# Aspects of emotional functioning following oesophageal cancer surgery in a population-based cohort study

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#### **Abstract**

*Objective*: The aim of this study was to establish the proportion of patients reporting emotional problems following oesophagectomy for cancer and identify the risk characteristics for emotional problems.

Methods: A Swedish population-based cohort study of patients with surgically treated oesophageal cancer was used. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 was used to assess tension, worry, irritation and depressed mood at 6 months and 5 years after surgery. Potential risk characteristics were retrieved from medical notes and data linkages to Swedish health registries. Multivariable logistic regression analyses were performed to examine risk characteristics for poor emotional recovery.

Results: Of 401 patients included at 6 months, 49% reported problems with tension, 61% worry, 62% irritation and 63% depressed mood. Of the 140 (35%) patients who completed the 5-year follow-up, 39% reported problems with tension and about half of the patients reported problems with worry, irritation, and depressed mood (49, 45 and 52%, respectively). Squamous cell carcinoma was identified as a risk characteristic for tension (OR 2.15, 95% CI 1.30–3.55), worry (OR 2.02, 95% CI 1.19–3.40) and depressed mood (OR 1.71, 95% CI 1.01–2.90) at 6 months compared with adenocarcinoma. Compared with higher education, lower education was associated with tension (upper secondary schooling: OR 1.97, 95% CI 1.02–3.79 and 9-year compulsory: OR 2.46, 95% CI 1.28–4.74), while non-cohabitating patients were less likely to report problems with worry at 6 months (OR 0.53, 95% CI 0.34-0.84) compared with cohabitating patients.

Conclusions: A substantial proportion of patients reports emotional problems following oesophagectomy, and risk characteristics include squamous cell carcinoma histology and low educational level. Copyright © 2014 John Wiley & Sons, Ltd.

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## Introduction

Oesophageal cancer is one of the most devastating cancer diseases worldwide. The overall survival is poor (<15% in Europe) [1] with only 25% of patients eligible for potentially curative surgery [2]. Oesophagectomy, often in combination with neoadjuvant therapy, is the most established curatively intended treatment to date [3]. The postoperative 5-year survival rate is only approximately 31%, and the risk of death from tumour recurrence is the highest during the first year postoperatively [4]. Oesophagectomy is an extensive surgical procedure and is associated with severe postoperative complications [5] and significantly impaired health-related quality of life (HRQOL), both in the short term and long term [6,7].

Indications of the psychological trauma experienced by patients with oesophageal cancer have recently been published in a large-scale Swedish cohort study [8]. These findings showed an increased risk of suicide following a

diagnosis of oesophageal cancer, with the highest risk observed within the first 12 weeks postdiagnosis. In addition, interview studies with survivors of oesophageal cancer have described the shock of receiving the diagnosis as 'coping with a death sentence' [9]. Uncertainty about the future following the operation and 'loss of control' has also been reported in interviews with long-term survivors [10]. Further, there is growing evidence of elevated symptoms of anxiety and depression from the time of diagnosis throughout the first year of illness [11]. However, the emotional adjustment following oesophageal cancer surgery has not been longitudinally studied in large-scale representative cohort studies [12]. Therefore, we aimed to establish the proportion of patients reporting problems with aspects of emotional functioning at 6 months and 5 years after oesophageal cancer surgery and to determine the risk characteristics for problems on these aspects, in a prospective and population-based cohort of patients with surgically treated oesophageal cancer.

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## **Methods**

### Data source

Data were drawn from the Swedish Oesophageal and Cardia Cancer database (SECC), a prospective nationwide population-based cohort study including 90% of all patients treated with oesophageal resection for cancer in Sweden between 2 April 2001 and 31 December 2005. Patients were identified through a nationwide network of clinicians at 174 hospital departments in Sweden who treated patients diagnosed with oesophageal cancer during this time period. Full details of the organization of the comprehensive network [13] and the design of the HRQOL research in the SECC have been described elsewhere [14]. In brief, patients were followed up with measures of HRQOL, to complete and return by post, including assessments at 6 months and 5 years following surgery. Informed consent was obtained from all patients, and the study was approved by the Regional Ethical Review Board in Stockholm, Sweden.

### Clinical characteristics

An extensive review of the prospectively collected medical records from histopathological, endoscopic and surgical units was performed in accordance with a predefined study protocol, in order to collect data on patient (age, sex, and body mass index) and tumour (stage, histologic type, and site) characteristics, as well as treatment (neoadjuvant therapy and surgical details) and predefined complications within 30 days of surgery. Tumours near the gastroesophageal junction were classified according to Siewert's definition [15], and tumour stage was classified according to International Union Against Cancer [16].

# Sociodemographic characteristics

Information on the sociodemographic variables education level and marital status was obtained through record linkage with the nationwide Swedish Population and Housing Census and the longitudinal integration database for health insurance and labour market studies (LISA) [17], held by Statistics Sweden. The individual record linkage between the SECC and the LISA was enabled by virtue of the unique personal identity number, assigned to all Swedish residents. Data on sociodemographic variables were collected for each patient as close to the date of operation as possible.

## Aspects of emotional functioning

Emotional functioning was assessed at 6 months and 5 years after oesophagectomy. The emotional functioning scale is one of four functioning scales within the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30)

[18]. This scale consists of four targeted questions assessing tension ('did you feel tense'), worry ('did you worry'), irritation ('did you feel irritable'), and depressed mood ('did you feel depressed') during the past week. Each item is scored on a four-point scale: (1) 'not at all', (2) 'a little', (3) 'quite a bit', and (4) 'very much'. These four items represent the aspects of emotional functioning evaluated in the present study. The EORTC QLQ-C30 is a widely used questionnaire with good validity and reliability [18]. When screening for symptoms of anxiety and depression in different cancer groups, the overlap between the emotional functioning scale on the QLQ-C30 and the Hospital Anxiety and Depression Scale (HADS) [19] has repeatedly been shown [20–22].

# Statistical analyses

For the purposes of the present study, the four items comprising the emotional functioning scale from the EORTC QLQ-C30 were included in the statistical analyses. Patients were grouped into reporting no problems (score of 1) or problems (scores of 2–4) on each of the four aspects of emotional functioning, that is, tension, worry, irritation and depressed mood, at 6 months and 5 years following oesophageal cancer surgery. Baseline characteristics of the patients were assessed using chi-square test between the two groups, that is, problems versus no problems, on each aspect of the emotional functioning scale. Multivariable logistic regression, providing odds ratios (ORs) with 95% confidence intervals (CIs), was used to assess the association between clinical and sociodemographic characteristics and problems with tension, worry, irritation and depressed mood, at 6 months and 5 years postsurgery. P-values less than 0.05 were considered as statistically significant. The multivariable model included age (categorised into <60, 60-74, or >75 years old), sex (male or female), tumour stage (0–I, II, or III–IV), tumour histology (adenocarcinoma or squamous cell carcinoma), education (9-year compulsory schooling, upper secondary schooling, or higher education), and marital status (non-cohabitating [never married or widowed/divorced] or cohabitating [married or remarried]). Patients with missing data were excluded from the analyses. The statistical software programme SAS (version 9.2, SAS Institute Inc, Cary, NC) for Windows was used for all statistical analyses.

## **Results**

# Patient characteristics

Throughout the study period, 616 patients underwent curatively intended surgery for oesophageal cancer. Of these, 110 (18%) patients died between surgery and 6-month follow-up and therefore were not eligible for inclusion. Among the 506 patients eligible for 6-month follow-up, 104 (21%) patients declined to answer the

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HRQOL questionnaire, and one patient was excluded because of missing data on the item assessing depressed mood in the EORTC QLQ-C30. The remaining 401 (79%) patients were included in the analyses performed on data collected at 6 months following surgery. A further 248 (49%) patients died before the 5-year follow-up, leaving 153 eligible patients. Of these, 12 patients (8%) declined to answer the HRQOL questionnaire at 5 years, and one patient was excluded because of missing data on the item assessing worry on the EORTC QLQ-C30. The remaining 140 (92%) patients were included in the 5-year analyses. There were no statistically significant differences between responders and non-responders at 6 months and 5 years on any of the baseline clinical or sociodemographic characteristics (data not shown).

Baseline characteristics of the total sample at 6 months (n=401) are presented in Table 1. The majority of the patients were male (81%) and aged between 60 and 74 years old (58%). The most common histological type was adenocarcinoma (76%), and most patients were diagnosed with tumour stages II or III (70%). Patients were predominantly cohabitating (66%) and had low educational attainment (9-year compulsory, 46%).

# Clinical and sociodemographic characteristics in relation to aspects of emotional functioning at 6 months postsurgery

Almost half of the patients reported problems with tension at 6 months (n = 195, 49%), whereas nearly two thirds of

**Table 1.** Clinical and sociodemographic characteristics of oesophageal cancer patients 6 months postsurgery

Characteristic, n (%)	Total sample (n = 401)
Sex	
Female	75 (19)
Male	326 (81)
Age	
>74	69 (17)
60–74	231 (58)
<60	101 (25)
Tumour histology	
Adenocarcinoma	303 (76)
Squamous cell carcinoma	98 (24)
Tumour stage <sup>a</sup>	
IV	33 (9)
III	160 (40)
II	120 (30)
0–I	84 (21)
Marital status <sup>a</sup>	
Cohabitating	264 (66)
Non-cohabitating	133 (34)
Education level <sup>a</sup>	. ,
Higher education	58 (15)
Upper secondary schooling	153 (39)
Nine-year compulsory	183 (46)

n = number.

patients reported problems with worry, irritation, and depressed mood (n = 246, 61%; n = 248, 62%; and n = 251, 63%, respectively).

After adjusting for the other clinical and sociodemographic variables, patients with squamous cell carcinoma had about twofold higher odds of reporting problems with tension (OR 2.15, 95% CI 1.30–3.55), worry (OR 2.02, 95% CI 1.19-3.40), and depressed mood (OR 1.71, 95% CI 1.01–2.90) at 6 months compared with patients with adenocarcinoma (Table 2). Patients with fewer years of education, that is, 9-year compulsory and upper secondary schooling, were more likely to report problems with tension (OR 2.46, 95% CI 1.28-4.74 and OR 1.97, 95% CI 1.02-3.79, respectively) than patients with higher education. Compared with cohabitating patients, non-cohabitating was associated with decreased odds of reporting problems with worry (OR 0.53, 95% CI 0.34–0.84). No statistically significant associations were observed between sex, age and tumour stage, and the four aspects of emotional functioning at 6 months (Table 2).

# Clinical and sociodemographic characteristics in relation to aspects of emotional functioning at 5 years postsurgery

At 5 years, 39% (n = 55) of the patients reported problems with tension, and almost half of the patients reported problems with worry, irritation, and depressed mood (n = 69), 49%; n = 63, 45%; and n = 73, 52%, respectively). Noncohabiting patients were less likely to report problems with worry (OR 0.35, 95% CI 0.15-0.84) compared with cohabitating patients. No other statistically significant associations were observed between any of the clinical or sociodemographic characteristics and these four aspects of emotional functioning at 5 years after adjustment for potential confounding factors (Table 2). Of patients with complete data on both the 6-month and 5-year assessments (n=116), approximately two thirds of patients reporting emotional problems at 5 years had also reported problems at 6 months (65, 62, 63 and 69% for tension, worry, irritation and depressed mood, respectively). However, a minority of patients who did not report problems at 6 months did report problems with tension (15%), worry (18%), irritation (16%) and depressed (24%) mood at 5 years following surgery.

## **Discussion**

This study of surgically treated oesophageal cancer patients shows that a substantial proportion of patients report problems with tension, worry, irritation and depressed mood at 6 months following surgery, which appear to persist in the majority of patients at 5 years. Of the clinical and sociodemographic characteristics assessed, histological type, marital status and educational level emerged as statistically significantly associated with

<sup>&</sup>lt;sup>a</sup>Missing data: tumour stage n = 4, marital status n = 4, and education level n = 7.

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**Table 2.** Associations expressed as odds ratios (ORs) with 95% confidence intervals (CIs) between clinical and sociodemographic characteristics and aspects of emotional functioning, that is, tension, worry, irritation and depressed mood, from the EORTC QLQ-C30 at 6 months and 5 years following oesophagectomy for cancer

enstic		ODICINS AL O MONCHE	Problems at 6 months postsurgery $(n=401)$	(10		Froblems at 3 years postsurgery (n = 140)	postsurgery (II = II+	(1
acteristic nale	Tension	Worry	Irritation	Depressed mood	Tension	Worry	Irritation	Depressed mood
male	(n = 195, 49%) OR $(95\% \text{ CI})^3$	(n = 246, 61%) OR $(95\% \text{ CI})^3$	(n = 248, 62%) OR (95% CI) <sup>a</sup>	(n = 251, 63%) OR (95% CI) <sup>a</sup>	(n = 55, 39%) OR (95% CI) <sup>a</sup>	(n = 69, 49%) OR $(95\% \text{ CI})^3$	(n = 63, 45%) OR (95% CI) <sup>a</sup>	(n = 73, 52%) OR (95% CI) <sup>a</sup>
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		0.1	0.1	0.1	0.1	0.1	0.1	0.1
Male 1.33	1.33 (0.77–2.28)	1.20 (0.69–2.08)	1.15 (0.66–1.98)	0.78 (0.45–1.37)	0.82 (0.33–2.04)	0.76 (0.3–1.90)	2.11 (0.81–5.50)	0.49 (0.17–1.16)
Age, years								
>74		0.1	0.1	0.1	0.1	0.1	0.1	0.1
60–74	0.87 (0.49-1.54)	1.01 (0.57–1.79)	0.85 (0.47-1.52)	0.90 (0.5–1.62)	0.54 (0.15–1.96)	0.28 (0.07–1.13)	1.03 (0.25-4.18)	0.93 (0.26–3.38)
<60 1.85	1.85 (0.95–3.61)	1.90 (0.96–3.78)	1.58 (0.79–3.15)	1.51 (0.76–3.01)	1.07 (0.27–4.18)	0.54 (0.13–2.30)	1.89 (0.43–8.32)	1.82 (0.45–7.32)
Histologic tumour type								
Adenocarcinoma 1.0		0.1	0.1	0.1	0.1	0.1	0.1	0:1
Squamous cell carcinoma 2.15	2.15 (1.30–3.55)	2.02 (1.19-3.40)	1.26 (0.76–2.09)	1.71 (1.01–2.90)	1.01 (0.43–2.38)	0.81 (0.34–1.90)	0.78 (0.32–1.85)	0.74 (0.31–1.74)
Tumour stage								
1.0		0.1	0.1	0.1	0.1	0.1	0.1	0:1
89:0	0.68 (0.31–1.50)	1.49 (0.68–3.28)	0.81 (0.36–1.81)	1.82 (0.83–3.99)	2.09 (0.17–25.42)	(91.9–80.0) 69.0	0.43 (0.05-4.06)	1.95 (0.17–22.73)
II 0.54	0.54 (0.24-1.22)	1.11 (0.49–2.49)	1.09 (0.47–2.52)	1.25 (0.56–2.79)	2.04 (0.18–23.61)	0.50 (0.06-4.28)	0.95 (0.11–8.21)	2.15 (0.19–23.84)
0-1	0.57 (0.25-1.33)	1.56 (0.67–3.66)	0.66 (0.28–1.57)	1.22 (0.53–2.79)	2.29 (0.20–26.00)	0.59 (0.07-4.84)	0.64 (0.08–5.40)	3.02 (0.28–32.68)
Marital status								
Cohabitating 1.0		0.1	0.1	0:1	0.1	0.1	0.1	0:1
ating	0.81 (0.52-1.26)	0.53 (0.34-0.84)	0.66 (0.42–1.03)	0.84 (0.53–1.31)	1.10 (0.49–2.51)	0.35 (0.15-0.84)	0.49 (0.21–1.13)	0.56 (0.25-1.28)
Education level								
Higher education 1.0		0.1	0.1	0:1	0.1	0.1	0.1	0:1
Upper secondary schooling 1.97	1.97 (1.02–3.79)	1.48 (0.77–2.81)	1.48 (0.79–2.78)	1.05 (0.56–1.98)	1.17 (0.41–3.32)	1.05 (0.38–2.92)	1.98 (0.70–5.62)	2.07 (0.74–5.85)
Nine-year compulsory 2.46	2.46 (1.28–4.74)	1.21 (0.64–2.28)	1.78 (0.95–3.35)	1.55 (0.82–2.94)	1.65 (0.58–4.70)	1.67 (0.60–4.70)	1.35 (0.43–3.80)	1.27 (0.46–3.52)

 $^{4}$ Adjusted for sex, age, tumour stage, histological tumour type, marital status and education level with exclusion of the study variable (i.e. characteristic). Note: ORs in bold indicate statistically significant results (p < 0.05).

problems in emotional adjustment at 6 months, while sex, age, and tumour stage were not. Only marital status was associated with problems with worry at 5 years.

Some methodological aspects of the study need to be considered. The main strengths include the longitudinal and prospective data collection based on an almost nationwide complete cohort of patients who underwent surgery for oesophageal cancer and the high quality data on exposures and outcomes. On the other hand, some level of non-participation and missing data might introduce a risk of selection bias. Confounding by known and unknown variables is a threat to all observational studies, which can never be entirely dismissed, but we adjusted all point estimates for several potential confounding factors. Finally, the large sample size at 6 months provided good statistical power, but the 5-year assessment was hampered by limited precision. In order to reduce chance errors because of multiple testing, only clinically significant characteristics were included in the multivariable analysis, and these were based on previously published studies regarding the association between clinical variables and emotional functioning [23].

Previous studies using the HADS screening instrument have indicated that patients with oesophageal cancer suffer significant emotional distress from the time of diagnosis throughout the first year of illness [11] and up to 4 years following surgery [24,25]. Further, cross-sectional studies addressing emotional outcomes after resection for oesophageal cancer have suggested that a substantial proportion of 1-year survivors have felt depressed (64%) and expressed fear of death and metastases (80%) [26]. Among patients surviving 2 years postsurgery, emotional aspects such as worry and irritability have been shown to be associated with overall quality of life [27]. Although these studies are limited because of small sample sizes, cross-sectional designs, and the use of general questionnaires and symptom checklists for measuring emotional aspects and quality of life, our results are generally in line with the results of these previous studies. Interestingly, in previous studies of postoperative HRQOL among patients treated with surgery for oesophageal cancer, emotional functioning has been shown to improve over time when measured by the EORTC QLQ-C30 questionnaire [7]. Improvements in emotional functioning from presurgery to postsurgery have also been shown to be associated with better survival [28], which underlines the importance of assessing emotional adjustment among these patients. However, symptoms of anxiety and depression measured by the HADS questionnaire have been reported to remain elevated or even increase up to 2 years after surgery [24]. In the present study, a validated and widely used questionnaire was used to assess aspects of emotional functioning. The high agreement between the emotional functioning scale in EORTC QLQ-C30 and the well-established screening instrument for symptoms of anxiety and

depression, HADS, has been described elsewhere [21]. However, compared with the HADS questionnaire, the sensitivity and specificity of the emotional functioning scale in the EORTC QLQ-C30 are slightly lower [20], and the unavailability of established cut-off levels for caseness of poor emotional functioning [21] is a limitation of the measurement. In addition, self-report questionnaires might be limited in detecting psychological morbidity, compared with clinical interviews [29]. Interestingly, a recently published meta-analysis showed that prevalence rates of depression in different cancer groups ranged from 8 to 24% depending on the type of screening instrument, type of cancer and treatment period [30]. These results highlight the complexity in choosing the appropriate instruments when screening for emotional distress in patients with cancer.

As summary scores on scales may disguise divergent item responses, each of the four items comprising the emotional functioning scale was analysed separately in the multivariable model, in order to identify differences in the proportion of problems reported and the potential risk characteristics. In the present study, a large proportion of patients reported problems with the four aspects of emotional functioning both at 6 months and 5 years. The majority of patients with problems at 6 months also reported problems at 5 years. However, a substantial minority of patients appeared to deteriorate over time, which is consistent with earlier studies investigating HRQOL among survivors of oesophageal cancer, where a subgroup of patients was identified who appeared to deteriorate over time, reporting worsened HRQOL after 5 years [14].

The somewhat rough categorization of patients reporting 'problems' versus 'no problems' on each of the four aspects from the emotional functioning scale might contribute to the high proportion of patients reporting problems over time. Within the group of patients reporting emotional problems, responses were distributed with the highest proportion of patients scoring 'a little' or 'quite a bit' on individual items, even though a small group of patients scored 'very much' on all the aspects at both time points. Nevertheless, we aimed to identify all patients reporting emotional problems following surgery, regardless of the burden of the problem. This might be a novel, straight forward way of communicating the postoperative emotional status of patients with oesophageal cancer to clinical practice because of the sometimes debatable and subjective interpretation of clinical significance of the EORTC QLQ-C30 questionnaire [31].

When conducting longitudinal studies using self-reported outcomes in patients who are exposed to a significant event, the patient's experiences may change over time, and adaptation to new life situations is often required. Consequently, the patients in this study might cope with the disease and report better emotional recovery than expected after 5 years. This methodological phenomenon is called response shift and should be considered when interpreting the results of the present study [32].

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We found that the histological tumour-type squamous cell carcinoma was associated with worry and depressed mood at 6 months, compared with patients diagnosed with adenocarcinoma. These results are in line with those of previous studies where patients with adenocarcinoma were found to have a decreased risk of poor HRQOL 6 months after surgery compared with patients with squamous cell carcinoma [23]. Patients with squamous cell carcinoma have a risk factor profile that includes lower socioeconomic status, increased alcohol use and tobacco smoking, compared with patients with adenocarcinoma [33]. These interrelated factors are associated with increased risk of mental health disorders [34] and may, at least in part, explain the differences observed in worry and depressed mood at 6 months. The results from this study might indicate the need for additional psychosocial support for patients diagnosed with squamous cell carcinoma.

Contrary to previous studies where non-cohabitating patients reported more depressive symptoms than cohabitating patients with cancer [35], we found that non-cohabitating patients less often reported problems with worry and possibly also with tension, irritation and depressed mood at 6 months than cohabitating patients did. Recently, published results from one large-scale study of mixed cancers showed a higher risk of death, metastases and under-treatment among unmarried patients compared with married patients [36]. Because of small numbers, we collapsed the marital status categories into a binary variable. Therefore, the 'non-cohabitating' category consisted of both never married and widowed/divorced patients, and the 'cohabitating' group included both married and remarried patients, which may have influenced the results. In addition, information on marital quality was unknown.

Previous studies of HRQOL in mixed cancer groups show that more highly educated patients report less anxiety and better overall HRQOL [35]. Similarly, we found that patients with lower education were more likely to report problems with tension at 6 months. However, more research is warranted regarding the association between socioeconomic status and emotional distress in order to investigate if, for example, sick leave and occupation might explain the increased reporting of tension among patients with lower educational attainment in this patient group.

With the exception of marital status, no other statistically significant associations between the clinical and sociodemographic characteristics and problems with aspects of emotional functioning appeared to persist after

5 years postsurgery. One possible reason for this could be that the 5-year results were much hampered by limited precision. It is also possible that patients who died before the 5-year follow-up assessment, with lower educational background, would have reported more severe problems also, but this is not known. However, the presence of response shift should not be ruled out as an additional potential explanation.

In conclusion, this prospective and population-based cohort study indicates that a significant proportion of patients with oesophageal cancer treated with surgery have problems with aspects of emotional functioning over time. Histological type, educational level and marital status seem to be the risk characteristics for problems with tension, worry and depressed mood at 6 months after adjustment for several potential confounding factors. In order to develop appropriate supportive interventions, further research is needed, using emotional distress specific measures, to establish the prevalence of and risk characteristics for psychological morbidity in this vulnerable patient group.

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### **Author contributions**

AW, PL and YH designed the study. AJ and YH performed the data analyses. YH and AW drafted the manuscript. All authors contributed to the interpretation of data and revised it critically for important intellectual content. All authors read and understand all parts of the study and approved the final manuscript.

# Role of the funding source

The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. The funders do not bear any responsibility for the analyses or interpretations presented here.

## **Conflict of interest**

The authors have declared no conflicts of interest.

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