



## OPEN Emerging burden of post-cancer therapy complications on unplanned hospitalisation and costs among Australian cancer patients: a retrospective cohort study over 14 years

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Cancer treatment using systemic therapy and radiotherapy may cause post-therapy complications, resulting in increased unplanned hospitalisation. The evidence on such complications, their impact on unplanned hospitalisations, and associated costs is scant in Australia. We aimed to estimate the prevalence of post-therapy complications, evaluate their impact on unplanned hospitalisation, length of stay (LOS) and investigate the associated medical costs. A retrospective cohort study was conducted among 8,633 cancer patients (1.03 million emergency hospital admissions) in Victoria, Australia from July 2006 to June 2020, from the Australian healthcare system perspective. Multivariate generalised linear regression models were employed to estimate the adjusted association between post-therapy complications and clinical characteristics with hospital LOS and associated hospitalisation medical costs. Approximately 52% of patients were male with an average patient age of 59.9 years. Annually, post-therapy complications leading to unplanned hospitalisations increased by 7.25%, outpacing the growth in overall hospitalisation admissions, which was 5.66% for overall hospitalisation admissions. A significant proportion of patients (71%) experienced multiple complications, with the most common being anemia (26%), sepsis (15%), nausea and vomiting (14%), and neutropenia (11%). Patients undergoing combined systemic and radiotherapy exhibited higher odds of post-therapy complications (OR = 8.24, 95%CI: 7.48 to 9.08) compared with those who only received systemic therapy. Mean hospital stay among patients who experienced post-therapy complications was 2.23 days per admission (360 days per patient), an extra 1.72 days per admission [95%CI: 1.68 to 1.76; 354 days per patient, 95%CI: 336 to 371 days] longer than patients without complications (0.51 days per admission and 6.48 days per patients). Overall, per-admission medical hospitalisation costs among patients with post-therapy complications were \$8,791 higher than for patients who did not experience complications (\$11,418 vs. \$2,627 per admission, 95%CI: \$8,685 to \$8,897). Per-patient costs for unplanned hospitalisation due to post-therapy complications were significantly \$1.82 million higher among patients than those without complications (\$1.86 million vs. \$33,599 per patient, 95%CI: \$1.71 million to \$1.94 million). The cost and hospitalisation stay (in days) varied by the type of therapy and cancer type. The study results indicate that post-therapy complications in cancer patients varied by the type of cancer and increased over the study period, leading to longer unplanned hospital stays and higher hospitalisation medical costs. The results highlight the need for better-customized treatment delivery strategies to address this burden and optimise resources in cancer care.

**Keywords** Post-therapy complications, Unplanned hospitalisation, Length of stay, And cancer patients, Retrospective cohort

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Cancer continues to be a major global health challenge<sup>1</sup>, contributing to the disease burden worldwide, including in Australia where it accounts for approximately 17% of the total disease burden in 2022<sup>2</sup>. In 2023, about 165,000 Bangladeshi were diagnosed with cancer, facing a mortality rate of 195 per 100,000 individuals<sup>3</sup>. These numbers are projected to rise dramatically by 2044, with incidence and mortality rates expected to be 51% and 36%, respectively. The economic impact of cancer is also substantial, with expenditures reaching AU\$10.1 billion in 2016, representing 8.6% of total disease expenditures in Australia<sup>4</sup>. The cost associated with hospital admissions for cancer treatments, including systemic therapy and radiotherapy, significantly contributes to this financial burden.

Advances in cancer treatment over the last decade have improved patient outcomes significantly<sup>5</sup>. Around 323,000 cancer patients in Australia receive systemic therapy or radiotherapy annually, with around 160,000 patients receiving both<sup>6,7</sup>, which are essential components of cancer treatment protocols. These modalities not only enhance quality of life but also extend overall survival<sup>8</sup>. However, the effectiveness of these treatments varies based on the severity of the disease<sup>9</sup>, and is not without risks<sup>10,11</sup>. Notably, severe post-therapy complications often lead to unplanned hospitalisations, straining healthcare resources. A study highlighted that 90% of cancer patients hospitalised after emergency visits suffered from post-therapy complications, with a significant impact on hospital length of stay (LOS) and associated costs<sup>12</sup>.

Despite the benefits, systemic therapy and radiotherapy can lead to adverse effects<sup>13–15</sup> such as sepsis, neutropenia, and pneumonia<sup>14–18</sup>, necessitating hospital care<sup>14</sup>, particularly for older adults and advanced-stage patients<sup>16</sup>. These complications not only exacerbate patient suffering but also interrupt ongoing cancer treatment, potentially derailing therapeutic outcomes<sup>13,19</sup>. Additionally, these unplanned hospitalisations represent a heavy economic burden on patients, families<sup>14</sup>, and the healthcare system, with the primary treatment phase alone costing over \$6 billion annually<sup>20</sup>.

The growing prevalence of cancer and the consequential increase in therapy-related complications underscore the need for comprehensive research to inform clinical and policy decisions. To our knowledge, there is currently no clear evidence-based research at a local or national level in Australia that examines the diversity of emergency admissions and inpatient care based on the cancer type and stage. In addition, evidence on post-therapy complications is limited in Australia which could help develop an oncology care model and reflect the reality of cancer care in the Australian healthcare system. To address this evidence gap, this study aimed to estimate the incidence of post-therapy complications due to systemic therapy and radiotherapy complications, measure their impact on hospitalisations, including LOS, and estimate that associated hospitalisation costs and factors associated hospitalisation among cancer patients in Victoria, Australia.

We hypothesise that different post-therapy complications occurring from systemic therapy and radiotherapy have significant impacts on healthcare systems, resulting in longer unplanned hospital LOS and higher hospitalisation medical costs, with some potential factors contributing more significantly than others.

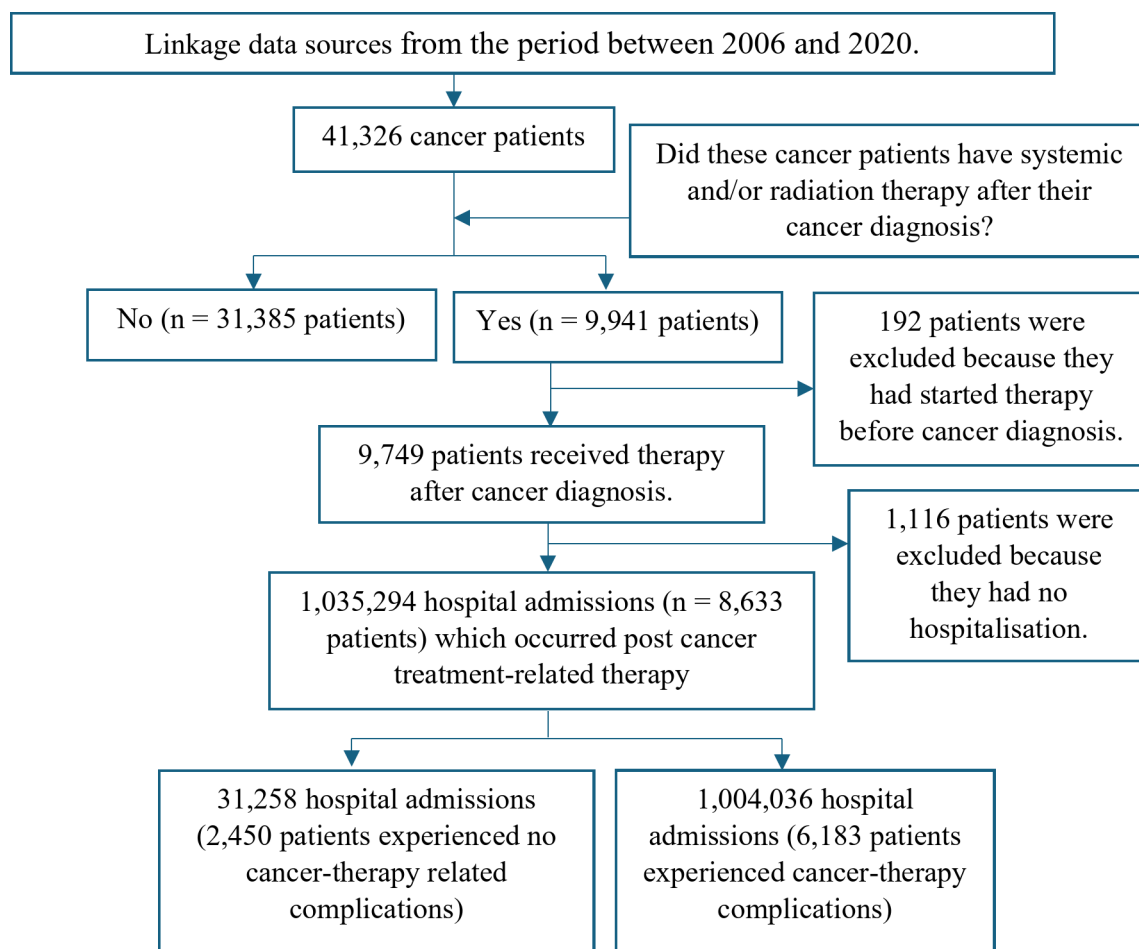
## Methods

### Study design and setting

A retrospective cohort study was conducted in Victoria, Australia, to investigate the post-therapy complications of systemic therapy and radiotherapy among cancer patients over a 14-year period (2006–2020). This study analysed administrative health data of the admitted patients to comprehensively examine treatment-related complications, and hospitalisation events, and their associated medical costs from the Australian healthcare system perspective. Patient demographics, clinical characteristics, clinical and administrative details for admitted episode of care records were extracted from linked data source (i.e., Victorian Admitted Episodes Dataset, VAED) from 2006 to 2020. The VAED provides a comprehensive dataset of the causes, effects and nature of illness, and the usage of health services in Victoria.

### Study population

The study population included patients at their first cancer diagnosis, even if they were diagnosed with multiple types of cancer. The study included patients who fulfilled the following criteria: (i) having a diagnosis of any cancer (only considered the first cancer diagnosis), (ii) have received systemic therapy and/or radiotherapy between 2006 and 2020, and (iii) have complete medical record data available, including ‘International Classification of Diseases (ICD) 10th version (ICD-10) codes or Australian Classification of Health Intervention (ACHI) codes for treatment. The records of cancer patients who could not meet these criteria were excluded from the analysis (Fig. 1). Systemic therapy and radiotherapy were defined based on available data (ACHI codes



**Fig. 1.** Distribution of study participants.

or ICD-10codes, see Appendix Table A1). In addition, we excluded patients who experienced post cancer-therapy related complications more than 5 years after the first date of therapy.

### Outcome measures

This study considered outcome measures: (i) post-therapy complication status, (ii) unplanned LOS in days due to post-therapy complications, and (iii) associated hospitalisation costs, valued in Australian dollars.

### Hospital length of stay (LOS)

Unplanned hospital LOS for post-cancer treatment-related therapy was defined as the number of days from hospital admission to discharge. Therefore, the LOS was calculated as the discharge date minus the hospital admission date for both patients with treatment-related complications and without complications. We calculated a LOS for each admission. If a patient did not experience any cancer-therapy related complications, their hospital admission was solely for post-cancer treatment-related therapy. Then after, the comparative analysis of LOS between these two groups (complication vs. non-complication) were conducted. We have detailed the hospitalisation process in Fig. 1.

### Hospitalisation costs for post-therapy complications

From the perspective of the Australian healthcare system, the medical costs associated with hospitalisation are calculated based on a unit of measurement known as 'National Weighted Activity Units (NWAUs)', which are assigned to each inpatient hospital admission<sup>21</sup>. NWAUs are used as the standard unit of measurement of hospital activity in Australia, against which the 'National Efficient Price (NEP)' is applied, and 'activity-based funding (ABF)' is provided to hospitals. To calculate the total hospitalisation medical cost for each admission, the NWAU for that admission is multiplied by the NEP, which is currently AU\$ 5,134 per national weighted activity unit for the fiscal year 2019-20, to determine the cost to the healthcare system. Admitted acute ABF costs were calculated based on the AR-DRG classification related to systemic therapy and radiotherapy-related complications. National cost weights as determined by the 'Independent Hospital Pricing for each AR-DRG code' were then applied to determine admitted acute hospital costs<sup>22</sup>. Each patient's hospitalisation medical cost

comprised the total cost of an admitted acute ABF AR-DRG presentation. Costs were reported as mean and rounded to the nearest whole Australian dollars (AU\$), using the 2020 reference year<sup>22</sup>.

**Measure of post-therapy complications** Occurrence of systemic therapy and radiotherapy-related complications, which were defined according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) codes was the main exposure variables in the study (Appendix Table A2). We considered any post-therapy complications that emerged subsequent to the first administration date of systemic therapy or radiotherapy. The prevalence of treatment-related complications was calculated based on the most reported complications. In addition, the status of post-therapy complications was categorised as follows: 1 indicates patients who reported at least one therapy (i.e., systemic therapy and/or radiotherapy) related complication during the post-therapy period and reported on subsequent hospitalisation, while 0 indicates patients who did not report any such complication.

### Covariates

Relevant covariates with a known or hypothesised association with the exposure variables or outcomes of interest (unplanned hospital LOS and hospitalisation medical costs) were identified from published literature<sup>14,19,23–31</sup>. Several covariates were included in regression models to answer each research question as outlined below. Sociodemographic factors were ascertained, including age (categorised as 18–25 years; 26–35 years; 36–45 years; 46–55 years; 56–65 years; >65 years), sex (male or female), Indigenous status, and year of cancer diagnosis.

### Statistical considerations

In the descriptive analyses, patient's characteristics were presented using frequencies, n (%) for categorical variables or mean (standard deviation, SD) for continuous data. A single imputation approach was applied to replace missing data with a single predicted value for estimating hospitalisation medical costs, such as the mean for a given case<sup>32</sup>. Continuous nature of data (i.e. unplanned hospital LOS in days and associated hospitalisation costs) was presented as mean with SD and mean differences between the two groups (with and without a diagnosis of post-therapy complications). The univariate analysis consisted of a non-parametric bootstrapping approach (with 1,000 replications) through a Generalised Linear Models (GLM) to assess the statistical significance of differences with 95% confidence intervals [CIs] in unplanned hospital LOS days [or hospitalisation medical costs]. For categorical data, the chi-square test was used to compare the post cancer therapy-related complications status (present or absent), by patients' characteristics.

For the univariate and multivariable analyses, the estimation approach was based on the nature of the outcome variables in each model. Unadjusted and adjusted associations were estimated between unplanned hospital LOS (or hospitalisation medical costs) and the main exposure variables using the GLM with a log-link, gamma distribution, and robust estimates of variance. In addition, a logistic regression model was used to determine the association between post-therapy complications and patients' characteristics. The reference group selected was the lower risk category of covariates. All statistical significance was considered as  $p$ -value < 0.05. All analyses were performed using the statistical software Stata/BE 18. This study has reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for cohort studies<sup>33</sup>. All methods were carried out in accordance with relevant national guidelines and institutional regulations.

## Results

### Characteristics of the study population

A total of 8,633 patients with cancer were included in this study (Table 1). The mean age of the patients was 59 years, and approximately 65% of them were 56 years or older, and 52% were male. Most patients (98%) were not of Aboriginal or Torres Strait background. About 92% of patients received systemic therapy and 4.33% of them received radiotherapy, whereas 4% of the participants received both systemic therapy and radiotherapy (Table 1). Between 2006 and 2020, there were 1,035,294 hospital admissions associated with these patients, out of which 1,004,036 were identified as being associated with post-therapy complications (Appendix Table A3).

### Diagnosis of post-therapy complications due to systemic therapy and radiotherapy

The most common complications were reported as follows: anemia at 26%, sepsis at 15%, nausea and vomiting at 14%, neutropenia at 11% and pneumonia at 9% (Fig. 2).

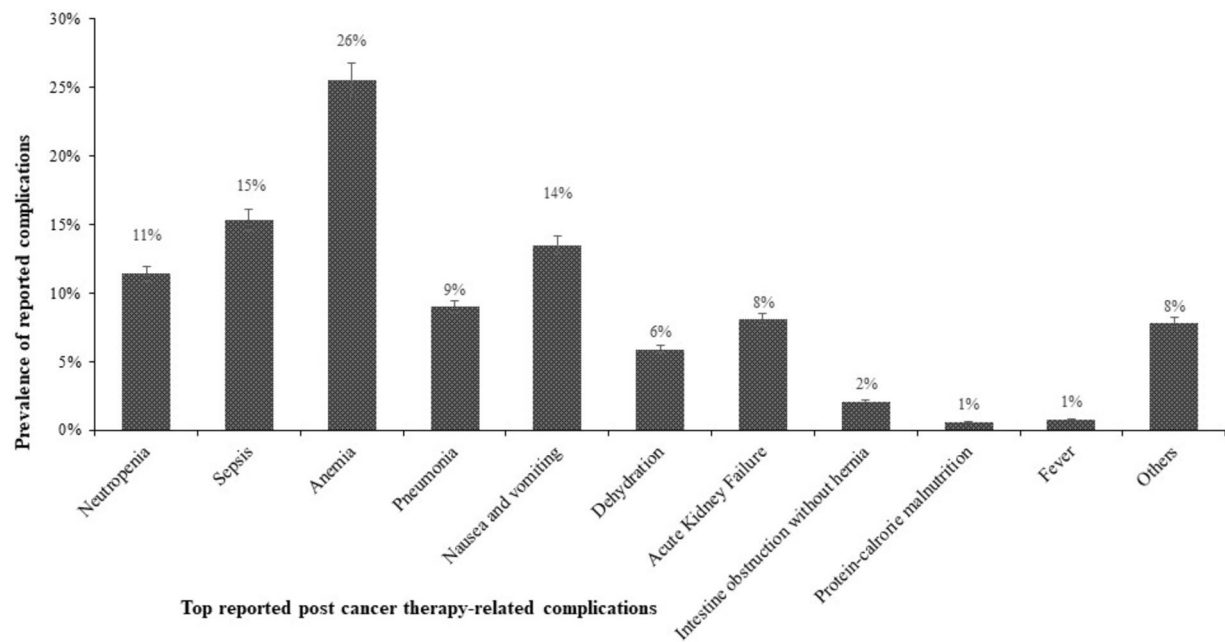
A significant majority of hospital admissions (94%;  $n = 945,846$ ) were associated with post-cancer therapy complications among patients undergoing systemic therapy (Appendix Table A3). Notably, patients who received both systemic therapy and radiotherapy exhibited an 8.24-fold increase in the odds of experiencing post-therapy-related complications (OR = 8.24, 95% CI: 7.48 to 9.08,  $p < 0.001$ ) compared with those who received systemic therapy alone. The odds of having post-therapy complications varied significantly with cancer type. Patients with acute lymphoblastic leukemia (OR = 16.99, 15.42 to 18.71), multiple myeloma (OR = 9.72, 9.00 to 10.5), melanoma (OR = 3.62, 3.20 to 4.09) showed the highest odds of complications. Increased odds were also noted for cancers of the kidney (OR = 3.54, 2.85 to 4.40), Hodgkin lymphoma (OR = 2.97, 2.75 to 3.20), esophageal cancer (OR = 2.43, 1.96 to 3.10), non-Hodgkin lymphoma (OR = 2.19, 2.06 to 2.33), and stomach cancer (OR = 2.30, 1.81 to 2.91) (Appendix Table A3).

Approximately 41% of female patients experienced at least one post-therapy complication. Compared to male patients, female patients had 16% lower odds of developing complications (OR = 0.84, 0.81 to 0.86). The odds of experiencing post-cancer therapy increased significantly with patient age ( $p < 0.001$ , Table 1). Patients aged 56 to 65 years had a 1.44-fold higher odd (OR = 1.44, 1.28 to 1.62), and or those older than 65 years had a 1.51-fold higher odd (OR = 1.99, 1.77 to 2.25) compared to were found to be 1.51 times more likely to experience post-therapy complications that the younger counterparts. Moreover, approximately 62% of post-therapy

Variables	Number of patients	
	n	%
Patient diagnosed with post-therapy complications		
No	2450	28.38
Yes	6183	71.62
Type of therapy		
Systemic therapy	7919	91.73
Radiation therapy	374	4.33
Systemic therapy and radiotherapy	340	4.00
Cancer group		
Oral	8	0.09
Bladder	499	5.78
Pancreatic cancer	2	0.002
Brain	56	0.65
Cervical cancer	15	0.17
Stomach cancer	76	0.88
Esophageal cancer	75	0.87
Gastric cardia	230	2.66
Colorectal cancer	42	0.49
Hodgkin lymphoma	336	3.89
Non-Hodgkin lymphoma	902	10.45
Multiple myeloma	794	9.20
Anal canal	454	5.26
Liver	261	3.02
Melanoma of the skin	211	2.44
Pancreas	216	2.50
Lung	790	9.15
Breast	1045	12.10
Ovary	57	0.66
Kidney	42	0.49
Thyroid	118	1.37
III-defined sites	2	0.02
Unspecified malignant neoplasm	765	8.86
Rectal cancer	98	1.14
Bone and bone marrow	200	2.32
Acute lymphoblastic leukemia	635	7.36
Others	704	8.15
Patient's characteristics		
Mean age of patients in years, mean (SD)	59.94	14.75
Patients age group, n (%)		
18–25 years	152	1.76
26–35 years	448	5.19
36–45 years	820	9.50
46–55 years	1471	17.04
56–65 years	2185	25.31
>65 years	3557	41.20
Gender		
Male	4515	52.30
Female	4118	47.70
Indigenous status		
Aboriginal or Torres Strait	585	6.78
Neither aboriginal nor Torres Strait	7908	91.60
Patient refused or unable asked	140	1.62
Year of cancer diagnosis		
2006–2009	1764	20.43
2010–2012	2116	24.51
Continued		

Variables	Number of patients	
	n	%
2013–2015	2465	28.55
2016–2018	1683	19.49
2019–2020	605	7.01
Total number of patients	8633	100

**Table 1.** Patient’s background characteristics.



**Fig. 2.** Top reported post-cancer therapy–related complications.

complications associated with this age group. There was a notable decline in the prevalence of post-therapy complications from 31% in 2006–2009 to 10% in 2016–2018.

**Distribution of hospitalisation length of stay (LOS) in days and hospitalisation medical costs**

Patients experiencing post-therapy complications had a significantly longer mean hospital stay, with 2.23 days per admission (Table 2), equating to 360 days per patient (Table 3), compared to those without complications, who had 0.51 days per admission and a total of 6.48 days per patient. This difference in LOS resulted in an additional 1.72 days per admission (95%CI: 1.68 to 1.76) and 354 days per patient (336 to 371).

Patients undergoing both systemic therapy and radiotherapy with complications also exhibited extended hospital LOS, with a mean difference of 1.38 days, resulting in 354 days per patient as opposed to 19.87 days per patients for those without complications. Male patients with complications had a longer LOS of 2.29 days compared to 0.54 days for those without, showing a significant difference of 1.72 days per admission ( $p < 0.001$ ).

Patients with post-therapy complications incurred substantially higher hospitalisation costs, averaging AU\$11,418 per admission in stark contrast to AU\$2,627 for those without complications. This difference led to an excess cost of AU\$8,791 per admission (8,685 to 8,897;  $p < 0.001$ ; Table 4).

Per-patient costs for unplanned hospitalisation due to complications were dramatically higher at \$1.82 million compared to AU\$33,599 for those without complications, with a confidence interval ranging from AU\$1.71 million to AU\$1.94 million (Table 5). Cost disparities were also notable in patients receiving systemic therapy alone or in combination with radiotherapy, with those having complications incurring AU\$11,335 and AU\$12,279 per admission, respectively, significantly higher than those without complications (AU\$2,371 and AU\$5,281 per admission, respectively). Male patients with post-therapy complications faced an average hospitalisation cost of AU\$11,729 per admission, significantly higher by AU\$2,806 than those without complications (AU\$ 8923 per admission). This trend was similar among female patients. Over time, hospitalisation costs have increased notably, with expenses for patients with complications tripling from AU\$10,642 per admission in 2006–2009 to AU\$27,930 per admission in 2019–2020 (Table 4).



Variables	No post-therapy complications		At least one post-therapy complications		Mean difference	
	Mean LOS in days per admission	SD	Mean LOS in days per admission	SD	Mean difference of hospital LOS in days (95% CI) <sup>§</sup>	p-value
Type of therapy						
Systemic therapy	0.46	2.09	2.21	6.76	1.75 (1.73 to 1.77)	<0.001
Radiation therapy	4.59	11.64	3.09	7.53	-1.50 (-2.77 to -0.23)	0.021
Systemic therapy and radiotherapy	1.02	3.18	2.40	6.68	1.38 (1.12 to 1.65)	<0.001
Cancer group						
Oral	na		7.12	24.77		
Bladder	0.36	2.31	2.30	6.88	1.94 (1.84 to 2.04)	<0.001
Pancreatic cancer	na		14.06	16.37		
Brain	0.69	2.79	2.73	5.20	2.04 (1.53 to 2.55)	<0.001
Cervical cancer	1.05	4.77	2.50	4.42	1.45 (-0.11 to 3.01)	0.124
Stomach cancer	0.88	2.87	1.91	4.52	1.03 (0.34 to 1.72)	<0.001
Esophageal cancer	0.41	0.79	1.64	5.30	1.23 (1.01 to 1.45)	<0.001
Gastric Cardia	0.59	2.37	1.74	6.19	1.15 (0.97 to 1.33)	<0.001
Colorectal cancer	0.73	4.89	1.51	4.87	-0.78 (-0.17 to 1.73)	0.061
Hodgkin lymphoma	0.28	0.95	1.16	4.08	0.88 (0.81 to 0.95)	<0.001
Non-Hodgkin lymphoma	0.56	2.08	2.87	7.10	2.31 (2.21 to 2.41)	<0.001
Multiple myeloma	0.28	1.62	2.71	8.12	2.43 (2.32 to 2.54)	<0.001
Anal canal	0.46	2.05	1.46	4.77	1.00 (0.90 to 1.10)	<0.001
Liver	0.62	3.14	1.34	4.84	0.72 (0.52 to 0.92)	<0.001
Melanoma of the skin	0.99	3.20	1.61	4.99	0.62 (0.25 to 0.99)	<0.001
Pancreas	0.50	2.81	1.32	3.36	0.82 (0.61 to 1.03)	<0.001
Lung	0.67	3.54	1.70	5.18	1.03 (0.88 to 1.79)	<0.001
Breast	0.41	1.60	1.42	3.98	1.01 (0.96 to 1.06)	<0.001
Ovary	0.22	0.43	1.76	4.89	1.54 (1.38 to 1.71)	<0.001
Kidney	0.30	0.81	1.55	5.05	1.25 (1.04 to 1.46)	0.002
Thyroid	2.20	3.32	3.60	8.85	1.40 (0.72 to 2.08)	0.001
III-defined sites	na		2.25	3.36		
Unspecified malignant neoplasm	0.44	1.78	1.61	5.22	1.17 (1.09 to 1.24)	<0.001
Rectal cancer	0.40	1.55	1.60	5.34	1.20 (0.96 to 1.44)	<0.001
Bone and bone marrow	0.85	3.03	1.93	6.58	1.08 (0.83 to 1.32)	<0.001
Acute lymphoblastic leukemia	0.37	1.93	2.67	7.67	2.30 (2.13 to 2.47)	<0.001
Others	0.89	4.21	2.06	6.28	1.17 (0.99 to 1.35)	<0.001
Patient's characteristics						
Patients age group						
18–25 years	0.30	0.81	1.89	6.61	1.59 (1.52 to 1.67)	<0.001
26–35 years	0.42	1.67	2.18	5.69	1.76 (1.65 to 1.88)	<0.001
36–45 years	0.47	2.05	2.41	7.29	1.95 (1.86 to 2.03)	<0.001
46–55 years	0.46	1.94	2.54	7.98	2.07 (2.01 to 2.13)	<0.001
56–65 years	0.44	1.96	1.95	6.43	1.52 (1.48 to 1.55)	<0.001
>65 years	0.62	3.15	2.35	6.49	1.72 (1.67 to 1.77)	<0.001
Gender						
Male	0.54	2.53	2.29	6.89	1.72 (1.69 to 1.80)	0.001
Female	0.48	2.37	2.14	6.57	1.66 (1.60 to 1.72)	<0.001
Indigenous status						
Aboriginal or Torres Strait	0.57	1.79	1.95	5.82	1.38 (1.29 to 1.47)	<0.001
Neither Aboriginal nor Torres Strait	0.51	2.50	2.24	6.80	1.73 (1.69 to 1.76)	<0.001
Patient refused or unable to asked	0.18	0.89	2.69	8.50	2.50 (2.23 to 2.78)	<0.001
Year of cancer diagnosis						
2006–2009	0.64	2.53	2.07	6.68	1.44 (1.36 to 1.51)	<0.001
Continued						

Variables	No post-therapy complications		At least one post-therapy complications		Mean difference	
	Mean LOS in days per admission	SD	Mean LOS in days per admission	SD	Mean difference of hospital LOS in days (95% CI) <sup>§</sup>	p-value
2010–2012	0.52	2.90	1.78	5.36	1.26 (1.17 to 1.35)	<0.001
2013–2015	0.51	2.15	2.23	6.78	1.72 (1.78 to 1.66)	<0.001
2016–2018	0.45	2.43	3.74	9.62	3.29 (3.19 to 3.39)	<0.001
2019–2020	0.33	1.55	5.53	10.19	5.20 (5.02 to 5.37)	<0.001
Overall	0.51	2.44	2.23	6.76	1.72 (1.68 to 1.76)	<0.001

**Table 2.** Comparison of average hospital length of stay per admission by post-therapy complications status among cancer patients. <sup>§</sup>Bootstrap confidence intervals with 1000 replications using generalised linear regression model, p-value = the probability value. *na* not available, *SD* standard deviation, *LOS* length of stay, *CI* confidence interval.

Therapy and cancer group	Per-patient mean hospital LOS (SD)			
	No post-therapy complications		Diagnosed at least post-therapy complications	
	Mean LOS in days (SD)	Mean LOS in days (SD)	Mean difference of LOS in days (95% CI) <sup>§</sup>	p-value
Type of therapy				
Systemic therapy	6.12 (10.63)	369.71 (1060.25)	363.6 (330.51 to 396.68)	<0.001
Radiation therapy	10.12 (19.55)	108.88 (219.48)	98.77 (71.46 to 126.07)	<0.001
Systemic therapy and radiotherapy	19.87 (17.96)	373.66 (783.4)	353.8 (248.76 to 458.84)	<0.001
Cancer group				
Oral	na	311.15 (483.74)	-	-
Bladder	6.07 (13.58)	323.3 (771.92)	317.24 (244.74 to 389.73)	<0.001
Pancreatic cancer	na	63.27 (87.87)	-	-
Brain	8.09 (14.63)	57.11 (70.19)	49.02 (22.56 to 75.48)	<0.001
Cervical cancer	6.1 (12.18)	262.5 (414.13)	256.4 (−29.99 to 542.79)	0.087
Stomach cancer	7.56 (6.86)	110.12 (141.72)	102.56 (74.46 to 130.66)	<0.001
Esophageal cancer	2.99 (3.18)	144.44 (196.98)	141.45 (67.62 to 215.28)	<0.001
Gastric Cardia	8.03 (11.44)	191.45 (412.42)	183.42 (122.76 to 244.09)	<0.001
Colorectal cancer	5.31 (13.61)	105.13 (115.79)	99.82 (49.68 to 149.97)	<0.001
Hodgkin lymphoma	3.42 (4.89)	340.38 (929.59)	336.95 (244.8 to 429.1)	<0.001
Non-Hodgkin lymphoma	4.85 (10.46)	448.94 (1075.73)	444.09 (381.83 to 506.36)	<0.001
Multiple myeloma	5.08 (8.95)	812.86 (1452.64)	807.78 (688.87 to 926.69)	<0.001
Anal canal	6.61 (9.45)	208.76 (494.82)	202.16 (169.89 to 234.43)	<0.001
Liver	6.71 (11.44)	127.08 (260.18)	120.37 (71.29 to 169.44)	<0.001
Melanoma of the skin	6.06 (12.39)	235.67 (688.49)	229.61 (127.77 to 331.45)	<0.001
Pancreas	8.21 (12.56)	100.62 (129.28)	92.41 (73.05 to 111.76)	<0.001
Lung	8.23 (13.94)	114.44 (212.59)	106.21 (92.86 to 119.56)	<0.001
Breast	5.93 (10.28)	99.48 (244.21)	93.55 (70.89 to 116.22)	<0.001
Ovary	1.84 (1.57)	239.66 (405.98)	237.82 (76.54 to 399.11)	<0.001
Kidney	3.7 (2.99)	257.76 (516.34)	254.06 (88.38 to 419.75)	<0.001
Thyroid	4.62 (6.91)	184.55 (467.05)	179.93 (−17.85 to 377.71)	0.076
III-defined sites	na	na	-	-
Unspecified malignant neoplasm	7.75 (9.81)	130.49 (256.45)	122.73 (102.31 to 143.15)	<0.001
Rectal cancer	10.7 (14.12)	134.23 (202.2)	123.53 (56.63 to 190.43)	<0.001
Bone and bone marrow	8.75 (12.04)	173.28 (323.06)	164.53 (125.09 to 203.96)	<0.001
Acute lymphoblastic leukemia	5.05 (7.89)	946.04 (21.37)	940.99 (760.89 to 1121.09)	<0.001
Others	7.59 (15.58)	253.49 (669.49)	245.91 (194.99 to 296.83)	<0.001
Overall	6.48 (11.52)	360.12 (1029.53)	353.65 (336.28 to 371.02)	<0.001

**Table 3.** Comparison of average hospital length of stay (in days) per patient by post-therapy complications status among cancer patients. <sup>§</sup>Bootstrap confidence intervals with 1000 replications using generalised linear regression model, p-value = the probability value. *na* not available, *SD* standard deviation, *LOS* length of stay, *CI* confidence interval.



Variables	Patients experienced no post-therapy complications		Patients experienced at least post-therapy complications		Difference	
	Mean costs per admission (AU\$)	SD	Mean costs per admission (AU\$)	SD	Mean difference of costs (95% CI) <sup>§</sup>	p-value
Type of therapy						
Systemic therapy	2,371	10,744	11,335	34,628	8964 (8881 to 9047)	<0.001
Radiation therapy	23,187	59,072	15,776	38,425	-7411 (-13543 to -1279)	0.018
Systemic therapy and radiotherapy	5,281	16,187	12,279	34,081	6998 (5873 to 8124)	<0.001
Cancer group						
Oral	na		36,577	127,192	na	
Bladder	1,840	11,876	11,803	35,197	9963 (9540 to 10386)	<0.001
Pancreatic cancer	na		72,184	84,047	na	
Brain	3,551	14,317	14,022	26,721	10,472 (7862 to 13081)	<0.001
Cervical cancer	5,371	24,513	12,701	22,338	7329 (-1549 to 16207)	0.106
Stomach cancer	4,495	14,740	9,820	23,171	5325 (1739 to 8912)	0.004
Esophageal cancer	2,194	4,098	8,428	27,124	6234 (5218 to 7250)	<0.001
Gastric Cardia	3,060	12,138	8,935	31,675	5875 (5013 to 6737)	<0.001
Colorectal cancer	3,774	24,984	7,769	24,905	3995 (938 to 7052)	0.010
Hodgkin lymphoma	1,442	4,892	5,960	20,930	4518 (4165 to 4871)	<0.001
Non-Hodgkin lymphoma	2,868	10,655	14,704	36,372	11,836 (11255 to 12417)	<0.001
Multiple myeloma	1,429	8,309	13,885	41,649	12,455 (11777 to 13134)	<0.001
Anal canal	2,397	10,523	7,480	24,439	5083 (4488 to 5679)	<0.001
Liver	3,180	16,125	6,886	24,792	3705 (2729 to 4681)	<0.001
Melanoma of the skin	5,128	16,350	8,248	25,562	3120 (1450 to 4790)	<0.001
Pancreas	2,576	14,408	6,783	17,227	4208 (3068 to 5347)	<0.001
Lung	3,463	18,130	8,743	26,493	5279 (4599 to 5960)	<0.001
Breast	2,093	8,205	7,316	20,358	5223 (4887 to 5558)	<0.001
Ovary	1,151	2,224	9,016	25,095	7865 (7175 to 8555)	<0.001
Kidney	1,535	4,162	7,940	25,746	6405 (5247 to 7564)	<0.001
Thyroid	11,296	17,060	18,470	45,438	7174 (4576 to 9771)	<0.001
III-defined sites	na		na		na	
Unspecified malignant neoplasm	2,279	9,135	8,277	26,738	5998 (5662 to 6333)	<0.001
Rectal cancer	2,053	7,945	8,234	27,361	6181 (5313 to 7049)	<0.001
Bone and bone marrow	4,380	15,523	9,914	33,712	5534 (4657 to 6411)	<0.001
Acute lymphoblastic leukemia	1,890	9,895	13,693	39,341	11,803 (11263 to 12343)	<0.001
Others	4,593	21,563	10,547	32,186	5954 (4692 to 7216)	<0.001
Patient's characteristics						
Patients age group						
18–25 years	1,541	4,164	9,711	33,903	8170 (7260 to 9081)	<0.001
26–35 years	2,180	8,548	11,206	29,177	9026 (8391 to 9662)	<0.001
36–45 years	2,405	10,533	12,371	37,386	9966 (9534 to 10397)	<0.001
46–55 years	2,394	9,964	12,999	40,886	10,605 (10236 to 10974)	<0.001
56–65 years	2,251	10,075	10,014	32,933	7763 (7506 to 8020)	<0.001
>65 years	3,211	16,168	12,022	33,245	8811 (8487 to 9135)	<0.001
Gender						
Male	2,806	12,955	11,729	35,302	8923 (8749 to 9096)	<0.001
Female	2,487	12,160	10,976	33,663	8489 (8286 to 8692)	<0.001
Indigenous status						
Aboriginal or Torres Strait	2,918	9,201	9,984	29,790	7066 (6578 to 7554)	<0.001
Neither Aboriginal nor Torres Strait	2,656	12,828	11,497	34,865	8841 (8698 to 8984)	<0.001
Patient refused or unable to ask	955	4,579	13,802	43,631	12,847 (11499 to 14195)	<0.001
Year of cancer diagnosis						
2006–2009	3,280	12,971	10,642	34,254	7363 (6981 to 7745)	<0.001
Continued						

Variables	Patients experienced no post-therapy complications		Patients experienced at least post-therapy complications		Difference	
	Mean costs per admission (AU\$)	SD	Mean costs per admission (AU\$)	SD	Mean difference of costs (95% CI) <sup>§</sup>	p-value
2010–2012	2,673	14,867	9,127	27,507	6454 (6144 to 6764)	<0.001
2013–2015	2,608	11,015	11,419	34,737	8811 (8518 to 9104)	<0.001
2016–2018	2,347	12,473	19,048	49,044	16,701 (16199 to 17204)	<0.001
2019–2020	1,733	7,942	27,930	51,807	26,197 (25478 to 26916)	<0.001
Overall	2,627	12,515	11,418	34,637	8791 (8685 to 8897)	<0.001

**Table 4.** Distribution and comparison of per admission hospitalisation medical costs (AU\$) by post-therapy complications status among cancer patients. <sup>§</sup>Bootstrap confidence intervals with 1000 replications using generalised linear regression model, p-value = the probability value. *na* not available, *SD* standard deviation, *LOS* length of stay, *CI* confidence interval.

Therapy and cancer group	Per-patient mean hospital costs in AU\$ (SD)			
	No post-therapy complications	Diagnosed at least post-therapy complications	Difference	
	Mean costs in AU\$ (SD)	Mean costs in AU\$ (SD)	Mean difference of costs in AU\$ (95% CI) <sup>§</sup>	<i>p</i> -value
Type of therapy				
Systemic therapy	31,692 (54804)	1,904,443 (5457699)	1,872,751 (1701884 to 2043617)	<0.001
Radiation therapy	52,570 (100713)	563,621 (1138623)	511,050 (369222 to 652878.5)	<0.001
Systemic therapy and radiotherapy	105,876 (92881)	1,938,516 (4037320)	1,832,640 (1289555 to 2375724)	<0.001
Cancer group				
Oral	<i>na</i>	1,597,451 (2483528)	-	
Bladder	31,446 (70040)	1,670,388 (3973787)	1,638,943 (1263786 to 2014099)	<0.001
Pancreatic cancer	<i>na</i>	324,828 (451099)	-	
Brain	42,032 (75163)	293,600 (360193)	251,567 (115655 to 387479)	<0.001
Cervical cancer	31,360 (62543)	1,396,021 (2241343)	1,364,661 (−184807 to 2914128)	0.084
Stomach cancer	38,822 (35232)	567,747 (726597)	528,924 (385774 to 672075)	<0.001
Esophageal cancer	16,129 (16125)	746,692 (1010441)	730,563 (352396 to 1108730)	<0.001
Gastric Cardia	41,754 (60749)	992,009 (2128121)	950,255 (637872 to 1262639)	<0.001
Colorectal cancer	27,268 (69874)	544,484 (600855)	517,216 (255136 to 779295)	<0.001
Hodgkin lymphoma	17,703 (25205)	1,757,482 (4783267)	1,739,779 (1264646 to 2214913)	<0.001
Non-Hodgkin lymphoma	25,142 (54219)	2,311,476 (5534690)	2,286,334 (1965442 to 2607227)	<0.001
Multiple myeloma	26,317 (46264)	4,181,140 (7464618)	4,154,824 (35439904 to 4765743)	<0.001
Anal canal	34,322 (49013)	1,080,488 (2566112)	1,046,166 (878955.2 to 1213376)	<0.001
Liver	34,441 (58711)	661,040 (1359791)	626,600 (373493 to 879707)	<0.001
Melanoma of the skin	31,870 (63635)	1,217,749 (3568219)	1,185,879 (655485 to 1716273)	<0.001
Pancreas	42,953 (64603)	519,467 (664065)	476,514 (375426 to 577603)	<0.001
Lung	42,891 (71657)	591,954 (1093989)	549,063 (480476 to 617650)	<0.001
Breast	30,742 (52955)	517,964 (1272254)	487,222 (369801 to 604643)	<0.001
Ovary	9465 (8054)	1,234,330 (2082324)	1,224,865 (394806.9 to 2054924)	<0.001
Kidney	18,984 (15365)	1,338,223 (2665533)	1,319,239 (456601 to 2181877)	<0.001
Thyroid	23,740 (35493)	947,493 (2397821)	923,752 (−91648 to 1939153)	0.075
III-defined sites	<i>na</i>	<i>na</i>	-	
Unspecified malignant neoplasm	40,276 (50704)	672,776 (1317938)	632,500 (527713 to 737287)	<0.001
Rectal cancer	54,924 (72478)	690,164 (1037722)	635,240 (291668 to 978812)	<0.001
Bone and bone marrow	44,906 (61836)	893,316 (1658943)	848,410 (646756 to 1050063)	<0.001
Acute lymphoblastic leukemia	25,949 (40547)	4,868,592 (1100037)	4,842,643 (3914453 to 5770832)	<0.001
Others	39,309 (80345)	1,306,230 (3441043)	1,266,921 (1006059 to 1527783)	<0.001
Overall	33,599 (59464)	1,855,879 (5299788)	1,822,280 (1705155 to 1939405)	<0.001

**Table 5.** Distribution and comparison of per patient hospitalisation medical costs (AU\$) by post-therapy complications status among cancer patients. <sup>§</sup>Bootstrap confidence intervals with 1000 replications using generalised linear regression model, p-value = the probability value. *na* not available, *SD* standard deviation, *LOS* length of stay, *CI* confidence interval.

## Factors associated with length of stay (LOS) in days per admission and hospitalisation medical costs

Table 6 presents the results of two different models for analysing hospitalisation LOS and the associated costs per admission. Potential variables were adjusted based on qualified variables from the unadjusted explorations (Appendix Table A4). The regression analysis revealed that patients who had complications after therapy had a significantly longer hospital LOS ( $\beta = 1.30, 1.25$  to  $1.35$ ) and higher medical costs ( $\beta = 1.29, 1.26$  to  $1.33$ ). However, the results varied depending on the patient's characteristics and of the specific cancer diagnosis. For instance, patients aged 65 and above had a significantly longer hospital LOS per admission ( $\beta = 0.37, 0.33$  to  $0.40$ ) and higher hospitalisation medical costs ( $\beta = 0.36, 0.34$  to  $0.39$ ) compared with younger patients aged 18 to 25 years.

## Discussion

This study provides a comprehensive analysis of post-therapy complications among cancer patients, highlighting significant increases in hospitalisation length of stay (LOS) and medical costs. Notably, 72% of patients developed complications post-systemic and/or radiation therapy, predominantly manifesting as anemia, sepsis, nausea and vomiting, and neutropenia. The types of cancer most frequently associated with these complications were acute lymphoblastic leukemia, multiple myeloma, melanoma, kidney, Hodgkin lymphoma, esophageal cancer, non-Hodgkin lymphoma, and stomach among the participants. Patients experiencing post-therapy complications had an average increase in hospital LOS by 1.72 additional days, reflecting unplanned extensions beyond their initial treatment plans. These patients also faced significantly higher hospitalisation costs, with additional expenses averaging AU\$8,791 compared to those without complications.

Our analysis revealed that patients who underwent both systemic therapy and radiotherapy had an 8.24 times higher chance of experiencing post-therapy complications compared with those who only received systemic therapy. These findings are consistent with previous studies that also showed a correlation between receiving cancer therapies and post-therapy complications<sup>34–37</sup>. This increased risk might be attributable to the cumulative toxic effects of multiple therapies on patient health, as suggested in other studies<sup>34–37</sup>. This comparative insight is crucial for healthcare providers in strategising care to mitigate these risks, particularly in treatments involving multiple therapy modalities<sup>38</sup>.

This study highlighted the significance of post-therapy and revealed that patients who experienced complications, such as prolonged following therapy, had significantly longer unplanned hospital stays and compared with those who did not experience any complications. This finding is consistent with published data that indicates patients with post-therapeutic complications have longer hospital stays and higher treatment costs<sup>12,14,18,19,39</sup>. These results reinforce the critical need for effective monitoring and management of patients during and after cancer treatment to mitigate the risks associated with post-therapy complications. Such complications not only impose a substantial economic burden on patients and the healthcare system but also potentially delay ongoing cancer treatment<sup>40</sup>, adversely affecting patient outcomes. It is imperative that healthcare providers implement robust strategies for early identification and management of potential complications. Assessing factors such as performance status, organ function, comorbidity, and patient frailty can guide clinicians in tailoring treatment plans that minimise the risk of adverse effects<sup>18,34,41</sup>. Moreover, proper communication with patients about the potential for hospitalisations and other treatment-related adverse events is essential. Providing detailed information helps patients make informed decisions about their treatment options, balancing the benefits against the risks. This approach can significantly improve the quality of care, reduce the impact on healthcare resources, and enhance the overall quality of life for patients and their caregivers.

Treatment-related complications, including anemia, sepsis, and neutropenia that occur after systemic and radiotherapy, have been found to be associated with longer hospitalisation stay per admission. Cancer patients undergoing active treatment are often immunocompromised, which makes them more susceptible to sepsis leading to mortality. Previous studies show that cancer patients have a higher incidence of severe sepsis, which results in increased hospitalisation and mortality<sup>14,18</sup>. For example, cancer patients with severe sepsis stayed in hospital for almost three times as long as cancer patients without severe sepsis<sup>14,18</sup>. Anemia is also prevalent among cancer patients and can lead to longer hospitalisation in the oncology unit<sup>31,42</sup>. These occurrences can adversely impact overall survivorship, quality of life, and increase length of hospital stay<sup>43</sup>. Neutropenia is another severe complication of chemotherapy among cancer patients. Patients who experience neutropenia mostly have longer hospitalisation periods<sup>44</sup>. Another study found that neutropenia is a life-threatening toxic effect of chemotherapy that can be responsible for longer hospital LOS<sup>39</sup>. However, the toxicity profile of each cancer treatment modality varies according to dosages, treatment duration, and patient characteristics. These findings highlight the need to manage these complications effectively with supportive measures at home or by increasing outpatient monitoring. Furthermore, it underlines the importance of preventing hospitalisation due to therapy-related complications to optimise patient outcomes. While the reasons for prolonged LOS without complications were not directly examined in this study. However, previous studies indicated that factors including pain, infection and dyspnea can influence hospitalisation<sup>14,24,31,41,45</sup>.

## Study strengths and limitations

The main strength of this study was the use of a large cohort of cancer patients from Victoria, Australia. Data was extracted from administrative linked data sources, including the Victorian Admitted Episodes Dataset, for the period between 2006 and 2020. These administrative datasets are based on hospital data compiled by individual public and private hospitals through two hospital networks in Victoria, Australia. This study conducted a 14-year longitudinal analysis among medically diagnosed cancer patients, allowing the identification of trends and changes in the burden of post-therapy complications over time. By capturing associations, this analysis aids in understanding how therapy practices and patient health outcomes have evolved. It is important to note that

Variables	Adjusted model for hospitalisation length of stay (LOS)		Adjusted model for hospitalisation costs (AU\$)	
	$\beta$ -coefficient (95% CI)	p-value	$\beta$ -coefficient (95% CI)	p-value
Type of therapy				
Systemic therapy (= ref)				
Radiation therapy	0.58 (0.50 to 0.66)	<0.001	0.57 (0.51 to 0.65)	<0.001
Systemic therapy and radiotherapy	0.15 (0.12 to 0.18)	<0.001	0.14 (0.12 to 0.18)	<0.001
Patient experience of complications (ref = no)	1.30 (1.25 to 1.35)	<0.001	1.29 (1.26 to 1.33)	<0.001
Cancer group (ref = other type of cancer)				
Bladder	-0.78 (-1.09 to -0.47)	<0.001	-0.76 (-1.14 to -0.44)	<0.001
Pancreatic cancer	0.29 (-0.47 to 1.06)	0.454	0.24 (-1.76 to 2.36)	0.778
Brain	-0.65 (-1.03 to -0.27)	0.001	-0.65 (-1.05 to -0.25)	0.001
Cervical cancer	-0.78 (-1.16 to -0.40)	<0.001	-0.80 (-1.21 to -0.39)	<0.001
Stomach cancer	-0.89 (-1.21 to -0.58)	<0.001	-0.90 (-1.26 to -0.54)	<0.001
Esophageal cancer	-1.09 (-1.42 to -0.77)	<0.001	-1.10 (-1.46 to -0.74)	<0.001
Gastric cardia	-1.01 (-1.32 to -0.69)	<0.001	-1.01 (-1.36 to -0.66)	<0.001
Colorectal cancer	-1.13 (-1.48 to -0.77)	<0.001	-1.13 (-1.50 to -0.75)	<0.001
Hodgkin lymphoma	-1.29 (-1.60 to -0.98)	<0.001	-1.29 (-1.64 to -0.94)	<0.001
Non-Hodgkin lymphoma	-0.40 (-0.71 to -0.09)	0.011	-0.41 (-0.76 to -0.06)	0.022
Multiple myeloma	-0.53 (-0.84 to -0.22)	0.001	-0.53 (-0.88 to -0.18)	0.003
Anal canal	-1.12 (-1.43 to -0.81)	<0.001	-1.13 (-1.48 to -0.78)	<0.001
Liver	-1.19 (-1.50 to -0.88)	<0.001	-1.20 (-1.55 to -0.85)	<0.001
Melanoma of the skin	-1.04 (-1.35 to -0.73)	<0.001	-1.04 (-1.39 to -0.69)	<0.001
Pancreas	-1.29 (-1.60 to -0.97)	<0.001	-1.29 (-1.64 to -0.94)	<0.001
Lung	-1.04 (-1.35 to -0.73)	<0.001	-1.05 (-1.40 to -0.70)	<0.001
Breast	-1.13 (-1.44 to -0.82)	<0.001	-1.14 (-1.49 to -0.79)	<0.001
Ovary	-0.89 (-1.21 to -0.57)	<0.001	-0.89 (-1.25 to -0.53)	<0.001
Kidney	-1.31 (-1.63 to -0.99)	<0.001	-1.31 (-1.67 to -0.96)	<0.001
Thyroid	-0.42 (-0.75 to -0.09)	0.013	-0.42 (-0.80 to -0.05)	0.028
III-defined sites	-0.61 (-0.93 to -0.29)	<0.001	-0.62 (-1.00 to -0.24)	0.001
Unspecified malignant neoplasm	-1.00 (-1.31 to -0.69)	<0.001	-1.00 (-1.35 to -0.65)	<0.001
Rectal cancer	-1.05 (-1.38 to -0.73)	<0.001	-1.06 (-1.42 to -0.70)	<0.001
Bone and bone marrow	-0.86 (-1.17 to -0.54)	<0.001	-0.86 (-1.22 to -0.51)	<0.001
Acute lymphoblastic leukemia	-0.47 (-0.78 to -0.16)	0.003	-0.48 (-0.83 to -0.13)	0.007
Patient's characteristics				
Patients age group (ref = 18–25 years)				
26–35 years	0.21 (0.17 to 0.25)	<0.001	0.20 (0.17 to 0.24)	<0.001
36–45 years	0.29 (0.26 to 0.33)	<0.001	0.26 (0.26 to 0.33)	<0.001
46–55 years	0.34 (0.30 to 0.37)	<0.001	0.33 (0.30 to 0.37)	<0.001
56–65 years	0.12 (0.08 to 0.15)	<0.001	0.12 (0.09 to 0.15)	<0.001
>65 years	0.37 (0.33 to 0.40)	<0.001	0.36 (0.34 to 0.40)	<0.001
Gender				
Female (ref = male)	0.001 (-0.02 to 0.01)	0.539	0.003 (-0.02 to 0.01)	0.565
Indigenous status				
Aboriginal or Torres Strait (= ref)	reference		reference	
Neither Aboriginal nor Torres Strait	0.11 (0.08 to 0.13)	<0.001	0.09 (0.08 to 0.14)	<0.001
Patient refused or unable asked	0.17 (0.08 to 0.26)	<0.001	0.16 (0.09 to 0.25)	<0.001
Year of diagnosis (ref = 2006–2009)				
2010–2012	-0.09 (-0.10 to -0.07)	<0.001	-0.08 (-0.10 to -0.07)	<0.001
2013–2015	0.12 (0.10 to 0.14)	<0.001	0.11 (0.10 to 0.14)	<0.001
2016–2018	0.53 (0.51 to 0.55)	<0.001	0.52 (0.50 to 0.55)	<0.001
2019–2020	0.78 (0.75 to 0.81)	<0.001	0.75 (0.72 to 0.82)	<0.001

**Table 6.** Association of post-therapy complications with length of stay (LOS) and hospitalisation medical costs on unplanned hospitalisation from an Australian healthcare system perspective. A generalised linear regression model was used to estimate the regression coefficient. ref = reference group.

while this study identifies associations, it does not establish causality between treatment practices and patient outcomes. This study adopted a comprehensive approach by investigating complications from several aspects, including clinical characteristics, hospitalisation, and healthcare system costs from the Australian healthcare system perspective. This multifaceted exploration improves the understanding of the complexities surrounding post-therapy complications.

This study has some limitations such as data was collected from only two hospital networks in metropolitan Victoria. However, it is important to note that the results may not be fully representative of the entire state and might be biased towards a particular population. To ensure accurate and reliable results, a more comprehensive study would be required, which would involve collecting data from a state-wide cancer registry and including data from all state hospitals. By doing so, we can ensure that our findings are based on extensive and diverse data, and that we can make confident and reliable conclusions. The study was conducted from the Australian healthcare system perspective and assessed the direct medical costs of unplanned hospitalisation due to post-therapy complications in cancer patients. However, patients who experience post-therapy complications may also incur greater indirect costs, such as psychological stress, reduced productivity in daily activities, and increased time off from work and additional care burdens on their family members. In order to perform rigorous explorations for the economic analysis of post-therapy complications, healthcare utilisation data, including Medicare claims through the Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Schedule (PBS) claims data, is required. Unfortunately, we were unable to capture all aspects of healthcare use and assess the long-term economic impact of these cancer patients due to a lack of data access and funding. The substantial group size imbalance, with the majority of patients receiving systemic therapy only, may have impacted the precision of estimates, and this limitation should be considered when interpreting the findings. We acknowledge that the stages of cancer among patients may significantly influence the choice of treatment modalities and subsequent risk of complications, which may not be fully captured by the analysis of this specific subgroup within our study. Moreover, the study considered post-therapy complications according to the study design and research questions, while cancer patients may also be diagnosed with non-cancer chronic comorbid conditions or diseases, which may contribute to a higher disease burden and hospitalisation events. However, we acknowledge that the inclusion of performance status, comorbidity indices, frailty, and organ function could enrich the analysis, providing a more nuanced understanding of risk factors associated with post-therapy complications and their economic impact. The absence of these variables in our analysis is indeed a limitation, as it could affect the depth of risk stratification and potentially influence the interpretation of our findings. Therefore, future research is required using a similar study design that captures all relevant aspects of healthcare use in an economic assessment to provide robust evidence for policymakers and stakeholders. In addition, we recommend that future clinical studies with larger subsets of patients receiving combined therapies be conducted to validate and expand upon these findings.

### Implications and key recommendations

The research findings have several policy implications for the Australian healthcare system, addressing various aspects of cancer care and post-therapy complications. This study proposes some key recommendations:

- (1) Develop risk stratification models to accurately identify patients at a higher risk of post-therapy complications. This should focus on factors such as age, gender, health conditions, and specific cancer types. Implement targeted interventions for these high-risk groups to ensure early detection, monitoring, and effective management of complications.
- (2) Given the observed higher risk of complications among patients receiving both systemic therapy and radiotherapy—despite the small size of this subgroup—, it is prudent to advocate, for a more cautious approach. We recommend the implication of tailored treatment protocols for these patients, which include enhanced monitoring and coordinated care. These protocols should focus on active surveillance, early detection, and prompt management of potential complications. This approach may help mitigate the risks associated with combined treatment modalities and improve patient outcomes.
- (3) Establish strategies for continuous monitoring and enhancement of the quality of cancer care. Consistently assess the occurrence of post-therapy complications, evaluate the impact on hospitalisation, and adjust healthcare practices accordingly. This could involve regular assessments and incorporating lessons learned into clinical guidelines.

### Conclusion

This study provides evidence of the economic impact of post-therapy complications and associated unplanned hospitalisation on cancer patients and the healthcare system. The research offers a compilation of the most reported complications, highlighting the prevalence of anemia, sepsis, nausea and vomiting, neutropenia, pneumonia, and acute kidney failure. This information is essential for adopting or introducing interventions that may mitigate and effectively manage these specific complications in cancer care. The study also revealed that post-therapy complications significantly increase unplanned hospitalisation LOS and associated hospitalisation medical costs. This underscores the importance of effective management of post-therapy complications to optimise the use of healthcare resources.

### Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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### Author contributions

All authors critically reviewed earlier versions of the draft and approved the final manuscript. RAM and OW conceived the paper. RAM, OW, KA, JG, MS, PKD, and MPM developed the analysis plan. RAM did the analysis and wrote the initial draft. RAM, MS, PKD, MPM, KA, JG, AMNR, MGH, SKM, KNK, SHC and OW contributed to the write up and editing.

### Declarations

### Competing interests

The authors declare no competing interests.

### Ethical approval

To ensure compliance with ethical standards and participant confidentiality, we obtained ethical approval from the ‘Royal Melbourne Hospital Human Research Ethics Committee’ (approval # 202201/1). The data were de-identified to maintain anonymity prior to analysis. Due to the retrospective nature of the study, Royal Melbourne Hospital Human Research Ethics Committee waived the need of obtaining informed consent. All methods were performed in accordance with the relevant guidelines and regulations.

### Additional information

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-89247-y>.

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