

REVIEW

# Measuring financial toxicity in head and neck cancer: a systematic review

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## SUMMARY

**Objective.** The current study systematically reviews the literature about financial toxicity (FT) in head and neck cancer patients. Three databases were reviewed: PubMed, Scopus and Web of Science.

**Methods.** Full text English papers published from 2000 to 2022 reporting on quantitative results about FT in head and neck cancer survivors collected through structured questionnaires or interviews were included.

**Results.** Twenty-seven articles were included. Most of the articles were published after 2015 and from United States. There was a slight prevalence of papers dealing with oropharyngeal cancer, squamous-cell carcinoma and locally advanced head and neck cancer. Measures of FT were obtained through validated questionnaires like COST, FIT and FDQ. Collected data were mostly referable to financial spending, financial resources, psychosocial aspect, support seeking, coping care and coping lifestyle subdomain. FT scores by COST were found to be worse in the COVID era. Financial counseling and adequate information about the costs of treatment were two effective strategies to mitigate FT.

**Conclusions.** FT is a relatively new challenge in head and neck cancer treatment, whose expenses are higher than therapies for other cancers. A universal method to assess FT and a unified guideline for the administration of questionnaires are needed to mitigate FT and to improve patient outcomes.

**KEY WORDS:** head and neck, cancer, financial toxicity, out-of-pocket cost, financial distress

## Introduction

The term financial toxicity (FT), first mentioned in medical literature in 2011<sup>1</sup>, encompasses both the objective and subjective financial burden from the perspective of the patient with cancer. Out-of-pocket (OOP) expenses include drugs and medications to cure treatment toxicity, complementary care, home-care assistance, travel and lodging to follow the treatment regimen, and are referable to objective financial burden. These direct costs as well as indirect costs such as losing income or work lead to subjective financial distress, which means worrying for one's financial situation, looking for economical support and using coping strategies to afford all the expenses<sup>2-4</sup>.

Patients with high level of FT at baseline have worse outcomes in term of overall survival and cancer specific survival<sup>5,6</sup>. The explanation for this can be multiple. The most obvious is the possibility to decrease the quality of treatments because of limited financial resources; this aspect is highly dependent on the organization of the Health National System (public and universal, or private). Moreover, a selection bias may exist, since patients with higher FT are likely to have more advanced and heavily treated disease, less qualitative health insurance, and lower socio-economic status. Finally, a possible "biologic" explanation relies on the stimulation of the sympathetic adrenergic path-

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way by financial hardship, which is a well-known promoter of immunosuppression and tumour growth <sup>6</sup>.

The evident negative impact on clinical outcomes underlines the importance to quantify, compare and prevent FT with adequate instruments. On one hand, available scales to measure financial toxicity include Financial Index of Toxicity (FIT), COmprehensive Score for financial Toxicity (COST), Financial Distress Questionnaire (FDQ), Subjective Financial Distress Questionnaire (SFDQ), Incharge Financial Distress/Financial Wellbeing Scale, Socioeconomic WellBeing Scale (SWBS) <sup>7-9</sup> and Patient-Reported Outcome for Fighting Financial Toxicity (PROFFIT) <sup>10</sup>. On the other hand, several questionnaires explore many aspects of patients' quality of life after cancer diagnosis and treatment also including the financial situation: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), short form Patient Satisfaction Questionnaire (PSQ-18), Cancer Self-Administered Questionnaire (CSAQ) supplement, Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium Patient Survey and Social Difficulties Inventory (SDI) <sup>9</sup>.

The multidimensional measure of FT in cancer patients has been firstly classified in three broad aspects (material conditions, psychological response, and coping behaviors). Then, a recent systematic review, which defined FT as a potential consequence of subjective financial distress due to cancer-related treatment costs, subdivided the three aspects in a six subdomains framework (financial spending, financial resources, psychosocial affect, support seeking, coping care, coping lifestyle) <sup>3,11</sup>.

Currently, FT has been investigated in several non-head and neck sites, while the evidence in the head and neck is still sparse. However, the impact of FT in the head and neck may be particularly severe in view of the relevant treatment toxicity and high burden of treatment-related symptoms. Moreover, the heterogeneity of definitions, terms, and measures in different healthcare systems make it difficult to obtain comparable data; therefore, an overview on the published evidence on this topic could provide both clinicians and researchers with precious insights.

The aim of this systematic review is to depict the overall burden of FT in head and neck cancer. Due to the lack of a single method of measuring FT, we referred to the above-mentioned six subdomains framework to subdivide the results and to make the comparison easier. Moreover, we describe the impact of FT on prognosis, and the factors that most affect FT and OOP expenses. Finally, we try to highlight the existing critical issues in measuring FT in head and neck that should be addressed by future research.

## Materials and methods

### Search strategy

A systematic review of the literature was conducted according to the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) 2020 statement <sup>12</sup>. The search was conducted on the PubMed, Scopus and Web of Science online databases up to September 27, 2022. We restricted the research to English language articles published from 2000 onward, using appropriate filters.

The following query (“head” OR “neck” OR “mouth” OR “pharynx” OR “oral cavit\*” OR “paranasal sinus\*” OR “accessory sinus\*” OR “nose” OR “nasal cavit\*” OR “middle ear” OR “larynx” OR “minor salivary gland\*” OR “major salivary gland\*” OR “thyroid” OR “skin”) AND (“cancer\*” OR “tumo#i\*” OR “neoplasm\*” OR “oncolog\*”) AND (“poverty” OR “financial toxicity” OR “financial distress” OR “financial stress\*” OR “financial burden” OR “financial well-being” OR “financial hardship” OR “financial worr\*” OR “financial difficult\*” OR “financial consequence\*” OR “material hardship\*” OR “economic burden” OR “economic hardship” OR “material hardship” OR “out-of-pocket cost\*” OR “out-of-pocket expens\*” OR “retirement” OR “bankrupt\*” OR “debt\*” OR “income” OR “work income” OR “earned income” OR “employment income”) was launched. Two authors (E.R. and G.Z.) together screened the titles and abstracts and selected articles according to inclusion and exclusion criteria. Discrepancies were clarified between two authors and consultation with a senior otolaryngologist (D.M.).

### Eligibility criteria

The Participants, Interventions, Comparisons, Outcomes, and Study design (PICOS) model was adopted.

Inclusion criteria were as follows:

1. Full text publications (peer review) with at least 20 patients;
2. FT in adult patients (> 18 years) with malignant head and neck tumours of different histology including thyroid, salivary glands, skin, and unknown primary;
3. Articles with quantitative results about FT obtained through structured questionnaires or interviews;
4. Articles with data about objective costs (direct and/or indirect costs) and patients' subjective perception of their financial situation.

Exclusion criteria were as follows:

1. Abstracts, case reports, clinical conferences, comments, congress reports, editorial, letters, published erratum;
2. Qualitative studies without published or structured questionnaires;
3. Articles about FT in paediatric patients or in patients with benign head and neck tumour or lymphoma;

4. Series of cancers from multiple sites, where data on head and neck tumours could not be extrapolated;
5. FT in patients with HPV-related tumours, where data on head and neck tumours could not be extrapolated.

#### Quality assessment

The quality assessment of each study included was estimated by two authors (E.R. and G.Z.) independently through the Newcastle Ottawa Scale (NOS)<sup>13</sup> adapted for cross-sectional and cohort studies. In case of discrepancies, a definitive evaluation was reached by discussion and consultation with the same senior otolaryngologist (D.M.).

#### Data collection

We created a dedicated database collecting most relevant features of the selected articles on country, study design, period of observation, healthcare system (according to Böhm classification, 2013)<sup>14</sup>, demographics data, tumour features with type (surgical vs non-surgical) and intent of treatment (curative or palliative).

In view of the heterogeneity of the articles included, we grouped them into 4 classes according to their focus: a) impact of different therapies in terms of FT; b) impact of FT on patient QoL; c) relation between FT and prognosis; and d) impact of OOP expenses (drugs and medication, complementary care, home care, travel, and accommodation) on FT. In the absence of a standardized taxonomy and a universal method of measuring FT, two authors (E.R. and G.Z.) independently analyzed definitions of financial stress and strain and the questionnaires or interviews used to collect data in the selected articles.

Percentages from collected articles related to the different aspects of financial distress were classified according to the six-subdomain framework proposed by Witte et al.<sup>3</sup> and questions from Subjective Financial Distress Questionnaire (SFDQ).

Data on sufficient financial funds to cover costs related to cancer treatment, loss of income/employment/work due to cancer diagnosis and treatment and selling properties or savings used were referred to *financial resources*.

Data on difficulties in paying for cancer-related treatment costs (travel, food, lodging, drugs, tests) or daily household expenses, financial burden due to OOP expenses, reaching credit card limit of bankruptcy, making debts after treatment or percentage of health-related spending in relation to household income were collected in the *financial spending* subdomain.

In the *psychosocial domain*, we included concerns about current financial situation, financial hardship complained by patients on their families and worsening of financial conditions after cancer treatment.

Data on looking for financial aid (governmental or not, borrowing money or credit, loans, or mortgage), need for a

family member to work more or discussing financial concerns with oncologist/radiotherapist or surgeon were collected in the *support seeking* subdomain.

Data on cutting back on medications, skipping follow-up visits, refusing or delaying treatment or tests were collected in the *coping care* subdomain, whereas results on cutting back on essentials (food, clothing), moving from home or turning off utilities were classified as *coping lifestyle*.

Lastly, absolute values of FT obtained from validated questionnaires were considered as follows: SFDQ percentages were representative of all the six subdomains, COST and FIT scores were comprehensive of all subdomains excluding behavioral domain (*coping care*, *coping lifestyle* and *support seeking*), whereas FDQ values were referred to *financial spending* subdomain only.

## Results

#### Article collection and quality assessment

The bibliographic search returned 5964 titles: 1695 from PubMed, 2470 from Scopus and 1799 from Web of Science. A total of 3375 records were screened through title and abstract evaluation after removal of duplicates (n = 2589).

Since no article about FT in skin cancers with deducible data on head and neck was found, all skin related articles were excluded (n = 176).

Seventy-eight full-text articles were assessed for eligibility. Fifty-one were excluded because they were related to FT from caregivers' perspective (n = 3), evaluated QoL after head and neck cancer treatment with no specific focus on FT (n = 42), compared FT in benign and malignant head and neck tumours (n = 2) or focused on financial barriers to cancer treatment (n = 4). Twenty-seven articles were finally included (Fig. 1). According to the NOS<sup>13</sup> the overall quality of the included studies was good (median value 7.9; range 7-9).

#### General features

Most of the studies included (Tab. I) were conducted after 2015 (n = 25/27)<sup>5,7,9,15-36</sup> and mostly in the United States (n = 15)<sup>5,15,17,20,21,24-28,31-35</sup>. There were 5 studies from Asia<sup>9,16,22,23,29</sup>, 4 of which were conducted in India<sup>9,16,22,29</sup>. There were only 5 studies from Europe<sup>18,19,36-38</sup>, all from Northern Europe: 2 from United Kingdom<sup>37,38</sup>, 2 from Ireland<sup>18,19</sup> and 1 from Norway<sup>36</sup>.

Most of the studies were retrospective (n = 21)<sup>5,9,15-20,23-29,31,33-35,37,38</sup> and unicentric (n = 19) series<sup>5,7,9,15-17,21,22,24,26,29-32,34-38</sup>. Prospective or combined retrospective and prospective data collection was conducted in 6 cases<sup>7,21,22,30,32,36</sup>. Two retrospective studies were multicentric<sup>18,23</sup>, whereas six articles analysed financial data from national databases<sup>19,20,25,27,28,33</sup>.

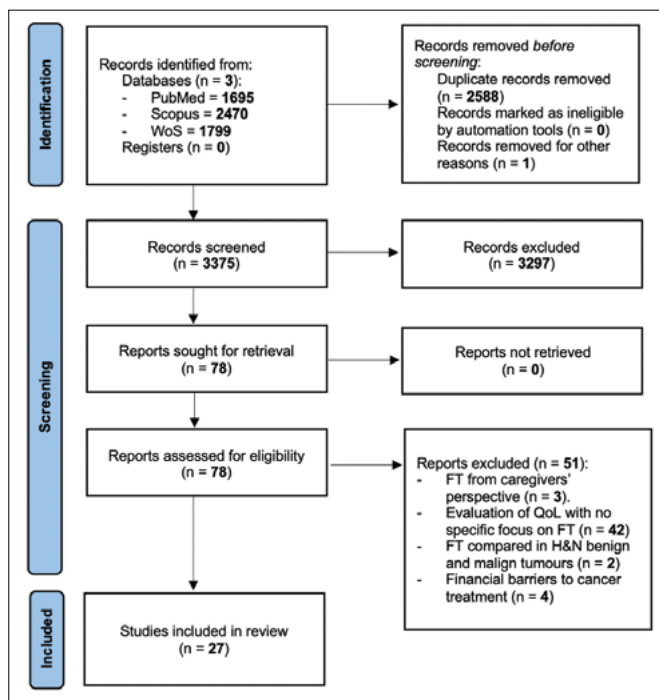


Figure 1. Flow-chart for selection of publications.

### Demographics

The sample sizes ranged from 29 to 470,772 participants whose cancer-related financial burden was collected with the Medical Expenditure Panel Survey (MEPS).

Mean age, reported in 22<sup>5,7,15-18,20,21,24-36,38</sup> of 27 studies, was 58.8 years (SD = 5.7). Five studies did not report the mean age of patients but divided the sample into decades<sup>9,19,22,23,37</sup>. Except for the articles dealing with FT in thyroid cancers (n = 4)<sup>24,25,27,31</sup>, there was a clear predominance of male gender (75.9%, SD = 10.4). Of the four thyroid-related articles, one dealt with a sample of Hispanic women with thyroid cancer<sup>27</sup>.

Eighteen articles reported data on patients' income<sup>7,9,15,16,20-25,27,28,30-32,34,37,38</sup> and 16 about employment status (before and after treatment)<sup>9,15-21,24,25,29,31,32,35,37,38</sup>. Eleven articles reported both income and employment status data<sup>9,15,20,21,24,25,31,32,32,37,38</sup>, whereas four studies did not specify either<sup>5,26,33,36</sup>.

Thirteen of the 18 studies<sup>5,9,16-22,25-28,31-35</sup> in which insurance status was specified were from the United States<sup>5,17,20,21,25-28,31-35</sup>. Due to the private healthcare system, these articles also reported the percentage of patients with different types of insurance. The mean percentage of uninsured patients ranged from 3.1% (SD = 2.8) in United States private healthcare system to 60.3% (SD = 30.6) in Ireland and in the Indian mixed public-private healthcare system. Further information is available in Table II.

### Tumour relevant characteristics

Most of the articles (n = 24) specified the head and neck cancer site and/or subsite included in the sample<sup>5,7,9,15-19,23-38</sup>. Six articles analysed FT in a single specific site, i.e. thyroid (n = 4)<sup>24,25,27,31</sup> and oral cavity (n = 2)<sup>23,29</sup>. Two articles included all head and neck cancer sites also considering the thyroid and salivary glands<sup>9,16</sup>. Three articles considered the oral cavity, pharynx and larynx, clearly excluding skin and salivary gland cancers<sup>7,37,38</sup>. Among these three articles, one also excluded thyroid cancers<sup>7</sup>. One article, comparing FT in head and neck cancer with other cancer survivors, included also skin and thyroid cancers in the latter group<sup>28</sup>. Excluding articles focused on one site or subsite, the oropharynx was the most frequently represented site (n = 8)<sup>5,7,15,17,30,32,34,35</sup>, followed by the oral cavity (n = 7)<sup>9,16,18,19,36-38</sup>. Excluding articles dealing with FT in thyroid cancers, only six studies described HPV status<sup>5,7,26,32,34,35</sup>.

Regarding histological type, six articles included only head and neck squamous cell carcinomas (SCC)<sup>15,17,23,35,37,38</sup>. The remaining included histological types other than SCC (n = 3)<sup>5,7,34</sup> or did not specify the histological types (n = 14)<sup>9,16,18-22,26,28-30,32,33,36</sup>. Two of the four thyroid-related cancer articles specified the most frequent histological type, which was papillary carcinoma<sup>24,31</sup>.

For the disease stage, there was a slight prevalence of percentage of locally advanced (i.e., stage III-IV) head and neck carcinomas (n = 10, > 50%)<sup>7,15,17,22,23,29,30,32,34,35</sup>. One article dealt with only locally advanced SCC<sup>9</sup>, whereas seven did not specify the disease stage<sup>9,16,20,25,28,31,33</sup>.

The treatment modality was heterogeneous: four articles considered patients who had surgical (n = 1) or nonsurgical (n = 3) treatment alone<sup>21,31,32,36</sup>. Most of the articles (n = 18) considered surgical, nonsurgical, or combined treatments<sup>5,7,9,15-19,22,24,26,27,29,30,34,35,37,38</sup>. Five studies did not specify treatment modality<sup>20,23,25,28,33</sup>. The intent of treatment was curative (n = 7)<sup>26,27,29,30,36-38</sup>, curative or palliative (n = 3)<sup>9,16,32</sup> or not specified (n = 17)<sup>5,7,15,17-25,28,31,33-35</sup>. These features are summarized in Table III.

### Measuring financial toxicity

Structured and validated questionnaires were used to measure FT in 12 articles<sup>5,7,9,16,17,25,26,29,32,34-36</sup>. The most used was COST (n = 5)<sup>16,29,32,34,35</sup>, followed by EORTC QLQ-C30 (n = 3)<sup>5,26,36</sup>, FDQ (n = 2)<sup>34,35</sup>, SFDQ (n = 1)<sup>9</sup>, FIT (n = 1)<sup>7</sup>, PSQ-18 (n = 1)<sup>17</sup> and CSAQ supplement (n = 1)<sup>25</sup>. Two articles used both COST and FDQ<sup>34,35</sup>. The remaining 15 articles used self-adapted survey tools to measure FT<sup>15,18-24,27,28,30,31,33,37,38</sup>. Most of the studies measured FT after treatment (n = 20)<sup>7,9,15,16,18-20,23-25,27-29,31-35,37,38</sup>. In other articles, the timing of measurement of FT was heterogeneous: during and after treatment (n = 5)<sup>5,22,26,30,36</sup>, after 13 months on

**Table I.** Most relevant characteristics of studies included in the systematic review.

Author	Year	Country	Study design		Period of observation	Healthcare system
Rogers et al. <sup>37</sup>	2012	UK	R	U	Jan - Dec 2008	NHS type
Rogers et al. <sup>38</sup>		UK	R	U	Jan 2002 - Dec 2008	NHS type
Egestad et al. <sup>36</sup>	2015	Norway	P	U	May 2009 - Nov 2012	NHS type
O' Brien et al. <sup>18</sup>	2016	Ireland	R	M	Apr 2012	Mixed public-private HS
De Souza et al. <sup>21</sup>	2017	USA	P	U	May 2013 - Nov 2014	Private HS
Massa et al. <sup>15</sup>	2018	USA	R	U	May - Oct 2017	Private HS
Lu et al. <sup>19</sup>	2019	Ireland	R	NCRI	2012	Mixed public-private HS
Massa et al. <sup>20</sup>		USA	R	MEPS	Jan 1997 - Dec 2015	Private HS
Chauhan et al. <sup>22</sup>		India	P, R	U	2015-2016	Mixed public-private HS
Amarasinghe et al. <sup>23</sup>		Sri Lanka	R	M	2016	Totally free HS to all
Mady et al. <sup>35</sup>		USA	R	U	Jan - Apr 2018	Private HS
Mongelli et al. <sup>24</sup>	2020	USA	R	U	Jan - Jun 2017	Private HS
Barrows et al. <sup>25</sup>		USA	R	MEPS	2011	Private HS
Hueniken et al. <sup>7</sup>		Canada	P	U	2014-2018	NHI type
Beeler et al. <sup>32</sup>		USA	P	U	May 2016 - Jun 2018	Private HS
Dar et al. <sup>16</sup>	2021	India	R	U	NS	Mixed public-private HS
Ma et al. <sup>5</sup>		USA	R	U	Jan 2013 - Aug 2017	Private HS
Farrugia et al. <sup>26</sup>		USA	R	U	Oct 2013 - Dec 2020	Private HS
Chen et al. <sup>27</sup>		USA	R	SEER	Jan 2014 - Dec 2015	Private HS
Khan et al. <sup>30</sup>		Canada	P	U	2015-2018	NHI type
Broekhuis et al. <sup>31</sup>		USA	R	U	2019	Private HS
Jella et al. <sup>33</sup>		USA	R	NHIS	2013-2018	Private HS
Baddour et al. <sup>34</sup>		USA	R	U	Jan - Aug 2018	Private HS
Lenze et al. <sup>17</sup>	2022	USA	R	U	May 2012 - July 2016	Private HS
Dar et al. <sup>9</sup>		India	R	U	Jan - Aug 2021	Mixed public-private HS
Mott et al. <sup>28</sup>		USA	R	NHIS	2013-2018	Private HS
Thaduri et al. <sup>29</sup>		India	R	U	May 2020 - Oct 2021	Mixed public-private HS

R: retrospective; P: prospective; U: unicentric; M: multicentric; NCRI: National Cancer Registry of Ireland; MEPS: Medical Expenditure Panel Survey; SEER: Surveillance Epidemiology End Results; NHIS: National Health Interview Study; NHS: National Health Service, HS: Health Service; NHI: National Health Insurance; NS: not specified.

average from diagnosis (n = 1) <sup>17</sup> and once a month during concurrent chemoradiation (n = 1) <sup>21</sup>.

Five studies reported a mean score of FT using COST: the lowest and the higher scores were, respectively, 10.8/44 (Grade 2) <sup>16</sup> and 26.5 (Grade 0) <sup>32</sup> (median value = 21.1 ± 5.9). Four of these five articles reported data on FT in terms of financial resources (n = 4) <sup>16,29,32,35</sup>, financial spending (n = 2) <sup>32,34</sup>, psychosocial effect (n = 2) <sup>16,32</sup> and behavioural aspect (n = 2) <sup>16,32</sup>. Two of these five articles reported that high FT was experienced by 45% and 40.5% of patients, respectively, by FDQ, whose items are referable to financial spending subdomain <sup>34,35</sup>. Only one study used the FIT score to assess FT (median value = 11.1/100) and reported data about financial spending <sup>7</sup>.

Considering each subdomain, the most reported data were on financial spending (n = 18) <sup>15,17-25,27,28,30-33,37,38</sup>, followed by financial resources (n = 15) <sup>9,15-17,21,22,24,25,27,29,31-33,35,37</sup>, psy-

chosocial aspect (n = 14) <sup>5,15,16,18,19,24-28,31,32,36,38</sup>, support seeking (n = 10) <sup>9,16,21,22,24,25,31,32,37,38</sup>, coping care (n = 3) <sup>15,31,32</sup> and coping lifestyle (n = 3) <sup>27,32,37</sup>. Data about both material aspects of subjective financial distress (i.e., financial resources and spending) were reported in 11 articles <sup>15,17,21,22,24,25,27,31-33,37</sup>, whereas data about all three behavioural subdomains were reported in one article <sup>32</sup>. Only a single article reported percentages for each subdomain of subjective financial distress <sup>32</sup>. For further information see Table IV.

#### *The impact of financial toxicity*

Few articles addressed the factors affecting FT and the impact of FT on prognosis and QoL (Tab. V).

Three found a correlation between the type of treatment and FT <sup>15,19,29</sup> and two found a significant impact of OOP costs on FT <sup>21,34</sup>, while only one demonstrated worse overall survival and cancer specific survival in patients with high

**Table II.** Most relevant patient characteristics of studies included.

	N	Age	M (%)	I	E	U (%)
Dar et al. <sup>16</sup>	29	49.5	82.8%	1	1	93.1%
Rogers et al. <sup>38</sup>	51	61	82.4%	1	1	NS
Beeler et al. <sup>32</sup>	63	64.1	89%	1	1	0%
Egestad et al. <sup>36</sup>	67	60	73.1%	0	0	NS
Amarasinghe et al. <sup>23</sup>	69	NS	87%	1	0	NS
Baddour et al. <sup>34</sup>	71	63	67.7%	1	0	0%
Souza et al. <sup>21</sup>	73	58	78.1%	1	1	0%
Thaduri et al. <sup>29</sup>	79	49	91.1%	0	1	NS
Massa et al. <sup>15</sup>	100	62.3	74%	1	1	NS
Mady et al. <sup>35</sup>	104	64	76.9%	0	1	3.4%
Dar et al. <sup>9</sup>	142	NS	85.9%	1	1	96.5%
Broekhuis et al. <sup>31</sup>	147	51	27%	1	1	1%
Lenze et al. <sup>17</sup>	202	59.6	77.4%	0	1	4%
Chen et al. <sup>27</sup>	273	47	0%	1	0	0%
Ma et al. <sup>5</sup>	284	61	77.5%	0	0	6.7%
Mott et al. <sup>28</sup>	311	65.9	69%	1	0	8.8%
Farrugia et al. <sup>26</sup>	387	62	78%	0	0	5%
Hueniken et al. <sup>7</sup>	430	61.6	77.2%	1	0	NS
Rogers et al. <sup>37</sup>	447	NS	71.6%	1	1	NS
Chauhan et al. <sup>22</sup>	447	NS	90%	1	0	64.2%
Massa et al. <sup>20</sup>	489	65	64.5%	1	1	2.6%
Lu et al. <sup>19</sup>	531	NS	68%	0	1	4.9%
O'Brien et al. <sup>18</sup>	583	62.9	67%	0	1	52.5%
Khan et al. <sup>30</sup>	657	62.5	77.3%	1	0	NS
Jella et al. <sup>33</sup>	710	59.9	42%	0	0	3.8%
Mongelli et al. <sup>24</sup>	1743	51	12%	1	1	NS
Barrows et al. <sup>25</sup>	470772	53.8	29.1%	1	1	5.4%

N: number; M: male; I: income; E: employment status; U: uninsured; NS: not specified. Stratification of financial toxicity by income and employment (1, Yes; 0, No).

level of FT <sup>5</sup> and seven underlined the impact of FT on patient QoL <sup>17,19,24,29,35,37,38</sup>.

## Discussion

Cancer diagnosis and treatment-related FT, along with physical and psychological burden, is a recent field of research associated with poor patient satisfaction and compliance, QoL and survival. Khera et al. suggested to consider FT as a traditional side effect of treatment <sup>39</sup>. Publications on this topic are now increasing, but there is still heterogeneity in definitions and tools of measurement along with healthcare systems in different countries. In this context, this systematic review tried to provide an overview on FT in patients with head and neck cancer.

### General features and demographics

Most of the publications included were conducted in the

United States, followed by India and Northern European countries. Financial burden of patients in USA with a mainly private healthcare system was not comparable to the one of patients from European countries with national health services or mixed private-public healthcare systems and from India, where, despite a mixed private-public healthcare system, 4.9% of patients on average are below the poverty line for treatment expenses <sup>22</sup>. In the articles included, the percentage of uninsured patients ranged from 3.1% in United States private healthcare system to 84.6% in India and 35.9% in Ireland mixed public-private healthcare systems.

Besides these discrepancies, the comparison is even more difficult considering the different level of development of the different countries. European patients benefit from a more uniform healthcare coverage and Americans are covered through the Affordable Care Act since March 2010, whereas Indians, who live in a low-middle income country, support the healthcare system through OOP payments <sup>3,9</sup>. In Sri Lanka, where the highest cost portion is borne by the health system and household costs decrease with the disease stage, the OOP cost for patients with late advanced oral cancer is 8.7% of the total cost, compared to 28% of those with an earlier stage of disease <sup>23</sup>.

### Tumour relevant characteristics

Only 4 articles found a relation between site or stage of disease and FT. Patients with laryngeal and hypopharyngeal cancer and those with advanced disease (stage IV or nodes positive) reported statistically significant <sup>15,26,35</sup> or near significant <sup>34</sup> higher levels of FT. In addition, patients with oropharyngeal cancer were found to have higher OOP costs <sup>30</sup>. Despite the definition of head and neck malignancies from the American Joint Committee on Cancer, which comprises tumours between the thoracic inlet and skull base <sup>40</sup>, the 27 articles collected in this systematic review revealed a clear heterogeneity in considering thyroid tumours in the group of head and neck cancers.

The psychosocial impact in terms of financial difficulties due to treatment and concern for one's own financial situation reported by thyroid cancer patients ranged from 43% to 50% (30.5% in the article dealing with financial hardship in Hispanic women), resorting to savings from 23.7% to 38%, reaching one's credit card limit from 12% to 17.7%, and bankruptcy from 3% to 9% <sup>24,27,31</sup>.

The worse psychological (46.1% vs 24%) and material (28.1% vs 19.9%) financial hardship experienced by thyroid cancer patients compared to patients with breast, prostate, colon, and lung cancer may be due to the younger age of patients with thyroid cancer, less savings, children still dependent, and employment linked insurance with higher OOP costs and not to Medicare yet <sup>25</sup>.

**Table III.** Tumour characteristics of studies.

	Site	Anatomopathological features			Treatment		
		HPV+ (%)	PH (%)	Stage III-IV (%)	S	NS	S, NS, S + NS
<b>One included</b>							
Mongelli et al. <sup>24</sup>	T		Papillary (85%)	25%			+
Barrows et al. <sup>25</sup>			-	NA		NA	
Chen et al. <sup>27</sup>			-	27.3%			+
Broekhuis et al. <sup>31</sup>			Papillary (38%)	NA	+		
Amarasinghe et al. <sup>23</sup>	OC	-	SCC (100%)	91.3%		NA	
Thaduri et al. <sup>29</sup>		-	-	73.4%			+
<b>Prevalent if more than one specified</b>							
Massa et al. <sup>15</sup>	Or	-	SCC (100%)	67%			+
Lenze et al. <sup>17</sup>		-	SCC (100%)	69.4%			+
Ma et al. <sup>5</sup>		40.1%	SCC (93%)	49%			+
Hueniken et al. <sup>7</sup>		42.1%	SCC (87.2%)	73.3%			+
Khan et al. <sup>30</sup>		-	-	71.8%			+
Beeler et al. <sup>32</sup>		33%	-	86%		+	
Baddour et al. <sup>34</sup>		31%	SCC (84.5%)	73.2%			+
Mady et al. <sup>35</sup>		43.1%	SCC (100%)	79.2%			+
Dar et al. <sup>16</sup>	OC	-	-	NA			+
O'Brien et al. <sup>18</sup>		-	-	37%			+
Lu et al. <sup>19</sup>		-	-	37.7%			+
Dar et al. <sup>9</sup>		-	-	NA			+
Rogers et al. <sup>37</sup>		-	SCC (100%)	26.4%			+
Rogers et al. <sup>38</sup>		-	SCC (100%)	33%			+
Egestad et al. <sup>36</sup>		-	-	23.8%		+	
Jella et al. <sup>33</sup>	T/P	-	-	NA		NA	
Farrugia et al. <sup>26</sup>	P	43.9%	-	48.6%			+
Massa et al. <sup>20</sup>	NA	-	-	NA		NA	
Souza et al. <sup>21</sup>		-	-	100%		+	
Chauhan et al. <sup>22</sup>		-	-	62.9%			+
Mott et al. <sup>28</sup>		-	-	NA		NA	

HPV: human papillomavirus; T: thyroid; OC: oral cavity; Or: oropharynx; P: pharynx; PH: prevalent histology; S: surgical; NS: non-surgical; SCC: squamous cell carcinoma; NA: not available.

### Impact of treatment strategy

As expected, multimodality treatment was associated with higher FT <sup>15,19,29</sup>. One article, comparing surgical and nonsurgical treatments in India, showed that patients experience higher financial distress after surgery along with chemo-radiotherapy than after radiation alone <sup>22</sup>. Likewise, multimodality treatments were associated with higher OOP expenses. Patients who underwent chemoradiation, surgery plus chemoradiation, or radiotherapy alone had to face higher OOP costs than surgery alone <sup>30</sup>.

### Measuring financial toxicity

Instruments used to assess FT were divided into validated or self-adapted questionnaires <sup>15,18-24,27,28,30,31,33,37,38</sup>. Validated

scales include Comprehensive Score for financial Toxicity (COST) <sup>16,29,32,34,35</sup>, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) <sup>5,26,36</sup>, Financial Distress Questionnaire (FDQ) <sup>34,35</sup>, Financial Index of Toxicity (FIT) <sup>7</sup>, Subjective Financial Distress Questionnaire (SFDQ) <sup>9</sup>, Patient Satisfaction Questionnaire (PSQ-18) <sup>17</sup> and Cancer Self-Administered Questionnaire (CSAQ) supplement from Medical Expenditure Panel Survey (MEPS) <sup>25</sup>. These instruments use different questions to assess and quantify financial burden, as seen in Table VI.

While EORTC QLQ-C30, PSQ-18 and CSAQ explore different aspects of QoL and satisfaction in cancer and non-cancer patients, COST, FDQ, FIT and SFDQ have been spe-

**Table IV.** Measuring financial toxicity.

	Subjective financial distress					
	Material		Psychosocial	Behavioural		
	Financial resources	Financial spending	aspect	Support seeking	Coping care	Coping lifestyle
Massa et al. <sup>15</sup>	+	+	+			
Dar et al. <sup>16</sup>		COST score (mean) = <b>10.8/44</b>				
	+		+	+	+	
Lenze et al. <sup>17</sup>	+	+				
Ma et al. <sup>5</sup>			+			
O'Brien et al. <sup>18</sup>		+	+			
Lu et al. <sup>19</sup>		+	+			
Massa et al. <sup>20</sup>		+				
Souza et al. <sup>21</sup>	+	+		+		
Dar et al. <sup>9</sup>			SFDQ = <b>NA</b>			
	+			+		
Chauhan et al. <sup>22</sup>	+	+		+		
Amarasinghe et al. <sup>23</sup>		+				
Mongelli et al. <sup>24</sup>	+	+	+	+		
Barrows et al. <sup>25</sup>	+	+	+	+		
Farrugia et al. <sup>26</sup>			+			
Chen et al. <sup>27</sup>	+	+	+			+
Mott et al. <sup>28</sup>		+	+			
Thaduri et al. <sup>29</sup>		COST score (mean) = <b>17.9/44</b>				
	+					
Hueniken et al. <sup>7</sup>		FIT score (median) = <b>11.1/100</b>				
Khan et al. <sup>30</sup>		+				
Broekhuis et al. <sup>31</sup>	+	+	+	+	+	
Beeler et al. <sup>32</sup>		COST score (mean) = <b>26.5/44</b>				
	+	+	+	+	+	+
Rogers et al. <sup>37</sup>	+	+		+		+
Rogers et al. <sup>38</sup>		+	+	+		
Jella et al. <sup>33</sup>	+	+				
Baddour et al. <sup>34</sup>		COST score (mean) = <b>24.8/44</b>				
		FDQ = <b>45%</b>				
Mady et al. <sup>35</sup>		COST score (mean) = <b>25.3/44</b>				
	+	FDQ = <b>40.5%</b>				
Egestad et al. <sup>36</sup>			+			

*COST: COmprehensive Score for financial Toxicity; SFDQ: Subjective Financial Distress Questionnaire; NA: not available; FIT: Financial Index of Toxicity; FDQ: Financial Distress Questionnaire.*

cifically validated to assess FT. Compared to SFDQ, COST, FDQ and FIT items do not cover all the six subdomains of subjective financial distress <sup>9</sup>. COST was developed in United States and validated in patients with advanced solid cancers. FIT was developed in Canada and validated in head and neck cancer patients of any stage. Both FIT and COST were validated in patients after chemotherapy. SFDQ is the most recently developed questionnaire, and has been validated in head and neck radiation oncology patients. Its items cover all

the six subdomains, also exploring FT from the perspective of the patients' family. On the other hand, FDQ, developed at the University of Pittsburgh, is a 2-item questionnaire to assess FT in cancer patients and in those with chronic diseases <sup>3,7,9,35</sup>. Given the heterogenous scales available to quantify FT that emerged, we followed the subdomains framework proposed by Witte et al. <sup>3</sup> to ease comparison of the results. Twelve articles reported data on material aspects of financial distress. In addition the direct medical expenditures on treat-



**Table V.** Impact of financial toxicity.

	Correlation between financial toxicity and:			
	Treatment	QoL	Survival	OOP costs
Massa et al. <sup>15</sup>	+			
Dar et al. <sup>16</sup>				
Lenze et al. <sup>17</sup>		+		
Ma et al. <sup>5</sup>			+	
O'Brien et al. <sup>18</sup>				
Lu et al. <sup>19</sup>	+	+		
Massa et al. <sup>20</sup>				
Souza et al. <sup>21</sup>				+
Dar et al. <sup>9</sup>				
Chauhan et al. <sup>22</sup>				
Amarasinghe et al. <sup>23</sup>				
Mongelli et al. <sup>24</sup>		+		
Barrows et al. <sup>25</sup>				
Farrugia et al. <sup>26</sup>				
Chen et al. <sup>27</sup>				
Mott et al. <sup>28</sup>				
Thaduri et al. <sup>29</sup>	+	+		
Hueniken et al. <sup>7</sup>				
Khan et al. <sup>30</sup>				
Broekhuis et al. <sup>31</sup>				
Beeler et al. <sup>32</sup>				
Rogers et al. <sup>37</sup>		+		
Rogers et al. <sup>38</sup>		+		
Jella et al. <sup>33</sup>				
Baddour et al. <sup>34</sup>				+
Mady et al. <sup>35</sup>		+		
Egestad et al. <sup>36</sup>				

QoL: quality of life; OOP: out of pocket.

ment, cancer is associated with indirect costs like loss of income and change in employment status. Several studies analysed the relation between employment status and head and neck cancer treatment, reporting that 34-52% of working patients left their job due to the treatment regimen<sup>15,41</sup>. Patients complained about changing their employment status<sup>9,15,16,24,25,29,32,37</sup> or income<sup>15,24,31,37</sup>, resorting to savings<sup>16,21,24,27,32,33,35</sup>, selling possessions<sup>16,21,22</sup> and not having sufficient financial funds to cover the cost of cancer treatment<sup>16,17</sup>. The highest percentage of patients that was forced to stop working after cancer treatment was around 70% (in India and USA)<sup>9,32</sup> and one article reported that almost half of patients who experienced financial burden complained about loss of income<sup>31</sup>. Patients were forced to use coping strategies, such as using savings (62%) or selling properties (25%)<sup>21</sup>.

OOP expenses (medical tests, travel and transportation, drugs or consumables, dental treatment after radiotherapy, petrol, park-

ing, taxi fares and paying medical bills) were another relevant source of financial distress. In fact, because of these payments 43% of patients were forced to work more<sup>17</sup> and about 50% were not able to make ends meet<sup>18,19</sup>. Referring to the United States, 14.9% reached their credit card limit<sup>24,27</sup>, 13% went into debt<sup>31</sup> and 4.4% experienced bankruptcy<sup>24,25,31</sup>. Chauhan et al. reported that 34% of patients suffered from catastrophic health expenditures, while Rogers et al. found that half of patients felt that the financial burden was large or unbearable<sup>22,38</sup>.

In comparison with other cancer survivors, those with head and neck cancer must afford higher OOP expenses (3.9% vs 3%)<sup>20</sup>. Fourteen articles reported data on the psychosocial aspect, which includes concerns about financial situation<sup>15,18,32</sup> and related effect on families<sup>16,19,32</sup> as well as worsening of their financial condition after cancer treatment<sup>5,24,26,27,36,38</sup>. Two articles reported comprehensive percentages of psychosocial domain of subjective financial distress. Both are FT comparison articles. In the first one, the psychosocial impact on patients with thyroid cancer was compared with breast, prostate, lung, and colon (46.1% vs 24%)<sup>25</sup>. In the second, the psychosocial impact in patients with head and neck tumours was compared with skin, thyroid, breast, genitourinary, gynaecological, gastrointestinal, melanoma, haematological, lung tumours and patients with multiple synchronous tumours (73.3% vs 72.3%)<sup>28</sup>. Data on the behavioural consequences of financial distress were available in 11 articles, but only one reported data on each of the three subdomains<sup>32</sup>. To afford medical expenses, more than 80% of patients asked for government or non-government aid (India)<sup>9,16</sup>, borrowed money (28.2% in United States and India)<sup>16,21,24,25,32</sup>, took out a mortgage (4.4% and 7% in United States and India, respectively)<sup>24,37</sup>, applied for benefits (63%, United Kingdom)<sup>38</sup>, or asked for a family member to work more (23%, United States)<sup>21</sup>. Nevertheless, 7% of patients skipped follow-up visits<sup>16,32</sup>, 9% refused or delayed tests or treatment<sup>31,32</sup> and 26% did not adhere to medications<sup>32</sup>. Patients also had to cut spending on food or clothes<sup>27,32,37</sup>, move from home or turn off utilities<sup>27</sup>. One article reported that mean FT scores from COST in cancer survivors (oral, breast and cancer of various sites) slightly worsened between the pre- and post-COVID era (21.1 [SD = 0.7] versus 15.6 [SD = 1.2])<sup>29</sup>. Patients reporting high financial distress by FDQ, used in two articles, were 45% and 40.5%, respectively<sup>34,35</sup>.

#### *Financial toxicity, prognosis, quality of life and OOP expenses*

Only one article underlined that a high level of financial difficulty at baseline was associated with worse overall survival and cancer specific survival in both multivariate and match paired analysis<sup>5</sup>. Interestingly, this finding attributes a prognostic weight to FT just like other major clinical and pathological factors, which should prompt physicians to address greater attention to this treatment-related aspect.

**Table VI.** Scales to measure FT and their characteristics.

Questionnaire	Items	Score
<b>COST</b> De Souza <sup>8</sup> USA	11/11. 8: psychosocial aspect 2: financial resources 1: financial spending	0-4/44 Grade 0 (> 26): no impact Grade 1 (14-25): mild Grade 2 (1-13): moderate Grade 3 (0): high
<b>EORTC QLQ-C30</b> Bjordal et al. <sup>45</sup> Europe	1/30. 1: financial difficulty	1-4/120 (Likert Scale) Higher score: better QoL
<b>FDQ</b> USA	2/2. 2: financial spending	Yes/no 1-3 Grade 1 (mild): Y + no difficulties Grade 2 (moderate): Y + some difficulties Grade 3 (severe): No + some/extreme difficulties
<b>FIT</b> Hueniken <sup>7</sup> Canada	9/9. 3: financial stress 4: financial strain 2: loss of productivity	Low tox (grade 1) High tox (grade 2+3) 0-1 (+ intermediate levels) Mean of all responses x 100/9 = score/100 Lower score: mild FT
<b>SFDQ</b> Dar <sup>9</sup> India	14/14. 2: financial resources 5: financial spending 3: psychosocial 2: coping behaviour 2: support seeking	0-2/28 Grade 1 (0-7): low Grade 2 (8-14): mild Grade 3 (15-21): moderate Grade 4 (22-28): high
<b>PSQ-18</b> Marshall et al. <sup>46</sup> USA	2/18. 2 financial distress	1-5/90 (Likert Scale) Higher score: satisfaction with financial situation
<b>CSAQ</b> ACS, 2011 USA	6/93 (Section 6) 3: support seeking 2: financial spending 1: psychosocial aspect	MEPS collects data on expenditures related to medical events. The survey includes 8 sections, and the 6 <sup>th</sup> focuses on the effects of cancer and its treatment on finances.

*COST: C*omprehensive Score for financial Toxicity; *EORTC QLQ-C30: E*uropean Organization for Research and Treatment of Cancer Quality of Life Questionnaire; *FDQ: F*inancial Distress Questionnaire; *FIT: F*inancial Index of Toxicity; *SFDQ: S*ubjective Financial Distress Questionnaire; *PSQ-18: P*atient Satisfaction Questionnaire; *CSAQ: C*ancer Self-Administered Questionnaire; *MEPS: M*edical Expenditure Panel Survey; *QoL: q*uality of life; *ACS: A*merican Cancer Society.

Further analyses are warranted to confirm the prognostic impact of FT in patients with head and neck cancer. Health related quality of life, assessed by Functional Assessment of Cancer Therapy - General (FACT-G) <sup>17,19</sup>, Patient-Reported Outcomes Measurement Information System (PROMIS) <sup>17,24</sup>, University of Washington Quality Of Life (UW-QOL) questionnaire <sup>35,37,38</sup> and Depression-Anxiety-Stress Scale (DASS-21) <sup>29</sup>, was negatively correlated with cancer-related FT. Two studies also found a significant correlation between COST scores and QoL: the lower the COST scores, the worse the QoL <sup>29,35</sup>. Of

these seven publications, one dealt with QoL in survivors of thyroid cancer <sup>24</sup>. OOP expenses were associated with higher financial stress <sup>21</sup> and lower COST scores <sup>34</sup>.

#### *Managing financial toxicity*

Along with coping strategies to reduce the impact of FT in terms of QoL and outcomes, mitigation strategies for FT in patients with head and neck cancer are needed. In addition to cost-effective strategies within clinical guidelines, financial counseling can help patients during treatment. Farrugia et al. found a signif-

icant increase in financial difficulty score by EORTC QLQ-C30 at the end of treatment in patients who did not undergo financial counseling ( $p = 0.002$ ) compared to patients who benefited from a financial counselor and who had no significant different scores in pre- and post-treatment questionnaires<sup>26,42,43</sup>.

Moreover, patients often complain about the lack of treatment cost-related information received. Broekhuis et al.<sup>31</sup> analysed financial burden in thyroid cancer survivors and found that 25% of patients were not adequately informed about treatment costs. Giving adequate information about treatment costs and discussing this with patients would be another way to mitigate the impact of the expenses of the treatment regimen on both patients and family<sup>31,44</sup>.

### Limitations

This is the first systematic review that has attempted to collect data about FT in patients with head and neck cancer. Our review has some limitations. Due to the heterogeneous taxonomy, we could have missed some relevant articles even after the hand-search. A certain degree of subjectivity in classifying data in each of the six subdomains may be present, although we tried to limit this via consensus. The heterogeneity in healthcare systems and in patient cohorts made comparisons almost impossible. In view of this, when reporting outcomes, we always specified the country where the study was conducted, and we advise the reader to consider the specific health system for better interpretation of data. Due to the heterogeneity among different questionnaires and since only a few studies found significant correlations between tumour features, type of treatment, prognosis and FT, a meta-analysis could not be conducted, and the evidence related to these correlations is still sparse.

### Conclusions

FT is a relatively new field of research. Its impact in head and neck cancer is relevant since these patients have to face higher OOP expenses than other cancer patients. Among current questionnaires specifically validated to assess FT (COST, FDQ, FIT, SFDQ), only FIT and SFDQ were developed to measure it in patients with head and neck cancer. FT often translates into psychological distress. We suggest following the framework proposed by Witte et al.<sup>3</sup> to intercept and classify it in terms of material, psychosocial and behavioural subdomains. The current evidence showed a correlation of FT with the request for financial aid and the consequent psychosocial distress, as well as its detrimental effect on QoL and psychological well-being of patients. Multimodality treatments and advanced disease are associated with both greater FT and higher OOP expenses. In turn, FT negatively impacts prognosis.

Patients who did not undergo financial counselling had greater financial difficulty as revealed by questionnaires at the end of treatment.

These findings should prompt clinicians to evaluate and discuss this aspect with the patient and his/her family before the beginning of treatment to guarantee the best compliance to the treatment plan. Heterogeneity of questionnaires and healthcare systems makes comparisons among studies almost impossible, and hinders a clear depiction of FT. Improvement of questionnaires and other analytic methods (including healthcare system type, socioeconomic patient status, site, stage of disease and type of treatment intent) are warranted to better profile the risk of FT for the individual patient at baseline, during treatment and follow-up, and properly address it. Moreover, a universal guideline for the timing of administration of questionnaires is needed.

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### Author contributions

ER, GZ, PB: concept; ER, GZ: data collection; ER, DM: writing – original draft; CP, PB, DM: writing – review and editing.

### Ethical consideration

Not applicable.

### References

- Zafar SY, Abernethy AP. Financial toxicity, Part I: a new name for a growing problem. *Oncology (Williston Park)* 2013;27:80-149.
- Zafar SY, Peppercorn JM, Schrag D, et al. The financial toxicity of cancer treatment: a pilot study assessing out-of-pocket expenses and the insured cancer patient's experience. *Oncologist* 2013;18:381-390. <https://doi.org/10.1634/theoncologist.2012-0279>
- Witte J, Mehliis K, Surmann B, et al. Methods for measuring financial toxicity after cancer diagnosis and treatment: a systematic review and its implications. *Ann Oncol* 2019;30:1061-1070. <https://doi.org/10.1093/annonc/mdz140>
- Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: understanding and stepping-up action on the financial toxicity of cancer treatment. *CA Cancer J Clin* 2018;68:153-165. <https://doi.org/10.3322/caac.21443>
- Ma SJ, Iovoli AJ, Attwood K, et al. Association of significant financial burden with survival for head and neck cancer patients treated with radiation therapy. *Oral Oncol* 2021;115:105196. <https://doi.org/10.1016/j.oraloncology.2021.105196>
- Qiao G, Chen M, Bucsek MJ, et al. Adrenergic signaling: a targetable checkpoint limiting development of the antitumor immune response. *Front Immunol* 2018;9:164. <https://doi.org/10.3389/fimmu.2018.00164>
- Hueniken K, Douglas CM, Jethwa AR, et al. Measuring financial toxicity incurred after treatment of head and neck cancer: development and validation of the Financial Index of Toxicity questionnaire. *Cancer* 2020;126:4042-4050. <https://doi.org/10.1002/cncr.33032>

- 8 de Souza JA, Yap BJ, Wroblewski K, et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: the validation of the Comprehensive Score for financial Toxicity (COST): measuring financial toxicity. *Cancer* 2017;123:476-484. <https://doi.org/10.1002/ncr.3036>
- 9 Dar MA, Chauhan R, Murti K, et al. Development and validation of Subjective Financial Distress Questionnaire (SFDQ): a patient reported outcome measure for assessment of financial toxicity among radiation oncology patients. *Front Oncol* 2022;11:819313. <https://doi.org/10.3389/fonc.2021.819313>
- 10 Riva S, Arenare L, Di Maio M, et al. Cross-sectional study to develop and describe psychometric characteristics of a patient-reported instrument (PROFFIT) for measuring financial toxicity of cancer within a public healthcare system. *BMJ Open* 2021;11:E049128. <https://doi.org/10.1136/bmjopen-2021-049128>
- 11 Altice CK, Banegas MP, Tucker-Seeley RD, et al. Financial hardships experienced by cancer survivors: a systematic review. *JNCI J Natl Cancer Inst* 2016;109:djw205. <https://doi.org/10.1093/jnci/djw205>
- 12 Page MJ, Moher D, Bossuyt C, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;Mar 29;372:n160. <https://doi.org/10.1136/bmj.n160>
- 13 Ottawa Hospital Research Institute. [https://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). Accessed September 20, 2023.
- 14 Böhm K, Schmid A, Götze R, et al. Five types of OECD healthcare systems: empirical results of a deductive classification. *Health Policy*. 2013;113:258-269. <https://doi.org/10.1016/j.healthpol.2013.09.003>
- 15 Massa ST, Rohde RL, Mckinstry C, et al. An assessment of patient burdens from head and neck cancer survivorship care. *Oral Oncol* 2018;82:115-121. <https://doi.org/10.1016/j.oraloncology.2018.04.024>
- 16 Dar MA, Chauhan R, Sharma KK, et al. Assessing the reliability and validity of comprehensive score for financial toxicity (COST) among radiation oncology patients in India: a cross-sectional pilot study. *Ecancermedicalscience* 2021;15:1219. <https://doi.org/10.3332/ecancer.2021.1219>
- 17 Lenze NR, Bensen JT, Farnan L, et al. Association of self-reported financial burden with quality of life and oncologic outcomes in head and neck cancer. *Head Neck* 2022;44:412-419. <https://doi.org/10.1002/hed.26934>
- 18 O'Brien KM, Timmons A, Butow P, et al. Associations between neighbourhood support and financial burden with unmet needs of head and neck cancer survivors. *Oral Oncol* 2017;65:57-64. <https://doi.org/10.1016/j.oraloncology.2016.12.019>
- 19 Lu L, O'Sullivan E, Sharp L. Cancer-related financial hardship among head and neck cancer survivors: risk factors and associations with health-related quality of life. *Psychooncology* 2019;28:863-871. <https://doi.org/10.1002/pon.5034>
- 20 Massa ST, Osazuwa-Peters N, Adjei Boakye E, et al. Comparison of the financial burden of survivors of head and neck cancer with other cancer survivors. *JAMA Otolaryngol Head Neck Surg* 2019;145:239-249. <https://doi.org/10.1001/jamaoto.2018.3982>
- 21 de Souza JA, Kung S, O'Connor J, et al. Determinants of patient-centered financial stress in patients with locally advanced head and neck cancer. *J Oncol Pract* 2017;13:E310-E318. <https://doi.org/10.1200/JOP.2016.016337>
- 22 Chauhan AS, Prinja S, Ghoshal S, et al. Economic burden of head and neck cancer treatment in North India. *Asian Pac J Cancer Prev APJCP* 2019;20:403-409. <https://doi.org/10.31557/APJCP.2019.20.2.403>
- 23 Amarasinghe H, Jayasinghe RD, Dharmagunawardene D, et al. Economic burden of managing oral cancer patients in Sri Lanka: a cross-sectional hospital – based costing study. *BMJ Open* 2019;9:E027661. <https://doi.org/10.1136/bmjopen-2018-027661>
- 24 Mongelli MN, Giri S, Peipert BJ, et al. Financial burden and quality of life among thyroid cancer survivors. *Surgery* 2020;167:631-637. <https://doi.org/10.1016/j.surg.2019.11.014>
- 25 Barrows CE, Belle JM, Fleishman A, et al. Financial burden of thyroid cancer in the United States: an estimate of economic and psychological hardship among thyroid cancer survivors. *Surgery* 2020;167:378-384. <https://doi.org/10.1016/j.surg.2019.09.010>
- 26 Farrugia M, Yu H, Ma SJ, et al. Financial counseling is associated with reduced financial difficulty scores in head and neck cancer patients treated with radiation therapy. *Cancers* 2021;13:2516. <https://doi.org/10.3390/cancers13112516>
- 27 Chen DW, Reyes-Gastelum D, Veenstra CM, et al. Financial hardship among hispanic women with thyroid cancer. *Thyroid* 2021;31:752-759. <https://doi.org/10.1089/thy.2020.0497>
- 28 Mott NM, Mierzwa ML, Casper KA, et al. Financial hardship in patients with head and neck cancer. *JCO Oncol Pract* 2022;18:E925-E937. <https://doi.org/10.1200/OP.21.00683>
- 29 Thaduri A, Garg PK, Malhotra M, et al. Financial toxicity and mental well-being of the oral cancer survivors residing in a developing country in the era of COVID 19 pandemic – a cross-sectional study. *Psychooncology* 2023;32:58-67. <https://doi.org/10.1002/pon.6030>
- 30 Khan MN, Hueniken K, Manojlovic-Kolarski M, et al. Out-of-pocket costs associated with head and neck cancer treatment. *Cancer Rep* 2021;5:E1528. <https://doi.org/10.1002/ctr2.1528>
- 31 Broekhuis JM, Li C, Chen HW, et al. Patient-reported financial burden in thyroid cancer. *J Surg Res* 2021;266:160-167. <https://doi.org/10.1016/j.jss.2021.03.051>
- 32 Beeler WH, Bellile EL, Casper KA, et al. Patient-reported financial toxicity and adverse medical consequences in head and neck cancer. *Oral Oncol* 2020;101:104521. <https://doi.org/10.1016/j.oraloncology.2019.104521>
- 33 Jella TK, Cwalina TB, Sachdev R, et al. Prevalence, trends, and demographic characteristics associated with self-reported financial stress among head and neck cancer patients in the United States of America. *Am J Otolaryngol* 2021;42:103154. <https://doi.org/10.1016/j.amjoto.2021.103154>
- 34 Baddour K, Fadel M, Zhao M, et al. The cost of cure: examining objective and subjective financial toxicity in head and neck cancer survivors. *Head Neck* 2021;43:3062-3075. <https://doi.org/10.1002/hed.26801>
- 35 Mady LJ, Lyu L, Owoc MS, et al. Understanding financial toxicity in head and neck cancer survivors. *Oral Oncol* 2019;95:187-193. <https://doi.org/10.1016/j.oraloncology.2019.06.023>
- 36 Egestad H, Nieder C. Undesirable financial effects of head and neck cancer radiotherapy during the initial treatment period. *Int J Circumpolar Health* 2015;74:26686. <https://doi.org/10.3402/ijch.v74.26686>
- 37 Rogers SN, Harvey-Woodworth CN, Hare J, et al. Patients' perception of the financial impact of head and neck cancer and the relationship to health related quality of life. *Br J Oral Maxillofac Surg* 2012;50:410-416. <https://doi.org/10.1016/j.bjoms.2011.07.026>
- 38 Rogers SN, Harvey-Woodworth CN, Lowe D. Patients' perspective of financial benefits following head and neck cancer in Merseyside and Cheshire. *Br J Oral Maxillofac Surg* 2012;50:404-409. <https://doi.org/10.1016/j.bjoms.2011.07.020>
- 39 Khera N, Chang YH, Hashmi S, et al. Financial burden in recipients of allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant* 2014;20:1375-1381. <https://doi.org/10.1016/j.bbmt.2014.05.011>
- 40 Cohen N, Fedewa S, Chen AY. Epidemiology and demographics of the head and neck cancer population. *Oral Maxillofac Surg Clin N Am* 2018;30:381-395. <https://doi.org/10.1016/j.coms.2018.06.001>
- 41 Buckwalter AE. Patient-reported factors associated with discontinuing employment following head and neck cancer treatment. *Arch Otolaryngol Head Neck Surg* 2007;133:464. <https://doi.org/10.1001/archoto.133.5.464>
- 42 Cherny NI, Sullivan R, Dafni U, et al. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol* 2015;26:1547-1573. <https://doi.org/10.1093/annonc/mdv249>
- 43 Schnipper LE, Davidson NE, Wollins DS, et al. American Society of Clinical Oncology Statement: a conceptual framework to assess the value of cancer treatment options. *J Clin Oncol* 2015;33:2563-2577. <https://doi.org/10.1200/JCO.2015.61.6706>
- 44 Henrikson NB, Tuzzio L, Loggers ET, et al. Patient and oncologist discussions about cancer care costs. *Support Care Cancer* 2014;22:961-967. <https://doi.org/10.1007/s00520-013-2050-x>
- 45 Bjordal K, Ahiner-Elmqvist M, Tollefson E, et al. Development of a European Organization for Research and Treatment of Cancer (EORTC) Questionnaire module to be used in quality of life assessments in head and neck cancer patients. *Acta Oncologica* 1994;33:879-885. <https://doi.org/10.3109/02841869409098450>
- 46 Marshall GN, Hays RD. The Patient Satisfaction Questionnaire Short-Form (PSQ-18). Santa Monica CA: RAND, 1994.