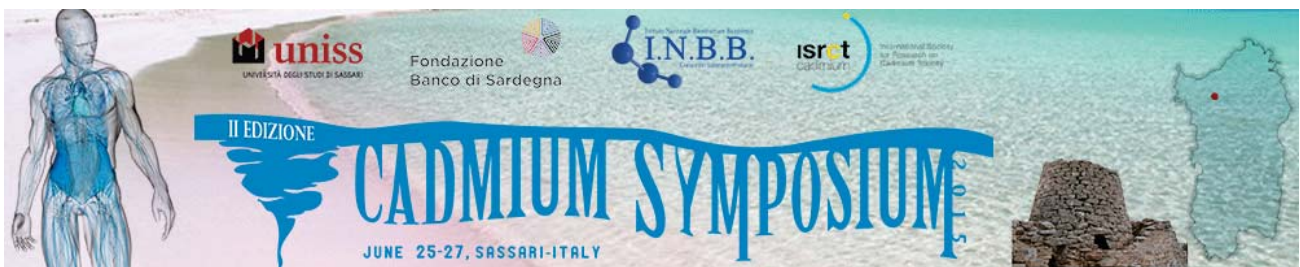


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Congress Proceedings

Sassari | June 25-27, 2015

DIETARY CADMIUM INTAKE AND BREAST CANCER RISK: A META-ANALYSIS OF LONGITUDINAL STUDIES AND RESULTS OF THE ORDET COHORT STUDY

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Cadmium is a heavy metal with estrogenic activity and established human carcinogenicity, but uncertainties exist about the amounts of exposure and the cancer types involved. In particular, the possibility that dietary cadmium may increase breast cancer risk was suggested by one cohort study, but results of the other four longitudinal investigations were inconsistent. We meta-analyzed these studies using a random-effects model, and we computed the summary relative risk (RR) of breast cancer along with its 95% confidence interval (CI) in subjects with the highest versus the lowest cadmium intake category. Summary RR was 1.00 (95% CI 0.87-1.15), while limiting the analysis to estrogen-receptor positive breast cancer RR was 1.05 (0.94-1.16). We also investigated the relation between cadmium intake and breast cancer risk in the ORDET cohort, a prospective study of 9,343 healthy women of Varese province, Northern Italy, recruited between 1987 and 1992 and followed for cancer occurrence until December

2009. Dietary habits and the corresponding estimated cadmium intake were assessed at baseline via a food frequency questionnaire. During 158,190 person-years of follow-up, 419 breast cancer cases occurred. In a multivariate Cox regression model adjusting for several potential confounders, the hazard ratio (HR) of breast cancer increased with increasing quintiles of cadmium intake, with values of 1.19, 1.23, 1.36 and 1.66, respectively (P trend=0.019) compared with bottom category. HR associated with 1-unit increase of Cd intake was 1.12 (1.03-1.21). After stratifying the analysis according to estrogen-receptor, human epidermal growth factor-receptor 2 and progesterone-receptor status, the receptor-positive breast cancer subtypes showed the strongest association with cadmium intake. Overall, these results suggest that dietary cadmium increases breast cancer risk, particularly for some disease subtypes, though the possibility of unmeasured confounding must also be considered.