

# Impact of pre-existing cardiometabolic diseases on cancer stage at diagnosis in the EPIC study

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**Background:** Among chronic non-communicable diseases, cardiometabolic diseases and cancer are the leading causes of morbidity and mortality worldwide. Shared risk factors and population aging contribute to an increased lifetime risk of an individual to concomitantly develop cardiometabolic diseases and cancer, resulting in multimorbidity. Multimorbidity can impact cancer screening and may affect both ongoing cardiometabolic diseases and cancer treatment. Stage at cancer diagnosis is an important prognostic factor for cancer survival. Existing evidence suggests that participation to cancer screening may be lower among individuals with type 2 diabetes (T2D) or cardiovascular diseases (CVD) compared to individuals without cardiometabolic diseases. Therefore, cardiometabolic diseases may lead to late cancer detection and advanced stage at diagnosis. This study aimed to investigate whether pre-existing cardiometabolic diseases are associated with stage at cancer diagnosis.

**Methods:** Within the European Prospective Investigation into Cancer and Nutrition cohort (EPIC), incident localised and metastatic cancers were diagnosed between 1992 and 2012 from 400,577 cancer-free participants from 6 European countries (i.e., Denmark, Germany, Italy, Spain, Sweden, and the UK). Participants with incident diagnosis of cardiometabolic diseases, including CVD and T2D, prior to cancer were identified (participants with a history of CVD and/or T2D at recruitment were excluded). Logistic regression models were used to estimate odds ratio (OR) and 95% confidence intervals (CI) of diagnosis of metastatic cancer according to the presence of CVD, T2D, both or no cardiometabolic disease among EPIC participants diagnosed with cancer. Models were adjusted for country, age at cancer diagnosis, sex, physical activity, BMI, alcohol intake, smoking status, education level, and self-reported hypertension at baseline. Analyses were carried out for all cancers combined and separately for screened cancers (breast and colorectal cancer) and non-screened (all cancers except breast and colorectal cancer) according to the availability of population-based cancer screening programs in Europe.

**Results:** During a median follow-up of 15 years, 11,945 incident cancers were diagnosed, of which 35.1% were metastatic and 53.6% were diagnosed in women. Overall, 86.8% had no pre-existing cardiometabolic diseases at cancer diagnosis, 4.8% of cancers followed a CVD diagnosis, 7.1% a T2D diagnosis, and 1.3% both CVD and T2D. The ORs for metastatic vs. localized cancer comparing participants with T2D, CVD, and T2D/CVD to those without a cardiometabolic disease prior to cancer were 1.12 [95% CI 0.95-1.30], 1.02 [95% CI 0.79-1.16], and 1.11 [95% CI 0.78-1.58], respectively. The corresponding ORs for non-screened cancers were 1.26 [95% CI 1.04-1.55], 1.07 [95% CI 0.85-1.34], and 1.18 [95% CI 0.78-1.78], respectively. No associations were found for screened cancers.

**Discussion:** The findings of this multi-national cohort study suggest an increased risk of advanced tumour stage at diagnosis, particularly for non-screened cancers, among individuals with pre-existing T2D compared to individuals without cardiometabolic diseases. In addition, among individuals with T2D, the results underline the importance of encouraging participation of the eligible population in screening programmes by healthcare professionals and pay special attention to the detection of cancers not included in screening programmes.

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