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# BMJ Open

## Protocol for a systematic review of the financial burden experienced by people affected by head and neck cancer

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Manuscripts

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3 **Protocol for a systematic review of the financial burden experienced by**  
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6 **people affected by head and neck cancer**  
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9 **Running title:** Protocol of a systematic review of financial burden in head and neck cancer  
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13 Nikki McCaffrey, PhD (corresponding author)  
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15 Deakin University, Geelong, Deakin Health Economics, Institute for Health Transformation,  
16  
17 School of Health and Social Development, Victoria, Australia.  
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19  
20 Cancer Council Victoria, 615 St Kilda Road, Melbourne, Victoria, Australia.  
21

22  
23 nikki.mccaffrey@deakin.edu.au  
24

25  
26 Phone 03 924 68767, mobile 04 4726 1668, fax 03 924 46261  
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29 Lidia Engel, PhD  
30

31 Deakin University, Geelong, Deakin Health Economics, Institute for Health Transformation,  
32  
33 School of Health and Social Development, Victoria, Australia  
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12 planned systematic review of published literature.  
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For peer review only

## Abstract

**Introduction:** Head and neck cancer is the seventh most common cancer worldwide.

Treatment may be associated with the inability to work and substantial out-of-pocket expenses. However, to date, there is little research synthesising quantitative evidence on the financial burden experienced by people affected by head and neck cancers (HNC), including family members and informal carers. The purpose of this systematic review is to estimate out-of-pocket costs, reduced or lost income and informal care costs associated with HNC, identify categories of financial burden and investigate which costs predominate when considering financial burden in this population.

**Methods and analysis:** A comprehensive search of peer-reviewed literature will be conducted for articles published since 2010 (CINAHL; Cochrane library; Econlit; Embase; Medline Complete). Published, English-language articles describing primary and secondary research directly related to the topic and quantitative cost data will be included. One researcher will complete the searches and screen results for potentially eligible studies. Three other researchers will independently screen the titles and abstracts of a subset of 30% citations. Full text articles will be independently screened by three reviewers. Any disagreement will be resolved by consensus among the team. Study and patient characteristics, cost categories and financial burden will be independently extracted by one reviewer and checked by a second. Methodological quality will be evaluated independently by two reviewers using appropriate critical appraisal checklists. Descriptive analyses will be undertaken and a narrative summary of the included studies will be provided.

**Ethics and dissemination:** Ethics approval is not required to conduct this research because this is a planned systematic review of published literature. Findings will be presented at

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2  
3 leading cancer and health economic conferences, published in a peer-reviewed journal and  
4  
5 disseminated via website postings and social media channels.  
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9 **Systematic review registration number:** CRD42021252929  
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### 11 12 **Strengths and limitations of this study**

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15 • The planned systematic review will provide insights into the financial burden faced by  
16  
17 patients and families to inform the development of appropriate strategies for improving  
18  
19 financial wellbeing in people affected by head and neck cancer.  
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- 22  
23 • The systematic review protocol is reported according to the recommendations of the  
24  
25 Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-  
26  
27 P) statement and is registered with the International Prospective Register of Systematic  
28  
29 Reviews (PROSPERO).  
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- 32  
33 • The total number of studies investigating the financial burden experienced by people  
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35 affected by head and neck cancer may be small; study methods may be heterogeneous;  
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37 and cost estimates may be derived from diverse health financing systems, limiting study  
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39 findings.  
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## INTRODUCTION

Head and neck cancer (HNC) is ranked as one of the top ten cancers globally with over 850,000 new cases diagnosed each year<sup>1 2</sup>. Incidence is anticipated to continue rising with more than one million new cases each year predicted by 2030<sup>2</sup>. Generally, HNC begins in the squamous cells of the mouth, throat and nose and includes cancers of the oral cavity, nasal cavity and paranasal sinuses, salivary glands, pharynx and larynx<sup>3</sup> and thus far, there is no effective screening strategy for HNC. Meticulous physical examination is the key approach for early detection<sup>4</sup>. Treatment may involve chemotherapy, radiotherapy, surgery or typically, a combination of these approaches, particularly in later stages<sup>3</sup>. Many patients experience substantial functional impairment due to the location of the tumour, such as loss of speech, difficulties with swallowing and speech and challenges with eating<sup>5</sup> and symptoms associated with HNC and its treatment include pain, breathlessness, dry mouth, fatigue, depression<sup>6 7</sup>.

People affected by cancer can experience substantial out-of-pocket expenses associated with treatment costs, travel expenses, and reduced household income from a diminished ability to continue or maintain paid employment, irrespective of universal health coverage status<sup>8 9</sup>. Informal carers, i.e. people who provide ongoing, regular assistance to a person with chronic, progressive, or life-limiting illness, typically without receiving payment for the assistance they provide<sup>10-12</sup> also report significant financial burden particularly related to reduced income and the costs of care time<sup>13 14</sup>. Financial burden has been associated with greater mortality risk, poorer quality of life (QOL), worse symptoms and reduced concordance with treatment advice<sup>15-18</sup>. Consequently, promoting financial wellbeing is a vital component of supportive care for people affected by cancer. Increasingly, clinical

1  
2  
3 practice guidelines recommend discussion of the possible costs of cancer care and potential  
4 financial burden to patients and families, particularly in vulnerable groups such as low  
5 socioeconomic status populations<sup>19</sup>. As socioeconomically deprived groups are  
6 disproportionately affected by HNC<sup>20-22</sup>, managing financial burden is particular germane for  
7 people with this type of cancer.  
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11 Whilst attempts have been made to summarise and quantify the financial burden  
12 experienced by people affected by a broad range of cancer types<sup>8 23-27</sup>, thus far, such  
13 information for people impacted by HNC is lacking. This information will help inform the  
14 development of appropriate policies, programs and strategies for improving financial  
15 wellbeing in this population. Consequently, the aim of this systematic review is to address  
16 this gap in knowledge by synthesising evidence on the constituents and magnitude of  
17 financial burden faced by patients and families affected by HNC.  
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### 34 **Review questions**

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37 This systematic review addresses three related research questions:

- 38 1. What is the financial burden faced by people affected by head and neck cancer?
- 39 2. What are the main categories of out-of-pocket expenses faced by people affected by  
40 head and neck cancer?
- 41 3. Which types of cost cause the greatest financial burden for people affected by head and  
42 neck cancer?

### 43 **METHODS**

44  
45 This protocol is reported according to the recommendations of the Preferred Reporting  
46 Items for Systematic Reviews and Meta-Analyses statement<sup>28</sup>.  
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## Eligibility criteria

Published, peer-reviewed, English-language articles reporting primary and secondary research directly related to the topic and quantitative cost data will be eligible for inclusion in the systematic review.

### Inclusion criteria:

- Studies including people affected by HNC, i.e. patients, families and informal carers;
- Studies reporting and quantifying costs borne by patients and families; and
- Primary and secondary research directly related to the topic, i.e. there will be no restrictions regarding research design.

### Exclusion criteria

- Studies reporting qualitative data only;
- Studies which do not report cost estimates;
- Economic evaluations;
- Non-English articles and those not peer reviewed, including comment or discussion papers, editorials, conference abstracts or papers and the grey literature.

## Search strategy

A comprehensive search of the literature will be conducted from January 1, 2010 to the date of the search (CINAHL; Cochrane library; Econlit; Embase; and MEDLINE Complete) to identify relevant published studies fitting the inclusion criteria. Studies published before 2010 were considered less relevant due to changes in HNC management over time<sup>29-31</sup>.

Keywords and subject headings, derived from previously conducted systematic reviews of

1  
2  
3 financial burden or toxicity in people affected by cancer<sup>9 23 26</sup> and the advice of the Deakin  
4  
5 University School of Health and Social Development liaison librarian include the following:  
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7 patient, family, carer, caregivers, cancer survivors, HNC, head and neck neoplasms, financial  
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9 burden, financial toxicity, financial stress, economic hardship, costs and cost analysis and  
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11 economics. An example search strategy is presented in Table 1.  
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16 [Insert Table 1]  
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19 Backwards and forwards citation tracing of included articles will be conducted for additional  
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21 literature unidentified by the search. Searches will be restricted to the English language  
22  
23 only. Search results will be downloaded into Thomson Reuters EndNote V. X9.2 (2019)  
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25 libraries and Rayyan software<sup>32</sup> will be used manage records throughout the review.  
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### 29 **Selection process**

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31 The titles and abstracts of the studies identified by the search will be screened  
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33 independently by one researcher to determine eligibility for inclusion in the review. Full text  
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35 articles will be retrieved when there is insufficient information to judge relevance.  
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39 Corresponding authors will be contacted to ascertain whether studies meet inclusion  
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41 criteria if necessary. Three other researchers will independently screen a subset of 30%  
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43 citations. Agreement between the reviewers will be assessed using the Kappa statistic to  
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45 determine if further duplicate title and abstract reviewing is required (Kappa <0.4, i.e. fair  
46  
47 agreement)<sup>33</sup>. An additional 25% of citations will be screened by all reviewers if required.  
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51 Any disagreement will be resolved by consensus amongst the team. The full text articles of  
52  
53 potentially eligible studies will be retrieved and independently assessed by three reviewers.  
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57 Any disagreement will be resolved by consensus amongst the team. Backwards and  
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3 forwards citation tracing of included articles will be conducted for additional literature  
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5 unidentified by the search.  
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### 8 **Risk of bias assessment**

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11 The methodological quality of the included studies will be evaluated independently by two  
12  
13 reviewers using appropriate critical appraisal checklists such as Larg & Moss's guide to  
14  
15 critical evaluation of cost-of-illness studies<sup>34</sup> and the *Strengthening the Reporting of*  
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17 *Observational Studies in Epidemiology* guidelines for observational studies<sup>35</sup>. Any  
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19 disagreement will be resolved by consensus amongst the team.  
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### 23 **Data collection**

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26 A table will be created in Microsoft Office Excel 2013 to extract data from the included  
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28 studies and summarise information about the constituents and magnitude of the financial  
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30 burden for people affected by HNC. This software will be used to handle data throughout  
31  
32 the review. The form will be piloted with two of the included articles and updated  
33  
34 accordingly. Extracted information will include study characteristics (first author's name,  
35  
36 publication date, country of origin, design), study population (age, gender, primary tumour  
37  
38 site, sample size), timeframe, and costs categorised in line with the recommendations of the  
39  
40 second panel on cost-effectiveness in health and medicine (formal health care sector,  
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42 informal health care sector and non-health care sectors)<sup>36</sup>. The views of a third reviewer will  
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44 be sought where there is ambiguity or disagreement.  
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### 51 **Data synthesis**

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54 A narrative synthesis of the included studies will be provided in accordance with guidance  
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56 from the Cochrane Collaboration<sup>37</sup>. A meta-analysis will not be conducted given the  
57  
58 anticipated heterogeneity between studies<sup>38</sup>. Three tables summarising the key features of  
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3 the included studies, cost components and quality assessment will be presented. Similarities  
4  
5 and differences between the studies and results will be reported and cost estimates will be  
6  
7 converted into 2020 Australian dollars using the CCEMG - EPPI-Centre Cost Converter<sup>39</sup>. If  
8  
9 feasible, average costs per category will be calculated and all costs will be converted to  
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11 annual figures to enable comparability. All relevant studies will be included in the review  
12  
13 and an assessment of how risk of bias may have affected the main results and outcome  
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15 measures will be presented. Finally, the strength of the body of evidence will be  
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17 independently assessed by two reviewers using the GRADE guidelines<sup>40</sup>. The views of a third  
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19 reviewer will be sought where there is ambiguity or disagreement.  
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## 26 **Ethics and dissemination**

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29 Ethics approval to conduct this research is not required because this study is a planned  
30  
31 systematic review of published literature. The protocol is registered with PROSPERO  
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33 (CRD42021252929). Findings will be presented at leading cancer and health economic  
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35 conferences, published in a peer-reviewed journal and disseminated via website postings  
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37 such as the Deakin University Institute for Health Transformation LinkedIn website and  
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39 social media channels such as Twitter (e.g. @DHE\_Deakin, @IHT\_Deakin) and Facebook.  
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52  
53 NM drafted the work and LE revised the protocol and manuscript critically for content. Both  
54  
55 authors approved the final version to be published and are accountable for all aspects of the  
56  
57 work. NM is the guarantor for the overall content.  
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**Open access**

**Table 1 EMBASE draft search strategy**

Concept 1	
S1	Patient*:ab,ti
S2	Family:ab,ti
S3	Carer*:ab,ti
S4	Caregiver*:ab,ti
S5	Survivor*:ab,ti
S6	Patient/de
S7	Family/de
S8	Caregiver/de
S9	"Cancer survivor"/de
Concept 2	
S10	((head OR neck OR "nasal cavity" OR "nasal cavities" OR "oral cavity" OR "oral cavities" OR larynx OR mouth OR pharynx OR "middle ear" OR "accessory sinuses" OR "accessory sinus") NEAR/4 (cancer OR cancers OR tumor OR tumors OR tumour OR tumours OR neoplasm OR neoplasms)):ab,ti
S11	Head/de
S12	Neck/de
S13	Mouth/de
S14	Pharynx/de
S15	"Nose Cavity"/de
S16	Ear/de
S17	Nose/de

S18	Larynx/de
S19	"Head and neck tumor"/de
<b>Concept 3</b>	
S20	"financial burden*":ab,ti
S21	"financial toxicit*":ab,ti
S22	"financial hardship*":ab,ti
S23	"financial stress*":ab,ti
S24	"financial distress*":ab,ti
S25	"material hardship*":ab,ti
S26	"out of pocket":ab,ti
S27	Bankruptcy:ab,ti
S28	Debt*:ab,ti
S29	"economic burden":ab,ti
S30	"economic hardship*":ab,ti
S31	cost*:ab,ti
S32	"Financial stress"/de
S33	"Financial management"/de
S34	Cost/de
S35	Economics/de
S36	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
S37	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
S38	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35
S39	#36 AND #37 AND #38
S40	#39 AND [2010-2021]/py
S41	#40 AND English: la

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06/07/21

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9 Dear Mr Aldcroft,

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11 **Re: Protocol for a systematic review of the financial burden experienced by people affected by**  
12 **head and neck cancer (HNC)**

13 We submit the above systematic review protocol manuscript for consideration for publication in  
14 your journal.  
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16 This systematic review protocol is reported according to the recommendations of the Preferred  
17 Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement, and is  
18 registered with the International Prospective Register of Systematic Reviews. i.e. PROSPERO  
19 (CRD42021252929).  
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22 The protocol manuscript describes a systematic review being undertaken to estimate out-of-  
23 pocket costs, reduced or lost income and informal care costs associated with HNC, and to  
24 investigate which costs predominate when considering financial burden in this population.  
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26 Although there is a growing body of research on financial burden among patients and families  
27 affected by cancer more generally, to our knowledge, there is no published systematic review  
28 investigating the financial burden experienced by people specifically affected by HNC. As  
29 socioeconomically deprived groups are disproportionately affected by HNC, managing financial  
30 burden is particular germane for people with this type of cancer. The systematic review findings  
31 will help inform the development of appropriate policies, programs and strategies for improving  
32 financial wellbeing in this population.  
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35 This protocol manuscript has not been published previously and is not under consideration for  
36 publication elsewhere. The article has been approved by all authors and the responsible  
37 authorities where the work was carried out, and if accepted, will not be published elsewhere.  
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40 Possible reviewers for this manuscript include Dr Alison Pearce, University of Sydney,  
41 (alison.pearce@sydney.edu.au), Professor Afaf Girgis, UNSW (girgisafaf@gmail.com) and  
42 Professor Claire Hulme, University of Exeter (C.T.Hulme@exeter.ac.uk).  
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45 We look forward to receiving your comments on the article in due course.

46 Yours sincerely

47  
48 Handwritten signature of Dr Nikki McCaffrey in black ink.

49  
50 **Nikki McCaffrey, PhD**

51 Senior Research Fellow (Health Economics – Cancer)

52 Deakin Health Economics, Faculty of Health, **Deakin University**

53 Deakin University CRICOS Provider Code 00113B

54 Telephone: +61 3 924 68767 Mobile: 04 4726 1668 Facs: +61 3 924 46261

55 Web Site: [www.deakin.edu.au/strategic-research/population-health/deakin-health-economics/](http://www.deakin.edu.au/strategic-research/population-health/deakin-health-economics/)  
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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Section of the manuscript
<b>ADMINISTRATIVE INFORMATION</b>			<b>Page numbers</b>
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	The title identifies the manuscript as a protocol of a systematic review (p1)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	The protocol is <i>not</i> an updated of a previous systematic review.
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	The protocol is registered with the International Prospective Register of Systematic Reviews, i.e. PROSPERO (CRD42021252929) (p2).
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	The names, institutional affiliations, e-mail addresses of all protocol authors and the physical mailing address of the corresponding author are provided (p1).
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	The contributions of the protocol authors and guarantor of the review are described (p10). "NM led the conception and design of the work with input from LE. NM drafted the work and LE revised the protocol and manuscript critically for content. Both authors approved the final version to be published and are accountable for all aspects of the work. NM is the guarantor for the overall content."
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	The protocol <i>does not</i> represent an amendment of a previously completed or published protocol. Important protocol amendments will be updated in the PROSPERO record. (p2)
Support:			
Sources	5a	Indicate sources of financial or other support for the review	There is no financial or other support for the review.
Sponsor	5b	Provide name for the review funder and/or sponsor	N/A

Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	<p>The rationale for the review is explained (pp5-6). "Financial burden has been associated with greater mortality risk, poorer quality of life (QOL), worse symptoms and reduced concordance with treatment advice. Consequently promoting financial wellbeing is a vital component of supportive care for people affected by cancer. Increasingly, clinical practice guidelines recommend discussion of the possible costs of cancer care and potential financial burden to patients and families, particularly in vulnerable groups such as low socioeconomic status populations. As socioeconomically deprived groups are disproportionately affected by HNC, managing financial burden is particular germane for people with this type of cancer. Whilst attempts have been made to summarise and quantify the financial burden experienced by people affected by cancer more generally, thus far, similar information for people impacted by HNC is lacking. Such information will help inform the development of appropriate policies, programs and strategies for improving financial wellbeing in this population."</p>
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<p>As described on page 6, "This systematic review addresses three related research questions:</p> <ol style="list-style-type: none"> <li>1. What is the financial burden faced by people affected by head and neck cancer?</li> <li>2. What are the main categories of out-of-pocket expenses faced by people affected by head and neck cancer?</li> <li>3. Which types of cost cause the greatest financial burden for people affected by head and neck cancer?"</li> </ol>
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	<p>The study characteristics and eligibility criteria are described (p7).        "Published, peer-reviewed, English-language articles reporting primary and secondary research directly related to the topic and quantitative cost data will be eligible for</p>

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			<p>inclusion in the systematic review.</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> <li>• Studies including people affected by HNC, i.e. patients, families and informal carers</li> <li>• Studies reporting and quantifying costs borne by patients and families; and</li> <li>• Primary and secondary research directly related to the topic, i.e. there will be no restrictions regarding research design.</li> </ul> <p>Exclusion criteria</p> <ul style="list-style-type: none"> <li>• Studies reporting qualitative data only;</li> <li>• Studies which do not report cost estimates;</li> <li>• Economic evaluations;</li> <li>• Non-English articles and those not peer reviewed, including comment or discussion papers, editorials, conference abstracts or papers and the grey literature.”</li> </ul>
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	The intended information sources are described in the methods (pp7-8). See also eligibility criteria above. “A comprehensive search of the literature will be conducted from January 1, 2010 to the date of the search (CINAHL; Cochrane library; Econlit; Embase; and MEDLINE Complete) to identify relevant published studies fitting the inclusion criteria. Backwards and forwards citation tracing of included articles will be conducted for additional literature unidentified by the search. Searches will be restricted to the English language only.” “Corresponding authors will be contacted to ascertain whether studies meet inclusion criteria if necessary”.
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	The draft Embase search strategy is presented in Table 1 (pp11-12), including the planned limits.
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Endnote, Rayyan and Excel will be used throughout the review to manage records and data (pp8-9)

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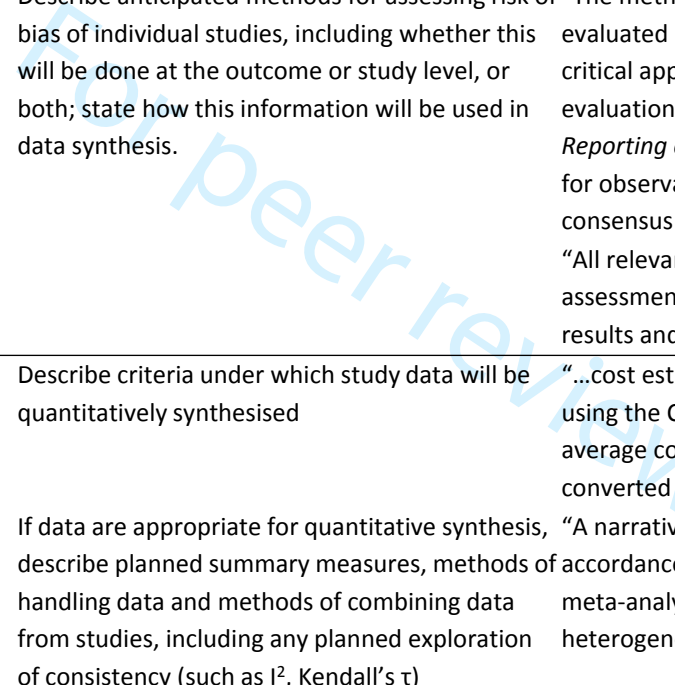
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	The process for selecting studies is described in the selection process (p8). "The titles and abstracts of the studies identified by the search will be screened independently by one researcher to determine eligibility for inclusion in the review. Full text articles will be retrieved when there is insufficient information to judge relevance. Corresponding authors will be contacted to ascertain whether studies meet inclusion criteria if necessary. Three other researchers will independently screen a subset of 30% citations. Agreement between the reviewers will be assessed using the Kappa statistic to determine if further duplicate title and abstract reviewing is required (Kappa <0.4, i.e. fair agreement). An additional 20% of citations will be screened by all reviewers if required. Any disagreement will be resolved by consensus amongst the team. The full text articles of potentially eligible studies will be retrieved and independently assessed by three reviewers. Any disagreement will be resolved by consensus amongst the team. Backwards and forwards citation tracing of included articles will be conducted for additional literature unidentified by the search."
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	"A table will be created in Microsoft Office Excel 2013 to extract data from the included studies and summarise information about the constituents and magnitude of the financial burden for people affected by HNC. This software will be used to handle data throughout the review. The form will be piloted with two of the included articles and updated accordingly...The views of a third reviewer will be sought where there is ambiguity or disagreement." (p9).
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	"Extracted information will include study characteristics (first author's name, publication date, country of origin, design), study population (age, gender, primary tumour site, sample size), timeframe, and costs categorised in line with the recommendations of the second panel on cost-effectiveness in health and medicine (formal, informal and non-health care)." (p9).
Outcomes and	13	List and define all outcomes for which data will be	costs categorised in line with the recommendations of the

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prioritization		sought, including prioritization of main and additional outcomes, with rationale.	second panel on cost-effectiveness health and medicine (formal, informal and non-health care)” to answer the review research questions (p9). “...cost estimates will be converted to 2020 Australian dollars using the CCEMG - EPPI-Centre Cost Converter (https://eppi.ioe.ac.uk/costconversion/default.aspx). If feasible, average costs per category will be calculated.” (p9).
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis.	“The methodological quality of the included studies will be evaluated independently by two reviewers using appropriate critical appraisal checklists such as Lorg & Moss’s guide to critical evaluation of cost-of-illness studies and the <i>Strengthening the Reporting of Observational Studies in Epidemiology</i> guidelines for observational studies. Any disagreement will be resolved by consensus amongst the team.” (p9) “All relevant studies will be included in the review and an assessment of how risk of bias may have affected the main results and outcome measures will be presented.” (p10)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	“...cost estimates will be converted to 2020 Australian dollars using the CCEMG - EPPI-Centre Cost Converter. If feasible, average costs per category will be calculated and all costs will be converted to annual figures to enable comparability..” (p9)
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall’s τ)	“A narrative synthesis of the included studies will be provided in accordance with guidance from the Cochrane Collaboration. A meta-analysis will not be conducted given the anticipated heterogeneity between studies.” (p9)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	There are no additional analyses proposed.
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	“A narrative synthesis of the included studies will be provided in accordance with guidance from the Cochrane Collaboration. A meta-analysis will not be conducted given the anticipated heterogeneity between studies.” (p9)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) - <a href="http://bmjopen.bmj.com/etabias(es).guidelines.xhtml">http://bmjopen.bmj.com/etabias(es).guidelines.xhtml</a>	As a meta-analysis is not planned given the anticipated heterogeneity between studies, there is no planned assessment of meta-bias(es).

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Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	The strength of the body of evidence will be assessed independently by two reviewers using the GRADE guidelines. The views of a third reviewer will be sought where there is ambiguity or disagreement. (p10).
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**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

## Protocol for a systematic review of the financial burden experienced by people affected by head and neck cancer

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055213.R1
Article Type:	Protocol
Date Submitted by the Author:	09-Dec-2021
Complete List of Authors:	McCaffrey, Nikki; Deakin University, Deakin Health Economics, School of Health and Social Development; Cancer Council Victoria Engel, Lidia; Deakin University, Deakin Health Economics, School of Health and Social Development
<b>Primary Subject Heading</b>:	Health economics
Secondary Subject Heading:	Oncology, Health policy
Keywords:	Head & neck tumours < ONCOLOGY, HEALTH ECONOMICS, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Manuscripts

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3 **Protocol for a systematic review of the financial burden experienced by**  
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9 **Running title:** Protocol of a systematic review of financial burden in head and neck cancer  
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12  
13 Nikki McCaffrey, PhD (corresponding author)  
14

15 Deakin University, Geelong, Deakin Health Economics, Institute for Health Transformation,  
16  
17 School of Health and Social Development, Victoria, Australia.  
18

19  
20 Cancer Council Victoria, 615 St Kilda Road, Melbourne, Victoria, Australia.  
21

22  
23 nikki.mccaffrey@deakin.edu.au  
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26 Phone 03 924 68767, mobile 04 4726 1668, fax 03 924 46261  
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29 Lidia Engel, PhD  
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31 Deakin University, Geelong, Deakin Health Economics, Institute for Health Transformation,  
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33 School of Health and Social Development, Victoria, Australia  
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36 **Number of figures:** 0  
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39 **Number of references:** 40  
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42 **Word count:** 1,548  
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45 **Abstract word count:** 290  
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48 **Keywords:** Financial burden, cost, carer, caregiver, head and neck cancer  
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51 **Number of pages:** 18  
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54 **Number of tables:** 0  
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57 **Supplemental file:** 1  
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3 **Ethics approval:** Ethics approval is not required to conduct this research because this is a  
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6 planned systematic review of published literature.  
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9 **Trial registration number:** CRD42021252929.  
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## Abstract

**Introduction:** Head and neck cancer is the seventh most common cancer worldwide.

Treatment may be associated with the inability to work and substantial out-of-pocket expenses. However, to date, there is little research synthesising quantitative evidence on the financial burden experienced by people affected by head and neck cancers (HNC), including family members and informal carers. The purpose of this systematic review is to estimate out-of-pocket costs, reduced or lost income and informal care costs associated with HNC, identify categories of financial burden and investigate which costs predominate when considering financial burden in this population.

**Methods and analysis:** A comprehensive search of peer-reviewed literature will be conducted for articles published from 01/01/2010 – 19/03/2021 (CINAHL; Cochrane library; Econlit; Embase; Medline Complete). Published, English-language articles describing primary and secondary research directly related to the topic and quantitative cost data will be included. One researcher will complete the searches and screen results for potentially eligible studies. Three other researchers will independently screen the titles and abstracts of a subset of 30% citations, i.e. 10% each. Full text articles will be independently screened by three reviewers. Any disagreement will be resolved by consensus among the team. Study and patient characteristics, cost categories and financial burden will be independently extracted by one reviewer and checked by a second. Methodological quality will be evaluated independently by two reviewers. Descriptive analyses will be undertaken and a narrative summary of the included studies will be provided.

**Ethics and dissemination:** Ethics approval is not required to conduct this research because this is a planned systematic review of published literature. Findings will be presented at

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3 leading cancer and health economic conferences, published in a peer-reviewed journal and  
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5 disseminated via website postings and social media channels.  
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9 **Systematic review registration number:** CRD42021252929  
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### 11 **Strengths and limitations of this study**

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15 • The planned systematic review will provide insights into the financial burden faced by  
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17 patients and families to inform the development of appropriate strategies for improving  
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19 financial wellbeing in people affected by head and neck cancer.  
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- 22 • The systematic review protocol is reported according to the recommendations of the  
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26 P) statement and is registered with the International Prospective Register of Systematic  
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28 Reviews (PROSPERO).  
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- 30 • The total number of studies investigating the financial burden experienced by people  
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32 affected by head and neck cancer may be small; study methods may be heterogeneous;  
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34 and cost estimates may be derived from diverse health financing systems, limiting study  
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## INTRODUCTION

Head and neck cancer (HNC) is ranked as one of the top ten cancers globally with over 850,000 new cases diagnosed each year<sup>1 2</sup>. Incidence is anticipated to continue rising with more than one million new cases each year predicted by 2030<sup>2</sup>. Generally, HNC begins in the squamous cells of the mouth, throat and nose and includes cancers of the oral cavity, nasal cavity and paranasal sinuses, salivary glands, pharynx and larynx<sup>3</sup> and thus far, there is no effective screening strategy for HNC. Meticulous physical examination is the key approach for early detection<sup>4</sup>. Treatment may involve chemotherapy, radiotherapy, surgery or typically, a combination of these approaches, particularly in later stages<sup>3</sup>. Many patients experience substantial functional impairment due to the location of the tumour, such as loss of speech, difficulties with swallowing and speech and challenges with eating<sup>5</sup> and symptoms associated with HNC and its treatment include pain, breathlessness, dry mouth, fatigue and depression<sup>6 7</sup>.

People affected by cancer can experience substantial out-of-pocket expenses associated with treatment costs, travel expenses, and reduced household income from a diminished ability to continue paid employment<sup>8 9</sup>. Informal carers, i.e. people who provide ongoing, regular assistance to a person with chronic, progressive, or life-limiting illness, typically without receiving payment for the assistance they provide<sup>10-12</sup> also report significant financial burden particularly related to reduced income and the costs of care time<sup>13 14</sup>. Financial burden has been associated with greater mortality risk, poorer quality of life (QOL), worse symptoms and reduced concordance with treatment advice<sup>15-18</sup>.

Consequently, promoting financial wellbeing is a vital component of supportive care for people affected by cancer. Increasingly, clinical practice guidelines recommend discussion of

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3 the possible costs of cancer care and potential financial burden to patients and families,  
4 particularly in vulnerable groups such as low socioeconomic status populations<sup>19</sup>. As  
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6 socioeconomically deprived groups are disproportionately affected by HNC<sup>20-22</sup>, managing  
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8 financial burden is particular germane for people with this type of cancer.  
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14 Whilst attempts have been made to summarise and quantify the financial burden  
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16 experienced by people affected by a broad range of cancer types<sup>8 23-27</sup>, thus far, such  
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18 information for people impacted by HNC is lacking. This information will help inform the  
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20 development of appropriate policies, programs and strategies for improving financial  
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22 wellbeing in this population. Consequently, the aim of this systematic review is to address  
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24 this gap in knowledge by synthesising evidence on the constituents and magnitude of  
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26 financial burden faced by patients and families affected by HNC.  
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### 31 32 **Review questions**

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35 This systematic review addresses three related research questions:  
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- 38 1. What is the financial burden faced by people affected by head and neck cancer?
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40 2. What are the main categories of out-of-pocket expenses faced by people affected by  
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42 head and neck cancer?
- 43  
44 3. Which types of cost cause the greatest financial burden for people affected by head and  
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46 neck cancer?  
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### 50 51 **METHODS**

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53 This protocol is reported according to the recommendations of the Preferred Reporting  
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55 Items for Systematic Reviews and Meta-Analyses statement<sup>28</sup>.  
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### 58 59 **Eligibility criteria**

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3 Published, peer-reviewed, English-language articles reporting primary and secondary  
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5 research directly related to the topic and quantitative cost data will be eligible for inclusion  
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7 in the systematic review.  
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#### 10 Inclusion criteria:

- 11 • Studies including people affected by HNC, i.e. patients, families and informal carers;
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- 14 • Studies reporting and quantifying costs borne by patients and families; and
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- 17 • Primary and secondary research directly related to the topic, i.e. there will be no
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#### Exclusion criteria

- Studies reporting qualitative data only;
- Studies which do not report cost estimates;
- Economic evaluations;
- Non-English articles and those not peer reviewed, including comment or discussion papers, editorials, conference abstracts or papers and the grey literature.

#### Search strategy

A comprehensive search of the literature will be conducted from January 1, 2010 to the date of the search (CINAHL; Cochrane library; Econlit; Embase; and MEDLINE Complete) to identify relevant published studies fitting the inclusion criteria. Studies published before 2010 were excluded due to more recent advances in HNC management which will affect the relative level of financial burden experienced by people by HNC.<sup>29-31</sup> Keywords and subject headings, derived from previously conducted systematic reviews of financial burden or

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3 toxicity in people affected by cancer<sup>9 23 26</sup> and the advice of the Deakin University School of  
4 Health and Social Development liaison librarian include the following: patient, family, carer,  
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6 caregivers, cancer survivors, HNC, head and neck neoplasms, financial burden, financial  
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8 toxicity, financial stress, economic hardship, costs and cost analysis and economics. The  
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10 search strategies are described in the online supplemental file.  
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16 Backwards and forwards citation tracing of included articles will be conducted for additional  
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18 literature unidentified by the search. Searches will be restricted to the English language  
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20 only. Search results will be downloaded into two Thomson Reuters EndNote V. X9.2 (2019)  
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22 libraries and Rayyan software<sup>32</sup> will be used to manage records throughout the review.  
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### 26 **Selection process**

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29 Step 1: The titles and abstracts of the studies identified by the search will be screened  
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31 independently by one researcher (SK) to determine eligibility for inclusion in the review. Full  
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33 text articles will be retrieved when there is insufficient information to judge relevance.  
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35 Corresponding authors will be contacted to ascertain whether studies meet inclusion  
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37 criteria if necessary. Three researchers (NM, LE, SA) will independently screen a subset of  
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39 30% citations, i.e. 10% each. Agreement between the reviewers will be assessed using the  
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41 Kappa statistic to determine if further duplicate title and abstract reviewing is required  
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43 (Kappa <0.4, i.e. fair agreement)<sup>33</sup>. If required, an additional 25% of citations will be  
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45 screened (NM, LE, SA).  
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52 Step 2: The full text articles of potentially eligible studies will be retrieved and  
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54 independently assessed by three reviewers (NM, LE, SK). Backwards and forwards citation  
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56 tracing of included articles will be conducted for additional literature unidentified by the  
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58 search.  
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3 Any disagreement will be resolved by consensus amongst the team.  
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### 6 **Risk of bias assessment**

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9 The methodological quality of the included studies will be evaluated independently by two  
10 reviewers (NM, LE) using Larg & Moss's guide to critical evaluation of cost-of-illness  
11 studies<sup>34</sup> and the *Strengthening the Reporting of Observational Studies in Epidemiology*  
12 guidelines for observational studies<sup>35</sup> critical appraisal checklists. Any disagreement will be  
13 resolved by consensus amongst the team.  
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### 22 **Data collection**

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24 A table will be created in Microsoft Office Excel 2013 to extract data from the included  
25 studies and summarise information about the constituents and magnitude of the financial  
26 burden for people affected by HNC. This software will be used to handle data throughout  
27 the review. The form will be piloted with two of the included articles and updated  
28 accordingly. Extracted information will include study characteristics (first author's name,  
29 publication date, country of origin, design, intervention), study population (age, gender,  
30 primary tumour site, sample size, subgroup), timeframe, costs categorised in line with the  
31 recommendations of the second panel on cost-effectiveness in health and medicine (formal  
32 health care sector, informal health care sector and non-health care sectors)<sup>36</sup>, and lost  
33 patient income and lost informal carer income. The views of a third reviewer (SA) will be  
34 sought where there is ambiguity or disagreement.  
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### 52 **Data synthesis**

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54 A narrative synthesis of the included studies will be provided in accordance with guidance  
55 from the Cochrane Collaboration<sup>37</sup>. A meta-analysis will not be conducted given the  
56 anticipated heterogeneity between studies<sup>38</sup>. Three tables summarising the key features of  
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3 the included studies, cost components and quality assessment will be presented. Similarities  
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5 and differences between the studies and results will be reported and cost estimates will be  
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7 converted into 2020 Australian dollars using the CCEMG - EPPI-Centre Cost Converter<sup>39</sup>. If  
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9 feasible, average costs per category will be calculated and all costs will be converted to  
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11 annual figures to enable comparability. All relevant studies will be included in the review  
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13 and an assessment of how risk of bias may have affected the main results and outcome  
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15 measures will be presented. Finally, the strength of the body of evidence will be  
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17 independently assessed by two reviewers (NM, LE) using the GRADE guidelines<sup>40</sup>. The views  
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19 of a third reviewer (SA) will be sought where there is ambiguity or disagreement.  
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## 26 **Ethics and dissemination**

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29 Ethics approval to conduct this research is not required because this study is a planned  
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31 systematic review of published literature. The protocol is registered with PROSPERO  
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33 (CRD42021252929). Findings will be presented at leading cancer and health economic  
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35 conferences, published in a peer-reviewed journal and disseminated via website postings  
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37 such as the Deakin University Institute for Health Transformation LinkedIn website and  
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39 social media channels such as Twitter (e.g. @DHE\_Deakin, @IHT\_Deakin) and Facebook.  
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44 **Patient or public involvement:** Patients or the public were not involved in the design, or  
45  
46 conduct, or reporting, or dissemination plans of our research.  
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56 abstracts.  
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4  
5 NM drafted the work and LE revised the protocol and manuscript critically for content. Both  
6  
7  
8 authors approved the final version to be published and are accountable for all aspects of the  
9  
10 work. NM is the guarantor for the overall content.

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16 **Open access**

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3 **Protocol for a systematic review of the financial burden experienced by people affected**  
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5 **by head and neck cancer**  
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9 **Database Search Strategies**  
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- 11 **1. CINAHL (VIA EBSCO)**
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**CINAHL via EBSCO****Concept 1**

- S1 TI patient\* OR AB patient\*
- S2 TI family OR AB family
- S3 TI families OR families
- S4 TI carer\* OR AB carer\*
- S5 TI caregiver\* OR AB caregiver\*
- S6 TI survivor\* OR AB survivor\*
- S7 (MH "patients") OR (MH "family") OR (MH "cancer survivors") OR (MH "caregivers")

**Concept 2**

- S8 TI ((head OR neck OR mouth OR pharynx OR "oral cavity" OR "oral cavities" OR "accessory sinuses" OR "accessory sinus" OR "nasal cavity" OR "nasal cavities" OR "middle ear" OR larynx) N4 (cancer\* OR tumo#r OR neoplasm\*)) OR AB ((head OR neck OR mouth OR pharynx OR "oral cavity" OR "oral cavities" OR "accessory sinuses" OR "accessory sinus" OR "nasal cavity" OR "nasal cavities" OR "middle ear" OR larynx) N4 (cancer\* OR tumo#r OR neoplasm\*))
- S9 (MH "head and neck neoplasms") OR (MH "head") OR (MH "neck") OR (MH "mouth") OR (MH "pharynx") OR (MH "nose") OR (MH "nasal cavity") OR (MH "ear") OR (MH "larynx")

**Concept 3**

- S10 TI "financial toxicity" OR AB "financial toxicity"
- S11 TI "financial toxicities" OR AB "financial toxicities"
- S12 TI "financial worry" OR AB "financial worry"
- S13 TI "financial worries" OR AB "financial worries"

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3 S14 TI “financial burden” OR AB “financial burden”  
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5 S15 TI “financial burdens” OR AB “financial burdens”  
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8 S16 TI “financial hardship\*” OR AB “financial hardship\*”  
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10 S17 TI “financial distress\*” OR AB “financial distress\*”  
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13 S18 TI “material hardship\*” OR AB “material hardship\*”  
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15 S19 TI “out of pocket” OR AB “out of pocket”  
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17  
18 S20 TI bankrupt\* OR AB bankrupt\*  
19  
20 S21 TI “economic burden\*” OR AB “economic burden\*”  
21  
22  
23 S22 TI “economic hardship\*” OR AB “economic hardship\*”  
24  
25 S23 TI debt\* OR AB debt\*  
26  
27 S24 TI cost\* OR AB cost\*  
28  
29  
30 S25 (MH “economics”) OR (MH “costs and cost analysis”) OR (MH “bankruptcy”) OR (MH  
31  
32 “Debt, financial”)  
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34  
35 S26 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7  
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37 S27 S8 OR S9  
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40 S28 S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR  
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42 S21 OR S22 OR S23 OR S24 OR S25  
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45 S29 S26 AND S27 AND S28  
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47 S30 Limit to English and 01/01/2010 – 19/03/21  
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**Cochrane Library via Wiley****Concept 1**

#1 MeSH descriptor: [Patients] this term only

#2 (patient\*):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#3 (family):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#4 (families):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#5 MeSH descriptor: [Family] this term only

#6 (carer\*):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#7 MeSH descriptor: [Caregivers] this term only

#8 (caregiver\*):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#9 (survivor\*):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#10 MeSH descriptor: [Cancer Survivors] this term only

**Concept 2**

#11 ((( (head OR neck OR mouth OR pharynx OR "oral cavity" OR "oral cavities" OR "accessory sinuses" OR "accessory sinus" OR "nasal cavity" OR "nasal cavities" OR "middle ear" OR larynx) Near/4 (cancer\* OR tumo?r\* OR neoplasm\*) ))):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar 2021

#12 MeSH descriptor: [Head] this term only

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3 #13 MeSH descriptor: [Neck] this term only  
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5 #14 MeSH descriptor: [Mouth] this term only  
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8 #15 MeSH descriptor: [Pharynx] this term only  
9  
10 #16 MeSH descriptor: [Nose] this term only  
11  
12 #17 MeSH descriptor: [Nasal Cavity] this term only  
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14  
15 #18 MeSH descriptor: [Ear] this term only  
16  
17 #19 MeSH descriptor: [Larynx] this term only  
18  
19 #20 MeSH descriptor: [Head and Neck Neoplasms] this term only  
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21  
22 #21 MeSH descriptor: [Squamous Cell Carcinoma of Head and Neck] this term only  
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### Concept 3

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27 #22 ("financial toxicity"):ti,ab,kw with Cochrane Library publication date Between Jan  
28  
29 2010 and Mar 2021  
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31 #23 ("financial toxicities"):ti,ab,kw with Cochrane Library publication date Between Jan  
32  
33 2010 and Mar 2021  
34  
35 #24 ("financial worries"):ti,ab,kw with Cochrane Library publication date Between Jan  
36  
37 2010 and Mar 2021  
38  
39 #25 ("financial worry"):ti,ab,kw with Cochrane Library publication date Between Jan 2010  
40  
41 and Mar 2021  
42  
43 #26 ("financial burden"):ti,ab,kw with Cochrane Library publication date Between Jan  
44  
45 2010 and Mar 2021  
46  
47 #27 ("financial burden\*"):ti,ab,kw  
48  
49 #28 ("financial hardship"):ti,ab,kw with Cochrane Library publication date Between Jan  
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51 2010 and Mar 2021  
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3 #29 ("financial hardship\*"):ti,ab,kw with Cochrane Library publication date Between Jan  
4  
5 2010 and Mar 2021  
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8 #30 ("financial stress"):ti,ab,kw with Cochrane Library publication date Between Jan 2010  
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10 and Mar 2021  
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13 #31 ("financial distress"):ti,ab,kw with Cochrane Library publication date Between Jan  
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15 2010 and Mar 2021  
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18 #32 ("material hardship"):ti,ab,kw with Cochrane Library publication date Between Jan  
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20 2010 and Mar 2021  
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23 #33 ("material hardship\*"):ti,ab,kw with Cochrane Library publication date Between Jan  
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25 2010 and Jan 2021  
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28 #34 ("out of pocket"):ti,ab,kw with Cochrane Library publication date Between Jan 2010  
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30 and Mar 2021  
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33 #35 (bankrupt\*):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and  
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35 Mar 2021  
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38 #36 ("economic burden"):ti,ab,kw with Cochrane Library publication date Between Jan  
39  
40 2010 and Mar 2021  
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43 #37 ("economic burden\*"):ti,ab,kw with Cochrane Library publication date Between Jan  
44  
45 2010 and Jan 2021  
46  
47  
48 #38 ("economic hardship"):ti,ab,kw with Cochrane Library publication date Between Jan  
49  
50 2010 and Mar 2021  
51  
52  
53 #39 ("economic hardship\*"):ti,ab,kw with Cochrane Library publication date Between Jan  
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55 2010 and Jan 2021  
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57  
58 #40 (debt OR debtor OR debts):ti,ab,kw with Cochrane Library publication date Between  
59  
60 Jan 2010 and Mar 2021

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3 #41 (cost\*):ti,ab,kw with Cochrane Library publication date Between Jan 2010 and Mar  
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5 2021  
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8 #42 MeSH descriptor: [Costs and Cost Analysis] this term only  
9

10 #43 MeSH descriptor: [Economics] this term only  
11

12  
13 #44 ("costs and cost analysis"):ti,ab,kw with Cochrane Library publication date Between  
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15 Jan 2010 and Mar 2021  
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17 #45 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10  
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20 #46 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21  
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22 #47 #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32  
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**EconLit via EBSCO****Concept 1**

- S1 TI patient\* OR AB patient\*
- S2 TI family OR AB family
- S3 TI families OR families
- S4 TI carer\* OR AB carer\*
- S5 TI caregiver\* OR AB caregiver\*
- S6 TI survivor\* OR AB survivor\*

**Concept 2**

- S7 TI ((head OR neck OR mouth OR pharynx OR "oral cavity" OR "oral cavities" OR "accessory sinuses" OR "accessory sinus" OR "nasal cavity" OR "nasal cavities" OR "middle ear" OR larynx) N4 (cancer\* OR tumo#r OR neoplasm\*)) OR AB ((head OR neck OR mouth OR pharynx OR "oral cavity" OR "oral cavities" OR "accessory sinuses" OR "accessory sinus" OR "nasal cavity" OR "nasal cavities" OR "middle ear" OR larynx) N4 (cancer\* OR tumo#r OR neoplasm\*))

**Concept 3**

- S8 TI "financial toxicity" OR AB "financial toxicity"
- S9 TI "financial toxicities" OR AB "financial toxicities"
- S10 TI "financial worry" OR AB "financial worry"
- S11 TI "financial worries" OR AB "financial worries"
- S12 TI "financial burden" OR AB "financial burden"
- S13 TI "financial burdens" OR AB "financial burdens"
- S14 TI "financial hardship\*" OR AB "financial hardship\*"
- S15 TI "financial distress\*" OR AB "financial distress\*"

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3 S16 TI “material hardship\*” OR AB “material hardship\*”  
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6 S17 TI “out of pocket” OR AB “out of pocket”  
7  
8 S18 TI bankrupt\* OR AB bankrupt\*  
9  
10  
11 S19 TI “economic burden\*” OR AB “economic burden\*”  
12  
13 S20 TI “economic hardship\*” OR AB “economic hardship\*”  
14  
15 S21 TI debt\* OR AB debt\*  
16  
17 S22 TI cost\* OR AB cost\*  
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20 S23 S1 OR S2 OR S3 OR S4 OR S5 OR S6  
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23 S24 S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR  
24  
25 S19 OR S20 OR S21 OR S22  
26  
27 S25 S7 AND S23 AND S24  
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30 S26 Limit to English and 01/01/2010 – 19/03/21  
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**EMBASE via Elsevier****Concept 1**

S1 Patient\*:ab,ti

S2 Family:ab,ti

S3 Carer\*:ab,ti

S4 Caregiver\*:ab,ti

S5 Survivor\*:ab,ti

S6 Patient/de

S7 Family/de

S8 Caregiver/de

S9 "Cancer survivor"/de

**Concept 2**

S10 ((head OR neck OR "nasal cavity" OR "nasal cavities" OR "oral cavity" OR "oral cavities" OR larynx OR mouth OR pharynx OR "middle ear" OR "accessory sinuses" OR "accessory sinus") NEAR/4 (cancer OR cancers OR tumor OR tumors OR tumour OR tumours OR neoplasm OR neoplasms)):ab,ti

S11 Head/de

S12 Neck/de

S13 Mouth/de

S14 Pharynx/de

S15 "Nose Cavity"/de

S16 Ear/de

S17 Nose/de

S18 Larynx/de

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3 S19 "Head and neck tumor"/de  
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6 **Concept 3**  
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8 S20 "financial burden\*":ab,ti  
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10 S21 "financial toxicit\*":ab,ti  
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12 S22 "financial hardship\*":ab,ti  
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14 S23 "financial stress\*":ab,ti  
15

16 S24 "financial distress\*":ab,ti  
17

18 S25 "material hardship\*":ab,ti  
19

20 S26 "out of pocket":ab,ti  
21

22 S27 Bankruptcy:ab,ti  
23

24 S28 Debt\*:ab,ti  
25

26 S29 "economic burden":ab,ti  
27

28 S30 "economic hardship\*":ab,ti  
29

30 S31 cost\*:ab,ti  
31

32 S32 "Financial stress"/de  
33

34 S33 "Financial management"/de  
35

36 S34 Cost/de  
37

38 S35 Economics/de  
39

40 S36 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9  
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42 S37 #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19  
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44 S38 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30  
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46 OR #31 OR #32 OR #33 OR #34 OR #35  
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48 S39 #36 AND #37 AND #38  
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**MEDLINE Complete via EBSCO****Concept 1**

S1 AB (Patient\* OR "family members" OR family OR families OR carer\* OR caregiver\* OR survivor\*) OR TI (Patient\* OR "family members" OR family OR families OR carer\* OR caregiver\* OR survivor\*)

S2 (MH "patients") OR (MH "family") OR (MH "cancer survivors") OR (MH "caregivers")

**Concept 2**

S3 AB (Head OR Neck" OR "oral cavity" OR pharynx OR "nasal cavities" OR "nasal cavity" OR "middle ear" OR "accessory sinuses" OR larynx OR mouth) OR TI (Head OR Neck" OR "oral cavity" OR pharynx OR "nasal cavities" OR "nasal cavity" OR "middle ear" OR "accessory sinuses" OR larynx OR mouth)

S4 (MH "Head and neck neoplasms") OR (MH "Head") OR (MH "Neck") OR (MH "Mouth") OR (MH "Pharynx") OR MH (Nasal Cavity") OR (MH "Ear") OR (MH "Nose") OR (MH "Larynx")

**Concept 3**

S5 AB ("Financial burden" OR "financial burdens" OR "financial toxicity" OR "financial toxicities" OR "financial hardship" OR "financial hardships" OR "financial stress" OR "financial stresses" OR "financial distress" OR "financial distresses" OR "material hardship" OR "material hardships" OR "out of pocket" OR bankruptcy OR debt OR debts OR "economic burden" OR "economics burdens" OR "economic hardship" or "economic hardships" OR cost\*) OR TI ("Financial burden" OR "financial burdens" OR "financial toxicity" OR "financial toxicities" OR "financial hardship" OR "financial hardships" OR "financial stress" OR "financial stresses" OR "financial distress" OR "financial distresses" OR "material hardship" OR "material hardships" OR "out of pocket" OR bankruptcy OR debt OR debts OR "economic

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3 burden" OR "economics burdens" OR "economic hardship" or "economic hardships" OR  
4  
5 cost\*)

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7  
8 S6 (MH "Financial stress") OR (MH "Bankruptcy") OR (MH "Costs and cost analysis") OR  
9  
10 (MH "economics")

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12  
13 S7 S1 OR S2

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15 S8 S3 OR S4

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17 S9 S5 OR S6

18  
19 S10 S7 AND S8 AND S9

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21 S11 S10 limited to English and 01/01/2010 – 19/03/21  
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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Section of the manuscript
<b>ADMINISTRATIVE INFORMATION</b>			<b>Page numbers</b>
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	The title identifies the manuscript as a protocol of a systematic review (p1)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	The protocol is <i>not</i> an updated of a previous systematic review.
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	The protocol is registered with the International Prospective Register of Systematic Reviews, i.e. PROSPERO (CRD42021252929) (p2).
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	The names, institutional affiliations, e-mail addresses of all protocol authors and the physical mailing address of the corresponding author are provided (p1).
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	The contributions of the protocol authors and guarantor of the review are described (p10). "NM led the conception and design of the work with input from LE. NM drafted the work and LE revised the protocol and manuscript critically for content. Both authors approved the final version to be published and are accountable for all aspects of the work. NM is the guarantor for the overall content."
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	The protocol <i>does not</i> represent an amendment of a previously completed or published protocol. Important protocol amendments will be updated in the PROSPERO record. (p2)
Support:			
Sources	5a	Indicate sources of financial or other support for the review	There is no financial or other support for the review.
Sponsor	5b	Provide name for the review funder and/or sponsor	N/A

1	Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
2	<b>INTRODUCTION</b>			
3	Rationale	6	Describe the rationale for the review in the context of what is already known	The rationale for the review is explained (pp5-6). "Financial burden has been associated with greater mortality risk, poorer quality of life (QOL), worse symptoms and reduced concordance with treatment advice. Consequently promoting financial wellbeing is a vital component of supportive care for people affected by cancer. Increasingly, clinical practice guidelines recommend discussion of the possible costs of cancer care and potential financial burden to patients and families, particularly in vulnerable groups such as low socioeconomic status populations. As socioeconomically deprived groups are disproportionately affected by HNC, managing financial burden is particular germane for people with this type of cancer. Whilst attempts have been made to summarise and quantify the financial burden experienced by people affected by cancer more generally, thus far, similar information for people impacted by HNC is lacking. Such information will help inform the development of appropriate policies, programs and strategies for improving financial wellbeing in this population."
4	Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	As described on page 6, "This systematic review addresses three related research questions: 1. What is the financial burden faced by people affected by head and neck cancer? 2. What are the main categories of out-of-pocket expenses faced by people affected by head and neck cancer? 3. Which types of cost cause the greatest financial burden for people affected by head and neck cancer?"
5	<b>METHODS</b>			
6	Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	The study characteristics and eligibility criteria are described (p7). "Published, peer-reviewed, English-language articles reporting primary and secondary research directly related to the topic and quantitative cost data will be eligible for

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			<p>inclusion in the systematic review.</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> <li>• Studies including people affected by HNC, i.e. patients, families and informal carers</li> <li>• Studies reporting and quantifying costs borne by patients and families; and</li> <li>• Primary and secondary research directly related to the topic, i.e. there will be no restrictions regarding research design.</li> </ul> <p>Exclusion criteria</p> <ul style="list-style-type: none"> <li>• Studies reporting qualitative data only;</li> <li>• Studies which do not report cost estimates;</li> <li>• Economic evaluations;</li> <li>• Non-English articles and those not peer reviewed, including comment or discussion papers, editorials, conference abstracts or papers and the grey literature.”</li> </ul>
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	The intended information sources are described in the methods (pp7-8). See also eligibility criteria above. “A comprehensive search of the literature will be conducted from January 1, 2010 to the date of the search (CINAHL; Cochrane library; Econlit; Embase; and MEDLINE Complete) to identify relevant published studies fitting the inclusion criteria. Backwards and forwards citation tracing of included articles will be conducted for additional literature unidentified by the search. Searches will be restricted to the English language only.” “Corresponding authors will be contacted to ascertain whether studies meet inclusion criteria if necessary”.
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	The draft Embase search strategy is presented in Table 1 (pp11-12), including the planned limits.
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Endnote, Rayyan and Excel will be used throughout the review to manage records and data (pp8-9)

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	The process for selecting studies is described in the selection process (p8). "The titles and abstracts of the studies identified by the search will be screened independently by one researcher to determine eligibility for inclusion in the review. Full text articles will be retrieved when there is insufficient information to judge relevance. Corresponding authors will be contacted to ascertain whether studies meet inclusion criteria if necessary. Three other researchers will independently screen a subset of 30% citations. Agreement between the reviewers will be assessed using the Kappa statistic to determine if further duplicate title and abstract reviewing is required (Kappa <0.4, i.e. fair agreement). An additional 20% of citations will be screened by all reviewers if required. Any disagreement will be resolved by consensus amongst the team. The full text articles of potentially eligible studies will be retrieved and independently assessed by three reviewers. Any disagreement will be resolved by consensus amongst the team. Backwards and forwards citation tracing of included articles will be conducted for additional literature unidentified by the search."
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	"A table will be created in Microsoft Office Excel 2013 to extract data from the included studies and summarise information about the constituents and magnitude of the financial burden for people affected by HNC. This software will be used to handle data throughout the review. The form will be piloted with two of the included articles and updated accordingly...The views of a third reviewer will be sought where there is ambiguity or disagreement." (p9).
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	"Extracted information will include study characteristics (first author's name, publication date, country of origin, design), study population (age, gender, primary tumour site, sample size), timeframe, and costs categorised in line with the recommendations of the second panel on cost-effectiveness in health and medicine (formal, informal and non-health care)." (p9).
Outcomes and	13	List and define all outcomes for which data will be	costs categorised in line with the recommendations of the

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prioritization		sought, including prioritization of main and additional outcomes, with rationale.	second panel on cost-effectiveness health and medicine (formal, informal and non-health care)” to answer the review research questions (p9). “...cost estimates will be converted to 2020 Australian dollars using the CCEMG - EPPI-Centre Cost Converter (https://eppi.ioe.ac.uk/costconversion/default.aspx). If feasible, average costs per category will be calculated.” (p9).
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis.	“The methodological quality of the included studies will be evaluated independently by two reviewers using appropriate critical appraisal checklists such as Lorg & Moss’s guide to critical evaluation of cost-of-illness studies and the <i>Strengthening the Reporting of Observational Studies in Epidemiology</i> guidelines for observational studies. Any disagreement will be resolved by consensus amongst the team.” (p9) “All relevant studies will be included in the review and an assessment of how risk of bias may have affected the main results and outcome measures will be presented.” (p10)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	“...cost estimates will be converted to 2020 Australian dollars using the CCEMG - EPPI-Centre Cost Converter. If feasible, average costs per category will be calculated and all costs will be converted to annual figures to enable comparability..” (p9)
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall’s τ)	“A narrative synthesis of the included studies will be provided in accordance with guidance from the Cochrane Collaboration. A meta-analysis will not be conducted given the anticipated heterogeneity between studies.” (p9)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	There are no additional analyses proposed.
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	“A narrative synthesis of the included studies will be provided in accordance with guidance from the Cochrane Collaboration. A meta-analysis will not be conducted given the anticipated heterogeneity between studies.” (p9)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) - <a href="http://bmjopen.bmj.com/etabias(es).guidelines.xhtml">http://bmjopen.bmj.com/etabias(es).guidelines.xhtml</a>	As a meta-analysis is not planned given the anticipated heterogeneity between studies, there is no planned assessment of meta-bias(es).

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Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	The strength of the body of evidence will be assessed independently by two reviewers using the GRADE guidelines. The views of a third reviewer will be sought where there is ambiguity or disagreement. (p10).
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**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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