

TREATMENT-RELATED COMPLICATIONS IN CANCER: A SYSTEMATIC REVIEW OF OCCURRENCE, SEVERITY, MANAGEMENT AND QUALITY OF LIFE IMPACT

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ABSTRACT

Treatment-related complications pose a formidable challenge for the patient with cancer; regardless of what cancer or modality of treatment, dramatically impacting clinical outcomes, psychology, and overall quality of life. This full analysis combines findings from numerous studies of 598,751 cancer patients to assess the prevalence, magnitude, management strategies, and impact on quality of life of such complications. The results affirm that 49% of cancer patients endure financial stresses, tangible and intangible; for long-term survivors, the highest frequency complications seen are diminished physical performance (36.3%), fatigue (35.1%), sexual malfunction (34.7%), sleep disturbances (34.1%), and arthralgia (33.8%). Modality-specific complications differ greatly based on the modality being used: surgical patients have immediate post-operative perils with late onset dysfunctions, serious complications occurring for 33% of survivors of esophagectomy; radiation and hormone therapies produce mainly urinary, gastrointestinal, and sexual concerns; while modality-based approaches using precision medicine have a lower incidence of mortality due to treatment (1.5% vs. 2.3%). Psychological complications are prevalent, emotionally- and cognition-related functions being dramatically below population means, especially for female patients. The uninsured have twice the risk for financial stresses than do the insured, first periods of treatment showing greatest financial toxicity corresponding with medication non-compliance, weaker health-related quality of life (HRQOL). Efficient management strategies are multidisciplinary support care models, which enhance end-of-life findings, and modality-based approaches using precision medicine, which reduce mortality rates while retaining response rates. Despite available measures, persistent gaps persist between quality of life needs, especially between emotionally- and cognition-related functions, due to extensive surgical complications inducing permanent impairments for many quality of life measurements even 5 years post-treatment. These results signal a need for comprehensive planning for survivors, more integration of psychosocial support, and targeted interventions for managing a high volume of unmet needs for cancer care.

Keywords: Health-related quality of life, Cancer complications, Occurrence, Treatment, Severity, Survivors.

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INTRODUCTION

Cancer represents one of the most formidable global health challenges of the twenty-first century, contributing significantly to the disease burden worldwide. According to GLOBOCAN, there are about 10 million deaths from cancer globally, making it the leading cause of mortality in every country [1]. Incidence rates for cancer have been increasing, and future projections suggest that this trend will continue. In Australia, Cancer is responsible for 17% of all diseases and had expenditures of Australian dollar (AUD) 10.1 billion in 2016, or 8.6% of total expenditure on diseases in Australia. In France, the number of new cancer cases rose by 20% over a 10-year period, from 320,000 new cases in 2005 to 400,000 new cases projected in 2017 [17].

There are several modalities of management available for cancer, including surgical treatment, radiotherapy, and systemic therapies such as chemotherapy and targeted agents. Innovations in cancer treatments during the past 10 years have increased the number of cancer survivors over 10 years of age from about 50% (in 2000) to nearly 50% now.

Despite advancements in cancer treatment, complications associated with the therapies remain a major issue for affected individuals and the healthcare system. The oncological therapeutic strategy essentially relies on local or loco-regional treatment through surgical removal and radiotherapy, along with systemic administration of chemotherapy or targeted therapy, each carrying distinct adverse effect profiles [8].

The burden of treatment-related complications varies considerably according to cancer type and treatment modality. Patients receiving combined systemic therapy and radiotherapy exhibit an 24-times

increase in the odds of experiencing post-therapy complications (odds ratio [OR]: 8.24, 95% confidence interval [CI]: 7.48–9.08) compared to those receiving systemic therapy alone [2].

The impact of treatment-related complications extends beyond immediate clinical outcomes to encompass substantial healthcare utilization and economic burden. These unplanned hospitalizations represent a heavy economic burden on patients, families, and healthcare systems, with the primary treatment phase alone costing over AU\$6 billion annually [10].

OCCURRENCE AND SEVERITY OF TREATMENT-RELATED COMPLICATIONS

General occurrence across cancer types

In a systematic review of 598,751 cancer patients, 49% had reported material or psychological financial burdens as a result of treatment (95% CI: 41–56%) [2].

In long-term survivors (mean 4 years following diagnosis), the most commonly reported moderate or larger burdens were:

- Loss of physical performance: 36.3%
- Fatigue: 35.1%
- Sexual issues: 34.7%
- Sleep issues: 34.1%
- Arthralgia: 33.8%
- Anxiety: 28.0%
- Neuropathy: 25.6%
- Memory issues: 23.0%
- Concentration issues: 21.9% [5].

Complications by treatment modality surgery (e.g., prostatectomy, esophagectomy)

People undergoing prostate cancer treatment often face immediate post-operative along with long-term challenges such as urinary and sexual dysfunction [12]. Major post-operative complications after esophagectomy occurred in 33% of long-term survivors; associated with increased dyspnea (mean difference [MD]: 15), fatigue (MD: 13), and eating restrictions (MD: 10) [13].

Radiation therapy

Urinary, gastrointestinal, and sexual complications prevalent in prostate cancer; improved techniques have reduced incidence but not eliminated risk [12].

Hormone therapy

Urinary, gastrointestinal, and sexual complications are prevalent within prostate cancer; improved methods have reduced cases, yet never eliminated risks [12].

Targeted/precision therapies

Patients who received personalized treatment strategies had fewer treatment-related deaths compared to those on non-personalized approaches (1.5% vs. 2.3%, $p < 0.001$) [10].

Financial complications

Non-insured patients had twice the chances of experiencing financial burdens as compared to insured patients (pooled OR: 2.09; 95% CI: 1.33–3.30) [2].

Financial toxicity was worst early in treatment and was correlated with poorer Health related quality of life (HRQoL) and greater medication non-adherence (non-adherence pooled OR: 1.70; 95% CI: 1.13–2.56) [12].

Psychological complications

Emotional and cognitive functions were worse than population norms among survivors, especially women ($p < 0.01$) [17,22]. And psychological distress – including anxiety, depression, existential and spiritual distress – is common in advanced cancer patients [6].

STRATEGIES FOR MANAGING TREATMENT-RELATED COMPLICATIONS

Multidisciplinary supportive care

Integrated care service (ICS) model involving oncology, palliative care, social work, psychiatry, nutrition, and rehabilitation increased hospice discharges (23% vs. 7%; $p < 0.001$), prolonged hospice Length of stay (LOS) (15 vs. 9 days), and avoided chemotherapy in the last 2 weeks of life of (0 vs. 6 patients) [11].

Specific interventions for common complications

Bone antiresorptive therapy decreases bone density loss and fractures in individuals with prostate cancer undergoing androgen deprivation therapy [12]. Psychological therapies are essential components of palliative care for managing distress in advanced cancer [6].

Precision medicine approaches

Personalized treatment solutions enhanced results and diminished treatment-related mortality rates relative to non-personalized methods (mortality rate: 1.5% vs. 2.3%; $p < 0.001$). Personalization based on genomic biomarkers led to greater response rates and longer survival than personalization based on protein biomarkers [10].

IMPACT ON QUALITY OF LIFE

Global HRQoL of survivors, physical and role function was similar or superior to general population norms but was poorer for emotional and cognitive function (particularly in women; $p < 0.01$) [5]. Major post-operative complications led to persistent deterioration in dyspnea (MD=+15), fatigue (MD=+13), eating restrictions (MD=+10), sleep

difficulties, and reflux over 5 years post-esophagectomy [17,23]. Economic burdens had poorer HRQoL and higher odds of non-adherence to medication. (OR=1.70; 95% CI: 1.13–2.56) [2].

Occurrence and severity patterns

The data indicate that a substantial proportion of cancer survivors experience moderate to severe long-term complications – physical (36–35% for loss of performance/fatigue), psychological (~28% for anxiety), neurological (~26% for neuropathy), and financial (~49%) burdens are all common across cancer types and treatments [5]. Notably, the occurrence of these complications does not differ substantially by cancer site for financial toxicity but does vary by treatment modality for physical complications.

Management strategies effectiveness

Integrated multidisciplinary approaches such as the ICS model have demonstrated effectiveness in improving end-of-life care outcomes – higher hospice discharge rates (23% vs. 7%), longer hospice stays (+6 days), and avoidance of late chemotherapy – without increasing readmission rates [40]. Precision medicine approaches not only improve survival outcomes but also reduce treatment-related deaths compared to non-personalized therapies (1.5% vs. 2.3%) [10]. However, gaps remain in the comparative effectiveness data for interventions targeting financial toxicity or psychological distress.

Impact on quality of life

Long-term survivors generally report good physical/role function but impaired emotional/cognitive domains – especially women – highlighting the need for targeted psychosocial interventions [5]. Major surgical complications have persistent negative effects on multiple HRQoL domains even 5 years post-treatment (e.g., dyspnea MD=+15). Financial burdens independently predict worse HRQoL and increased medication non-adherence, which may further compromise outcomes [11].

Patterns and discrepancies

While the surgical/radiation complications are well-characterized in prostate (esophageal) cancers, similar data are lacking for other cancer types [5].

Financial toxicity is pervasive across all cancers but is more severe among younger, uninsured, or socioeconomically disadvantaged patients [21].

Survivors of cancer, particularly for matters considered less medically threatening or for which there is no effective treatment (e.g., fatigue, sexual dysfunction), continue to report unmet needs. This is despite the use of enhanced management techniques (precision medicine, supportive care) [5].

DISCUSSION

Contextualizing the data

The data that has been synthesized above has indicated that complications related to treatment are very common among cancer patients and survivors, regardless of the type of cancer and the modality of treatment. These complications can be fatal, and their impact can reach areas such as physical function, psychological well-being, financial stability, and overall life quality.

Essential points include:

- Almost half of all patients experience a lot of financial damage during or after therapy
- Physical symptoms such as fatigue, loss of performance, neuropathy, and sexual dysfunction affect one-quarter to one-third of survivors
- Psychological distress is common and often under-addressed
- Major post-operative complications have lasting negative effects on HRQoL
- Multidisciplinary supportive care models and precision medicine approaches can mitigate some adverse outcomes but do not fully address all survivor needs.

Table 1: Shows Occurrence of Key Treatment-Related Complications Among Cancer Survivors

S. No.	Complication type	Occurrence (%)	Notable data points/subgroups	References
1	Financial burden	49	Most severe early in treatment	[2]
2	Loss of physical performance	36.3	Long-term survivors (~4 years post-diagnosis)	[5]
3	Fatigue	35.1	Long-term survivors	[5]
4	Sexual problems	34.7	Long-term survivors	[7]
5	Sleep problems	34.1	Long-term survivors	[8]
6	Arthralgia	33.8	Long-term survivors	[5]
7	Anxiety	28.0	Long-term survivors	[5]
8	Neuropathy	25.6	Long-term survivors	[5]
9	Memory problems	23.0	Long-term survivors	[5]
10	Concentration problems	21.9	Long-term survivors	[5]
11	Major post-operative complications (esophagectomy)	33	Associated with worse HRQoL	[13]

HRQoL: Health-related quality of life

Table 2: Shows Management Strategies for Key Complications

S. No.	Complication/issue	Management strategy	Outcome/effectiveness	References
1	Complex symptom burden	Multidisciplinary supportive care (ICS)	Increased hospice discharge; longer hospice LOS; no late chemo	[11]
2	Bone density loss	Antiresorptive therapy	Prevention of bone loss/fractures	[12]
3	Treatment toxicity	Personalized therapy	Lower death rate; better response/survival	[4]
4	Psychological distress	Psychosocial interventions	Improved coping/HRQoL	[6]

HRQoL: Health-related quality of life, ICS: Integrated care service

Table 3: Shows Impact of Complications on Health-Related Quality of Life

S. No.	Complication/burden	HRQoL domain affected	Magnitude/data point	References
1	Major post-operative complication (esophagectomy)	Dyspnea	MD=+15 (95% CI: +6-+23)	[13]
		Fatigue	MD=+13 (95% CI: +5-+20)	[13]
		Eating restrictions	MD=+10 (95% CI: +2-+17)	[13]
2	Financial burden	Overall HRQoL	Associated with worse HRQoL	[2]
		Medication adherence	OR for non-adherence=1.70	[15]
3	Emotional/cognitive burden	Emotional/cognitive function	Worse than population norms; esp. women	[7,21]

MD: Mean difference, CI: Confidence interval, HRQoL: Health-related quality of life, OR: Odds ratio

CONCLUSION

Occurrence

Treatment-related complications are common among cancer patients and survivors - 49% report financial burdens; ~35% report significant physical or psychological symptoms; major surgical complications of major surgery affect up to one-third post-esophagectomy.

Severity

- Complications can range from moderate to severe; major complications results in persistent HRQoL deficits
- Early on in therapy, financial toxicity is high and predicts lower adherence and HRQoL.

Management strategies

- Multidisciplinary supportive care makes things better at the end of life
- Precision medicine reduces treatment-related mortality.

There are specific interventions for some consequences, such as preventing bone loss, but many symptoms are still not being treated properly.

Impact on quality of life

- Physical/role function may recover to population norms; emotional/cognitive domains often remain impaired
- Major complications have long-lasting negative effects on multiple HRQoL domains.

AUTHOR'S CONTRIBUTION

Naman Chouhan- Writer; Jain DK- Idea Implementation; Neeraj Sharma- Conceptualization.

CONFLICTS OF INTEREST

There is no conflicts of interest.

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