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Trends in cancer incidence by socioeconomic deprivation in Germany in 2007 to 2018: An ecological registry-based study

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Abstract

Age-standardized cancer incidence has decreased over the last years for many cancer sites in developed countries. Whether these trends led to narrowing or widening socioeconomic inequalities in cancer incidence is unknown. Using cancer registry data covering 48 million inhabitants in Germany, the ecological association between age-standardized total and site specific (colorectal, lung, prostate and breast) cancer incidence in 2007 to 2018 and a deprivation index on district level (aggregated to quintiles) was investigated. Incidence in the most and least deprived districts were compared using Poisson models. Average annual percentage changes (AAPCs) and differences in AAPCs between deprivation quintiles were assessed using Joinpoint regression analyses. Age-standardized incidence decreased strongly between 2007 and 2018 for total cancer and all cancer sites (except female lung cancer), irrespective of the level of deprivation. However, differences in the magnitude of trends across deprivation quintiles resulted in increasing inequalities over time for total cancer, colorectal and lung cancer. For total cancer, the incidence rate ratio between the most and least deprived quintile increased from 1.07 (95% confidence interval: 1.01-1.12) to 1.23 (1.12-1.32) in men and from 1.07 (1.01-1.13) to 1.20 (1.14-1.26) in women. Largest inequalities were observed for lung cancer with 82% (men) and 88% (women) higher incidence in the most vs the least deprived regions in 2018. The observed increase in inequalities in cancer incidence is in alignment with trends in inequalities in risk factor prevalence and partly utilization of screening. Intervention programs targeted at socioeconomically deprived and urban regions are highly needed.

KEYWORDS
cancer, deprivation, Germany, incidence, trends

Abbreviations: AAPC, average annual percentage change; DCO, death certificate only; GIMD, German Index of Multiple Deprivation; IRR, incidence rate ratio; PSA, prostate-specific antigen; SHI, statutory health insurance.

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What's new?
Age-standardized cancer incidence has decreased strongly between 2007 and 2018 for many cancer sites in developed countries. The authors investigated variations in these trends according to socioeconomic deprivation for cancer in total and for the sites colorectal, lung, prostate and breast cancer using German cancer registry data. The results indicated trend differentials across deprivation groups resulting in widening inequalities for cancer in total, colorectal and lung cancer in Germany.

1 | INTRODUCTION

Social inequalities on the individual as well as on the area-based level affect all stages of the cancer continuum, even in countries with universal health care.[1] In Germany, socioeconomic inequalities in cancer incidence, screening utilization, mortality and survival have been reported.[2-8] Cancer incidence is associated with area-based socioeconomic deprivation[2] as well as individual incomes in Germany.[3,4] For example, age-standardized cancer incidence in 2010 to 2013 was 7.3% higher in more deprived than in less deprived areas for all cancer sites combined (total cancer) in men. However, results varied by cancer site.[2] While a recent review on socioeconomic inequalities in cancer incidence in Europe showed that lower socioeconomic position was associated with elevated incidence for many cancer sites, the association was reversed for breast, prostate, thyroid and skin cancer.[9]

Studies on recent trends in socioeconomic inequalities in cancer incidence are generally rare but important, given the strong changes in cancer incidence for common cancer sites in developed countries in recent years. In Germany, age-standardized incidence has decreased for all cancer sites combined (since approximately 2008), colorectal cancer (since 2003), and breast cancer (since 2009).[10] Age-standardized lung cancer incidence has decreased among men and increased among women since the late 1990s. Prostate cancer incidence has first decreased since 2011 and stabilized in the last years. Whether these on-going changes are associated with changes in socioeconomic inequalities in cancer incidence is still an open research question. So far, only very few studies using health insurance claims data from the federal state of Lower Saxony (about 4% of the German population) provided initial evidence.[3,4] They showed persisting or even widening socioeconomic inequalities in cancer incidence in the last years, which varied by domain of deprivation and age. Studies from other countries did not show a common trend of increasing or decreasing socioeconomic inequalities in cancer incidence.[9,11-17]

The aim of this study is to investigate whether recent trends in age-standardized cancer incidence led to narrowing or widening socioeconomic inequalities in cancer incidence in Germany.

2 | MATERIALS AND METHODS

2.1 | Cancer registry data

This ecological study is based on pooled cancer registry dataset from the Centre for Cancer Registry Data (ZfKD) at the Robert Koch Institute. The analysis was restricted to federal states with estimated sufficient completeness of case ascertainment in the entire analysis period from 2007 (first year with complete data for the large federal state of North Rhine-Westphalia) to 2018 (the last available year). Consequently, the Eastern federal states and the federal states of Hesse and Baden-Württemberg were excluded, as the completeness of the data, based on estimates from the ZfKD,[18] in recent or earlier calendar years was insufficient. Thus, the cancer registry data of Schleswig-Holstein, Hamburg, Bremen, Lower Saxony, North Rhine-Westphalia, Rhineland-Palatinate, Saarland and Bavaria, covering a population of 48.6 million inhabitants (60% of the German population) and 254 of 401 districts in 2018, are included in the study. Death Certificate Only (DCO) cases were included with the date of death as date of diagnosis. Patients without information on their place of residence at the district level at the time of diagnosis were excluded ($N = 1282$).

2.2 | Deprivation data

Similar to several previous studies on cancer survival in Germany,[7] the German Index of Multiple Deprivation (GIMD)[19] at district level was used as a measure of area-based socioeconomic deprivation. The GIMD comprises seven single deprivation domains (ie, income, employment, education, municipal/district revenue, social capital, environment and security) as well as a composite index including all seven domains. For each single domain and the composite index, districts were categorized into pre-defined deprivation quintiles covering the whole of Germany from Q1 (lowest area deprivation quintile) to Q5 (highest area deprivation quintile). The main analyses focused on the composite index, but analyses using the seven single domains were additionally conducted. Three versions of the GIMD have been developed, based on official statistics mainly from 2006, 2010 and 2015, respectively. Over the three available versions of the GIMD, the index was quite stable (Table S1). Figure 1 shows the included regions with the assigned GIMD quintiles from 2015. Figure S1 shows maps of the other two versions.

The GIMD was linked to the cancer registry data set using the district information of the patient's place of residence at diagnosis (Amtlicher Gemeindeschlüssel, first 5 digits). The GIMD version closest to the year of diagnosis was linked to the registry data (GIMD 2006 for years of diagnosis 2007/2008, GIMD 2010 for 2009 to 2012 and GIMD 2015 for 2013 to 2018). District area reforms were

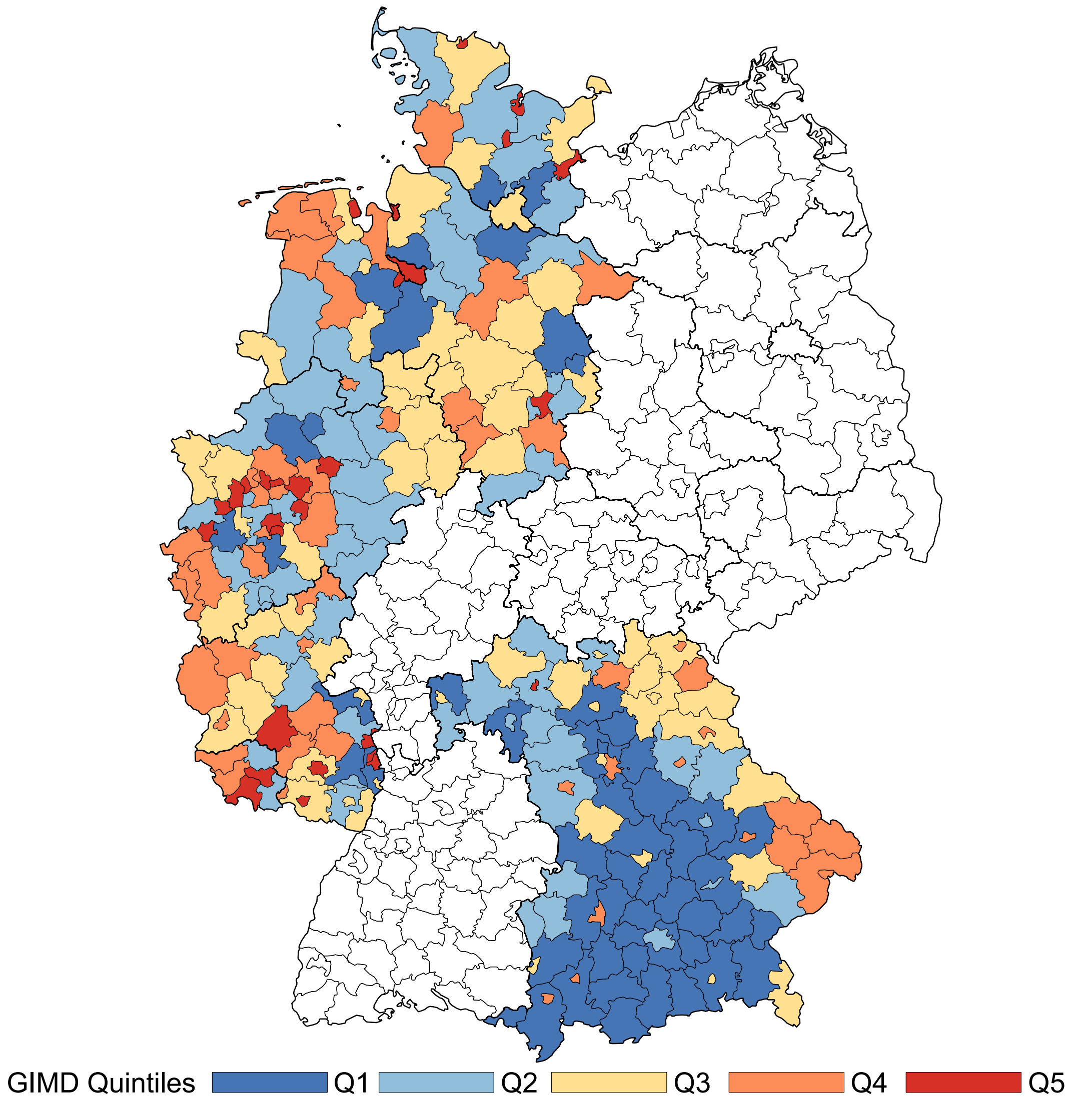

FIGURE 1 Map of the composite index of the German Index of Multiple Deprivation (GIMD), version 2015 (1 = least deprived quintile, 5 = most deprived quintile; excluded regions are shown in white).

taken into account by transforming the district to the status in 2018. The underlying population per district varies strongly from 34 239 to 1 835 882 individuals, with a mean and median population of 194 546 and 135 966 individuals, respectively.

2.3 | Statistical analyses: Main analyses

Age-standardized annual incidence for the years 2007 to 2018 for breast (female, ICD-10 C50), prostate (C61), colorectal (C18-C20), lung (C34) and total cancer (C00-C97, without C44, C77-C79) was calculated, stratified by GIMD quintile and sex, using population numbers by calendar year, GIMD quintile, sex and age (derived from district-level numbers published by the German Federal Statistical Office).[20] Estimates were age-standardized to the population in Germany in 2020 using 5-year age groups until 85+ years (Table S2).

Incidences were compared between the least and most deprived regions in 2007 and 2018 using Poisson models including the factors age group (0-29 years and 5-year age groups up to 85+ years) and deprivation quintile as fixed effects and district as random effect separately for females and males. The number of cases was modeled including the logarithm of the underlying population as offset. Incidence rate ratios (IRR) and 95% confidence intervals were extracted. Time trends were modeled using Joinpoint regression analysis.[21] A maximum number of two joinpoints was pre-specified, but it was visually checked whether this specification is sufficient. The model selection followed the permutation test with 5000 permutations and an overall significance level of 0.05.[21] Errors were assumed to be uncorrelated with constant variance. First, the trend was modeled by cancer site, sex and GIMD quintile. The average annual percentage change (AAPC) was extracted together with their corresponding 95% confidence intervals. The AAPC is computed as a weighted average of the annual percentage changes (APCs) from the Joinpoint model, with the weights equal to the length of the APC interval. This allows a comparison across groups over a common time interval, even if they have different joinpoints.[22] Second, trends were modeled for the least and most deprived quintile in one model, stratified by cancer site and sex, to test whether the trends were parallel and to estimate the difference in the AAPC between these groups if two trend curves were fitted (test of parallelism).[23]

Modeled incidence comparisons were restricted to the comparison of the least and most deprived quintile to decrease the number of false positive results. As the study is purely descriptive, no multiple comparison corrections were performed.

2.4 | Additional analyses: Age-specific trends

As a previous study on the association of individual income and lung cancer incidence reported that trends with respect to socioeconomic factors varied by age,[3] additional analyses stratified by age (0-64 years, 65+ years) were conducted. In these analyses, incidence was age-standardized within the age groups using the German population in 2020.

2.5 | Additional analyses: Domains of deprivation

Age-standardized sex-specific incidence for the selected cancer sites was additionally computed by domain of deprivation. Incidence in the most and least deprived quintile of a deprivation domain were compared using Poisson models, as described above for the GIMD quintiles. IRRs and confidence intervals for the comparison of the most and least deprived quintile were extracted.

2.6 | Sensitivity analyses: Exclusion of large districts

The GIMD does not reflect socioeconomic differences within districts even if they are larger and more heterogeneous. For example, in Hamburg, which is assigned one GIMD score, huge socioeconomic inequalities in cancer survival have been found.[8] Therefore, a sensitivity analysis was performed by excluding large districts with more than 500.000 inhabitants (Hamburg, Munich, region Hannover, Köln, Stuttgart, Düsseldorf, district Recklinghausen and district Rhein-Sieg) from the analyses.

2.7 | Statistical programs

Joinpoint regression was conducted with the Joinpoint Regression Program, version 4.9.1.0.[24] Data preparation and other statistical analyses were performed using SAS V9.4.

3 | RESULTS

In total, 3 385 729 incident cancer diagnoses were included in the study. The included regions covered an average annual population of 23.8 million men and 24.8 million women (Table S3). With an underlying population of 4.0 million inhabitants (8.2% of the total underlying population in this study), the most deprived quintile was underrepresented. Within the study population, an average of 147 003 men and 135 142 women were annually diagnosed with cancer.

Figure 2 shows age-standardized incidence rates by cancer site, sex, deprivation quintile between 2007 and 2018. Table 1 displays the corresponding estimates for 2007 and 2018 as well as the modeled AAPC over time and a comparison of the most and least deprived districts using IRRs. These IRRs are illustrated in Figure 3. Except for lung cancer in women, the age standardized incidence significantly decreased between 2007 and 2018 for all cancer sites and for each deprivation quintile. For example, total cancer incidence in the least deprived districts decreased from 2007 to 2018 annually by 2.4% in men and 1.5% in women. There was no gradual trend over the deprivation quintiles, but the AAPC was 1.2% (men) and 0.9% (women) lower in the most deprived compared to the least deprived districts. Consequently, inequalities increased over time resulting in a 23% higher cancer incidence in men and 20% higher cancer incidence in women in the most deprived compared to the least deprived districts (Table 1). Similar patterns were observed for colorectal and lung cancer among men. For colorectal cancer in women, the IRR between the most and least deprived districts increased from 1.11 (95% confidence interval: 1.02-1.21) to 1.21 (1.11-1.32), but the AAPCs were not significantly different. Lung cancer incidence in women increased between 2007 and 2018. The increase was stronger in the most deprived group resulting in increasing inequalities in 2018 (IRRs—2007:1.58 [1.37-1.81], 2018:1.88 [1.66-2.12]). However, there was no clear pattern among the other deprivation quintiles. For prostate and breast cancer, incidence decreased between 2007 and 2018 and the trends were not found to differ significantly between deprivation quintiles. In 2018, prostate and breast cancer incidence were not significantly different in the most and least deprived districts.

The previously described pattern of decreasing total cancer incidences between 2007 and 2018 but widening inequalities in incidence over time was also found in age-specific analyses (0-64 and 65+ years; Figure 4 and Table 2, estimates for Q2-Q5 are shown in Tables S4 and S5). Results by cancer sites are shown in Figures S2 and S3 and Tables 2, S4 and S5. For colorectal cancer, IRRs between the most and least deprived quintiles differed only in older individuals. The decrease in incidence between 2007 and 2018 in men and women was stronger in the least deprived districts resulting in higher inequalities in 2018 (men: 1.21 [1.11-1.33], women: 1.26 [1.12-1.38]). For lung cancer in men, patterns were similar in both age groups. For female lung cancer, incidence significantly increased between 2007 and 2018 only in older individuals. However, in both age groups inequalities in incidence were higher in 2018 than in 2007. The incidence of prostate cancer also decreased in both age groups. However, the AAPC did not differ significantly between the least and most

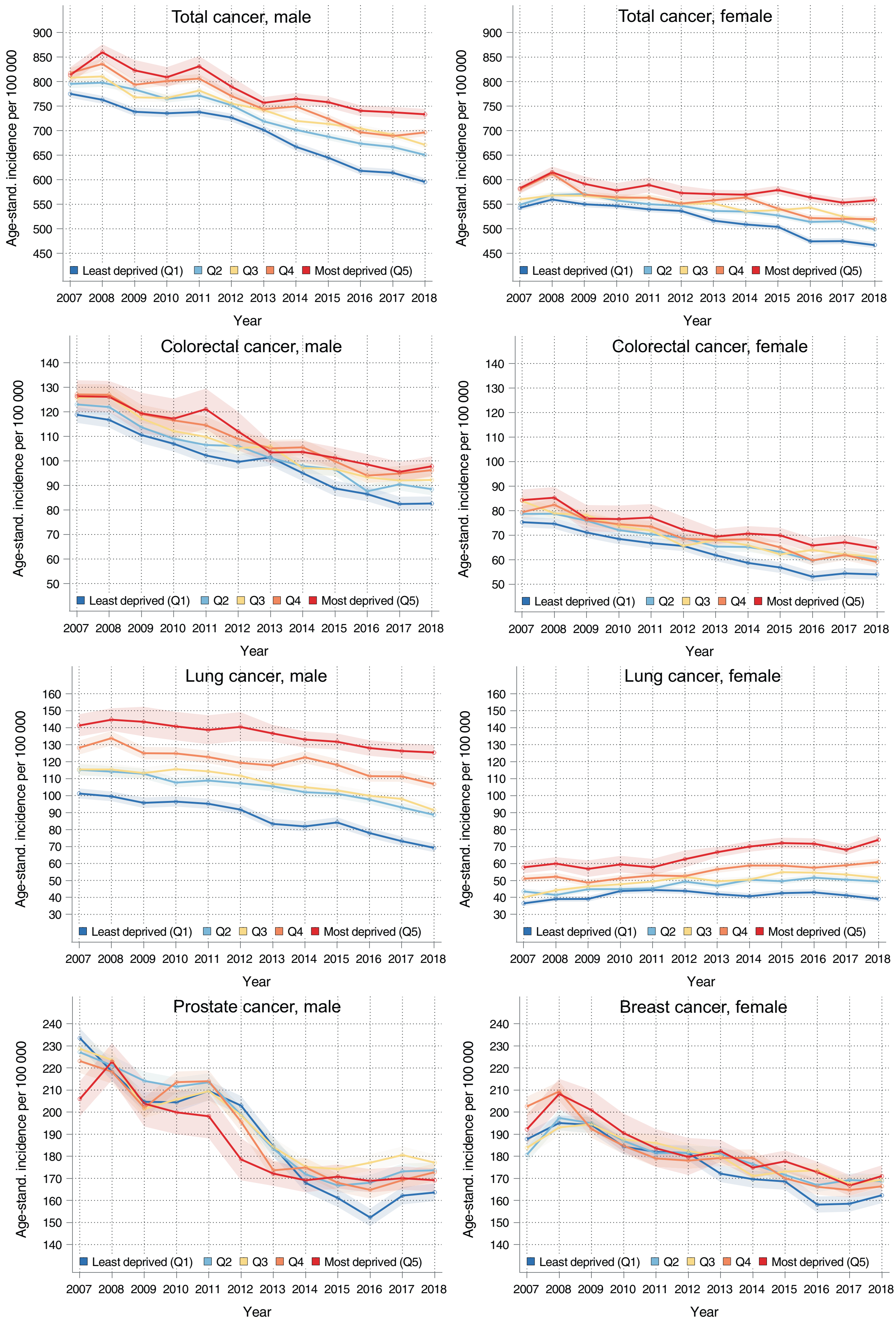

FIGURE 2 Age-standardized total, colorectal, lung, prostate and breast cancer incidence between 2007 and 2018 by sex and deprivation quintile.

TABLE 1 Age-standardized breast, prostate, colorectal, lung and total cancer incidence in 2007 and 2018 by sex and deprivation quintile.

Cancer site	Sex	Quintile	Incidence 2007	Incidence 2018	AAPC, CI[a] 2018 vs 2007
Total	Male	Q1 (least deprived)	775.3	595.7	**−2.4 (−2.9; −2.0)**
		Q2	795.5	650.6	**−1.8 (−2.4; −1.2)**
		Q3	808.2	671.2	**−1.6 (−1.9; −1.4)**
		Q4	817.7	696.5	**−1.8 (−2.2; −1.5)**
		Q5 (most deprived)	813.3	733.5	**−1.2 (−1.6; −0.9)**
		Q5 vs Q1; IRR/AAPC Diff, CI	**1.07 (1.01; 1.12)**	**1.23 (1.14; 1.32)**	**−1.2 (−1.7; −0.6)**
Total	Female	Q1	542.9	466.7	**−1.5 (−2.0; −0.9)**
		Q2	549.1	498.8	**−0.9 (−1.3; −0.4)**
		Q3	560.0	513.7	**−0.8 (−1.1; −0.6)**
		Q4	580.6	519.8	**−1.2 (−1.6; −0.8)**
		Q5	582.8	558.4	**−0.7 (−1.0; −0.3)**
		Q5 vs Q1; IRR/AAPC Diff, CI	**1.07 (1.01; 1.13)**	**1.20 (1.14; 1.26)**	**−0.9 (−1.6; −0.2)**
Colorectal	Male	Q1	118.8	82.6	**−3.4 (−3.8; −3.1)**
		Q2	123.0	88.5	**−3.1 (−3.5; −2.6)**
		Q3	125.6	92.2	**−3.0 (−3.4; −2.6)**
		Q4	127.1	96.2	**−2.8 (−3.3; −2.4)**
		Q5	126.4	97.8	**−2.5 (−3.1; −2.0)**
		Q5 vs Q1; IRR/AAPC Diff, CI	1.08 (1.00; 1.16)	**1.18 (1.09; 1.27)**	**−0.9 (−1.5; −0.4)**
Colorectal	Female	Q1	75.3	54.0	**−3.0 (−4.0; −2.0)**
		Q2	78.7	60.0	**−2.6 (−3.0; −2.3)**
		Q3	83.9	61.2	**−2.9 (−3.5; −2.2)**
		Q4	79.4	59.1	**−2.9 (−3.4; −2.4)**
		Q5	84.3	64.9	**−2.3 (−2.9; −1.8)**
		Q5 vs Q1; IRR/AAPC Diff, CI	**1.11 (1.02; 1.21)**	**1.21 (1.11; 1.32)**	−0.7 (−1.7; 0.4)
Lung	Male	Q1	101.2	69.2	**−3.3 (−3.9; −2.7)**
		Q2	115.2	88.7	**−2.4 (−2.8; −1.9)**
		Q3	115.4	91.4	**−1.9 (−2.5; −1.2)**
		Q4	128.1	106.8	**−1.7 (−2.1; −1.2)**
		Q5	141.2	125.4	**−1.2 (−1.7; −0.6)**
		Q5 vs Q1; IRR/AAPC Diff, CI	**1.43 (1.28; 1.61)**	**1.82 (1.60; 2.06)**	**−2.1 (−2.9; −1.4)**
Lung	Female	Q1	36.5	39.1	+0.8 (−0.3; +1.9)
		Q2	43.5	49.4	**+1.7 (+1.1; +2.3)**
		Q3	40.0	51.6	+2.3 (−0.5; +5.2)
		Q4	51.0	60.8	**+1.9 (+1.3; +2.5)**
		Q5	57.7	73.9	**+2.2 (+1.4; +3.0)**
		Q5 vs Q1; IRR/AAPC Diff, CI	**1.58 (1.37; 1.81)**	**1.88 (1.66; 2.12)**	**−1.4 (−2.7; −0.0)**
Prostate	Male	Q1	233.6	163.6	**−3.6 (−4.5; −2.7)**
		Q2	227.2	173.7	**−2.3 (−2.8; −1.7)**
		Q3	228.8	177.1	**−2.2 (−3.4; −0.8)**
		Q4	223.2	172.8	**−2.8 (−3.8; −1.9)**
		Q5	205.9	169.2	**−2.2 (−3.2; −1.3)**
		Q5 vs Q1; IRR/AAPC Diff, CI	**0.90 (0.83; 0.97)**	1.02 (0.92; 1.12)	[a]
Breast	Female	Q1	187.7	162.4	**−1.9 (−2.4; −1.4)**
		Q2	180.7	168.7	**−1.3 (−1.8; −0.8)**
		Q3	183.8	169.3	**−1.3 (−1.7; −0.9)**

TABLE 1 (Continued)

Cancer site	Sex	Quintile	Incidence 2007	Incidence 2018	AAPC, CI[a] 2018 vs 2007
		Q4	202.6	166.4	**−1.9 (−2.4; −1.4)**
		Q5	192.3	171.1	**−1.6 (−2.1; −1.1)**
		Q5 vs Q1; IRR/AAPC Diff, CI	1.02 (0.93; 1.12)	1.05 (1.00; 1.11)	[a]

Note: Significant differences are printed in bold.

Abbreviations: AAPC, average annual percentage change from 2007 to 2018; CI, 95% Confidence interval; Diff, difference; IRR, incidence rate ratio between Q5 and Q1; Q, quintile.

[a]The AAPCs for each quintile were derived from stratified analyses by quintile. The AAPC differences were derived from models including Q1 and Q5 provided that the test of parallelism was rejected. In case of parallelism of the AAPC of Q1 and Q5, the parallel model was preferred and, thus, the difference between the AAPC of Q1 and Q5 was not reported.

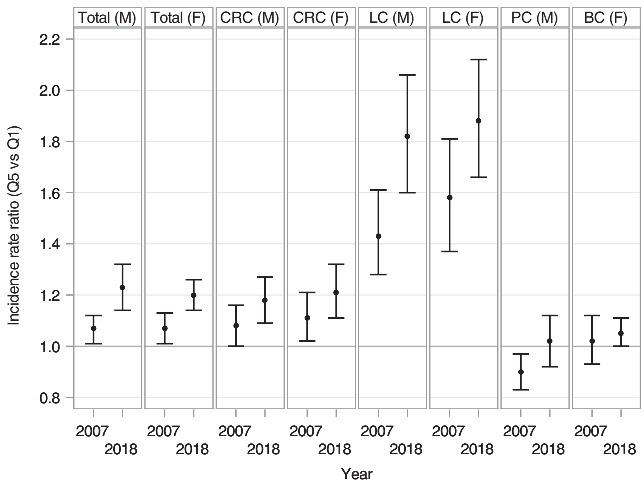

FIGURE 3 Incidence rate ratio between the most (Q5) and least deprived (Q1) quintile in 2007 and 2018 for total, colorectal (CRC), lung (LC), prostate (PC) and breast cancer (BC) by sex (M = male, F = female).

deprived districts. For younger men, a reversed gradient in inequalities between the most deprived and least deprived region was observed in 2007, which disappeared in 2018. In contrast, the typical gradient in inequality developed over time among men aged 65+, with higher incidences in the most deprived regions. For breast cancer, no significant differences between years or across deprivation quintiles in 2007 and 2018 were observed.

Areas with the most compared to the least employment deprivation had significantly higher cancer incidence rates for total cancer and all analyzed sites with a particularly strong association in lung cancer (men: 2.08 [1.89-2.29], women: 2.26 [2.10-2.44]; Table S6). Higher income deprivation was also associated with higher incidence rates for all cancer sites except for breast and prostate cancer. Education deprivation was only significantly associated with incidence differences in female lung cancer. No significant associations were found for municipality revenue and security deprivation. Districts with the highest social capital deprivation had a lower cancer incidence for all cancer sites except for total cancer and colorectal cancer in men. Environment deprivation was significantly associated with higher incidences of total, lung and breast cancer incidence in the most compared to the least deprived districts.

The sensitivity analysis shows that excluding districts with more than 500 000 inhabitants leads to comparable results, which emphasizes the robustness of the analyses of the study (Table S7).

4 | DISCUSSION

In Germany, age-standardized cancer incidence decreased strongly across all deprivation quintiles for total cancer and almost all analyzed cancer sites (except for lung cancer in females living in deprived areas) between 2007 and 2018. For total cancer, colorectal cancer, and male lung cancer the decrease was less pronounced in the most deprived districts resulting in widening socioeconomic inequalities over time.

Socioeconomic inequalities in cancer incidence have been widely documented internationally.[9] In Germany, higher incidence in more deprived districts in 2010 to 2013 were reported for total cancer in men but not in women, with a 7% higher incidence in the most compared to the least deprived districts.[2] A study on the association of individual income and cancer incidence in Lower Saxony (2006-2018) using data from a single health insurance provider reported socioeconomic inequalities for colon and lung cancer in men but not in women and a reverse association for prostate cancer.[4] While evidence for prostate and breast cancer was mixed, our study demonstrated consistent and large inequalities for total, colon and lung cancer, based on a larger sample and longer time frame than earlier studies. Yet, international and national comparisons are hampered by the use of different deprivation indices, different tools for standardization, variations in study design, that is, area-based vs individual level, and whether registry data or claims data were used.

To our knowledge, the question of whether declining incidence trends were comparable across deprivation groups has rarely been investigated. In our study, we observed widening inequalities between 2007 and 2018 for total cancer, lung cancer and for colorectal cancer in men based on data of eight German federal states. This adds to a smaller prior study on incidence trends in Lower Saxony, where inequalities tended to widen for total cancer among men and for colon, lung and breast cancer among women.[4] While there was no

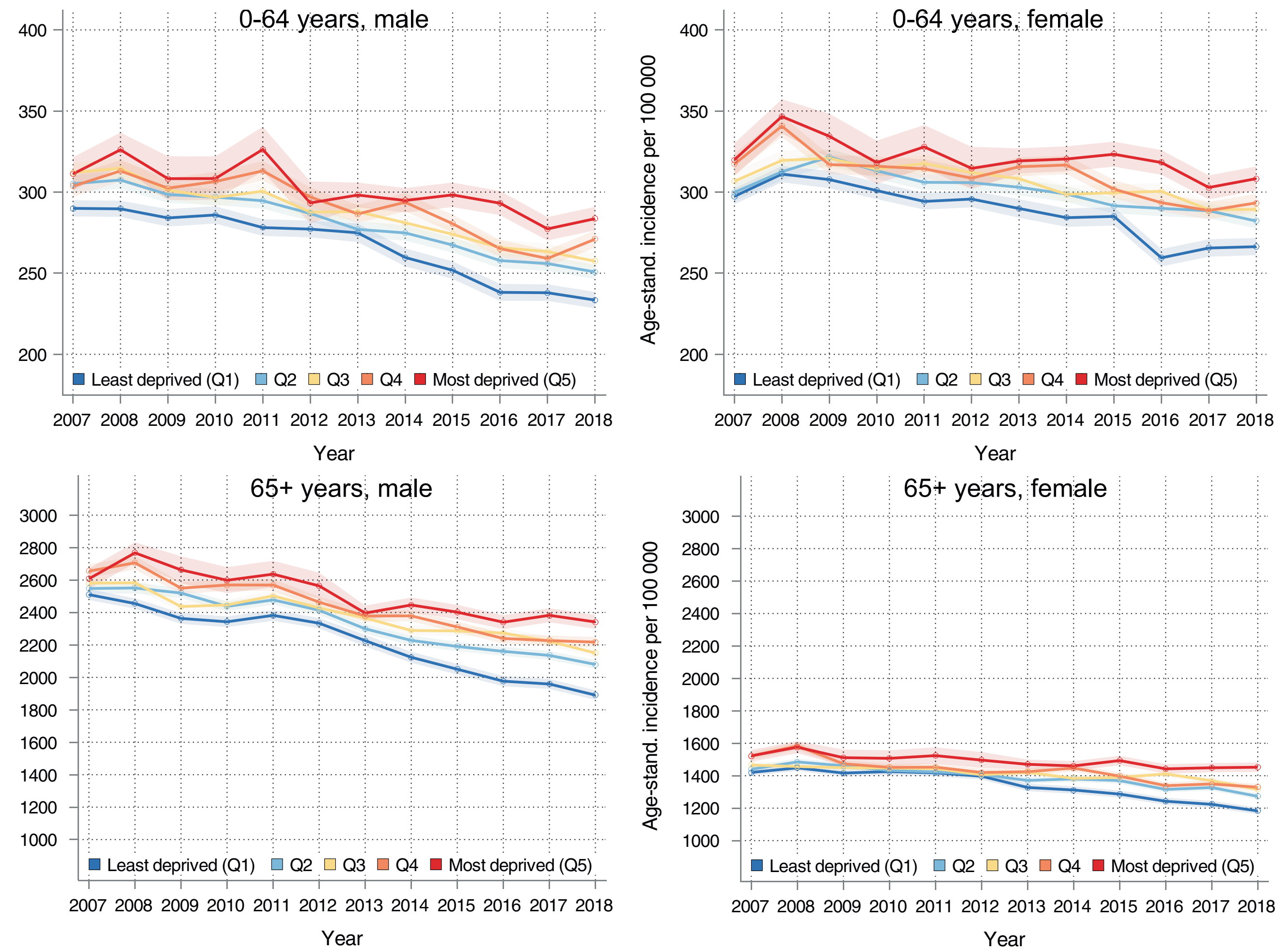

FIGURE 4 Age-standardized total cancer incidence for individuals aged 0 to 64 years and 65+ years between 2007 and 2018 by sex and deprivation quintile.

interaction with age in our study, a previous study found widening income inequalities in lung cancer incidence among the retired population and narrowing educational and occupational inequalities among the working-age population.[3] This underlines that different domains of socioeconomic inequalities differ in their impact on incidence trends by cancer site and sex, as shown in our analysis. Furthermore, an area-based design covers different aspects of inequality than analyses at the individual level so that findings and their interpretation necessarily vary from study to study.

Results from other countries on changes in socioeconomic inequalities vary by cancer site, country and choice of calendar years. In England, the deprivation gap for lung cancer incidence increased between 1990 and 2002.[14] In Norway, educational inequalities in breast cancer incidence have narrowed between 2000 and 2009,[16] whereas in Scotland screening-detected estrogen receptor positive breast cancer (but not other subtype) incidence increased between 2009 and 2016 mostly in the least deprived group leading to stronger inequalities.[13] In Iran, social disparities in breast cancer incidence did not change between 2003 and 2009.[12] In Canada, area-based income inequalities in prostate cancer incidence reversed over time from a higher incidence in higher income neighborhoods in 1996 to 2005 to higher incidence in lower income neighborhoods in 2006 to 2010.[11] In Scotland (2001-2012), similar to our results, inequalities in colorectal cancer and lung cancer incidence increased over time whereas there was no significant change for prostate and breast cancer.[17] In contrast, narrowing educational inequalities in colorectal cancer incidence were reported for Finland between 1976 and 2014.[15] Most likely, these cross-country variations are explained by differences in the magnitude and spread of risk factors, such as smoking, obesity and alcohol consumption and screening utilization in addition to the methodological aspects mentioned above.

To identify means to tackle the observed socioeconomic inequalities, it is important to look more closely at district characteristics (Table S8). Interestingly, the most deprived areas in our study did not exhibit observable disadvantages with respect to availability of and access to health care services, visible by a high degree of urbanity and population density, short distance to the nearest major center, pharmacy and family doctor as well as high rates of physicians,

TABLE 2 Age-standardized breast, prostate, colorectal, lung and total cancer incidence for individuals aged 0-64 years for individuals aged 0-64 years in 2007 and 2018 by sex and deprivation quintile.

			0-64 years			65+ years		
					AAPC, CI[a]			AAPC, CI[a]
Cancer site	Sex	Quintile	Incidence 2007	Incidence 2018	2018 vs 2007	Incidence 2007	Incidence 2018	2018 vs 2007
Total	Male	Q1	290.0	233.4	**−2.0 (−2.8; −1.1)**	2510.0	1890.6	**−2.5 (−3.1; −2.0)**
		Q5	311.2	283.6	**−1.2 (−1.6; −0.7)**	2607.8	2341.6	**−1.3 (−1.7; −0.8)**
		Q5 vs Q1 IRR/AAPC Diff, CI	**1.07 (1.01; 1.15)**	**1.21 (1.13; 1.31)**	−0.8 (−1.7; +0.1)	**1.06 (1.00; 1.12)**	**1.23 (1.14; 1.34)**	**−1.3 (−2.0; −0.6)**
Total	Female	Q1	297.4	266.4	**−1.4 (−1.9; −0.9)**	1420.3	1182.9	**−1.7 (−2.1; −1.3)**
		Q5	319.9	308.3	**−0.7 (−1.2; −0.3)**	1522.5	1452.4	**−0.6 (−0.9; −0.3)**
		Q5 vs Q1 IRR/AAPC Diff, CI	**1.07 (1.01; 1.13)**	**1.16 (1.10; 1.22)**	**−0.7 (−1.3; −0.1)**	**1.07 (1.00; 1.14)**	**1.23 (1.16; 1.30)**	**−1.1 (−1.6; −0.6)**
Colorectal	Male	Q1	37.9	29.9	**−2.3 (−2.7; −1.9)**	408.0	271.0	**−3.8 (−4.2; −3.4)**
		Q5	39.7	33.0	**−1.3 (−2.3; −0.3)**	436.2	329.5	**−2.9 (−3.5; −2.4)**
		Q5 vs Q1 IRR/AAPC Diff, CI	1.05 (0.90; 1.21)	1.10 (0.99; 1.22)	**−1.0 (−1.9; −0.1)**	**1.09 (1.00; 1.18)**	**1.21 (1.11; 1.33)**	**−0.9 (−1.5; −0.3)**
Colorectal	Female	Q1	23.3	21.0	**−1.5 (−2.4; −0.7)**	261.3	172.1	**−4.1 (−4.4; −3.7)**
		Q5	26.4	22.2	−1.3 (−2.6; +0.1)	291.4	217.3	**−2.7 (−3.2; −2.2)**
		Q5 vs Q1 IRR/AAPC Diff, CI	1.12 (0.99; 1.27)	1.06 (0.94; 1.21)	[a]	**1.11 (1.00; 1.22)**	**1.26 (1.15; 1.38)**	**−1.4 (−1.9; −0.9)**
Lung	Male	Q1	36.9	26.6	**−3.2 (−4.2; −2.2)**	330.8	221.5	**−3.3 (−3.9; −2.7)**
		Q5	56.0	47.5	**−1.6 (−2.4; −0.8)**	445.9	403.9	**−1.1 (−1.4; −0.8)**
		Q5 vs Q1 IRR/AAPC Diff, CI	**1.54 (1.33; 1.77)**	**1.77 (1.54; 2.04)**	**−1.6 (−2.8; −0.3)**	**1.39 (1.23; 1.57)**	**1.84 (1.61; 2.10)**	**−2.2 (−2.8; −1.6)**
Lung	Female	Q1	20.7	18.5	−1.0 (−2.5; +0.5)	93.1	112.4	**+1.9 (+0.6; +3.3)**
		Q5	32.4	38.0	0.6 (−0.9; +2.1)	148.3	202.3	**+3.3 (+2.5; +4.1)**
		Q5 vs Q1 IRR/AAPC Diff, CI	**1.57 (1.32; 1.85)**	**2.04 (1.73; 2.41)**	[a]	**1.58 (1.36; 1.83)**	**1.79 (1.60; 2.02)**	−1.4 (−2.9; +0.2)
Prostate	Male	Q1	69.7	50.4	**−2.5 (−4.2; −0.7)**	819.5	568.4	**−3.7 (−4.6; −2.8)**
		Q5	57.9	46.1	**−2.3 (−3.1; −1.4)**	734.9	608.9	**−1.9 (−3.4; −0.3)**
		Q5 vs Q1 IRR/AAPC Diff, CI	**0.83 (0.76; 0.90)**	0.91 (0.82; 1.01)	[a]	0.92 (0.84; 1.01)	**1.06 (0.95; 1.17)**	[a]
Breast	Female	Q1	127.8	110.5	**−2.0 (−2.6; −1.4)**	401.8	347.6	**−1.8 (−2.2; −1.3)**
		Q5	131.5	115.7	**−1.7 (−2.5; −0.9)**	409.6	368.9	**−1.5 (−1.9; −1.0)**

(Continues)

TABLE 2 (Continued)

Cancer site	Sex	Quintile	0-64 years			65+ years		
			Incidence 2007	Incidence 2018	AAPC, CI[a] 2018 vs 2007	Incidence 2007	Incidence 2018	AAPC, CI[a] 2018 vs 2007
		Q5 vs Q1 IRR/AAPC Diff, CI	1.02 (0.94; 1.11)	1.05 (0.99; 1.11)	[a]	1.02 (0.91; 1.14)	1.06 (0.99; 1.15)	[a]

Note: Significant differences are printed in bold.
Abbreviations: AAPC, average annual percentage change from 2007 to 2018; CI, 95% confidence interval; Diff, difference; IRR, incidence rate ratio between Q5 and Q1 (reference); Q, quintile.
[a]The AAPCs for each quintile were derived from stratified analyses by quintile. The AAPC differences were derived from models including Q1 and Q5 provided that the test of parallelism was rejected. In case of parallelism of the AAPC of Q1 and Q5, the parallel model was preferred and, thus, the difference between the AAPC of Q1 and Q5 was not reported.

hospital beds, nursing homes per 10 000 inhabitants. Yet, aspects of deprivation and/or socioeconomic disadvantage, that is, unemployment, municipality depth, rate of recipients of social welfare benefits, share of school leavers were indeed much more unfavorable in the group of districts of the least deprived quintiles. Thus, indeed social determinants of health seem to play a much greater role than aspects of medical care or more general infrastructure. This adds to prior evidence, demonstrating that unemployment rate and welfare benefits were better predictors of life expectancy at the district level than average income, population density and number of physicians per 100 000 inhabitants.[25] The fact that the most deprived districts are often also urban districts necessitates the investigation of socioeconomic inequalities within cities, as for example targeted by the World Health Organization within the European Healthy Cities Network.[26]

In order to explain the study results, individual risk factors need to be considered in addition to area-based indicators. The most prominent factors, such as tobacco consumption, alcohol abuse and obesity, typically also exhibit a socioeconomic gradient.[27] For example, results from the second wave of the European Health Interview Service (2013-2015) reported a higher prevalence of current smoking, obesity, physical activity below 150 min per week, heavy episodic drinking and nondaily fruit or vegetable intake among individuals with lower educational level.[28] In Germany, smoking prevalence decreased over the years but socioeconomic inequalities in smoking prevalence increased between 1995 and 2013.[29] It has been shown that smoking was a strong determinant for socioeconomic inequalities in mortality in Europe with decreasing impact over the years among men but not among women.[30] Obesity prevalence increased in the low and medium but not in high socioeconomic groups between 1990 and 2011.[31] These increasing inequalities in risk factor prevalence are in alignment with the less pronounced decrease of lung cancer incidence in men, total cancer and colorectal cancer in more deprived regions, which resulted in increasing inequalities in cancer incidence in recent years. For breast cancer incidence, no clear association with socioeconomic deprivation was observed. Here, a higher prevalence of hormone replacement therapy[32] and other reproductive factors,[33] such as lower birth rates,[34] might counterbalance generally more favorable health-related risk factors among women with higher socioeconomic status. Prostate cancer is known to be less associated with common cancer risk factors, likely explaining the absence of an association with deprivation in our study.

Utilization of screening is clearly associated with breast, colorectal and prostate cancer incidence.[35-37] The statutory health insurance (SHI), in Germany mandatory since 2009, bears all costs for approved diagnostics and treatments including screening.[38] Therefore, there should not be a financial barrier to early detection or cancer diagnostics. The increase in breast cancer incidence from 2007 to 2008 followed by a decrease in all deprivation quintiles could be related to national mammography screening program rolled out between 2005 and 2009.[39] Introduction of opportunistic colonoscopy screening led to a decrease of colorectal cancer incidence since its introduction in 2002, enabled by the detection and removal of precursor lesions.[40] Accordingly, we observed a strong downward trend for colorectal cancer incidence across all deprivation groups. There is no organized screening program for prostate cancer in Germany, but costs for an annual examination of men's sex organs including digital rectal exam are covered by the SHI. Costs for prostate-specific antigen (PSA) test are not covered, but the German S3 guideline on prostate cancer has long recommended proactively informing men of PSA testing.[41] In Germany, prostate cancer incidence increased between 1999 and 2007 followed by a decrease until 2013 and a slight increase in the last years.[42] This pattern of decrease since 2007 followed by a stagnation or slight increase after 2013 is broadly replicated in our data, while incidence trends did not seem to systematically differ across deprivation quintiles. Thus, there were no indications that PSA testing affected socioeconomic differences. Whether the slight tendency towards widening inequalities in breast cancer incidence and the more pronounced widening of inequalities in colorectal cancer incidence in our findings might be related to selective utilization of screening would be an interesting avenue for further studies. In general, it has been shown that organized compared to opportunistic screening might contribute to smaller inequalities in utilization of screening but also that it unlikely eliminates these inequalities.[5,43,44] Reported strategies to enhance access to screening among individuals with lower socioeconomic status, for example, screening invitations and reminder letters[45] or the involvement of primary-care physicians, mobile mammography, free tests and offering financial incentives is an important national public health challenge.[46-49]

Further research should disentangle the mechanism how area-based deprivation affects cancer incidence specifically taking time lags between exposure and disease into account. Although it is certainly true that early life circumstances affect cancer development, deprivation differentials in Germany are rather stable over time. Likewise, the GIMD was relatively stable between 2006 and 2015 in our study (Table S1). Thus, more recent indicators of deprivation likely provide a reasonable proxy for current and past exposures arising from less favorable living conditions. Also, internal migration rates were stable over time in Germany with a rate for migration across districts of 3.8% in 2018 mainly affecting younger people with low cancer incidence rates.[50,51] The sparse data on spatial mobility and socioeconomic factors indicate a higher migration rate among persons with higher education, yet again at age groups less relevant for cancer.[50] The same is true for the significant increase in immigration since 2011, primarily from the countries of the European Union, and the strong immigration of refugees in the mid-2010s. Whether the complex interplay of selective in- and outmigration and spatial mobility at younger age groups indeed affects cancer incidence at older ages remains a fascinating line of research.

The major strength of our study was the possibility to investigate trends in cancer incidence by regional socioeconomic deprivation using high-quality cancer registry data in combination with a well-established and validated deprivation index in a setting with universal and statutory health insurance. A limitation is the exclusion of cancer registry data from the Eastern Federal States due to data quality issues so that it is unknown to which extent the findings could be generalized to the entire German population. Since we used the quintiles calculated for the entire Germany districts to cover the entire spectrum of deprivation, the most deprived quintile was underrepresented in our study. Nonetheless, the sample size was large enough to detect inequalities in incidence and the results might represent a conservative estimate of actual socioeconomic differences. A further limitation is the lack of information on individual socioeconomic factors or data on individual risk factors. In our analysis, the main comparisons compared the least and most deprived quintile, which does not reflect the entire range of socioeconomic inequalities. Yet, tables and trends included all deprivation quintiles, allowing readers to perform more in-depth comparisons. A German standard population instead of a general standard population (eg, for Europe) was used for standardization of incidence rates to estimate the magnitude of inequalities for Germany perhaps hampering the comparison to studies from other countries in addition to the aspects mentioned above, such as the use of different indices.

In summary, decreasing prevalence of cancer risk factors, especially smoking, and partly increasing utilization of cancer screening may have led to an encouraging decline in age-standardized cancer incidence for total cancer and the most common cancer sites in all deprivation quintiles in Germany. However, this development was less pronounced in more deprived districts leading to widening socioeconomic inequalities in total cancer, colorectal cancer and lung cancer incidence. Further research is needed taking the impact of individual socioeconomic status, health-related behavior, utilization of screening and selective migration or social mobility into account. Interventions to promote a healthy lifestyle to reduce risk factor prevalence and to increase participation rates in screening programs should generally be targeted universally. However, their intensity should depend on the degree of need leading to a higher intensity in socioeconomically deprived and urban regions. This principle of proportional universalism[52] could be used by policy makers when designing future interventions to overcome the observed increasing inequalities in cancer incidence.

AUTHOR CONTRIBUTIONS

Lina Jansen: conceptualization, data curation, formal analysis, investigation, methodology, project administration, software, visualization, writing—original draft; Lars Schwettmann: data curation, investigation, writing—review & editing; Christian Behr: data curation, investigation, writing—review & editing; Andrea Eberle: data curation, investigation, writing—review & editing; Bernd Holleczek: data curation, investigation, writing—review & editing; Christina Justenhoven: data curation, investigation, writing—review & editing; Hiltraud Kajüter: data curation, investigation, writing—review & editing; Kirsi Manz: data curation, investigation, writing—review & editing; Frederik Peters: data curation, investigation, writing—review & editing; Andrea Schmidt-Pokrzywniak: data curation, investigation, writing—review & editing; Eunice Sirri: data curation, investigation, writing—review & editing; Ron Pritzkuleit: data curation, investigation, writing—review & editing; Fabian Tetzlaff: writing—review & editing; Sven Voigtländer: data curation, investigation, writing—review & editing; Volker Arndt: conceptualization, supervision, writing—review & editing. The authors have performed the work reported in the article, unless clearly specified in the text.

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CONFLICT OF INTEREST STATEMENT

The authors declared no potential conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request, following permission of the cancer registries.

ETHICS STATEMENT

Data collection within the Cancer Registries has been carried out according to state legislation of cancer registration. The study was conducted in accordance with the recommendations of the Declaration of Helsinki by the World Medical Association.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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