Table 2. Risk for developing second primary infection-related solid tumors among adult 1-y NHL survivors, 17 SEER registry areas, 2000 to 2014

Second primary malignancy site	First primary NHL subtype												
	CLL/SLL			DLBCL			FL			MZL			
	Obs	SIR†	95% CI†	Obs	SIR†	95% CI†	Obs	SIR†	95% CI†	Obs	SIR†	95% CI†	$P_{heterogeneity}$*
Oropharynx/tonsil	30	1.08	0.73-1.54	22	1.04	0.65-1.58	18	1.00	0.59-1.58	7	0.96	0.39-1.98	.99
Stomach	39	0.70‡	0.50-0.96	62	1.51‡	1.16-1.94	26	0.81	0.53-1.19	44	2.78‡	2.02-3.74	<.01
Anus	16	1.57	0.90-2.55	31	3.71‡	2.52-5.27	5	0.67	0.22-1.56	8	2.36‡	1.02-4.64	<.01
Liver	54	1.04	0.78-1.36	76	1.85‡	1.46-2.31	32	0.98	0.67-1.39	30	1.98‡	1.34-2.83	<.01
Cervix uteri	7	0.78	0.31-1.61	9	0.89	0.41-1.69	8	0.87	0.38-1.72	<5	0.68	0.14-1.98	.98

Obs, observed.

*P values to test differences in SIRs across NHL subtypes were computed using likelihood ratio test derived from Poisson regression models adjusted for age at first primary NHL, sex, and latency, with log of expected numbers of cases included as offset. Exact numbers of cases are not reported for categories with <5 observed cases to maintain patient confidentiality. All statistical tests were 2 sided.

†SIRs and exact Poisson-based 95% CIs compared number of observed cases with that expected in general population (additional details provided in "Methods").

‡Indicates 95% CI excludes 1.00, corresponding to 2-sided $P < .05$.

we observed significantly elevated SIRs among gastric MZL survivors (SIR, 6.70; 95% CI, 4.34-9.90) but not among nongastric extranodal MZL survivors (SIR, 1.67; 95% CI, 0.80-3.06; $P_{heterogeneity} < .01$; Figure 1) or nodal MZL survivors (data not shown; SIR, 1.48; 95% CI, 0.68-2.81). This risk after gastric MZL was similar across treatments (data not shown; SIR range, 5.98-9.15). Likewise, the SIR for stomach cancer was significantly increased after gastric DLBCL (SIR, 2.67; 95% CI, 1.07-5.50) but not after nongastric extranodal DLBCL (SIR, 1.32; 95% CI, 0.77-2.11), although the SIRs did not differ significantly ($P_{heterogeneity} = .12$). Additionally, the SIR for stomach cancer was elevated among survivors of nodal DLBCL (SIR, 1.50; 95% CI, 1.06-2.05). In secondary analyses stratifying DLBCL survivors by HIV/AIDS status at the time of diagnosis, the risk of anal cancer was much more strongly elevated among those with known HIV/AIDS (SIR, 68.34; 95% CI, 37.36-114.66) than those without known HIV/AIDS (SIR, 2.09; 95% CI, 1.22-3.34; Table 3).

Additional analyses of the most commonly occurring second cancers (liver and stomach cancers) evaluated SIR patterns by patient subgroup (Tables 4 and 5). In general, SIRs were largely consistent across age at first primary NHL diagnosis, sex, time since first primary NHL diagnosis, stage of first primary NHL, and initial treatment of first primary NHL, but there were a few exceptions. For stomach cancer (Table 4), the only indication of borderline heterogeneity was by stage for MZL survivors (early stage: SIR, 3.79; advanced stage: SIR, 2.00; $P_{heterogeneity} = .07$); notably, a majority of early-stage MZL cases (n = 21 of 31) were gastric MZL. For liver cancer (Table 5), the SIR among DLBCL survivors diagnosed before age 60 years was higher than that among patients diagnosed with DLBCL at older ages (SIR, 2.89 vs 1.21; $P_{heterogeneity} < .01$) and during the first 5 years after DLBCL compared with later periods (SIR, 2.23 vs 1.32; $P_{heterogeneity} < .01$). Liver cancer SIRs after DLBCL and MZL were significantly elevated only among males, but differences by sex were not statistically significant (DLBCL: SIR, 1.96 vs 1.48; $P_{heterogeneity} > .50$; MZL: SIR, 2.32 vs 1.14; $P_{heterogeneity} = .16$). Additionally, although there was no overall increase in liver cancer after FL, the SIR was significantly elevated highest among FL survivors who received initial chemotherapy and radiotherapy (SIR, 2.53; $P_{heterogeneity} = .02$), based on 7 observed cases. Across NHL subtypes, there was no evidence of heterogeneity in the SIRs for stomach or liver cancers by calendar year period of NHL diagnosis (data not shown).

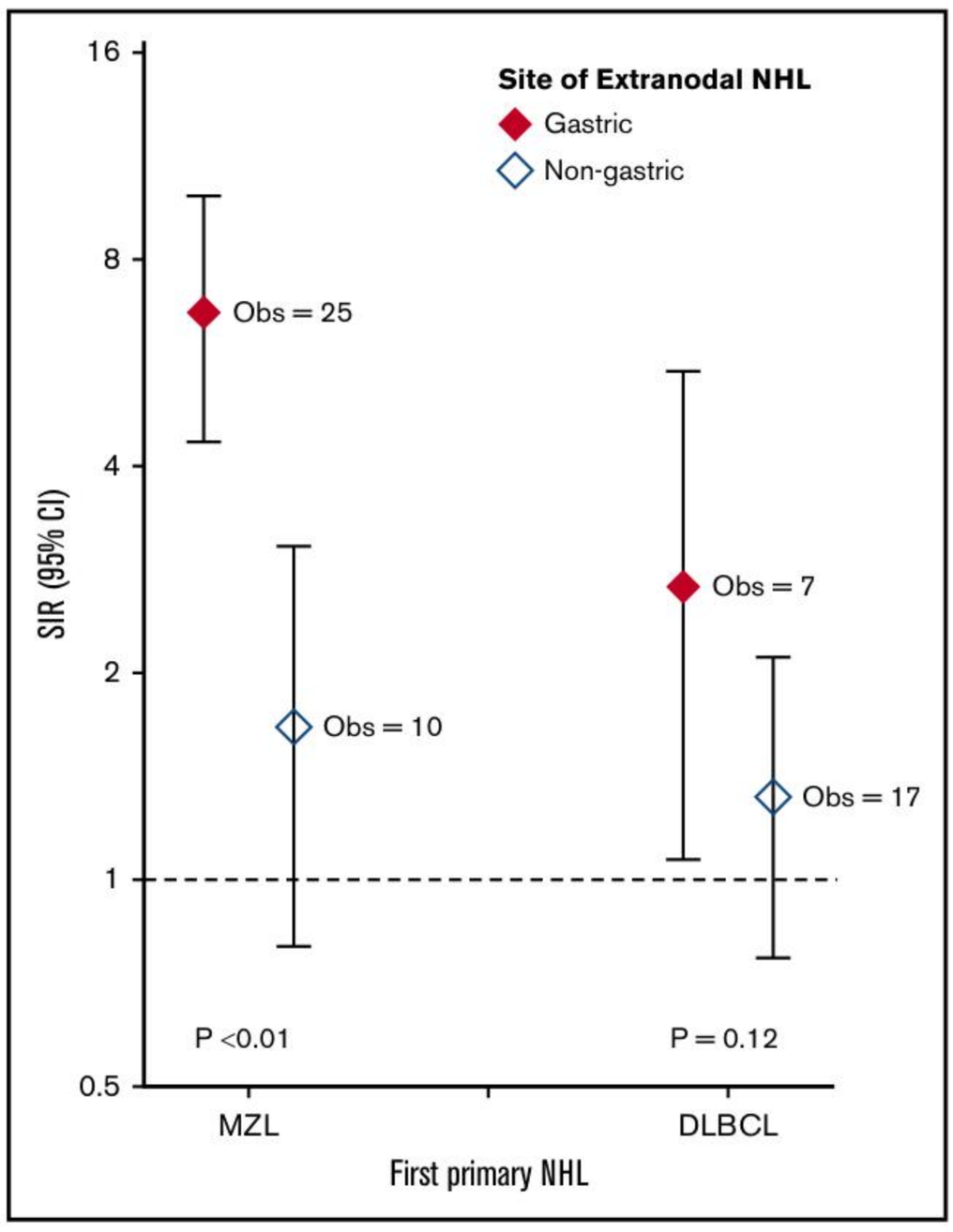

Figure 1. Risk for developing second primary stomach cancer among adult 1-year DLBCL and MZL survivors by site of DLBCL or MZL, 2000 to 2014. SIRs and exact Poisson-based 95% CIs compared the number of observed cases with that expected in the general population (additional details provided in "Methods"). P values to test differences in the SIRs were computed using a likelihood ratio test derived from Poisson regression models stratified by age at first primary NHL, sex, and latency, with the log of the expected numbers of cases included as an offset. All statistical tests were 2 sided. Created using GraphPad Prism (version 7; La Jolla, CA).