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## 264Response to Italian Group Letter (22 April)

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### Dear Editor,

Dr Coretta and colleagues have investigated the inverse association between esophageal adenocarcinoma (EAC) and gastric cancer (GC) incidence rates in 33 local cancer registries within Italy. They applied the same methodology we used in the cross-sectional part of our recent international study involving 51 countries<sup>1</sup> for analysing the correlation between the two cancers. The authors found non-significant correlations between EAC and either NCGC or total gastric cancer within the Italian population.

In the cross-sectional part of our international study, we had a group of countries including Italy with a low incidence of both TGC and EAC which we called group C in Figure 1. This group of countries did not contribute to the inverse correlation between the two cancers seen in our cross sectional study.

The Italian national incidence of 0.61 for EAC in men estimated in our study (which is calculated by pooling the data from registries meeting a minimum quality standard) is in the middle of the range (0.3 – 1.6) reported by the Italian investigators. Even the highest rates within these ranges (0.3 – 1.6 in men and 0 - 0.2 in women) for Italy are relatively low by international standards. If we had confined our analysis to countries where the rates of EAC were less than 1.6 (for men) or 0.2 (for women), we would also not have observed significant correlations with GC. What drives our observations are the high rates of EAC (exceeding the highest rates seen in Italy) that are associated with low rates of GC. Indeed, in our figure 1c, it is groups A and B that give rise to the correlation. The Italian situation is similar to only having populations in groups C and D, where there is no correlation.

Interestingly, when looking at the longitudinal part of our study (original Table 3), data from two Italian registries (Romagna and Torino) showed no correlations between TGC and EAC. This again confirms the fact that these populations did not contribute to overall worldwide inverse correlations between two cancers. We have discussed possible explanations for these observations in our paper including environmental factors, life style factors, and cancer registration quality.

### References:

1. Derakhshan MH, Arnold M, Brewster DH, Going JJ, Mitchell DR, Forman D, McColl KE. Worldwide Inverse Association between Gastric Cancer and Esophageal Adenocarcinoma Suggesting a Common Environmental Factor Exerting Opposing Effects. *Am J Gastroenterol*. 2016 Feb;111(2):228-39.