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Predicting return to work after head and neck cancer treatment is challenging due to factors that affect work ability

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Research Article

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Abstract

Purpose To prospectively investigate the factors that hinder and facilitate return to work (RTW) at 3 and 12 months after the end of treatment in head and neck cancer (HNC) survivors and whether these factors influence the ability to continue working after treatment.

Methods Participants (n=227) aged \leq 65 years at diagnosis with HNC were included. Data were collected before the start of treatment and 3 and 12 months after the end of treatment. The Rubin causal model was used for statistical analysis.

Results Within the 3-month follow-up period, 92 participants had RTW and 30 had retired. At the 12-month follow-up, 80 of these participants were still working, another 51 participants had RTW, and five patients working still suffered from cancer. The hindrances to RTW within 3 months were advanced tumour stage (III and IV) (p=0.0159) and multi-modality treatment (p=0.0366). Hindrance to RTW at the 12-month follow-up was oral cancer (p=0.0194), and the facilitator was a white collar job (p=0.0411). Participants living with a spouse or partner had an earlier RTW (p=0.0414).

Conclusions A high rate of early RTW was identified, with only 13% dropping out of work in one year. Disease and treatment factors were the most important hindrances to RTW, and type of work and living with a spouse or partner were nonclinical factors influencing RTW.

Implications for Cancer Survivors: More research is needed to understand the impact of cancer rehabilitation to facilitate RTW and the economic burden of being on sick leave.

Introduction

Striving to return to everyday life, including work, is of great importance for many cancer survivors, and the success rate is traditionally regarded as dependent on the site of the tumour, tumour stage, treatment, and comorbidities [1-3].

Head and neck cancer (HNC) includes a group of malignancies located at different sites in the upper aerodigestive tract, and squamous cell carcinoma (SCC) accounts for more than 90%. Earlier, this cancer type predominantly affected older people with heavy smoking and alcohol abuse. However, in recent decades, the demographics has changed due to the increasing incidence of human papillomavirus (HPV)-positive oropharyngeal cancer, which majorly affects the younger patients [4]. Treatment for HNC consists of single or combined treatment with surgery, radiotherapy, and medical treatment (such as chemotherapy and targeted therapy), which are included in the therapeutic arsenal [5]. The ability to return to work (RTW) and continue working are linked to several medical, physical, psychosocial, and social factors experienced by patients. Treatment-related acute toxicities and sequelae can result in early, late, and chronic problems for the cancer survivor [6]. Work-related and sociodemographic factors are also considered to play an important role in the effort to RTW after sick leave in connection with a long period of treatment for HNC [7, 8].

There is increasing awareness that RTW after cancer treatment can have important benefits for cancer survivors' wellbeing. Moreover, altered treatment regimens and the introduction of rehabilitation interventions suggest the need for further studies on HNC survivors. With the increasing incidence of HNC in young population, there is a need for more prospective cohort studies to evaluate the risk/beneficial factors that impact RTW. The purpose of this study was to prospectively investigate factors that hinder and facilitate RTW 3 and 12 months after the end of treatment in HNC survivors and to determine whether these factors influence the ability to continue working after treatment.

Methods

Study design and population

This is an ongoing multicentre prospective observational study of patients with HNC registered at ClinicalTrials.gov (identifier NCT03343236). Two hundred and twenty-seven participants aged 65 years or younger at the time of diagnosis were included in this study from October 2015 to August 2021. Inclusion criteria were age above 18 years, curable untreated HNC, and a performance status of 0–2 according to the Eastern Cooperative Oncology Group Performance Status/World Health Organization Performance Status (WHO PS) [9]. The exclusion criteria were malignant neoplasms previously treated within the last five years (except for skin cancer), inability to understand Swedish language, severe alcohol abuse, and cognitive impairments.

Data Collection

Data were collected on three occasions: before the start of HNC treatment (baseline) and 3 and 12 months after the end of treatment, and stored in a database (data.dynareg.se). This database was developed to facilitate easy, reliable, and safe data collection for prospective multicentre observational studies.

At baseline, clinical characteristics and sociodemographic data were collected by a research nurse who collected information from the participants about their age, sex, marital status, type of accommodation, educational level, smoking status, current working status, and occupation. Additional information was collected from the participants' medical records, including cancer site, tumour stage according to the Union for International Cancer Control (UICC) 8 staging system, and treatment.

The timing of RTW was tracked at three and 12 months after the end of treatment. The participants reported their working status and from the medical record, the outcome of treatment (cancer-free/recurrence or mortality from cancer/other diseases) was collected. Two categories of RTW were studied: early RTW (0–3 months after the end of treatment) and late RTW (3–12 months after the end of treatment).

The participants were classified into three occupational groups: 1) white-collar workers, defined as people performing professional, desk manager, and administrative work; 2) blue-collar workers, defined as people performing manual labour including machine operators, assemblers, and occupations with demand for elementary education; and 3) pink-collar workers, defined as healthcare workers (including physicians, nurses, assistant nurses, occupation- and physiotherapists, psychologists, and residential workers). The classification of workers was based on the Swedish standard system for the classification of occupations [10].

The study was performed in accordance with the principles of the Declaration of Helsinki of the World Medical Association [11], and approval was granted by the Regional Ethical Review Board in Uppsala, Sweden, No. 2014/447. Informed oral and written consent was obtained from all participants included in the study.

Statistical Analysis

Descriptive data for the continuous variable is presented as mean ± standard deviation (SD), and the categorical variables are presented as numbers (%). Pearson's chi-squared test was used to analyse cancer stage and RTW. Data were analysed using the statistical software IBM SPSS version 28.0 (IBM, Armonk, NY, USA).

The Rubin causal model [12–16] that conceptualises causal inference in terms of potential outcomes, was used to analyse RTW. A good starting point is to consider the question, "What causes the patient to RTW after being treated for HNC?". Evaluating the possible causal effect of the parameters in the dataset on the outcome of RTW will be of high relevance.

In the context of statistical causal inference, by defining certain parameters, an action variable W can be regarded as a potential cause of an outcome. Each observation in the dataset belongs to either the action group (W = 1) whose

members were exposed to the action variable or the control group (W = 0) whose members were not exposed to the action variable. Note that the action group in our study is sometimes termed the treatment group in other fields.

Now, suppose that there are two potential outcomes, $Y_i(1)$ and $Y_i(0)$ for RTW. The observed outcome is a mixture of two potential outcomes in the following manner:

$$Y_{i}^{obs} = Y_{i}(0) (1 - W_{i}) + Y_{i}(1) W_{i},$$

This is what we observed only in the data. This indicates that it is impossible for an individual to access $Y_i(1)$ and $Y_i(0)$. Only one potential outcome can be observed, whereas the other is counterfactual. This is the well known "missing observation" problem in causal effect analysis.

The estimate of interest under the causal inference context is the "average causal effect" (ACE) defined to be $ACE = E [Y_i(1) - Y_i(0)]$, where the average is over the population of the individuals. Both $Y_i(1)$ and $Y_i(0)$ are random because of the varying nature of the covariates and the latent error. ACE represents the average difference between two potential outcomes over the population; therefore, it indicates the causal effect or the action truly causes the parameter of interest if it is nonzero. To estimate the ACE consistently, we assume the following:

- 1. Probabilistic: Each individual in the study had a chance, no matter how low it was, to enter either the action or the control group.
- 2. Individualistic: There is no interference between the individuals in the study.
- 3. Unconfoundedness: The action assignment for each individual was not confounded by the two potential outcomes given the covariates. This implies that action assignment is independent of potential outcomes, given the covariates.

Based on the above assumptions, we can now identify the conditional causal effect within the levels of the covariates, and the average effect can be safely computed by marginalising the covariates as follows:

$$egin{array}{lll} \mathrm{ACE} &= \mathrm{E}_{\mathrm{X}}\left[\mathrm{E}\left[Y_{i}^{obs} \left|W_{i}=1,X_{i}
ight]
ight] - \mathrm{E}_{\mathrm{X}}\left[\mathrm{E}\left[Y_{i}^{obs} \left|W_{i}=0,X_{i}
ight]
ight]. \end{array}$$

Because the average event was identified, it could be estimated using the observed data. We used propensity score matching to balance the covariates and alleviate potential bias in the estimation. For details on the propensity score matching technique, see Rosenbaum and Rubin [17]. We assume linearity in function F in this project and employ logistic regression to estimate the propensity scores.

Data Manipulations

The variables of interest that we model and investigate in this study are the indicators of returning to work (IRTW) within certain periods (3 and 12 months) after corresponding medical treatments for each individual in the dataset.

The variables used after data manipulation as the dependent variable, covariates, and action variables in the analysis are presented in the following table. The indicator of returning to work (IRTW) was used as a common dependent variable in all models.

Results

Description of participants before the start of treatment

Of the 227 participants with HNC included in this study, 66 were women. The mean age of the participants was 55.1 years (range 22–65 years). The clinical, work-related, and sociodemographic characteristics of the study population are presented in Table 1.

Table 1 Clinical, work-related, and sociodemographic characteristics of 227 participants with head and neck cancer (n = numbers are given).

Characteristics	Sub-groups	n (%)
Age, mean years (± SD)		55.1 (± 8.65)
Age, range of years		22-65
Sex	Female	66 (29.1)
	Male	161 (70.9)
Marital status	Married, cohabiting	170 (74.9)
	Single or couple not living together	57 (25.1)
Living conditions	House	152 (67)
	Owned apartment	22 (9.7)
	Rental flat	53 (23.3)
Educational status	Mandatory	33 (14.5)
	High school/college	119 (52.4)
	Other post-high school education	7 (3.1)
	University	68 (30.0)
Type of work	White collar	112 (49.3)
	Blue collar	87 (38.3)
	Pink collar	25 (11.0)
	Unemployed	2 (0.9)
	Student	1 (0.4)
Tumour site	Oropharynx	113 (49.8)
	Oral cavity	60 (26.4)
	Larynx	19 (8.4)
	Nasopharynx	12 (5.3)
	Cancer of unknown primary	10 (4.4)
	Nasal and sinus	7 (3.1)
	Salivary glands	3 (1.3)
	Hypopharynx	2 (0.9)
	Other (Rhabdomyosarcoma in the left maxilla ethmoidal)	1 (0.4)
Tumour stage UICC† 8		93 (41.1)
	II	52 (22.9)
	III	42 (18.5)
	IV	39 (17.2)

Characteristics	Sub-groups	n (%)
	Not applicable	1 (0.4)
Treatment type	Surgery	20 (8.8)
	Radiotherapy (RT)	83 (36.6)
	Chemo* radiotherapy (CRT)	63 (27.8)
	Surgery and RT or CRT	61 (26.9)

⁺ The Union for International Cancer Control's (UICC).

*Cisplatin or Cetuximab

Early return to work (RTW)

Within the 3-month follow-up, 92 (41%) participants (age range 27–65 years, mean 53.2 years) had early RTW. Two were unemployed, 99 were on sick leave, 30 were retired, and 4 died (Fig. 1).

Late return to work (RTW)

Eighty of the 92 participants who had early RTW continued to work at the 12-month follow-up. The remaining 12 participants either retired (6), went back on sick leave (2), died (2), or dropped out of the study (2). Between the 3- and 12-month follow-up, another 51 (22%) participants returned to work. The remaining participants were unemployed (one) and were still on sick leave (26). Additionally, 7 participants retired and 11 died. At the 12 months follow-up a total of 131 of the 227 (58%) participants were employed (Fig. 1.).

The stage of cancer in participant RTW and not

Thirty participants (age range 47–65 years, mean 62.17 years) who retired early had stage I (14), II (6), III (5), and IV (5) cancer. The cancer stage distribution of the 92 participants with early RTW was 49, 23, 11, and 9 respectively. At the time of late RTW, the distribution of cancer stages in participants was I (64), II (29), III (22), and IV (16).

A total of 28 participants (18 males and 10 females) were on sick leave at the 12-month follow-up, with cancer stages I (n = 4), II (n = 7), III (n = 9), and IV (n = 8). Two had RTW at some point in time but were back on sick leave due to cancer recurrence, 4 of the 28 participants had a recurrence of their cancer, and the rest of the participants had not recovered and had not been able to RTW since treatment.

The RTW for all participants returning early and late divided by cancer stage (early and late stages) are presented in Table 2, which shows a less favourable situation for participants in the late stage. A significant difference was observed between participants working and those on sick leave regarding cancer stage at the 3-month follow-up ($X^{2=}$ 15.020, df = 4, p = 0.003) and at the 12-month follow-up ($X^{2=}$ 13.407, df = 3, p = 0.003).

Follow-up	Stage	Working	Unemployed	Sick leave	Retired	Dead	Missing data
3-month	I and II	72	-	53	20	-	-
	III and IV	20	2	45	10	4	-
	Not applicable	-	-	1	-	-	-
12-month	I and II	93	6	11	32	1	2
	III and IV	38	1	17	10	15	-
	Not applicable	-	-	-	-	1	-

Table 2 Return to work outcomes of 227 participants treated for head and neck cancer at the 3- and 12-month follow-up categorized by cancer stage

Of the 227 included participants, 11 were non-responders to cancer treatment or had early recurrence within 3 months of treatment completion. One of these 11 participants (diagnosed with cancer of unknown primary, stage IVB) had RTW early (at the 3-month follow-up) but was not working at the late follow-up. One participant was diagnosed with stage II laryngeal cancer with a partial response after RT, underwent transoral laser microsurgery, and was thereafter cancer-free, with an RTW between the 3- and 12-month follow-ups. None of the other non-responders or participants experienced early recurrence of RTW. Before the 3-month follow-up, three participants died: one participant was diagnosed with oral cancer, stage IVA, and two with nasal and sinus cancer, stages IVA and IVB, respectively. At the 12-month follow-up, two participants with early recurrence had died: one with oral cancer, stage IVA, and one with rhabdomyosarcoma in the left maxilla ethmoid.

Between the 3- and 12-month follow-ups, 31 participants (24 males and 7 females) were diagnosed with cancer recurrence. The sites of cancer recurrence were the oropharynx in 15 participants (stages I, II, III, and IVA), oral cavity in 12 participants (stages II, III, IVA, and IVB), and in four other sites (larynx stage II, nasal and sinus stage IVB, salivary gland stage IVA, or nasopharynx stage II). Of these 31 participants, seven had early RTW, and one was unemployed. At the 12-month follow-up, one of the seven participants with early RTW had died, and the other six continued to work, even though four of them were not cancer-free and the other two were cancer-free after salvage surgery. Additionally, two participants with cancer recurrence had RTW (cancer-free), and the unemployed participant had RTW (not cancer-free) between 3 and 12 months. In total, five participants with active cancer disease (two were unsuccessfully treated with salvage surgery) and four participants who were cancer-free after salvage treatment had RTW at 12 months. The remaining participants with cancer recurrence between the 3- and 12-month follow-ups had retired (n = 7), continued sick leave (n = 6), were unemployed (n = 1), or died (n = 7). Of the 31 participants with cancer recurrence, eight died and had stage III (n = 4), IVA (n = 3), and IVB (n = 1) cancer.

Clinical, work-related, and sociodemographic factors and return to work

Advanced cancer stage (p = 0.0159) and multi-modality treatment (p = 0.0366) hindered early RTW. Furthermore, oral cancer (p = 0.0194) was a hindrance to late RTW, and being a white-collar worker (p = 0.0411) was a facilitating factor at the 12-month follow-up. No other factors were significantly different (Table 3a).

The first column shows the results of RTW at some point within 3 months of treatment.

The second column shows the RTW results at some point within 12 months of treatment.

If the estimate is significant, a positive value implies that it facilitates RTW, whereas a negative value implies that it hinders RTW.

Excluded participants are those who retired or are deceased.

Table 3a. Factors influencing return to work (RTW) at 3 and 12 months after treatment completion for head and neck cancer.

	RTW 3-month follow-up							RTW 12-month follow-up					
VARIABLES	Yes	Yes RTW	No	Yes RTW	ACEe [†]	ACEp*	Yes	Yes RTW	No	Yes RTW	ACEe [†]	ACEp*	
IRTW	92		101				131		35				
University or college education	65	35	128	57	-0.1216	0.3686	59	50	107	81	-0.1205	0.3646	
Living in a relationship	143	68	50	24	-0.0578	0.6536	124	103	42	28	0.2167	0.0722	
Living in a house	128	66	65	26	0.1750	0.0854	111	92	55	39	-0.0142	0.8623	
White Collar	97	51	96	41	0.0555	0.6687	85	71	81	60	0.2806	0.0411	
Pink Collar	22	9	171	83	-0.3368	0.1627	20	14	146	117	-0.0492	0.8357	
Oropharynx	95	44	98	48	0.1913	0.3388	86	73	80	58	0.0526	0.7017	
Oral	52	26	141	66	-0.2789	0.2656	40	28	126	103	-0.5753	0.0194	
Larynx	16	5	177	87	-0.4560	0.1583	14	8	152	123	-0.7349	0.0056	
Advanced cancer stage (III or IV)	67	20	126	72	-0.2618	0.0159	56	38	110	93	-0.0728	0.4589	
Multi- modality treatment	110	44	83	48	-0.2605	0.0366	92	69	74	62	-0.1270	0.2006	
Smoking	102	45	91	47	-0.0206	0.8040	87	67	79	64	0.0266	0.7459	
⁺ estimated ch	ange in	percent											
* n-values													

* p-values

Table 3b reveals that a white collar job was a facilitating factor (p = 0.0353) for participants who returned to work at some point within 3 months after treatment and were still working at the 12-month follow-up (n = 80). Living with a spouse or partner was a facilitating factor for early RTW (p = 0.0414) compared to living alone. No other significant differences were observed (Table 3b).

The first column shows the results of the participants' return to work (RTW) at some point within 3 months after treatment and those who continued to work at the 12-month follow-up. Participants who had retired or died were excluded. If the estimate is significant, a positive one implies that it facilitates and a negative one implies that it hinders participants from continuing work.

The second column shows the results of early RTW (within the 3-month follow-up) compared with late RTW (within the 12-month follow-up). If the estimate is significant, a positive value implies an early return to work, and a negative value implies a late return to work.

Table 3b. Returning to work after head and neck cancer.

	RTW and continuing working						RTW at 3 or 12-month follow-up					
VARIABLES	Yes	Yes RTW	No	Yes RTW	ACEe [†]	ACEp*	Early RTW	Yes RTW	Late RTW	Yes RTW	ACEe [†]	ACEp*
IRTW	80		86				92		51			
University or college education	59	31	107	49	-0.1985	0.1032	54	35	89	57	-0.0233	0.8786
Living in a relationship	124	59	42	21	-0.0147	0.9127	112	68	31	24	-0.2768	0.0414
Living in a house	111	57	55	23	0.1474	0.1512	101	66	42	26	0.0321	0.7937
White Collar	85	47	81	33	0.2997	0.0353	75	51	68	41	0.1438	0.4287
Pink Collar	20	7	146	73	-0.3775	0.1247	16	9	127	83	-0.4452	0.1804
Oropharynx	86	40	80	40	0.1352	0.4831	77	44	66	48	-0.1802	0.3092
Oral	40	22	126	58	-0.2319	0.4056	32	26	111	66	0.2821	0.2478
Larynx	14	5	152	75	-0.4789	0.1233	8	5	135	87	0.2937	0.4002
Advanced cancer stage (III or IV)	56	18	110	62	-0.3373	0.0035	40	20	103	72	-0.2040	0.1150
Multi- modality treatment	92	38	74	42	-0.1908	0.1508	75	44	68	48	-0.1867	0.0967
Smoking	87	38	79	42	-0.0688	0.4786	74	45	69	47	-0.0983	0.3235
⁺ estimated c	hange i	n percer	nt									
* p-values												

Discussion

In this prospective multicentre observational study on participants with HNC, 227 participants with an age of 65 years or less at the initiation of treatment were assessed for RTW one year after the end of treatment. There were 92 participants (41%) who had early RTW. Among the 131 (58%) participants working 12 months after the end of treatment, 126 participants were tumour free, and five participants still suffered from cancer. The clinical factors found to hinder early RTW were advanced tumour stage and multi-modality treatment, and oral cancer hindered late RTW. Moreover, participants with more physically demanding jobs were less likely to RTW.

The percentage of participants' RTW in this study differed according to the site and stage of HNC. We have in an earlier study showed that 72% of 295 individuals with oropharyngeal cancer were working 15 months after diagnosis [18]. Other studies have shown that in individuals with oral cancer (n = 174), 55% had RTW at a follow-up of 6 months or more after the termination of treatment [19], and in a study of 111 individuals with different HNC diagnoses, 44.1% had RTW within 5 years [20]. In a review of follow-ups of HNC survivors, the rate of RTW varied between 32 and 90%, 3.6–11 months after the end of treatment [1]. The wide RTW range in that study may be explained by the heterogeneous nature of HNC which agrees with the importance of disease status and treatment revealed in the present study. In addition, HNC survivors have a complex burden of unresolved physical, psychological, and existential needs that add to their risk profile for not returning to work.

The recurrence rate in patients with HNC is highest during the two first years after initial treatment [21]. The present study included all participants enrolled at baseline, and not only patients who remained cancer-free during the disease trajectory, as the study aimed to prospectively describe a real-world situation for cancer survivors. A review of the literature shows that no exclusive definition of a cancer survivor or survivorship exists [22]. The definition of cancer survivor used in this study refers to Morgan's [23] definition of a cancer survivor which can be summarised as a person diagnosed with cancer regardless of when and who is alive. The RTW is not the same as that of a cancer-free individual. Of the 131 cancer survivors working at the 12-month follow-up, 9 had cancer recurrence after completion of treatment, and 5 of them were still not cancer-free even though they were working.

To better understand the time to RTW pattern, participants were followed-up at 3 and 12 months after the end of treatment. Early RTW was observed in 72 of 145 (49.7%) participants with stage 1–2 tumour whereas only 18 of 81 (22.2%) participants with stage 3–4 tumour demonstrated an early RTW. The advanced stage (III-IV) significantly hindered the participants from RTW and played a negative role in their ability to continue working. An inverse association with RTW has been demonstrated among earlier studies [20, 24].

The pattern of RTW was not shown to be robust or predictable, even in patients with early RTW, as periodic RTW was observed for medical and social reasons. Although 80 of 92 (87%) participants who had RTW at three months still were working nine months later, 12 participants practiced periodic RTW and had left the work sector for retirement, sick leave, dropped out, or were deceased. The inability to RTW or to discontinue working after cancer treatment was impacted by multiple factors: Among the 43 participants in this cohort, the sick leave period ended in retirement at any time during the study period, and 26 participants were on sick leave throughout the entire follow-up.

HNC is associated with a high degree of physical, psychological, and social burden related to the disease and treatment. HNC survivors may have significant problems related to eating, speech and voice, loss of hearing, and altered physical appearance [6, 25], and they may also struggle with fatigue, depression, and distress [26]. Most patients had the lowest QoL in the first year after treatment [27]. To examine RTW patterns, appropriate facilitators and hindrances were split into three categories and used as predictors: clinical, work-related, and sociodemographic factors. The oral cavity, oropharynx, and larynx are the three most common anatomical sites for head and neck squamous cell cancers. Although HNC affects individuals of different ages, occupations, and living conditions [5], the most important finding in the present study was that clinical factors affected RTW ability. This finding was not unexpected, as the study cohort displayed cancer at different HNC sites, stages, and treatments. Patients with advanced-stage disease were more prone to recurrence and cancer-related death which agrees with the finding that advanced-stage disease is a negative factor for RTW. Individuals treated for oral cavity and laryngeal cancers had a lower rate of RTW. Considering the different variables affecting RTW, it is difficult to construct a comprehensive model for predicting RTW in a mixed population of patients with HNC.

Psychosocial and physical demands are important aspects of the workload and RTW after HNC treatment. In the present study, the individuals were divided into three occupational categories where 49% were white collar workers, 38% blue collar workers, and 11% pink collar workers. The results show that white-collar work facilitates RTW. In another study of

80 patients with HNC, including more than six months after the latest treatment, pink-collar work was significantly associated with not returning to work [24].

RTW is important for many cancer survivors as it symbolises a regaining of normality and daily life [28], where work plays a meaningful aspect of life [29]. Support plays an important role in RTW, and in the present study, support from a spouse or partner was demonstrated to be most likely a facilitating factor for late RTW which is in agreement with the results of a systematic review of cancer survivors in Europe with different cancer diagnoses, including HNC [30]. However, international comparisons of RTW are complex, as several factors, such as the work environment and policy, cultural contexts, and economic issues, may affect RTW patterns [31]. Comparative approaches must also consider that different countries have different social security systems [32]. In the Swedish system [33], employers pay sick pay for the first 1– 14 days. Subsequently, the person on sick leave must apply for sickness benefits through the Swedish Social Insurance Agency. If an employee is assumed to be sick for more than 60 days, a rehabilitation plan needs to be implemented by the employer for easier RTW [33]. The support from the employer and the obligation to give support with a rehabilitation plan can play an important role for an individual with HNC to RTW [28]. The reduction in money when you are on sick leave may also directly impact the requirement for a person to RTW as soon as possible, or even if you are not on sick leave at all.

Healthcare also has an important task of identifying rehabilitation needs and using an experienced rehabilitation staff to effectively train the patients after treatment for HNC. Rehabilitation and screening for psychological and physical impairments are important for patients with cancer to preserve function and improve quality of life [34]. Efforts from different rehabilitation competencies such as occupational therapists, dietitians, physiotherapists, counsellors, speech therapists, and psychologists are often needed. Interdisciplinary rehabilitation programs are still lacking in many HNC centres [35]. Professionals must work together to address the complex symptoms and problems that can arise in patients with HNC [36].

Regarding the dearth of sociodemographic factors, further studies should address the economic burden of a person on sick leave and the impact it might have on RTW, and also focus on providing patient rehabilitation for a better chance of preparedness and success in RTW.

Limitations of this study are the rather short follow-up time, different tumour sites, and stages of HNC; and the inclusion of participants with a WHO performance > 2, which means that patients with less favourable status were excluded from the study. A more homogeneous group and a five-year follow-up period would have been preferable.

Conclusion

A clear RTW pattern is observed. Factors hindering RTW included advanced tumour stage, multi-modality treatment, and oral cancer. White-collar workers and participants living with spouses or partners were more likely to RTW. Further studies should address the economic burden of a person taking sick leave and its impact on RTW. Healthcare should focus on providing rehabilitation for a better chance and preparedness for success in RTW.

Declarations

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References

- 1. Zecena Morales C, Lisy K, McDowell L, Piper A, Jefford M. Return to work in head and neck cancer survivors: a systematic review. Journal of Cancer Survivorship. 2022:1-16; https://doi.org/10.1007/s11764-022-01298-6
- Mols F, Thong MS, Vreugdenhil G, van de Poll-Franse LV. Long-term cancer survivors experience work changes after diagnosis: results of a population-based study. Psychooncology. 2009;18(12):1252-60; https://doi.org/10.1002/pon.1522
- 3. Yoshida A, Motomura K, Natsume A, Chalise L, lijima K, Hara D, et al. Preoperative predictive factors affecting return to work in patients with gliomas undergoing awake brain mapping. J Neurooncol. 2020;146(1):195-205; https://doi.org/10.1007/s11060-019-03371-0
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49; https://doi.org/10.3322/caac.21660
- 5. Mody MD, Rocco JW, Yom SS, Haddad RI, Saba NF. Head and neck cancer. The Lancet. 2021; https://doi.org/10.1016/S0140-6736(21)01550-6
- 6. Trotti A. Toxicity in head and neck cancer: a review of trends and issues. International journal of radiation oncology, biology, physics. 2000;47(1):1-12; https://doi.org/10.1016/s0360-3016(99)00558-1
- 7. Verdonck-de Leeuw IM, van Bleek W-J, Leemans CR, de Bree R. Employment and return to work in head and neck cancer survivors. Oral oncology. 2010;46(1):56-60; https://doi.org/10.1016/j.oraloncology.2009.11.001
- Giuliani M, Papadakos J, Broadhurst M, Jones J, McQuestion M, Le LW, et al. The prevalence and determinants of return to work in head and neck cancer survivors. Support Care Cancer. 2019;27(2):539-46; https://doi.org/10.1007/s00520-018-4343-6
- 9. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5(6):649-55;
- 11. General Assembly of the World Medical A. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. J Am Coll Dent. 2014;81(3):14-8;
- 12. Holland PW. Statistics and causal inference. Journal of the American statistical Association. 1986;81(396):945-60;
- 13. Rubin DB. Estimating causal effects of treatments in randomized and nonrandomized studies. Journal of educational Psychology. 1974;66(5):688;
- 14. Rubin DB. Bayesian inference for causal effects: The role of randomization. The Annals of statistics. 1978:34-58;
- 15. Rubin DB. Comment: Neyman (1923) and causal inference in experiments and observational studies. Statistical Science. 1990;5(4):472-80;
- 16. Splawa-Neyman J, Dabrowska DM, Speed TP. On the Application of Probability Theory to Agricultural Experiments. Essay on Principles. Section 9. Statistical Science. 1990;5(4):465-72;

- 17. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika. 1983;70(1):41-55;
- Granström B, Tiblom Ehrsson Y, Holmberg E, Hammerlid E, Beran M, Tano K, et al. Return to work after oropharyngeal cancer treatment—Highlighting a growing working-age population. Head & Neck. 2020;42(8):1893-901; https://doi.org/10.1002/hed.26123
- 19. Chen SC, Huang BS, Hung TM, Lin CY, Chang YL. Impact of physical and psychosocial dysfunction on return to work in survivors of oral cavity cancer. Psycho-Oncology. 2019;28(9):1910-7; https://doi.org/10.1002/pon.5173
- 20. Tsai P-L, Wang C-P, Fang Y-Y, Chen Y-J, Chen S-C, Chen M-R, et al. Return to work in head and neck cancer survivors: its relationship with functional, psychological, and disease-treatment factors. Journal of Cancer Survivorship. 2022:1-10; https://doi.org/10.1007/s11764-022-01224-w
- 21. De Almeida JR, Li R, Magnuson JS, Smith RV, Moore E, Lawson G, et al. Oncologic outcomes after transoral robotic surgery: a multi-institutional study. JAMA Otolaryngology–Head & Neck Surgery. 2015;141(12):1043-51; https://doi.org/10.1001/jamaoto.2015.1508
- 22. Marzorati C, Riva S, Pravettoni G. Who is a cancer survivor? A systematic review of published definitions. Journal of Cancer Education. 2017;32(2):228-37; https://doi.org/10.1007/s13187-016-0997-2
- 23. Morgan MA, editor Cancer survivorship: history, quality-of-life issues, and the evolving multidisciplinary approach to implementation of cancer survivorship care plans. Oncology nursing forum; 2009. https://doi.org/10.1188/09.0NF.429-436
- 24. Rangabashyam M, Koh SQ, Sultana R, Tan NC, Iyer NG, Soo KC, et al. Factors associated with returning to work in head and neck cancer survivors in Singapore: A preliminary exploratory mixed-methods approach study. Head & Neck. 2021;43(5):1451-64; https://doi.org/10.1002/hed.26644
- 25. Strojan P, Hutcheson KA, Eisbruch A, Beitler JJ, Langendijk JA, Lee AWM, et al. Treatment of late sequelae after radiotherapy for head and neck cancer. Cancer Treat Rev. 2017;59:79-92; https://doi.org/10.1016/j.ctrv.2017.07.003
- 26. Hammermüller C, Hinz A, Dietz A, Wichmann G, Pirlich M, Berger T, et al. Depression, anxiety, fatigue, and quality of life in a large sample of patients suffering from head and neck cancer in comparison with the general population. BMC cancer. 2021;21(1):1-11; https://doi.org/ 10.1186/s12885-020-07773-6
- 27. Nyqvist J, Fransson P, Laurell G, Hammerlid E, Kjellén E, Franzén L, et al. Differences in health related quality of life in the randomised ARTSCAN study; accelerated vs. conventional radiotherapy for head and neck cancer. A five year follow up. Radiotherapy and Oncology. 2016;118(2):335-41; https://doi.org/0.1016/j.radonc.2015.12.024
- 28. Isaksson J, Wilms T, Laurell G, Fransson P, Ehrsson YT. Meaning of work and the process of returning after head and neck cancer. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2016;24(1):205-13; https://doi.org/10.1007/s00520-015-2769-7
- 29. Duijts SF, van Egmond MP, Gits M, van der Beek AJ, Bleiker EM. Cancer survivors' perspectives and experiences regarding behavioral determinants of return to work and continuation of work. Disability and Rehabilitation. 2017;39(21):2164-72; https://doi.org/10.1080/09638288.2016.1219924
- Paltrinieri S, Fugazzaro S, Bertozzi L, Bassi MC, Pellegrini M, Vicentini M, et al. Return to work in European Cancer survivors: a systematic review. Supportive Care in Cancer. 2018;26(9):2983-94; https://doi.org/10.1007/s00520-018-4270-6
- 31. Dewa CS, Trojanowski L, Tamminga SJ, Ringash J, McQuestion M, Hoch JS. Work-related experiences of head and neck cancer survivors: an exploratory and descriptive qualitative study. Disability and Rehabilitation. 2018;40(11):1252-8; https://doi.org/10.1080/09638288.2017.1291764
- 32. Mehnert A, de Boer A, Feuerstein M. Employment challenges for cancer survivors. Cancer. 2013;119 Suppl 11:2151-9; https://doi.org/10.1002/cncr.28067

- 33. The Swedish Social Insurance Agency. Sick leave regulations in Sweden. [Available from: https://www.forsakringskassan.se/.
- 34. Silver JK, Baima J, Mayer RS. Impairment-driven cancer rehabilitation: an essential component of quality care and survivorship. CA: a cancer journal for clinicians. 2013;63(5):295-317; https://doi.org/10.3322/caac.21186
- 35. Beck A-JC, Passchier E, Retèl VP, Stuiver MM, Van Der Molen L, Klop W, et al. Study protocol of a prospective multicenter study comparing (cost-) effectiveness of a tailored interdisciplinary head and neck rehabilitation program to usual supportive care for patients treated with concomitant chemo-or bioradiotherapy. BMC cancer. 2019;19(1):1-10; https://doi.org/10.1186/s12885-019-5874-z
- 36. Wells M, Semple C, Lane C. A national survey of healthcare professionals' views on models of follow-up, holistic needs assessment and survivorship care for patients with head and neck cancer. European Journal of Cancer Care. 2015;24(6):873-83; https://doi.org/10.1111/ecc.12285

Figures



Figure 1

A flow chart of returning to work (RTW) at 3 (early RTW) and 12 months (late RTW) after the end of treatment in 227 study participants with HNC. N = numbers are given. HNC: head and neck cancer.