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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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 measure 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, $I^2 = 63.7\%$), whereas the pooled OR of self-reported sedentary behaviour was 1.27 (95% CI, 1.18–1.36, $I^2 = 26.7\%$). 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, $I^2 = 4.2\%$), whereas the pooled OR of self-reported sedentary behaviour was 1.01 (95% CI, 0.92–1.11, $I^2 = 19.7\%$). 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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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;