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**Cancer of unknown primary: analysis of incidence trends, survival and familial risks
to suggest organs to search for primary tumors**

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The aim of this thesis was to analyze incidence trends, survival trends and familial risks to provide a basis for the search of primary tumors of CUP patients. This search is very important as the treatment of cancer patients is based on the primary organ. If the tumor remains undetected CUP patients have a very poor survival prognosis.

The CUP incidence declined for several locations of metastasis over the years. These effects might be explained by improved diagnostic methods such as CT, PSA testing, MRI and PET which might have especially helped in detecting lung and colorectal as well as prostate and breast cancers as these methods are especially sensitive in their detection. Similarly decreasing incidence trends were observed for most common primary sites for CUP.

The findings based on the survival analysis of CUP patients diagnosed with metastasis in the lymph nodes suggest, beside the already existing recommendations for those patients, a general focus on lung cancer detection for CUP patients. Even if diagnostic methods have improved in identifying lung cancer it has to be seen how this will improve survival in CUP patients with primary tumors in the lung. Different survival trends in lung and breast cancer by CUP with diagnosed metastasis in head, face and neck lymph nodes and in axillary lymph nodes that have been observed in these study may be a hint for distinct metastatic pathways for aggressive tumors.

The familial risk and survival analyses suggest that the primary tumor for metastatic CUP is located in the metastatic organ. Phenotypic modifications of the tumor let the primary look as a metastasis. This might explain the particular aggressiveness of CUP. These analyses support the hypothesis that many fatal CUP are phenotypically modified primary cancers rather than real cancers of unknown origin.