International Journal of Environmental and Biological Sciences
ISSN: 3054-3924
https://doi.org/10.63939/bx4r6q78
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Vol. 1 , No 4 , October 2026

RESEARCH Open Access

Smoking Status and Tobacco-Associated Cancer Site Profiles: A Multivariable Case-Case Analysis of Oncology Registry Records in Iraq

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Abstract:

Background: Tobacco smoking has been associated with a number of malignancies including the lung, larynx and urinary bladder. However, the smoking status patterns reported by Iraqi oncology registries are not properly characterized at the site-specific level. Hospital-based case–case analyzes may not be able to establish population-level cancer risks but they may offer useful insights into these patterns. Objective: To investigate the associations between relative representation of lung, laryngeal and urinary bladder

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cancers in the records of oncology registry in Iraq, after controlling for age, sex and registration year, and documented current and former smoking. Methods: We conducted a retrospective registry-based case-control study using five annual oncology datasets from 2022 to 2026. To be eligible, the records must have included a diagnosis of a recognizable malignant neoplasm (ICD-10 C00–C97), an interpretable age and sex, and a documented smoking status. Smoking was classified as current, former, or documented nonsmoking. Lung (C34), laryngeal (C32) and urinary bladder (C67) cancers were compared with other registered malignancies in separate multivariable logistic regression models, adjusted for age, sex and registration year. Six major smoking-cancer associations were evaluated. Benjamini–Hochberg procedure was selected for multiple testing correction. Sensitivity analyzes excluded records from 2026 and secondary analyzes estimated current or former smoking combined. Results: The reported analytical cohort included 11,664 eligible registry records, of which 2,092 (17.9%) current smokers, 1,518 (13.0%) former smokers, and 8,054 (69.1%) recorded nonsmokers. Current or previous smoking was recorded in 74.4% of lung cancer, 82.8% of laryngeal cancer and 66.5% of urinary bladder cancer records. Current smokers had higher adjusted odds of lung cancer (aOR 6.72; 95% CI 5.64-8.01), laryngeal cancer (aOR 9.81; 95% CI 6.13-15.71) and urinary bladder cancer (aOR 2.71; 95% CI 2.18-3.36) than recorded nonsmokers. Corresponding estimates for ex-smokers were 4.68 (95% CI 3.87-5.67), 9.06 (95% CI 5.47-14.99), and 2.12 (95% CI 1.67-2.69). The source analysis, corrected for multiple-testing, demonstrated statistically significant associations. Positive associations for lung and laryngeal cancers were retained in restricted-period analyzes, but a stable restricted-period bladder cancer estimate was not available. Conclusions: The relative percentages of lung, laryngeal and urinary bladder cancer diagnoses in this institutional oncology registry were associated with documented current and former smoking. These results are consistent with what is already known about tobacco-related cancers, but they should be interpreted as associations in individual cases, rather than as estimates of the risk of cancer in the population. Better documentation of smoking, identification of patients and validation of registry data is essential to reinforce future oncology research in Iraq.

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Keywords: Tobacco smoking; Oncology registry; Case–case study; Lung cancer; Laryngeal cancer; Urinary bladder cancer; Multivariable logistic regression; Iraq.

Introduction

Cancer remains a major global public health challenge, with approximately 20 million new cases and 9.7 million deaths worldwide in 2022 [1]. It has been well documented that tobacco smoking prevents many malignancies, including those of the lung, larynx and urinary bladder. Although carcinogens derived from tobacco contribute to DNA damage, genomic instability, and malignant transformation [2–5], the intensity of the risks of cancer associated with smoking depends on the individual susceptibility and exposure characteristics. Systemic uptake and elimination in urine of carcinogenic metabolites generated from tobacco are partly involved in the development of urinary bladder carcinogenesis, while lung and laryngeal cancers are strongly related to tobacco exposure [10–13]. These known associations provide a scientific basis to analyze the patterns of smoking status among the cancer diagnoses in clinical oncology registries. Cancer is a major health-care burden in Iraq, and tobacco-related cancers and significant differences in smoking exposure between men and women have been reported in previous studies [14–18]. The surveillance of tobacco-related cancers is further complicated by waterpipe and cigaret use, particularly when detailed information on smoking intensity, duration, tobacco product type and cessation history is not present in routine clinical records.

The association between tobacco smoking and multiple malignancies is well established, yet systematic characterization of the distributions of smoking status across cancer diagnoses in Iraqi oncology registries has important gaps. Existing institutional data may provide descriptive information on exposure to smoking, but adjusted comparisons across specific cancer sites are not well characterized. In addition, the absence of reliable patient-level identifiers, differences between annual registry datasets, incomplete documentation of exposure, and inconsistent smoking terminology may affect comparability of data and interpretation of statistical findings. A further methodological consideration concerns the interpretation of hospital-based cancer comparisons. Unlike conventional case–control studies, case–case analyses compare records of a selected

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malignancy with records of other malignancies rather than cancer-free individuals. Consequently, the resulting odds ratios describe differences in the relative representation of cancer diagnoses associated with smoking status, rather than population-level cancer risk. Their magnitude may also depend on the diagnostic composition of the comparison group, particularly when other tobacco-associated cancers are included.

To address these institutional and methodological evidence gaps, the present retrospective registry-based case–case study investigated associations between documented current and former smoking and three prespecified tobacco-associated malignancies—lung (ICD-10 C34), laryngeal (C32), and urinary bladder (C67) cancers—using Iraqi oncology registry records from 2022 to 2026. Multivariable analyses adjusted for age, sex, and registration year, with additional evaluation of combined smoking categories and restricted-period sensitivity analyses. The study seeks to provide a clearer characterization of smoking-related cancer-site representation within routinely collected oncology data while emphasizing appropriate epidemiological interpretation and the limitations of registry-based inference.

1.1. Study Objectives

Main Purpose

To investigate the relationships between the relative proportion of lung (ICD-10 C34), laryngeal (C32) and urinary bladder (C67) cancers in eligible Iraqi oncology registry records from 2022 to 2026 using multivariable case–case analyzes adjusted for age, sex and registration year.

2. Secondary Objectives

1. To describe the distribution of documented smoking status in the analytical cohort by recorded sex and selected cancer diagnoses.
2. To calculate and compare the adjusted case-case associations of current and former smoking with each prespecified cancer site, with recorded nonsmoking as the reference category.

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3. To evaluate the association of the relative proportion of the three selected malignancies with current or former smoking (ever-smoking).
4. To test the robustness of the main associations by conducting restricted-period sensitivity analyzes excluding the 2026 registry dataset that is capable of producing stable model estimates.
5. To detect limitations in registry data quality, documentation of smoking status and record-level analysis, which may influence the interpretation of observed associations.

2. Materials and Methods

2.1. Study Design

The present study employed a retrospective, observational, registry-based case-case study design to examine the associations between documented smoking status and the relative frequency of selected cancer diagnoses in Iraq's oncology registry data. The analysis compared records of three prespecified tobacco-associated malignancies (lung cancer, laryngeal cancer, and urinary bladder cancer) with those of other malignant neoplasms in the same institutional registry. The current study did not use cancer-free controls, as in a traditional case-control study. Consequently, the estimated odds ratios describe associations between smoking status and the relative distribution of cancer diagnoses among registered oncology records rather than population-level cancer incidence, etiological relative risks, or smoking-attributable cancer fractions. The methodological framework was developed with reference to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) extension [6,7].

2.2. Study Setting, Data Source, and Unit of Analysis

This retrospective study utilized routinely collected electronic oncology registry data from a tertiary cancer treatment center in Iraq. Five annual datasets covering 2022–2026

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were included, containing demographic characteristics, malignant neoplasm diagnoses classified according to the International Classification of Diseases, Tenth Revision (ICD-10), documented smoking status, and registration year. Annual data sets were transformed into a common analytic structure, by standardizing the terminology of smoking status, identifying recognizable malignant neoplasm codes, and assessing the completeness and interpretability of demographic data. These procedures provided for consistent classification of exposure and outcome throughout the study period. The unit of analysis was the individual record of the oncology registry. The lack of reliable unique patient identifiers prevented the systematic identification or exclusion of repeated registrations across years. Thus, the analytic cohort was comprised of registry records, not confirmed unique patients. The logistic regression models reported did not account for potential correlation within patients, which may have influenced the precision of the estimated associations.

2.3. Study Period

The research looked at five annual oncology registry datasets corresponding to calendar years 2022, 2023, 2024, 2025 and 2026. The 2021 data set was available but not included as there was no dedicated smoking status variable that could be used for the primary exposure classification. Patient-specific observations were extracted from the annual registry workbook worksheet for 2025, not from aggregate summary worksheets. The registration year was assigned from the annual source data set and included as a categorical covariate in the multivariable analyzes. Due to temporal inconsistencies in some records of the 2026 dataset, the primary full-period analysis was supplemented with a restricted-period sensitivity analysis (2022–2025). The objective of this methodology was to assess how reliant the major associations were on the inclusion of the 2026 reporting period. It didn't, however, address the fundamental concerns about the quality of the data.

2.4. Study Population and Eligibility Criteria

The source population was derived from oncology registry records. Malignant neoplasm diagnoses were coded to ICD-10 codes C00–C97. Eligible records were derived



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from one of the five annual datasets (2022–2026) and contained a recognizable diagnosis of malignant neoplasm, interpretable age, recorded sex, and smoking-status information classified into the predefined analytical categories. Plausible values were between 0 and 110 years of age. Records with missing or unrecognizable diagnostic codes, invalid or uninterpretable age values, missing sex information, or missing, ambiguous, or contradictory smoking-status entries were excluded from the complete-case analytical cohort. Missing smoking information was not categorized as nonsmoking and no statistical imputation was described. Application of these criteria yielded an analytical cohort of 11,664 eligible oncology registry records reported. However, the source manuscript did not report the initial number of extracted records and the numbers excluded for each criterion, and these had to be cross-checked with the original registry datasets. Analytically, the time inconsistencies found in the 2026 dataset were addressed by applying a restricted-period sensitivity analysis that excluded this year, as detailed in the statistical analysis section.

2.6. Smoking-Status Assessment and Classification

Documented smoking status was the primary explanatory variable. Smoking terminology recorded in the original registry datasets was standardized into mutually exclusive analytical categories: current smoking, former smoking, recorded nonsmoking, and unknown smoking status. The classification framework is presented in Table 1.

Table 1. Operational classification of recorded smoking status

Recorded terminology	**Analytical category**
Smoker / Current smoker	Current smoker
Former smoker / Ex-smoker	Former smoker
Nonsmoker / Non-smoker	Recorded nonsmoker
Missing, unclear, or contradictory smoking information	Unknown

The designation *recorded nonsmoker* was retained because the source documentation did not independently establish lifelong abstinence from tobacco. For the primary analyses,

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current and former smoking were represented by separate binary indicator variables, with recorded nonsmoking serving as the reference category. Records classified as having unknown smoking status were excluded from the complete-case analytical cohort. For secondary analyses, current and former smoking were combined into a single *ever-smoking* category, while recorded nonsmoking remained the reference category. The registry did not provide sufficiently reliable information on smoking intensity, duration, pack-years, age at smoking initiation, or time since cessation. Furthermore, cigarette smoking could not be distinguished from waterpipe tobacco use. Consequently, the exposure variables represented documented smoking categories rather than quantitatively measured lifetime tobacco exposure.

2.7. Cancer-Site Classification and Outcome Definitions

Three primary cancer-site outcomes were prespecified on the basis of established evidence concerning tobacco-associated malignancies. The selected outcomes were lung cancer (ICD-10 C34), laryngeal cancer (C32), and urinary bladder cancer (C67).

Table 2. Definitions of the primary cancer-site outcomes

Cancer site	ICD-10 code	Analytical comparison
Lung cancer	C34	C34 versus other eligible malignant neoplasms
Laryngeal cancer	C32	C32 versus other eligible malignant neoplasms
Urinary bladder cancer	C67	C67 versus other eligible malignant neoplasms

For each main outcome, a separate binary dependent variable was constructed. Records for the selected cancer diagnosis were assigned a value of 1, and records for other eligible malignant neoplasms were assigned a value of 0. Therefore, each logistic regression model evaluated the relative probability of a particular cancer diagnosis versus other malignancies in the analytic cohort. The comparison group was not cancer-free. It might also harbor malignancies not necessarily related to tobacco exposure. The magnitude of the estimated associations may therefore be partly driven by the diagnostic composition

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of the institutional registry. Secondary diagnostic categories including pancreatic cancer (C25), stomach cancer (C16) and breast cancer (C50) were descriptively analyzed.

2.8. Covariates and Potential Confounding

The primary multivariable models included age, recorded sex, and registration year as adjustment variables. Age was entered as a continuous variable, consistent with the reported original model specification. Recorded sex was incorporated as a categorical variable using the available registry classification. Registration year was represented using categorical indicator variables to account for differences in annual registry composition without imposing a linear temporal trend. These covariates were selected because demographic and temporal differences may influence both documented smoking status and the distribution of cancer diagnoses. The available registry did not provide sufficiently complete information on other potentially relevant factors, including occupational carcinogen exposure, socioeconomic characteristics, environmental tobacco exposure, alcohol consumption, or detailed tobacco-use history. Consequently, residual confounding could not be excluded.

2.9. Statistical Analysis

Categorical variables were summarized as frequencies and percentages. Smoking-status distributions were described for the overall analytical cohort, by recorded sex, and across the selected cancer diagnoses. For each cancer site, the proportion of current and former smokers was calculated using the total number of eligible records within that diagnostic category as the denominator. Separate multivariable binary logistic regression models were used to examine the associations between documented smoking status and the relative representation of lung (C34), laryngeal (C32), and urinary bladder (C67) cancers. Each cancer site was analyzed as a binary outcome against all other eligible malignant neoplasms. Current and former smoking were included as separate exposure categories, with recorded nonsmoking as the reference. Models were adjusted for age, sex, and registration year. Associations were expressed as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). All statistical tests were two-sided. The Benjamini–Hochberg

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procedure was applied to control the false discovery rate across six primary comparisons, comprising two smoking-status contrasts for each of the three cancer outcomes. Statistical significance was defined as a false discovery rate–adjusted p-value (q-value) below 0.05. Secondary logistic regression analyses combined current and former smokers into an ever-smoking category, using recorded nonsmokers as the reference group and retaining the same adjustment variables. These analyses were considered supportive of the primary findings. The 2026 dataset was excluded due to documented temporal inconsistencies and a sensitivity analysis was conducted for a restricted period using records from 2022–2025. The same exposure definitions and adjustment strategy were used to evaluate consistency of primary associations across reporting periods. Model limitations included potential for within-patient correlation, separation, convergence issues and sparse data which could have been caused by multiple registrations. There was no way to adjust for patient-level clustering due to the absence of reliable, unique patient identifiers. Therefore, the model estimates were interpreted within the limitations of record-level analysis. We interpreted odds ratios as representing the relative representation of cancer sites in the oncology registry rather than estimates of population-level cancer risk, since comparison groups were other malignancies instead of cancer-free individuals.

2.12. Ethical Approval and Considerations

The current study was ethically approved in 2026 by the Research Ethics Committee of the College of Medicine, University of Kufa, Iraq. The study was conducted following the ethical principles and institutional policies applicable to retrospective studies involving clinical and oncology registry data. Throughout the data collection, processing and statistical analysis, patient confidentiality and privacy of data were maintained. All research results were presented in aggregated form, and no personally identifiable patient information was released.

3. Results

3.1. Analytical Cohort and Annual Distribution

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The reported final analytical cohort comprised 11,664 eligible oncology registry records collected across five annual datasets from 2022 to 2026. The largest contribution was from 2025 (n = 2,719; 23.3%), followed by 2022 (n = 2,342; 20.1%), 2024 (n = 2,293; 19.7%), 2023 (n = 2,189; 18.8%), and 2026 (n = 2,121; 18.2%). The restricted dataset for 2022–2025 contained 9,543 eligible records, representing 81.8% of the full analytic cohort. Annual counts show the distribution of eligible registry observations, not the annual incidence of cancer.

Table 1. Annual distribution of eligible oncology registry records, 2022–2026.

Registration year	Eligible records (n)	Percentage (%)
2022	2,342	20.1
2023	2,189	18.8
2024	2,293	19.7
2025	2,719	23.3
2026	2,121	18.2
Total	11,664	100.0

Percentages were calculated using the full analytical cohort as the denominator.

3.2. Overall Distribution of Smoking Status

Among the 11,664 records eligible for analysis, 2,092 (17.9%) were classified as current smokers, 1,518 (13.0%) as former smokers, and 8,054 (69.1%) as nonsmokers by record. 3,610 (30.9%) of the records were of current and former smokers. The most important category was that of nonsmokers who recorded their exposure. These proportions are representative of the smoking status of eligible institutional oncology records recorded and not to be interpreted as the smoking prevalence in the general Iraqi population.

Table 2. Distribution of Smoking Status Among Oncology Registry Records (N = 11,664)

Smoking status	Frequency (n)	Percentage (%)
Current smoker	2,092	17.9
Former smoker	1,518	13.0

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Recorded nonsmoker	8,054	69.1
Total	11,664	100.0

3.3. Smoking Status According to Recorded Sex

Smoking status was significantly different in male and female registry records. Of the 5149 men, 1718 (33.4%) were current smokers, 1181 (22.9%) were former smokers, and 2250 (43.7%) were nonsmokers at the time of record. In total, 6,515 female records were classified as current smokers (374, 5.7%), former smokers (337, 5.2%) and recorded nonsmokers (5,804, 89.1%). In male records the combined proportion of current or former smokers was 56.3% whereas in female records it was 10.9%.

Table 3. Smoking-status distribution by recorded sex.

Recorded sex	Current smoker	Former smoker	Recorded nonsmoker	Total
Female	374	337	5,804	6,515
Male	1,718	1,181	2,250	5,149
Total	2,092	1,518	8,054	11,664

The counts have been copied from the original manuscript. The percentages in the accompanying text use the corresponding sex-specific denominators. These observed differences reflect the large heterogeneity in recorded smoking status by recorded sex and provide a descriptive rationale for the inclusion of sex in the multivariable models.

3.4. Smoking-Status Profiles Across the Three Primary Cancer Sites

The three prespecified cancer diagnoses revealed different distributions of smoking status. There were 1,089 lung cancer records classified as current smokers (488), former smokers (322) and recorded nonsmokers (279). 810 (74.4%) records were attributed to current or former smoking in combination. In total, 174 laryngeal cancer records were analyzed, with 86 classified as current smokers, 58 as former smokers and 30 as recorded nonsmokers. Current or former smoking in combination was assigned to 144 records (82.8%). Of the 585 urinary bladder cancer records, 230 were current smokers, 159 were

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former smokers and 196 were recorded as non-smokers. Current or former smoking in combination accounted for 389 records (66.5%

Table 4. Distribution of recorded smoking status among the three primary cancer diagnoses.

Cancer site	Current	Former	Nonsmoker	Total	Ever-smoking (%)
Lung (C34)	488	322	279	1,089	74.4
Larynx (C32)	86	58	30	174	82.8
Bladder (C67)	230	159	196	585	66.5

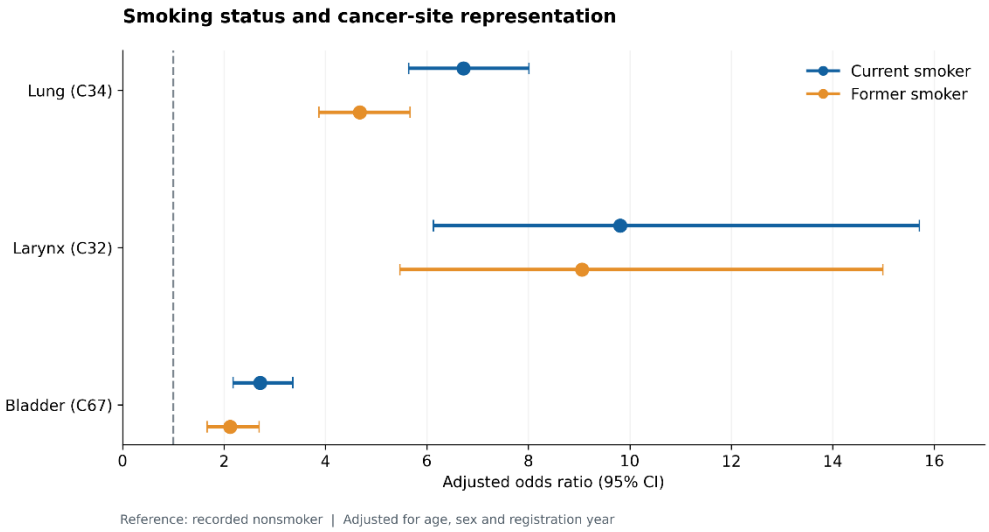


Figure 1. Adjusted Associations Between Smoking Status and Selected Cancer Sites in the Analytical Cohort (2022–2026)

The highest recorded proportion of current or former smoking was in the records of laryngeal cancer, followed by lung and urinary bladder cancer. Descriptive percents were calculated based on the reported counts of cancer sites. These descriptive differences do not establish differences in causal effects of smoking for cancer sites.

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3.5. Multivariable Associations Between Smoking Status and Cancer-Site Representation

Separate multivariable logistic regression models were used to analyze lung, laryngeal and urinary bladder cancers in comparison with all other eligible malignant neoplasms. Adjusted odds ratios for current smoking for lung cancer were 6.72 (95% CI 5.64–8.01) after adjustment for age, sex and registration year. 9.81 (95% CI 6.13–15.71) for laryngeal cancer, and 2.71 (95% CI 2.18–3.36) for urinary bladder cancer. Former smoking was also positively associated with all three outcomes. The reported adjusted odds ratios were 4.68 (95% CI 3.87–5.67) for lung cancer, 9.06 (95% CI 5.47–14.99) for laryngeal cancer, and 2.12 (95% CI 1.67–2.69) for urinary bladder cancer. All six reported confidence intervals excluded the null value of 1.0.

Table 5. Adjusted case–case associations of current and former smoking with selected cancer diagnoses.

Cancer site	Current smoking aOR (95% CI)	Former smoking aOR (95% CI)
Lung (C34)	6.72 (5.64–8.01)	4.68 (3.87–5.67)
Larynx (C32)	9.81 (6.13–15.71)	9.06 (5.47–14.99)
Bladder (C67)	2.71 (2.18–3.36)	2.12 (1.67–2.69)

aOR, adjusted odds ratio; CI, confidence interval. Reference category: recorded nonsmokers. Models were reported as adjusted for age, sex, and registration year.

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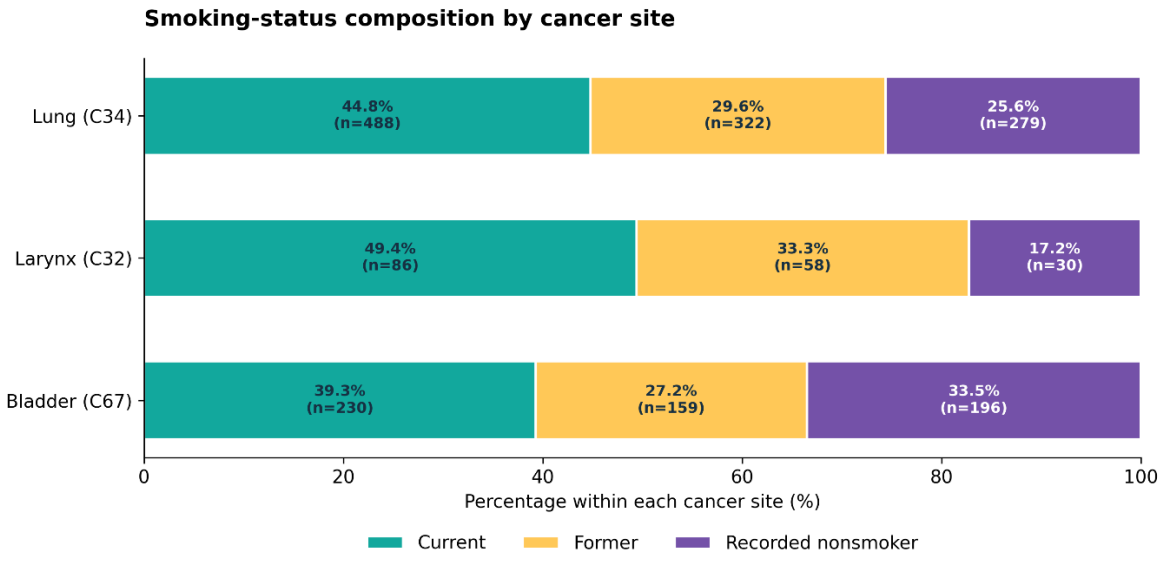


Figure 2. Distribution of Smoking Status Across Lung, Laryngeal, and Urinary Bladder Cancer Records

Reported aORs were numerically higher for current smoking than for former smoking at all three cancer sites. But there were no formal tests to compare the two smoking coefficients. Hence, the numerical differences cannot be understood as statistical differences between current and former smoking. Likewise, variations in the magnitude of the adjusted odds ratio (aOR) between cancer sites should not be interpreted as direct comparisons of the population level risk of cancer.

3.6. Multiple-Testing Correction

In the initial analysis, the Benjamini–Hochberg procedure was applied to six primary smoking-cancer-site comparisons. After correction for false discovery rate ($q < 0.001$) all six associations remained statistically significant. However, the maximum adjusted q-value for the association between urinary bladder cancer and former smoking reported in the original manuscript was 0.0004. This value needs to be verified because it is not compatible with the published aOR and 95% CI by a standard Wald approximation. Thus, the original claims of statistical significance are cautiously upheld, but the individual q-values are not reported as independently verified results.

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3.7. Secondary Ever-Smoking Analysis

In the secondary models combining current and former smokers into an ever-smoking category, all three of the primary cancer diagnoses had positive adjusted associations. In the reported study, aOR for lung cancer was 5.78 (95% CI 4.91–6.81), for laryngeal cancer was 9.52 (95% CI 6.05–14.98) and for urinary bladder cancer was 2.44 (95% CI 2.00–2.97).

Table 6. Adjusted associations between documented ever-smoking and primary cancer diagnoses.

Cancer site	aOR	95% CI
Lung (C34)	5.78	4.91–6.81
Larynx (C32)	9.52	6.05–14.98
Bladder (C67)	2.44	2.00–2.97

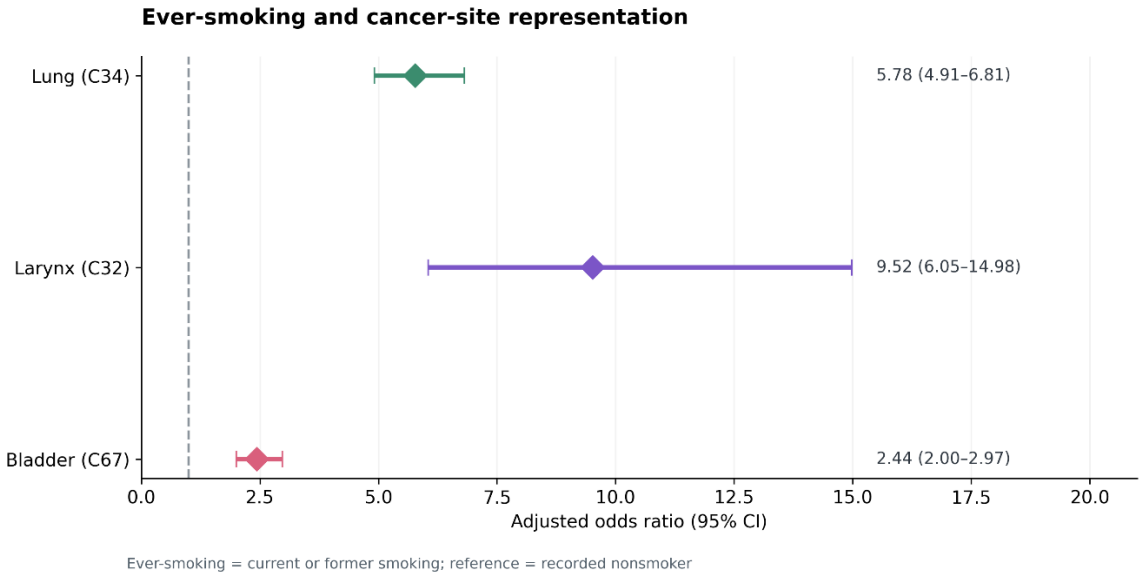


Figure 3. Adjusted Associations Between Ever Smoking and Selected Cancer Sites

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Ever smoking includes documented current and former smoking. The reference group was nonsmokers who have never smoked. Models were reported adjusted for age, sex, and year of registration. The primary analyzes confirmed the direction of the associations. However, the combined ever smoking category was not able to differentiate current from past tobacco exposure and the resulting estimates cannot be interpreted as measures of lifetime cumulative smoking exposure.

3.8. Sensitivity Analysis Excluding 2026

The 2026 data were excluded from the restricted-period sensitivity analysis owing to previously identified temporal inconsistencies so the analysis was limited to registry records from 2022 to 2025. Positive effects were still seen for lung and laryngeal cancer. Adjusted odds ratios for lung cancer were 7.58 (95% CI 6.21–9.27) among current smokers and 5.24 (95% CI 4.23–6.49) among former smokers. Corresponding estimates for laryngeal cancer were 8.64 (95 % CI 5.17-14.45) and 7.47 (95 % CI 4.31-12.95).

Table 7. Sensitivity analysis of smoking associations after exclusion of the 2026 registry dataset.

Cancer site	Current smoking aOR (95% CI)	Former smoking aOR (95% CI)
Lung (C34)	7.58 (6.21–9.27)	5.24 (4.23–6.49)
Larynx (C32)	8.64 (5.17–14.45)	7.47 (4.31–12.95)
Bladder (C67)	Not available	Not available

Restricted analytical period: 2022–2025. The source manuscript reports that the urinary bladder cancer model did not achieve stable convergence. No replacement estimate was calculated.

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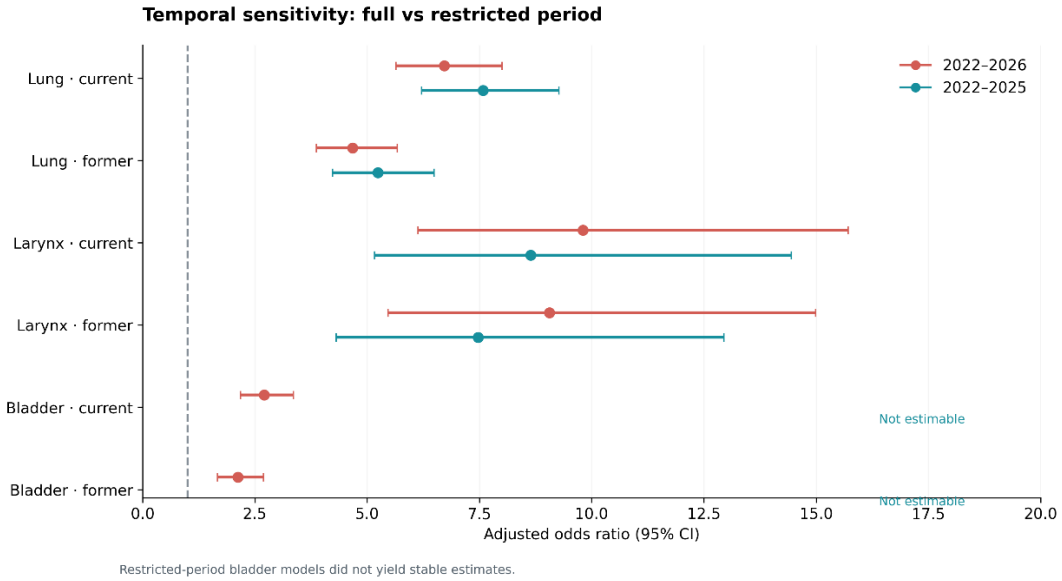


Figure 4. Comparison of Adjusted Smoking–Cancer Associations Between the Full Analytical Period (2022–2026) and the Restricted Period (2022–2025)

Lung and laryngeal cancers showed consistent directions of association in the restricted-period results, although the estimated associations were of a different magnitude to the full-period models. The corresponding model for urinary bladder cancer did not yield a stable estimate for the reported specification. Therefore, the sensitivity analysis could not assess the robustness of the main bladder cancer associations without 2026.

3.9. Smoking-Status Profiles of Selected Secondary Cancer Sites

Descriptive analyses were additionally reported for pancreatic, stomach, and breast cancer records. Current or former smoking was documented in 157 of 354 pancreatic cancer records (44.4%), 94 of 313 stomach cancer records (30.0%), and 180 of 2,770 breast cancer records (6.5%).

Table 8. Smoking-status distribution among selected secondary cancer diagnoses.

Cancer site	Current	Former	Nonsmoker	Total	Ever-smoking (%)
Pancreas (C25)	85	72	197	354	44.4

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Stomach (C16)	58	36	219	313	30.0
Breast (C50)	97	83	2,590	2,770	6.5

These secondary results were descriptive and were not accompanied by adjusted site-specific models in the source manuscript. Therefore, the observed differences should not be interpreted as comparative measures of tobacco carcinogenicity.

4. Discussion

4.1. Principal Findings

This retrospective registry-based case–case study examined the associations between documented smoking status and the relative representation of three tobacco-associated malignancies among 11,664 eligible oncology registry records collected in Iraq between 2022 and 2026. The reported findings demonstrated positive associations of both current and former smoking with lung, laryngeal, and urinary bladder cancers after adjustment for age, sex, and registration year. The largest numerical adjusted associations were observed for laryngeal cancer, followed by lung and urinary bladder cancers. Current or former smoking status was recorded in 82.8% of laryngeal cancer, 74.4% of lung cancer and 66.5% of urinary bladder cancer. The adjusted odds ratios for each of the six main smoking–cancer-site comparisons were all greater than unity. Thus, the reported multivariable analyzes showed associations in a consistent direction. Positive associations were also found across the three outcomes in secondary models combining current and former smoking. Positive associations for lung and laryngeal cancers were also maintained in the restricted-period analyzes excluding 2026, showing that the direction of these results was not solely due to the last year of registration.

However, the temporal robustness of all three outcomes was not fully assessed as the corresponding urinary bladder cancer model did not yield a stable estimate. These results are in agreement with the well-known evidence of tobacco carcinogenicity [2–5]. However, their interpretation must be adapted to the design case-by-case. The reported odds ratios are differences in cancer-site representation in the institutional registry, because only

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malignant neoplasm records were included in the analytical cohort, not population-level cancer risks.

4.2. Association Between Smoking and Lung Cancer

Lung cancer was significantly positively associated with smoking status recorded. Current smoking was associated with an adjusted odds ratio of 6.72 (95% CI 5.64–8.01) versus recorded nonsmoking, while former smoking was associated with an adjusted odds ratio of 4.68 (95% CI 3.87–5.67). These findings are biologically consistent with the well-known carcinogenic effects of tobacco smoke on the respiratory epithelial tissues. Tobacco smoke contains many carcinogens that can damage DNA, cause mutations and genomic instability, and result in malignant transformation [2–5]. Previous epidemiological studies have demonstrated that smoking is highly associated with the development of the major histologic types of lung cancer, including small cell lung cancer and squamous cell carcinoma [12]. The present results are also in agreement with the evidence that the risk of lung cancer is affected by duration, intensity and history of smoking [21]. However, the registry did not have the level of detail needed to directly study these relationships such as cumulative tobacco exposure, pack years, or timing of cessation.

The restricted-period analysis strengthened the consistency of the observed association. After excluding the 2026 dataset, the adjusted odds ratios remained elevated for current smoking (7.58; 95% CI 6.21–9.27) and former smoking (5.24; 95% CI 4.23–6.49). The numbers changed, but not the direction. This is especially true in the Iraqi context. The burden of lung cancer and importance of tobacco exposure, including cigaret and waterpipe smoking, have been highlighted in past national investigations [14,18]. Also, observational studies found association between waterpipe smoking and lung cancer [15,16]. However, the present registry did not differentiate between waterpipe tobacco use and cigaret smoking. Therefore, the observed associations are not limited to any single tobacco product. Note that the adjusted odds ratio 6.72 should not be interpreted as the risk of lung cancer among smokers in Iraqi population is 6.72 times higher. This is an important point. instead it is the adjusted relative odds of a lung cancer diagnosis relative to any other

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registered malignancy in records classified as current smokers versus recorded nonsmokers.

4.3. Association Between Smoking and Laryngeal Cancer

The highest numerical smoking-related associations among the three major cancer end-points were for laryngeal cancer. Adjusted odds ratios were 9.81 (95% CI 6.13-15.71) for current smoking and 9.06 (95% CI 5.47-14.99) for former smoking. In addition, 144 of 174 laryngeal cancer records (82.8%) were current or former smokers, which was the highest proportion among the three selected diagnoses. Such observations are in line with the well-known link between tobacco smoking and laryngeal carcinogenesis. The laryngeal epithelium is directly exposed to inhaled tobacco smoke, which contains carcinogenic compounds that can cause cellular injury and malignant transformation [2,22]. Previous systematic reviews and meta-analyses have shown significant associations between smoking and laryngeal cancer and the magnitude of the risk depends on the duration and intensity of exposure [11].

However, there are a number of limitations to the interpretation of the present findings. The laryngeal cancer subgroup was initially comprised of only 174 records, which was much smaller than the lung cancer subgroup. This smaller sample was associated with wider confidence intervals and lower precision. Second, the relatively high adjusted odds ratios do not indicate that tobacco smoking has a more pronounced causal effect on laryngeal cancer than on lung cancer. Such comparisons would need to be formally addressed by statistical methods and an appropriate epidemiologic design. Third, alcohol use is a known risk factor for laryngeal cancer that may interact with tobacco exposure, but this information was not available in the registry. Therefore, residual confounding due to alcohol consumption was not evaluated. In the restricted-period analysis, current smoking (aOR 8.64; 95% CI 5.17–14.45) and former smoking (aOR 7.47; 95% CI 4.31–12.95) were positively associated. However, the numerical estimates are subject to sampling variability and the limitations of regular registry documentation, although the results suggest a consistent direction of the association between the two analytical periods.

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4.4. Association Between Smoking and Urinary Bladder Cancer

Urinary bladder cancer was positively associated with documented current and former smoking, with reported adjusted odds ratios of 2.71 (95% CI 2.18–3.36) and 2.12 (95% CI 1.67–2.69), respectively. Current or former smoking was documented in 389 of 585 urinary bladder cancer records (66.5%). These findings are biologically plausible and consistent with established evidence identifying tobacco smoking as a major modifiable risk factor for urinary bladder cancer [2,3,10]. Unlike the direct exposure of respiratory tissues to inhaled tobacco smoke, the relationship between smoking and bladder carcinogenesis involves systemic absorption of tobacco-derived carcinogens, their metabolism, and subsequent urinary excretion. This process leads to exposure of the urinary bladder urothelial lining to carcinogenic metabolites. Previous epidemiological studies have reported an increased risk of bladder cancer among smokers with evidence of associations for both sexes and a reduction in risk after cessation of smoking [10,13,34].

Urinary tract bladder cancer, however, is multifactorial in etiology. The disease development may be associated with development of certain chronic inflammatory or infectious conditions, genetic susceptibility and occupational exposure to aromatic amines and other chemical carcinogens. In southern Iraq, historical studies have documented the relevance of schistosomiasis to bladder cancer patterns [31]. The present registry did not have the detail to evaluate the potential contribution of occupational carcinogen exposure and history of schistosomiasis. Another constraint relates to the sensitivity analysis of the restricted period. The models for bladder cancer for the full period showed positive adjusted associations; however, the model for the 2022-2025 period did not converge stably under the specification reported.

Thus, the temporal robustness of the bladder cancer associations could not be fully evaluated. This restriction does not independently invalidate the full period estimates, but does reduce the degree to which their stability can be assessed. Future analyzes should first explore the source of the convergence problem (sparse data, separation, model specification) before considering alternative estimation procedures.

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4.5. Current Versus Former Smoking: Interpretation and Limitations

The three selected cancer diagnoses showed positive adjusted associations with current and former smokers, with current smokers having numerically higher odds ratios. The present case-case findings cannot establish a protective effect of cessation or the magnitude thereof, although this pattern is consistent with established evidence of reduced risk of cancer with smoking cessation over time [4,25]. The observed differences reflect the relative representation of cancer diagnoses in the registry and not changes in the population risk of cancer. Interpretation is further limited by the lack of information on smoking intensity, duration, cumulative exposure and time since cessation. The temporal interpretation may have been further complicated by the possibility that smoking cessation happened after the onset of symptoms or the diagnosis of cancer. Also, there were no formal statistical comparisons of coefficients between current and former smoking. As such, differences in numbers should not be interpreted as statistically significant effects of cessation. The secondary ever-smoking analysis confirms the general direction of the associations, but is not able to differentiate between current and previous exposure or to establish dose–response relationships.

4.6. Sex Differences and Residual Confounding

There were large differences in reported smoking status between male and female registry records. Current or former smoking was reported in 56.3% of male records compared to only 10.9% of female records. This pattern is in line with the previously reported sex differences in tobacco use in Iraq [17]. But the smoking rates among Iraqi men and women in the institutional registry should not be taken to represent estimates of the smoking rates in Iraq. Sex is an important factor in comparisons of cancer sites because the distribution of malignancies differs between men and women. If these differences are not taken into account, the observed associations between smoking and specific cancer diagnoses may be affected. The multivariable models were therefore adjusted for the sex recorded, and the age and registration year. However, adjustment for these variables does not completely eliminate the potential for confounding. Detailed information on occupational exposures, socioeconomic characteristics, environmental tobacco smoke,

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alcohol consumption or other potentially relevant factors was not available from the registry. Male and female patients may differ in their smoking disclosure or documentation, which may also have influenced exposure misclassification. Residual confounding and differential exposure misclassification thus provide plausible explanations for some of the observed associations.

4.7. Epidemiological Interpretation of the Case–Case Design

The case–case design calls for careful interpretation because all records included in the study were malignant neoplasms. The selected cancer site was compared to other registered malignancies rather than to cancer-free controls. Therefore, the adjusted odds ratios are representative of differences in the representation of cancer sites in the institutional registry and not population incidence or etiological risk of cancer. The estimated associations were also somewhat driven by the diagnostic make-up of the registry, as the comparison groups included other potentially tobacco related cancers. This limits the generalizability of effect estimates beyond the study population and their direct comparisons across cancer sites. Nevertheless, the findings provide important institutional evidence for documented smoking patterns and reinforce the need for better oncology surveillance and future population-based studies.

4.8. Clinical Implications, Tobacco Control, and Oncology Registry Improvement

The findings highlight the need for a comprehensive assessment of tobacco exposure in the oncology services in Iraq. Standardized smoking documentation should include tobacco product type, smoking duration, intensity, cumulative exposure, and cessation history, and should differentiate current smokers, former smokers, lifelong nonsmokers, and those with unknown smoking status. Special attention should be given to waterpipe smoking that requires different exposure assessment from traditional cigaret measures. Accurate documentation can help with clinical risk assessment, smoking cessation counseling and comprehensive oncology care. Previous studies [25,26] have shown clinical benefits of smoking cessation, but the current analysis did not evaluate cessation effectiveness, treatment outcomes or survival. Improving the quality of oncology registry

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is also important to reinforce clinical research and cancer surveillance. Priority measures include standardized ICD-10 coding, electronic data validation procedures, reliable unique patient identifiers and regular quality audits. Separate recording of registration, diagnosis and treatment dates should be implemented to improve temporal accuracy. Use of consistent smoking-status definitions across institutions and reporting years would improve data comparability. Furthermore, multicenter registry collaboration could help to increase geographical coverage, improve the representation of rarer malignancies and allow for more robust epidemiological investigations. Taken together, these improvements would increase the scientific utility and reliability of oncology registry data in Iraq.

4.10. Study Strengths

Strengths of this study include the prespecified evaluation of three tobacco-associated cancer sites, separate evaluation of current and former smoking, and a large institutional dataset of 11,664 oncology registry records over a 5-year period. Some of the statistical outputs need to be verified independently. We strengthened the analytic framework by multivariable adjustment, secondary ever-smoking analyzes, and restricted-period sensitivity analyzes. Moreover, explicit interpretation of the results in the framework of the case-by-case approach allows their adequate application to institutional oncology research, as well as methodological transparency.

4.11. Study Limitations

There are several limitations that are important in the interpretation of the results.

1. This study was limited to data from a single tertiary oncology institution. Therefore, the distributions of smoking status and diagnostic composition may not accurately reflect the cancer populations in the whole of Iraq.
2. The unit of analysis was the registry record, not a confirmed unique patient. Since reliable patient-level identifiers were not available, the precision of the estimated confidence intervals might have been affected and statistical independence could not be confirmed.

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3. Smoking status was determined from routine clinical documentation and not from standardized research assessment. The extent of unmeasured smoking-status misclassification and the potential that the recorded nonsmoking category may not always represent lifelong abstinence.
4. Data regarding smoking intensity, duration, pack-years, type of tobacco product and timing of smoking cessation were not available in exact terms. This prevented differentiating between cigaret and waterpipe exposure and performing dose-response analyzes.
5. Uncertainty in the timing of smoking status documentation in relation to cancer diagnosis. Therefore, we could not determine temporal relationships between smoking cessation and cancer diagnosis.
6. Residual confounding may persist after controlling for age, gender and registration year. Occupational exposures, socioeconomic characteristics, alcohol consumption and relevant environmental or infectious exposures were not adequately captured.
7. Comparison groups were other malignancies including some tobacco-related cancers. Thus, the estimated odds ratios were conditional on the institutional cancer case-mix, and could not be interpreted as the population-level cancer risks. 8. The complete-case analytical approach may have led to selection bias if the probability of complete smoking information differed substantially by cancer site, demographic characteristics, or other factors. Complete exclusion counts were not available and it was not possible to determine the magnitude of this bias.
8. Temporal inconsistency in the 2026 dataset. Although analyzes of restricted period were available for lung and laryngeal cancers, the urinary bladder cancer model did not give a stable estimate when 2026 was excluded.
9. The original analytical outputs did not contain sufficient information to independently verify all model diagnostics, exact p-values, Benjamini-Hochberg adjusted q-values, or formal comparisons between current and former smoking coefficients.

Finally, the retrospective observational design and limitations of available registry variables do not allow for causal inferences regarding the severity of the risk of tobacco-related cancer. These limitations should be considered in combination

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when assessing the reliability, precision and generalizability of the reported associations.

5. Conclusions and Recommendations

5.1. Conclusions

The results of this retrospective registry-based case–case study led to the following conclusions:

1. The relative proportion of lung, laryngeal and urinary bladder cancers in records of oncology registries in Iraq was positively associated with documented current and ex-smoking, after adjustment for demographic and temporal factors.
2. Secondary analyzes backed up the general direction of the associations observed. However, the stability of the estimates of urinary bladder cancer in the restricted-period analysis was not shown.
3. The associations observed are indicative of differences in the representation of cancer sites within an institutional oncology registry, rather than population level cancer risks or the causal effects of smoking.
4. Incomplete smoking histories, possible repeated registrations and residual confounding limit the precision and interpretation of the findings.
5. The study emphasizes the importance of improved quality of oncology registries and standardized tobacco exposure documentation to enhance cancer surveillance and future epidemiological research in Iraq.

5.2. Recommendations

Based on the findings of the study and its methodological limitations, the following recommendations are proposed:

1. Oncology registries should standardize the assessment of tobacco exposure, including smoking status, intensity, duration, history of cessation, and type of tobacco product used, particularly cigaret and waterpipe use.

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2. There should be systematic procedures in place for data validation, accurate dates of registration, consistent diagnostic coding and reliable patient identifiers to minimize duplication of records, missing data and time inconsistencies.
3. Systematic smoking assessment and evidence-based cessation support should be incorporated into routine oncology care to enhance tobacco-related clinical management and preventive practices.
4. Multicenter and population-based studies with comprehensive risk-factor assessments and robust statistical tools are recommended to validate the observed associations, address residual confounding, and better characterize the risks of tobacco-associated cancer in Iraq.

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