more (although not much more) weight to the overall effect size, but including only one of the two measures of sedentary behaviour is also inappropriate.

In summary, we appreciate most of Lynch and Boyle’s comments and suggestions. Our meta-analysis indeed has some flaws, but these defects do not alter our main results and conclusions.

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Letters to the Editor

Coexistence of KRAS mutation with mutant but not wild-type EGFR predicts response to tyrosine-kinase inhibitors in human lung cancer

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Sir,

EGFR and KRAS mutations occur mutually exclusively in NSCLC, suggesting functional redundancy (Kosaka et al, 2004; Pao et al, 2005; Shigematsu et al, 2005; Tam et al, 2006). However, they predict contrasting response rates to tyrosine-kinase inhibitors (TKIs) – while EGFR mutation predicts longer progression-free survival rate (Lynch et al, 2004;