

Subsequent Primary Tumour risk after Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma in Germany: a nationwide analysis from 1970 to 2010

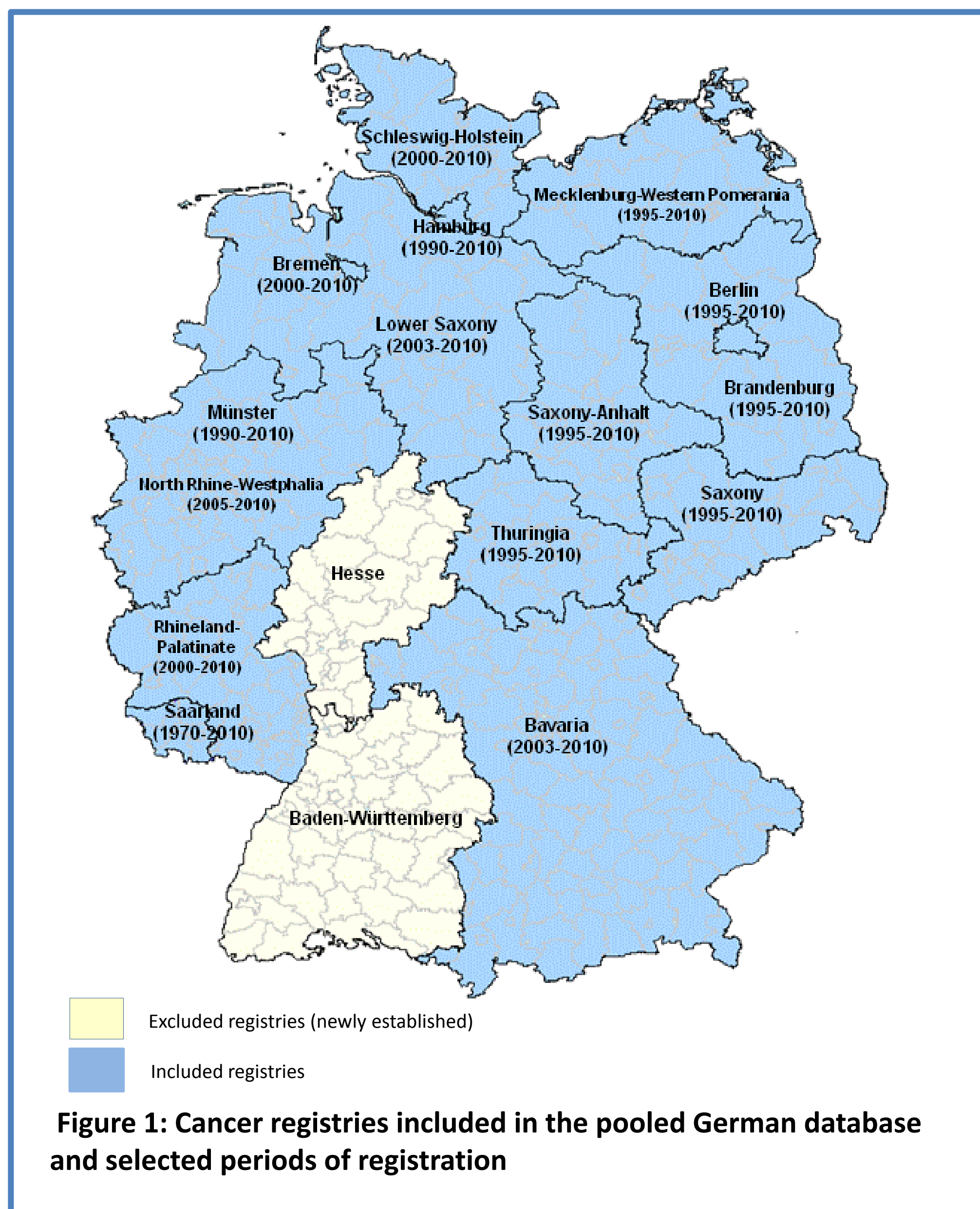


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Background

Reports from the U.S SEER registries (1), North European and international multicentre studies (2–5) indicate that survivors of Hodgkin's lymphoma (HL) and Non-Hodgkin's lymphoma (NHL) are at increased risk for developing subsequent malignancies. This risk is associated with long-term effects of chemo- and radiotherapy. Until now, there is only little information regarding this risk in Germany.



Methods

The German cancer registry database, pooled from 14 out of 16 federal states' cancer registries [Figure 1], was used to calculate the incidence of subsequent tumours among 108,378 cancer patients who had been diagnosed with first primary HL (ICD-10 C81) and NHL (C82-C85) at age ≥ 15 years between 1970 and 2010 [Table 1]. The ratio of the observed numbers of subsequent primary tumours and the expected numbers (standardized incidence ratio, SIR) was used as a measure of the relative risk. The expected numbers were obtained by applying site-, sex-, age-, period-, and registry-specific cancer incidence rates in the general German population to the corresponding person-years at risk in the cohort.

Discussion

Despite the limited follow-up time for some registries, the pooled German data showed an increased risk of developing subsequent malignancies for HL and NHL patients compared to the general population which is consistent with other population-based studies [Figure 4]. We found consistently increased risks for the following subsequent tumours after HL and NHL: oral cavity and pharynx, oesophagus, stomach, colorectal, lung, skin melanoma, female breast, thyroid, kidney and other lymphohaematopoietic neoplasms. Significant excess risks for subsequent cancers of the liver, pancreas, testis, urinary bladder and central nervous system were only found after NHL. Risks for some cancers increased with follow-up time and were higher at younger ages at diagnosis of both lymphomas indicating the long-term effects of treatments. Significant bi-directional relationships were found between the two lymphomas and cancers of the skin melanoma, colon, lung, thyroid, oral cavity, kidney, and liver suggesting common risk factors (immune suppression, infections, or tobacco) could play a role in addition to treatment effects; however, over-diagnosis and misclassification biases cannot be ruled out. Careful follow-up should be considered to reduce the burden of these tumours on long-term lymphoma survivors.

References

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Results

A total of 6,771 (6%) subsequent tumours, 5,714 of which were solid tumours (C00-C75), were observed following HL and NHL in both sexes. The median follow-up time was 4.5 years for HL and 3 years for NHL. There was about a 2.5-fold significant increase in risk of developing subsequent tumours at any site (C00-C97 excl. C44) for HL survivors, and a 1.6-fold for NHL survivors compared with the general population. The risk was highest (7-to 10-fold) among survivors who were younger than 30 years old at the time of their first cancer diagnosis [Figure 2]. The risk for solid tumours was increased by 90% (SIR 1.9, 95% CI: 1.75-2.06) after HL, and 48% (SIR 1.48, 95% CI: 1.44-1.52) after NHL. Figure 3 shows site-specific risks after HL and NHL.

First primary cancer site	Hodgkin's lymphoma (HL)	Non-Hodgkin's lymphoma (NHL)	Total
Number of Patients*	15330 (14.1%)	93048 (85.9%)	108378
Person-years of observation	342782.72	1367287.02	1710069.74
Observed number of subsequent cancers	836 (5.5%)	5935 (6.4%)	6771 (6.2%)
Synchronous (<2 months)**	135 (16.1%)	1323 (22.3%)	1458 (21.5%)
Metachronous (>2 months)**	701 (83.9%)	4612 (77.7%)	5313 (78.5%)
Expected number of subsequent cancers	339.4	3792.5	4131.9
Tumour sequence numbers			
One primary tumour	14544 (94.9%)	87402 (93.9%)	101946 (94.1%)
2 primaries	738 (4.8%)	5373 (5.8%)	6111 (5.6%)
3 primaries	46 (0.3%)	257 (0.3%)	303 (0.3%)
4 or more primaries	2 (0.0%)	16 (0.0%)	18 (0.0%)

*after excluding Death Certificate only (DCO) cases, preceding primary tumours, and patients aged less than 15 years old
**after the diagnosis of the first primary cancer

Table 1: Characteristics of patients in the cohort by the type of first primary cancer, both sexes, Germany (1970-2010)

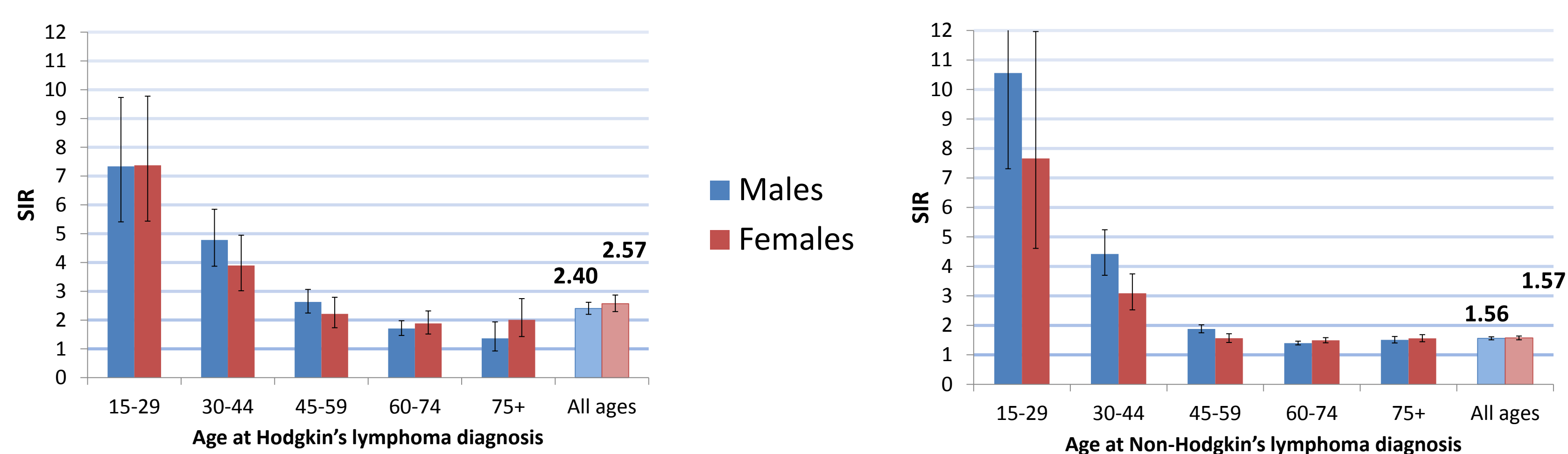


Figure 2: Overall risk and age-specific risk of subsequent cancers by sex after first primary HL and NHL, Germany (1970-2010)

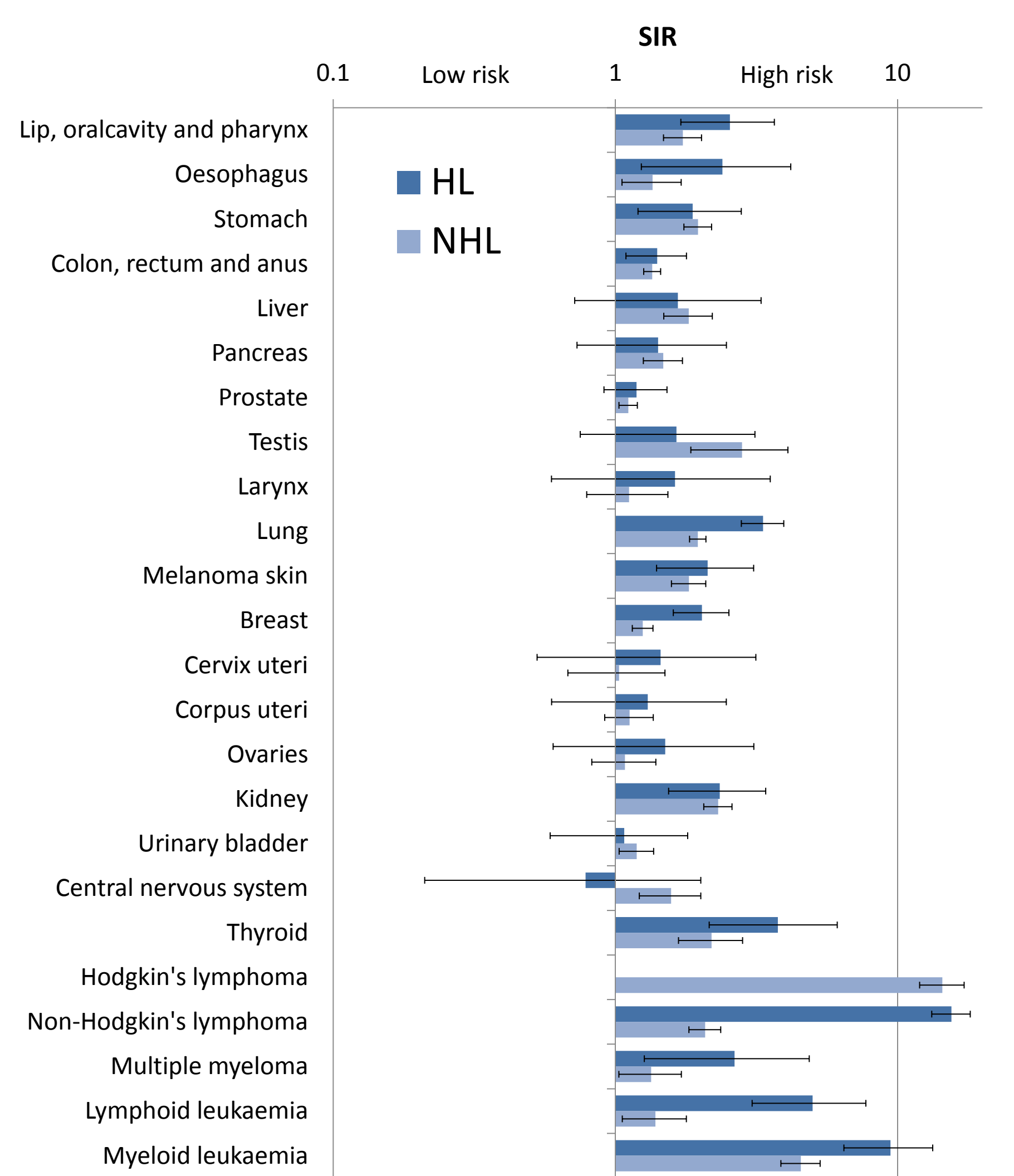


Figure 3: Risk of subsequent primary cancers at specific sites after first primary HL and NHL, both sexes, Germany (1970-2010)

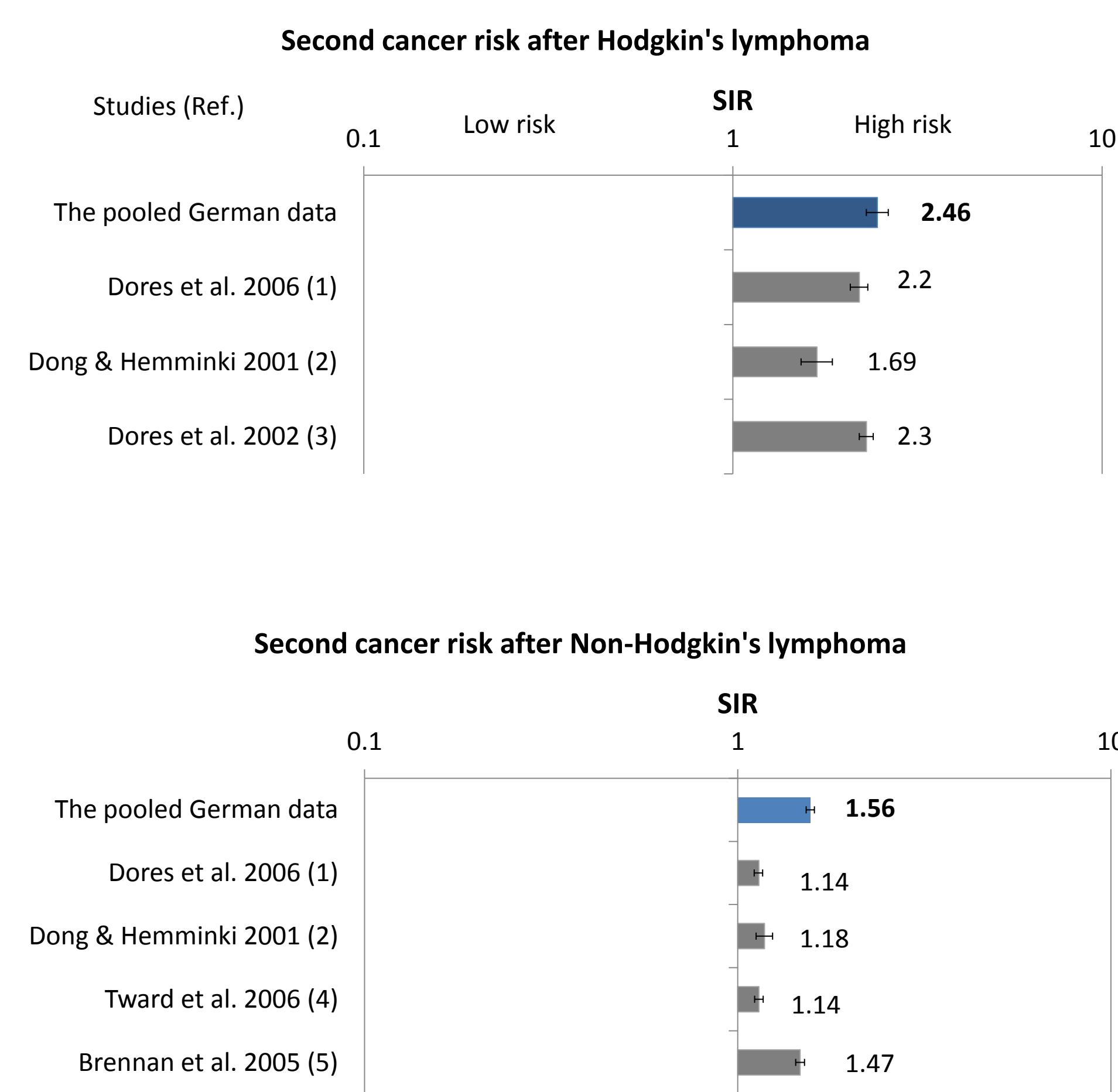


Figure 4: Overall risk (SIR) and 95% confidence interval after HL and NHL in Germany compared to results from other population-based studies

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