

Risk of severe COVID-19 outcomes in individuals with prior cancer diagnosis – A nationwide Swedish register-based cohort study

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ABSTRACT

Background: Individuals with cancer are recognized as a high-risk group for severe COVID-19, yet population-based evidence across cancer types remains limited. This study assessed associations between previous cancer diagnoses and COVID-19 outcomes among individuals diagnosed with different cancers.

Methods: We included the entire Swedish population on 1 Jan 2020 ($n = 10,390,479$). Cancer diagnoses from 2015 to 2019 were identified from the Swedish National Cancer Register. COVID-19 outcomes (infection, hospitalization, intensive care, and death) from 1 Jan 2020–31 Dec 2021 were retrieved from national registers. Cox regression estimated hazard ratios (HR) with 95% confidence intervals (CI), controlling for age, sex, comorbidity and sociodemographic factors.

Results: We identified 234,582 individuals with cancer diagnosis, among whom 20,329 had COVID-19 infection, 5010 were hospitalized, 423 admitted to intensive care, and 1664 died. Compared with individuals without recent cancer ($N = 10,155,897$), those with cancer had a slightly lower HR of COVID-19 infection (0.97, 95% CI 0.96–0.99) but higher HRs of hospitalization (1.18, 1.14–1.21) and death (1.18, 1.13–1.25). Those with respiratory cancer had the highest HR for hospitalization (1.51, 1.36–1.68) and death (2.35, 1.98–2.79), and those with breast or prostate cancer showed lower HR for COVID-19 infection (0.95, 0.92–0.98 and 0.83, 0.80–0.86). Only prostate cancer was associated with a slightly lower, non-significant, risk of COVID-19-related death (0.92, 0.81–1.04).

Conclusions: Overall, a previous cancer diagnosis was associated with a slightly lower hazard of recorded COVID-19 infection. The risk of severe COVID-19 outcomes differed across cancer types. Our results highlight heterogeneity in COVID-19 outcomes across types. These findings support consideration of cancer type when assessing vulnerability during public health crisis.

1. Introduction

Since early in the pandemic, it has been recognized that older individuals, men, and people with pre-existing medical conditions such as hypertension, COPD, diabetes, and cancer are at a higher risk of experiencing adverse outcomes from COVID-19 infection [1–3]. Studies conducted worldwide have shown that individuals with cancer are particularly vulnerable to severe outcomes of COVID-19, including hospitalization, intensive care unit (ICU) admission, and death [4–7].

This vulnerability may be related to underlying medical conditions, treatments, and compromised immune system [8,9].

Cancer patients often experience immune system challenges related to the nature of their specific cancer type, whether it is an invasive solid tumor or a hematological malignancy - which affects immune competence in different ways. Moreover, cancer treatments such as cytotoxic chemotherapy, steroids for supportive care, immunomodulatory therapies (e.g., checkpoint inhibitors), and surgery, can further compromise immune response. As a result, cancer patients may be more susceptible

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to both inadequate and dysregulated immune reactions to SARS-CoV-2 infection [10–13]. Individuals with cancer also tend to be older, in poorer overall health, and more likely to have multiple comorbidities [14].

Studies examining COVID-19 risk among cancer patients in Sweden were mostly conducted during the early phase of the pandemic (before October 2020) and focused on major cities such as Stockholm, Uppsala, and Gothenburg [15–17]. Later Nordic studies indicate that excess risk of severe disease and mortality persisted beyond the initial phase [18, 19]. Male sex, older age, terminal cancer disease, and comorbidities were associated with higher mortality [16–20]. A greater proportion of cancer patients were found to be infected with COVID-19 compared to the general population, with the clearest excess in lymphoma [15]. Early global evidence, including meta-analyses and hospital cohorts, also reported higher mortality and severe disease in patients with cancer [20–25]. More recent studies highlight substantial variation in risk across cancer types, with the highest severity observed in hematologic malignancies and lung cancer, and lower risk in prostate cancer. Thoracic cancer registries further report greater severity among those receiving recent treatment [24,26,27].

However, despite extensive research, few nationwide population-based studies have examined COVID-19 outcomes across all cancer types over an extended period of the pandemic. In Sweden, comprehensive analyses covering the entire population and later pandemic phases remain limited. The extent to which risks differ between specific cancer sites, and whether these patterns persist across multiple waves, is still not fully understood. Using nationwide register data over an extended period of the COVID-19 pandemic, this study aimed to examine and quantify the associations between a previous cancer diagnosis, overall and by cancer type, and COVID-19 infection, hospitalization, ICU admission, or death compared with individuals without a recent cancer diagnosis.

2. Methods

2.1. Study population and follow-up

The study population was derived from the Swedish Covid-19 Investigation for Future Insights - a Population Epidemiology Approach using Register Linkage (SCIFI-PEARL) project [28], currently extended to include all individuals residing in Sweden since 2015. For this analysis, we included all individuals of any age living in Sweden on 1 January 2020, resulting in a total study population of 10,390,479. The follow-up period in each outcome analysis spanned from 1 January 2020 to the earliest of: each outcome of interest, emigration, death, or the end of study period (December 31, 2021).

The Swedish Ethical Review Authority approved the study (2020–01800, with subsequent amendments).

2.2. Exposure

Individuals with a previous cancer diagnosis were identified through the Swedish National Cancer Register [29], excluding records of benign tumors. Cancer diagnoses from 2015 to 2019 were included and classified using International Classification of Diseases, 10th revision (ICD-10) codes, as malignancies of the respiratory system (C30–C39), colorectal (C18–C21), digestive system (C15–C29), breast (C50), prostate (C61), other female specific (C50–C58), other male specific (C60–C63), melanoma (C43), and oral (C00–C14). Individuals with multiple cancer diagnoses were included in all relevant cancer type categories. The comparison group consisted of individuals with no recorded cancer diagnosis during the same period.

2.3. COVID-19 outcomes

Four outcomes were defined:

- 1) COVID-19 infection, including all individuals with a record of positive SARS-CoV-2 test identified through the national notifiable disease register (SmiNet), or with relevant ICD-10 codes (U07.1 or U07.2) as primary or secondary diagnosis for inpatient or outpatient specialist care in the National Patient Register (NPR) or as underlying or contributing cause of death in the National Cause of Death Register (NCDR).
- 2) COVID-19 hospitalization, referring to all individuals with hospitalization with primary or secondary diagnosis for COVID-19 (codes as above) in the NPR.
- 3) COVID-19 ICU admission, including all individuals who were admitted to the ICU as identified from the Swedish Intensive Care register, with a diagnosis of COVID-19 (codes as above).
- 4) COVID-19-related death, i.e. those with COVID-19 as underlying or contributing cause of death (codes as above), based on data from the National Cause of Death Register.

2.4. Potential confounders

All potential confounders were measured or assessed before 1st January 2020: age, sex (male, female), employment (employed, unemployed), marital status (married, unmarried/widowed/divorced/separated), highest education level (primary, secondary, and tertiary), country of birth (Sweden, high income countries, upper-middle income countries, lower-middle income countries, low income countries), occupation group (essential/non-essential worker; essential worker included healthcare, education, sales, postal, cleaning, and transportation) [30], living in a retirement home (yes/no), and baseline comorbidities (from 2015 to 2019), including respiratory disease, cardiovascular disease, diabetes, kidney disease, liver disease, asthma, hypertension, stroke, pneumonia, chronic obstructive pulmonary disease (COPD), and psychiatric conditions (Suppl Table 1).

2.5. Statistical analysis

Sociodemographic characteristics and pre-existing comorbidities were described for both the cancer and non-cancer group, and cancer types were described for the cancer group. Continuous variables were summarized using median and range, and categorical variables using counts and percentages. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CI) for each outcome, both for overall cancer and by specific cancer types. Three models were run for each outcome: (1) unadjusted (Model 0, Suppl Table S2), (2) age-and-sex adjusted (Model 1, Suppl Table S3), and (3) fully adjusted (Final Model, Fig. 1 and Suppl Table S4) including all covariates listed above. Age was treated as a continuous variable, while all other variables were treated as categorical. All statistical analyses were performed using STATA version 18 (StataCorp, TX, USA).

2.6. Sensitivity analysis

As a sensitivity analysis, we expanded the cancer exposure to include diagnoses from 1993 to 2019. The start year 1993 was selected to align with the adoption of ICD-10 codes in the Swedish healthcare system (Suppl Table S5).

3. Results

The total study population comprised 10,390,479 individuals, of whom 234,582 (2.3%) had at least one cancer diagnosis recorded between 2015 and 2019. Prostate cancer, breast cancer and digestive system cancer were the most common (Table 1). The cancer group was substantially older, with a median of 71 years, compared with the non-cancer group (39 years). Across several sociodemographic characteristics the groups differed, with the cancer group comprising a slightly higher proportion of men (53% and 50%) and individuals born in

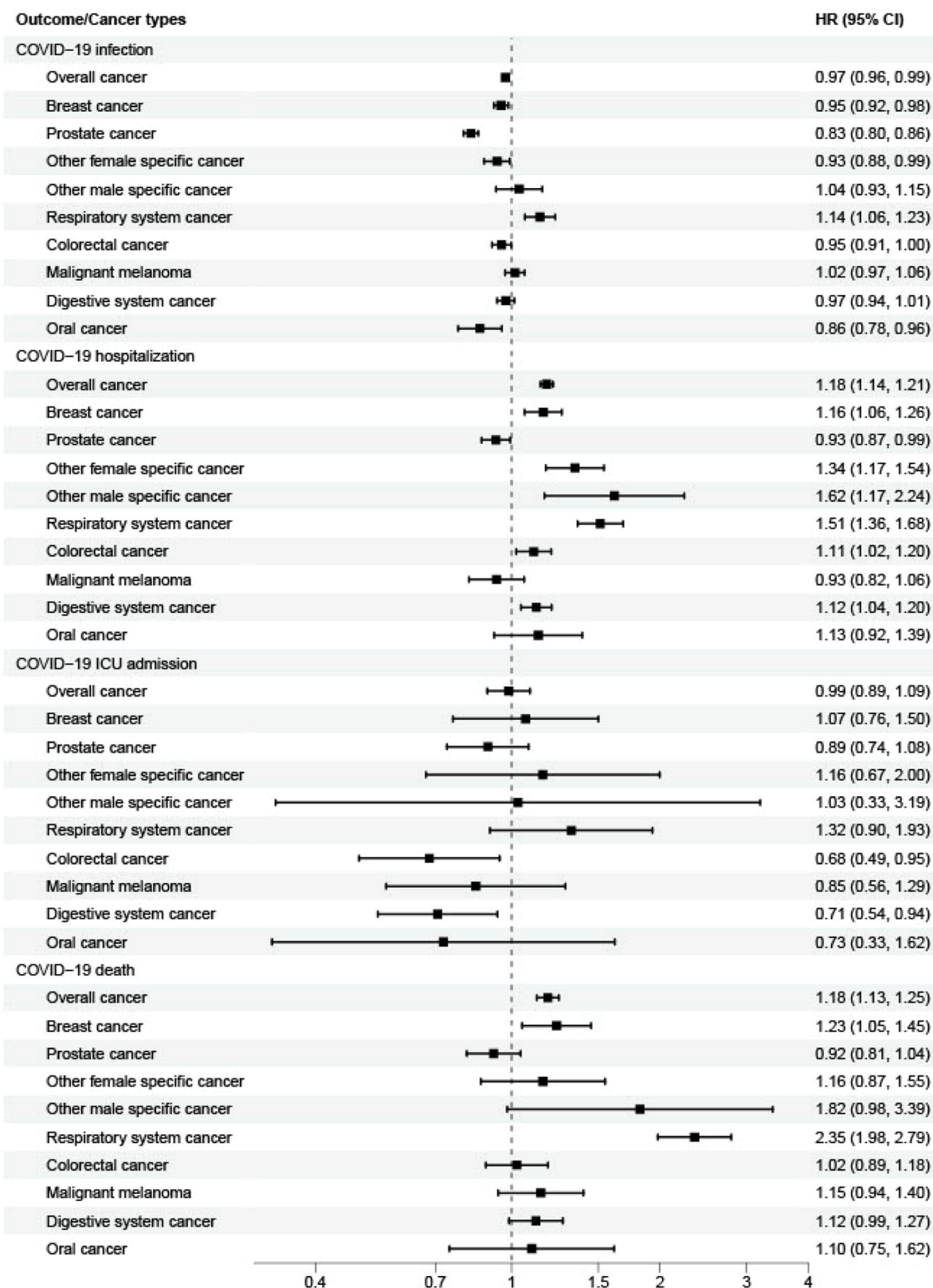


Fig. 1. Adjusted hazard ratios with 95% confidence intervals for associations between cancer type and four COVID-19 outcomes (infection, hospitalization, intensive care unit (ICU) admission and death) in Sweden 2020–2021. Model was adjusted for pre-existing comorbidities (respiratory disease, cardiovascular disease, diabetes, kidney disease, liver disease, asthma, hypertension, stroke, pneumonia, chronic obstructive pulmonary disease (COPD) and psychiatric conditions) and socio-demographic factors (age, sex, employment status, marital status, highest education, birth country, essential worker, SÄBO (Särskilt boende för äldre, an accommodation designated for the elderly population). Reference group: general Swedish population without cancer diagnosis during 2015–2019.

Table 1

Sociodemographic characteristics and pre-existing comorbidities of the study population on 1 January 2020; cancer patients with any cancer diagnosis between 01 Jan 2015 and 31 Dec 2019 and persons without cancer. All results are presented as count (percentage) except for age.

	Non-Cancer group	Cancer diagnosis group
Count	10,155,897 (97.7%)	234,582 (2.3%)
Cancer types		
Breast cancer		36,392 (15.5%)
Prostate cancer		48,522 (20.7%)
Other female specific cancer ^a		11,886 (5.1%)
Other male specific cancer ^b		2342 (1.0%)
Respiratory system cancers		9911 (4.2%)
Colorectal cancers		24,899 (10.6%)
Malignant melanoma		18,707 (8.0%)
Digestive system cancers		32,494 (13.9%)
Oral cancers		4606 (2.0%)
Sociodemographic		
Age, Median (Min - Max)	39 (0–118)	71 (0–109)
Sex		
Men	5106,288 (50%)	123,335 (53%)
Women	5049,609 (50%)	111,247 (47%)
Country of Birth		
Sweden	8109,241 (80%)	203,696 (87%)
High income	614,111 (6%)	16,652 (7.1%)
Low income	414,354 (4.1%)	2245 (1%)
Lower-middle income	301,256 (3%)	2746 (1.2%)
Upper-middle income	570,624 (5.6%)	7003 (3%)
Missing	146,311 (1.4%)	2240 (1%)
Education		
Primary	1565,801 (15%)	59,092 (25%)
Secondary	3416,846 (34%)	98,867 (42%)
Tertiary	2960,456 (29%)	73,487 (31%)
Missing	2212,794 (22%)	3136 (1.3%)
Employment		
Employed	5834,411 (57%)	99,020 (42%)
Unemployed	2461,913 (24%)	134,460 (57%)
Missing	1859,573 (18%)	1102 (0.5%)
Marital status		
Married	3283,715 (32%)	124,802 (53%)
Non-married	6853,749 (67%)	109,776 (47%)
Missing	18,433 (0.2%)	4 (0.0%)
Essential worker		
Non-essential worker	3324,298 (33%)	56,758 (24%)
Essential worker	1739,149 (17%)	26,611 (11%)
Missing	5092,450 (50%)	151,213 (64%)
Retirement home		
No	10,073,609 (99%)	229,324 (98%)
Yes	82,288 (0.8%)	5258 (2.2%)
Comorbidities		
Respiratory disease	1155,008 (11%)	50,155 (21%)
Cardiovascular disease	1146,498 (11%)	114,304 (49%)
Diabetes mellitus	314,898 (3.1%)	27,928 (12%)
Kidney disease	176,382 (1.7%)	18,836 (8%)
Liver disease	30,696 (0.3%)	3186 (1.4%)
Asthma	284,512 (2.8%)	8698 (3.7%)
Hypertension	704,374 (6.9%)	82,972 (35%)
Stroke	83,701 (0.8%)	7644 (3.3%)
Pneumonia	192,315 (1.9%)	17,490 (7.5%)
COPD ^c	81,564 (0.8%)	11,329 (4.8%)
Psychiatric conditions	347,036 (3.4%)	8943 (3.8%)

c COPD, Chronic obstructive pulmonary disease.

^a Other female specific cancer: malignant neoplasms of female genital organs (vulva, vagina, cervix uteri, corpus uteri, uterus unspecified, ovary, unspecified female genital organs, placenta (ICD-10 C51 – C58))

^b Other male specific cancer: malignant neoplasms of male genital organs (penis, prostate, testis, other and unspecified genital organs (ICD-10 C60 – C63))

Sweden (87% and 80%). Employment was lower in the cancer group (42% and 57%), whereas marriage was more common (53% and 32%). Educational levels differed, with a higher proportion of primary and secondary education among individuals with cancer.

The cancer group had a higher prevalence of prior comorbidities. The most common comorbidities were cardiovascular disease (49%), hypertension (35%) and respiratory disease (21%). In contrast, these

comorbidities were far less prevalent in the non-cancer group, with cardiovascular and respiratory diseases each reported in only 11% of individuals.

Findings from the Cox regression (Fig. 1, Suppl Table S4) showed that, after full adjustment for sociodemographic and pre-existing comorbidities (Final Model), cancer patients had only a slightly lower risk for COVID-19 infection (HR 0.97, 95% CI 0.96–0.99) compared with the non-cancer group. On the other hand, the cancer group had a higher HR for COVID-19-related hospitalization (1.18, 1.14–1.21) and death (1.18, 1.13–1.25). No association was observed for ICU admission (0.99, 0.89–1.09). In the other models (crude or less adjusted), the results were similar to those from the full model (Suppl Table S2 & S3).

When comparing COVID-19 outcomes across cancer types, several cancer groups showed slightly lower HRs for COVID-19 infection (Fig. 1, Suppl Table S4). Individuals with oral cancer had the lowest HR of COVID-19 infection (0.86, 0.78–0.96), whereas those with respiratory system cancer had a slightly elevated risk (1.14, 1.06–1.23).

Similar patterns were observed for the other COVID-19 outcomes. Individuals with prior other (non-prostate) male-specific cancer had an elevated HR for hospitalization (1.62, 1.17–2.24). Respiratory cancers were associated with the highest HR for ICU admission (1.32, 0.90–1.93) and COVID-19-related death (2.35, 1.98–2.79).

Notably, we observed decreased HRs for COVID-19 outcomes in patients with prostate cancer, with point estimates below 1.0 for all four outcomes. Several other cancer types also had lower HRs for COVID-19 infection and ICU admission, but not for hospitalization or death (Fig. 1, Suppl Table S4).

In the sensitivity analysis where cancer diagnoses during 1993–2019 were included for also identifying patients with more long-standing cancer, we identified almost twice as many patients (N = 545,307) with a previous cancer diagnosis. The demographic and socioeconomic characteristics were essentially the same as for the main analysis cohort. The analytical results were also essentially the same, with small changes in point estimates and 95% CIs (Suppl Table S5).

4. Discussion

The results of this study based on the full Swedish population provide valuable insights into the associations between various cancer diagnoses and COVID-19 outcomes during the pandemic. Individuals with cancer did not have a higher HR for COVID-19 infection overall, but had higher HRs for COVID-19-related hospitalization and death. HRs varied across cancer types, with the highest HRs for severe outcomes observed among individuals with respiratory cancers, whereas breast and prostate cancer were associated with lower HRs for infection, and prostate cancer was not associated with increased COVID-19 mortality.

In contrast to a previous Swedish study that found cancer patients had a slightly increased risk of COVID-19 infection [15], in our study, individuals with cancer overall had a slightly lower hazard of recorded COVID-19 infection. This difference may partly reflect the inclusion of predominantly more severe cases requiring medical care, which may have resulted in greater case detection among individuals with cancer. One possible explanation is that individuals with cancer may have adopted protective behaviors, such as social distancing and mask-wearing, more consistently because of greater awareness of their vulnerability. However, such behaviors were not measured in this study. It is well-established that individuals with pre-existing health conditions, including certain comorbidities and advanced age [10], have a higher risk of severe COVID-19 outcomes. Consequently, the Public Health Agency of Sweden recommended that these individuals take extra precautions [31]. Such recommendations and heightened risk awareness may therefore represent possible explanations for the slightly lower hazard of recorded COVID-19 infection observed among individuals with cancer. This interpretation is supported by previous evidence of greater adherence to distancing measures among individuals with cancer [32].

However, despite the slightly lower observed hazard of recorded COVID-19 infection, individuals with cancer had higher hazards of severe COVID-19 outcomes, i.e. hospitalization and death. This may reflect differences in underlying health status, cancer-related factors, treatment or other characteristics that could not be fully captured in the available data. These findings corroborate previous studies from other countries [3,33,34].

Among patients with different types of cancer, those with respiratory system cancers faced the highest risk of severe COVID-19 outcomes. Several mechanisms may contribute to this pattern. However, this observation aligns with the fact that SARS-CoV-2 primarily targets the respiratory system, and that many individuals with respiratory system cancer also have pulmonary or cardiovascular comorbidities [26,35].

Individuals with prostate cancer diagnosis generally had lower HR point estimates across the examined COVID-19 outcomes, and several plausible explanations exist. First, prostate cancer rarely directly affects the respiratory function [36]. Second, a possible explanation relates to differences in treatment patterns. Although not available in the study data, it has been reported that few individuals with prostate cancer are treated with chemotherapy or immunosuppressive therapies [37,38]. Third, most prostate cancer diagnoses in Sweden are made after prostate-specific antigen (PSA) testing. Selection related to PSA testing may also contribute, as men undergoing testing may differ in health status from those who did not undergo testing [39].

These observations suggest that cancer type may be relevant when assessing vulnerability to severe COVID-19 outcomes and planning strategies for future pandemics. Considering differences across cancer types may help identify groups that warrant particular attention when planning protective strategies and allocating healthcare resources.

The robustness of our findings was supported by additional analyses. The sensitivity analysis extending the cancer diagnosis period back to 1993 also yielded consistent results, with only small changes in the point estimates and confidence intervals. This supports the stability of the findings across the two cancer exposure definitions. Our findings contribute to cancer epidemiology by providing nationwide, population-based estimates of COVID-19 outcomes using consistent analysis methods across a wide range of cancer types, offering a more nuanced understanding of risk variation during the pandemic.

Strengths and Limitations

This study benefits from high-quality nationwide Swedish register data, providing comprehensive assessments of the associations between a wide range of cancer types and COVID-19 outcomes. The use of multiple linked health registers, including the National Cancer Register, supports comprehensive identification of cancer diagnoses and COVID-19 outcomes. The registers encompass rich data covering individuals' medical history and a wide range of sociodemographic information. The large sample size allowed stratified analyses by cancer type, providing a nuanced understanding of heterogeneity in COVID-19 risk across cancer groups. Sensitivity analyses further supported the stability and robustness of the associations.

The age/sex-adjusted model gave similar results were similar to those from the fully adjusted model, suggesting that additional adjustment for the measured sociodemographic factors and comorbidities did not materially change the observed associations.

However, some limitations also merit consideration. As with any observational study, a causal relationship cannot be inferred, and residual or unmeasured confounding cannot be fully ruled out. Some factors such as genetics, immune status, environmental exposures, and behavioral factors that might influence both cancer development and Covid-19 risk, were not captured in the available registers. Furthermore, the available data identified previous cancer diagnoses but did not include detailed information on cancer stage or disease status, specific treatment modalities, or timing of cancer treatment. We were therefore unable to examine whether the observed associations differed according to active disease, recent treatment, or treatment-related immunosuppression. Information on COVID-19 vaccination status was also not

incorporated into the present analyses. As vaccination became available during the study period, differences in vaccination uptake or timing may have influenced COVID-19 outcomes during 2021. In addition, biological measures of immune function were not available, preventing direct assessment of immunological mechanisms that may contribute to differences in COVID-19 severity. Future studies integrating detailed information on cancer stage, treatment modality and timing, vaccination, and markers of immune function could help clarify the mechanisms underlying the heterogeneous associations observed across cancer types.

In addition, COVID-19 case ascertainment varied over time, particularly early in the pandemic, potentially leading to under-detection of mild infections, although essentially population-wide testing was in place for the major part of the study period.

5. Conclusion

The findings of this study indicate heterogeneity in COVID-19 outcomes across cancer types. Risks varied substantially across cancer types and for different Covid-19 outcomes, with individuals with respiratory system cancers showing the highest risks of severe outcomes, while individuals with prostate cancer tended to have lower risks across the investigated outcomes. Overall, our results support consideration of cancer-type-specific risk assessment, rather than a one-size-fits-all approach. These findings suggest that treating all individuals with a previous cancer diagnosis as a homogeneous risk group may overlook important variation between cancer types. In future pandemics, consideration of cancer type may contribute to more refined identification of groups at increased risk of severe outcomes.

CRedit authorship contribution statement

Patricia Ernst: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Niranjan Ganeshkumar:** Writing – review & editing, Investigation. **Ailiana Santosa:** Writing – review & editing, Validation, Methodology, Conceptualization. **Chioma Nwaru:** Writing – review & editing, Validation, Methodology, Conceptualization. **Ola Bratt:** Writing – review & editing, Validation, Methodology. **Fredrik Nyberg:** Writing – review & editing, Validation, Resources, Methodology, Funding acquisition, Conceptualization. **Huiqi Li:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of Competing interest

F. Nyberg was an employee of AstraZeneca until 2019 and previously owned some AstraZeneca shares. F. Nyberg, A. Santosa, and H. Li report participation in a research project funded by a pharmaceutical company (regulator-mandated phase IV study; investigator-initiated study), with funds paid to the University of Gothenburg where they are employed (no personal fees) and with no relation to the work reported here. P. Ernst and C. Nwaru have nothing to disclose.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.canep.2026.103236](https://doi.org/10.1016/j.canep.2026.103236).

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