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Social Determinants of Health-Related Quality of Life Outcomes for Head and Neck Cancer Patients

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Abstract: The influence of area-based and individual indicators of socioeconomic status (SES) on health-related quality of life (HRQOL) and patient concerns following head and neck cancer is complex and under-reported. The aim of this study is to use baseline data collected as part of a randomised controlled trial to provide greater detail on the attribution of SES to University of Washington Quality of Life version 4 (UWQOL v4), Distress Thermometer and European Quality of Life Five-Dimension Five-Level (EQ-5D-5L) outcomes. A total of 288 trial patients attended baseline clinics a median (Interquartile (IQR)) of 103 (71–162) days after the end of treatment. Area-based SES was assessed using the Index of Multiple Deprivation (IMD) 2019. Thirty-eight per cent (110/288) of patients lived in the most deprived IMD rank quintile. Less than good overall quality of life (31% overall) was associated with current working situation ($p = 0.008$), receipt of financial benefits ($p < 0.001$), total household income ($p = 0.003$) and use of tobacco ($p = 0.001$). Income and employment were significant patient level indicators predictors of HRQOL outcomes after case-mix adjustment. The number of Patient Concerns Inventory items selected varied significantly by overall clinical tumour clinical stage ($p < 0.001$) and by treatment ($p < 0.001$) but not by area IMD or patient-level deprivation indicators. In conclusion, interventions to improve employment and finance could make a substantial positive effect on HRQOL outcomes and concerns.

Keywords: social determinants; financial toxicity; health-related quality of life; head and neck cancer; quality of life; survivorship

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1. Introduction

The term 'determinants of health' was introduced in the 1970s and refers to factors that have a significant influence, positive or negative, on health [1]. These may be biological, behavioural, sociocultural, economic and ecological [2]. The determinants of health can be divided into four categories: nutrition, lifestyle, environment and genetics [3]. Evidence shows that the incidence of cancer and chronic diseases share modifiable risk factors such as alcohol consumption, cigarette smoking, unhealthy diet and physical inactivity [4]. Some determinants are modifiable such as nutrition and lifestyle. People should be encouraged and supported in making modifications where possible, and this is an integral component of cancer care [4].

Head and neck cancer (HNC) is associated with social inequalities as reflected by its higher incidence in lower socio-economic groups (SESG) [5]. Of the determinants of health nutrition and lifestyle areas that can be usefully addressed in those with HNC, smoking and alcohol are the main risk lifestyle factors and are more prevalent in lower SESG [6]. After diagnosis and treatment, a high proportion of head and neck cancer survivors reduce their work capacity, and many do not return to work following cancer treatment. This can have further implications for their finances [7]. Socioeconomic position and deprivation have consequences in the utilisation of healthcare [8,9] and this is related to diagnosis and treatment and results in unmet needs. Regarding unmet needs, HNC patients tend not to actively pursue support compared to their less disadvantaged peers [10]. Socioeconomic and other demographic disparities predict survival even when there is equal access to care [11] and are associated with unmet needs and poor health-related quality of life (HRQOL).

Many factors are associated with poorer HRQOL outcomes following HNC, such as site, stage and treatment [12]. HNC cancer patients often live in poor socioeconomic areas and those most deprived do tend to report poor HRQOL [13]. Differences in HRQOL are reflected in differences in Index of Multiple Deprivation (IMD) scores [14].

The authors have been involved in a randomised trial involving the use of a patient prompt list (Patient Concerns Inventory) in routine review consultant consultations, a trial which indicated benefits in quality of life and socio-emotional dysfunction compared to standard care [15]. Trial casemix information included both area- and individual-based socio-economic characteristics [16]. With this detail, secondary analyses were possible; hence the aim of this study was to focus on SES and add greater definition and understanding to the contribution of the area and patient indicators of SES as factors affecting HRQOL outcomes after HNC. This information will allow for a better appreciation amongst the head and neck multi-professional team and for closer collaboration across primary and secondary care to potentially improve outcomes for more disadvantaged HNC patients.

2. Methods

The data came from a pragmatic cluster-controlled trial at two UK Cancer Centres, Aintree and Leeds. Consultants (clusters) were randomised to ‘using’ or ‘not using’ an intervention incorporating the Patient Concerns Inventory (PCI) prompt list at all their trial clinics. The full methodology has been described previously [17]. Eligible patients were treated curatively for primary HNC, with all sites, stages of disease and treatments included. Palliation and recurrence were exclusion criteria, as were cognitive impairment, psychoses or dementia. The PCI consists of 56 clinical items [18], which patients select from before their appointment, to help guide the outpatient consultation through the symptoms and problems experienced following treatment for HNC. Patients were first discussed at multi-disciplinary team (MDT) meetings (tumour board) between January 2017 and December 2018, with baseline clinics between April 2017 and October 2019. HRQOL data from the first post-treatment (trial baseline) consultation with consultant surgeon were analysed.

Ranks from the Index of Multiple Deprivation (IMD 2019) were derived from patient postcodes using publicly available data [19] for 32,844 small areas within England. Overall ranks were analysed as quintile categories ranging from the 20% of most deprived areas in England to the 20% least deprived. A baseline clinic questionnaire collected individual SES deprivation-related information as to whether patients lived alone or with others, were working, had ever been unemployed, were receiving financial benefits and their total household income before tax. Lifestyle factors regarding the use of tobacco and alcohol were also collected, as were patient ethnicity, gender and age. Clinical details about primary tumour site, grade, treatment and comorbidity were obtained from clinical records.

The UW-QOLv4 questionnaire contains 12 single-question domains, with 3–5 evenly scaled response options from 0 (worst) to 100 (best) [20]. Regarding overall QOL, patients were asked to consider not just physical and mental health, but also many other factors, such as family, friends, spirituality or personal leisure activities that were important to their enjoyment of life. Subsequent work developed subscale composite scores [21] and domain algorithms screening for significant problems/dysfunction [22]. Question domains for intimacy and fears of recurrence were also developed using a similar system of hierarchical responses, as for the UWQOL v4 [23,24]. HRQOL data also included the Distress Thermometer (DT) and EQ-5D-5L [25,26]. The pre-specified primary outcome measure of the trial was the percentage with less than good overall QOL (UWQOLv4) at 12 months after the baseline clinic. Two pre-specified secondary outcomes were the percentage with a DT score ≥4 and the mean social–emotional subscale score of the UWQOLv4. This paper analyses these and other HRQOL measures at the baseline clinic.

3. Statistical Analyses

Mann–Whitney (2 groups) or Kruskal–Wallis (>2 groups) tests were used to compare patient groups by UWQOL social–emotional and physical subscale scores, EQ5D-5L VAS and time trade-off (TTO) values, and by the total number of PCI items selected. Fishers exact test was used to assess the association between patient characteristics and of those with binary HRQOL outcomes. Logistic regression was used to assess whether any of the deprivation indicators (IMD 2019, living alone, currently working, receiving financial benefits, ever been unemployed, total household income, use of tobacco and alcohol) were predictive of HRQOL outcomes after adjustment for trial location, age, gender, tumour site, stage and treatment, and Adult Comorbidity Evaluation (ACE-27) comorbidity. The adjustment variables were all forced into the model as independent predictors, and then the deprivation indicators were considered as additional independent predictors with $p < 0.01$ criteria for stepwise entry. Analysis with SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, USA) gave the NagelKerke R2 statistic (range 0–1) as an estimate of how much variation in binary outcomes was explained by 'predictor' factors in the logistic regression model. In recognition of the numerous tests, $p < 0.01$ was taken as a better reflection of statistical significance.

The study was conducted according to the guidelines of the Declaration of Helsinki and approved given on 8 July 2016 by the North West-Liverpool Central Research Ethics Committee REC reference: IRAS 16/NW/0465, Project ID: 189554. It also has approval from the Health Research Authority (HRA) and the Research and Development Department at Aintree University Hospital National Health Service.

4. Results

The 288 trial patients attended baseline clinics a median (IQR) of 194 (125–249) days after diagnosis and 103 (71–162) days after the end of treatment. Median (IQR) age at baseline clinic was 62 (55–69) years and 69% (198) were male. Patient characteristics are shown in Table 1. Thirty-eight per cent (110/288) of patients lived in the most deprived 20% of small-area neighbourhoods in England as measured by IMD rank quintiles. The trial groups (140 PCI, 148 no PCI) were well matched at baseline in regard to the primary, secondary and other HRQOL measures analysed in this paper [16].

Table 1. Patient characteristics. (FF—Free flap; RT—Radiotherapy; CT—Chemotherapy).

		Patients	%
	Total	288	100
Location	Aintree	178	62
	Leeds	110	38
Age	<55	71	25
	55–64	116	40
	65–74	67	23
	≥75	34	12
Gender	Male	198	69
	Female	90	31
Tumour site	Oral cavity	134	47
	Oropharynx	91	32
	Larynx	41	14
	Other	22	8
Overall stage	Early 0–2	124	43
	Advanced 3–4	164	57

Table 1. *Cont.*

		Patients	%
Treatment	Surgery only, no FF	95	33
	Surgery only, and FF	21	7
	RT/CT only	58	20
	Surgery & RT/CT, no FF	68	24
	Surgery & RT/CT, and FF	46	16
ACE-27 comorbidity	None	137	48
	Mild	95	33
	Mod/severe	56	19
Ethnic group	Caucasian	279	97
	Other	9	3
IMD 2019 quintile	1 worst	110	38
	2	40	14
	3	49	17
	4	55	19
	5 best	34	12
Currently living in house or flat	With other	220	76
	Alone	65	23
	Not known	3	1
Currently working	Yes	88	31
	No	192	67
	Not known	8	3
Ever been unemployed	Yes	110	38
	No	162	56
	Not known	16	6
Financial Benefits	None	158	55
	Yes	107	37
	Not known	23	8
Total household income-all sources before tax	<GBP 12,000	52	18
	GBP 12,000–22,999	47	16
	GBP 23,000–34,999	46	16
	≥GBP 35,000	56	19
	Not known	87	30
Tobacco user	Current	37	13
	Former	163	57
	Never	80	28
	Not known	8	3
Alcohol user	Current	194	67
	Former	73	25
	Never	13	5
	Not known	8	3

Less than good overall quality of life (31% overall) was associated (Table 2) with current working situation ($p = 0.008$), receipt of financial benefits ($p < 0.001$), total household income ($p = 0.003$) and use of tobacco ($p = 0.001$). For working patients, this was 20% compared with 36% if not working. It was 43% for those on benefits and 22% without benefits, 50% for patients in households with <£12,000 annual income and 20–23% for higher-income groups. It was 57% for current users of tobacco. A distress thermometer score of ≥4 (45% overall) was associated (also Table 2) with ever having been unemployed ($p = 0.002$), receipt of financial benefits ($p < 0.001$) and use of alcohol ($p = 0.007$). It was 55% for patients having been unemployed compared with 36% otherwise. It was 58% if receiving benefits and 34% without benefits and 60% for former users of alcohol. The trends observed across the other four HRQOL measures in Table 2 suggest worse HRQOL reported by patients who were younger, had tumours located in the oral cavity or oropharynx, had tumours at an advanced stage, had ACE-27 comorbidity, were living in more deprived IMD neighbourhoods, were currently not working, had known unemployment, were receiving benefits, were living in lower income households and were current users of tobacco and former users of alcohol.

Table 2. HRQOL measures by casemix.

			Overall QOL: Less Than Good			Distress Thermometer (DT) Score ≥ 4			UWQOL Social–Emotional Subscale Score			UWQOL Physical Function Subscale Score			EQ-5D-5L VAS			EQ-5D-5L TTO		
		Patients	**%**	***n***	***p*-Value**	**%**	***n***	***p*-Value**	**Median**	**IQR**	***p*-Value**	**Median**	**IQR**	***p*-Value**	**Median**	**IQR**	***p*-Value**	**Median**	**IQR**	***p*-Value**
	Total	288	31	89		45	129		75	59–88		69	54–86		75	60–86		0.77	0.64–0.88	
Location	Aintree	178	26	47	0.05	45	80	>0.99	75	61–88	0.78	69	56–84	0.74	76	60–85	0.89	0.76	0.65–0.88	0.33
	Leeds	110	38	42		45	49		75	58–88		68	53–86		75	50–88		0.78	0.64–0.88	
Age	<55	71	37	26	0.13	52	37	0.02	68	55–87	0.002	66	54–87	0.41	75	60–89	0.59	0.74	0.59–0.84	0.04
	55–64	116	33	38		47	55		77	56–87		68	53–81		75	50–86		0.77	0.59–0.84	
	65–74	67	30	20		45	30		76	65–91		69	59–88		75	61–88		0.80	0.66–1.00	
	$\geq$75	34	15	5		21	7		87	71–96		75	56–93		80	70–85		0.84	0.72–0.91	
Gender	Male	198	30	60	0.78	44	88	0.90	78	61–91	0.15	69	55–86	0.43	75	60–86	0.74	0.77	0.65–0.88	0.62
	Female	90	32	29		46	41		71	57–87		68	54–82		77	51–85		0.76	0.63–0.88	
Tumour site	Oral cavity	134	37	49	0.27	47	63	0.11	71	55–87	0.002	66	50–82	<0.001	71	50–84	0.05	0.75	0.58–0.88	0.01
	Oropharynx	91	25	23		51	46		72	63–87		66	54–74		75	69–85		0.74	0.65–0.84	
	Larynx	41	29	12		34	14		87	75–95		90	73–95		80	64–90		0.84	0.72–1.00	
	Other	22	23	5		27	6		81	66–91		77	59–92		86	73–90		0.82	0.67–0.91	
Overall stage	Early 0–2	124	28	35	0.44	38	47	0.04	83	63–91	0.001	79	65–95	<0.001	79	53–88	0.49	0.77	0.64–0.88	0.22
	Advanced 3–4	164	33	54		50	82		71	58–87		63	50–73		75	60–86		0.76	0.64–0.84	
Treatment	Surgery only, no FF	95	19	18	0.01	33	31	0.03	84	68–92	<0.001	86	71–95	<0.001	80	67–90	0.07	0.84	0.70–0.91	0.09
	Surgery only, & FF	21	33	7		67	14		67	48–87		61	35–75		79	56–86		0.71	0.62–0.84	
	RT/CT only	58	38	22		50	29		75	59–88		65	50–79		75	60–85		0.75	0.61–0.88	
	Surgery & RT/CT, no FF	68	31	21		47	32		71	61–83		66	57–74		75	61–84		0.75	0.65–0.84	
	Surgery & RT/CT, and FF	46	46	21		50	23		66	52–83		53	39–68		70	50–85		0.74	0.53–0.91	
ACE27 comorbidity	None	137	24	33	0.02	40	55	0.32	78	63–91	0.21	71	61–89	0.007	80	69–90	0.003	0.80	0.70–0.88	0.02
	Mild	95	33	31		49	47		73	58–87		68	54–83		70	50–83		0.74	0.58–0.88	
	Mod/severe	56	45	25		48	27		75	54–88		61	39–81		71	51–81		0.69	0.53–0.88	
Ethnic group	White British	279	30	84	0.14	44	122	0.08	75	61–88	0.21	69	55–86	0.43	78	60–86	0.10	0.77	0.64–0.88	0.36
	Other	9	56	5		78	7		69	na		62	na		70	na		0.72	na	
IMD 2019 quintile	1 worst	110	37	41	0.19	50	55	0.29	70	54–87	0.05	65	50–83	0.09	70	50–82	0.004	0.74	0.54–0.88	0.19
	2	40	35	14		53	21		71	61–86		68	50–88		72	52–84		0.75	0.58–0.85	
	3	49	29	14		41	20		78	65–91		72	61–84		79	71–89		0.77	0.70–0.88	
	4	55	25	14		35	19		78	65–92		69	57–87		81	65–90		0.81	0.68–0.88	
	5 best	34	18	6		41	14		82	69–88		78	61–86		80	71–89		0.77	0.71–0.84	
Currently living in house or flat	With other	220	31	69	0.88	48	105	0.06	74	59–87	0.09	68	54–84	0.60	75	60–86	0.41	0.77	0.64–0.85	0.38
	Alone	65	29	19		34	22		83	61–91		71	53–88		75	54–84		0.77	0.63–0.91	
	Not known	3		1			2		55	na		67	na		90	na		0.72	na	
Currently working	Yes	88	20	18	0.008	40	35	0.25	82	70–91	<0.001	75	62–91	<0.001	80	70–90	<0.001	0.80	0.74–0.98	<0.001
	No	192	36	70		47	91		71	55–87		66	50–79		71	50–82		0.74	0.55–0.84	
	Not known	8		1			3		77	na		85	na		84	na		0.84	na	

Table 2. *Cont.*

			Overall QOL: Less Than Good			Distress Thermometer (DT) Score ≥ 4			UWQOL Social–Emotional Subscale Score			UWQOL Physical Function Subscale Score			EQ-5D-5L VAS			EQ-5D-5L TTO		
		Patients	**%**	***n***	***p*-Value**	**%**	***n***	***p*-Value**	**Median**	**IQR**	***p*-Value**	**Median**	**IQR**	***p*-Value**	**Median**	**IQR**	***p*-Value**	**Median**	**IQR**	***p*-Value**
Ever been unemployed	Yes	110	35	38	0.23	55	61	0.002	71	54–87	0.001	66	50–79	0.002	70	50–81	<0.001	0.72	0.56–0.84	0.001
	No	162	27	44		36	58		78	66–91		71	59–90		80	70–90		0.80	0.69–0.88	
	Not known	16		7			10		68	53–82		69	49–95		71	50–85		0.74	0.52–0.87	
Financial Benefits	None	158	22	34	<0.001	34	54	<0.001	81	68–91	<0.001	73	61–90	<0.001	80	70–90	<0.001	0.82	0.74–0.91	<0.001
	Yes	107	43	46		58	62		66	54–87		62	43–78		69	50–82		0.65	0.51–0.84	
	Not known	23		9			13		67	48–87		68	48–92		52	50–82		0.74	0.44–0.84	
Total household income from all sources before tax	< £12,000	52	50	26	0.003	53	28	0.26	62	46–80	<0.001	54	35–72	<0.001	60	50–81	<0.001	0.65	0.51–0.84	<0.001
	£12,000–22,999	47	23	11		45	21		79	63–96		72	61–90		80	70–90		0.84	0.68–1.00	
	£23,000–34,999	46	20	9		39	18		82	61–91		73	63–88		80	70–90		0.77	0.70–1.00	
	$\geq$ £35,000	56	23	13		36	20		78	70–90		71	61–90		79	68–90		0.80	0.70–0.88	
	Not known	87		30			42		71	61–87		67	55–82		72	50–82		0.77	0.65–0.84	
Tobacco user	Current	37	57	21	0.001	57	21	0.04	71	40–87	0.08	62	43–87	0.16	71	45–86	0.02	0.69	0.42–0.86	0.04
	Former	163	29	47		47	76		75	61–88		68	53–82		75	55–85		0.77	0.63–0.88	
	Never	80	24	19		34	27		78	66–91		72	59–87		80	70–90		0.80	0.70–0.90	
	Not known	8		2					66	na		68	na		66	na		0.72	na	
Alcohol user	Current	194	26	51	0.02	40	78	0.007	78	66–91	0.001	71	59–90	0.001	79	62–89	0.004	0.80	0.68–0.88	0.001
	Former	73	44	32		60	44		63	52–87		63	46–77		70	50–81		0.70	0.53–0.83	
	Never	13	23	3		31	4		78	70–91		66	43–78		74	51–85		0.77	0.67–1.00	
	Not known	8		3					67	na		71	na		73	na		0.74	na	

p-value: Fishers exact test (Overall QOL and DT); otherwise Mann–Whitney test (2 comparison groups) or Kruskal–Wallis test (3 or more comparison groups), excluding any categories not known. TTO: Time trade-off crosswalk values. VAS: Visual analogue scale.

Logistic regression methods were used (Table 3) to assess the significance of area-level IMD and patient-level deprivation indicators on HRQOL outcomes after adjustment for hospital location, gender, age, tumour site, stage, treatment and ACE27 comorbidity. Patient level indicators relating in one way or another to income and employment were significant predictors of these HRQOL outcomes after such adjustment. In separate analyses, the IMD area quintiles were collapsed into a binary variable, into the first two quintiles (i.e., those living in the 40% of more deprived English small area neighbourhoods) and those living in other less deprived areas. This binary IMD variable was significantly predictive in regard to the worst third of UWQOL social–emotional scores ($p = 0.005$), the worst third of EQ-5D-VAS ($p = 0.004$) and EQ-5D-TTO ($p = 0.001$) values, after similar casemix adjustment. For the other HRQOL outcomes of Table 3, it was of borderline significance ($0.05 < p < 0.10$).

Table 3. Association of deprivation indicators with HRQOL outcome after adjustment.

HRQOL Outcome	*n*	R^2 (for Adjustment Variables) *	SES Deprivation-Related Indicators ** Selected in Addition to Adjustment Variables (p for Entry, Stepwise Regression)	R^2 (Adjustment Variables + Selected SES Indicators)
Less than good overall QOL	254	0.24	Financial benefits (0.009)	0.27
Distress thermometer $\geq$4	254	0.15	Financial benefits 0.001)	0.21
Worst third of UWQOL Social–emotional subscale scores	254	0.23	Financial benefits (<0.001), Alcohol use (0.002)	0.37
Worst third of UWQOL Physical subscale scores	254	0.32	Currently working (<0.001)	0.38
Worst third of EQ-5D-5L VAS values	254	0.19	Financial benefits (<0.001)	0.30
Worst third of EQ-5D-5L TTO crosswalk values	254	0.21	Financial benefits (<0.001), Currently working (0.009)	0.39

* Adjustment for Age group, gender, trial location, tumour site, tumour staging, treatment and ACE-27 comorbidity as described in Table 1.
** Factors considered were IMD 2019 quintile, currently living in house or flat, currently working, ever been unemployed, financial benefits, total household income, tobacco use and alcohol use. The NagelKerke R^2 statistic (range 0–1) estimates the proportion of the variation in a binary outcome that can be explained by the predictor variables in the logistic regression model. Missing data were coded only for household income; otherwise, complete data were available for 254 patients. SES: Socio-Economic Status.

Table 4 shows the significant univariate associations of casemix and SES-related deprivation-relevant factors with dysfunction on specific UWQOL domains. After similar casemix adjustment, patient-level indicators relating in one way or another to income and employment were also significant predictors ($p < 0.01$) of dysfunction in pain, mood, swallowing and chewing. The binary-area IMD measure after similar adjustment was also predictive of dysfunction in mood ($p = 0.007$) and chewing ($p = 0.002$).

Table 4. Significant ($p < 0.01$) associations of casemix and deprivation-relevant variables with UWQOL domain dysfunction.

Variables Associated		***p* Value ***	**Observed Nature of Dysfunction**				
Casemix	**Dysfunction**						
Age	Mood	0.004	<55: 21% (15/71)	55–64: 20% (23/116)	65–74: 10% (7/67)	≥75: 0% (0/34)	
	Anxiety	0.008	<55: 25% (18/71)	55–64: 20% (23/116)	65–74: 10% (7/67)	≥75: 3% (1/34)	
	Fear of recurrence	0.002	<55: 21% (15/71)	55–64: 12% (14/116)	65–74: 4% (3/67)	≥75: 0% (0/34)	
Gender	Fear of recurrence	0.001	Male: 7% (13/198)	Female: 21% (19/90)			
Tumour site	Mood	0.003	Oral: 24% (32/134)	Oropharynx: 7% (6/91)	Larynx: 10% (4/41)	Other: 14% (3/22)	
	Taste	0.005	Oral: 16% (22/134)	Oropharynx: 25% (23/91)	Larynx: 7% (3/41)	Other: 41% (9/22)	
	Saliva	0.001	Oral: 28% (38/134)	Oropharynx: 48% (44/91)	Larynx: 17% (7/41)	Other: 45% (10/22)	
Overall stage	Taste	0.005	Early 0–2: 12% (15/124)	Advanced 3–4: 26% (42/164)			
	Saliva	<0.001	Early 0–2: 21% (26/124)	Advanced 3–4: 45% (73/164)			
Treatment *	Shoulder	0.003	S no FF: 15% (14/95)	S & FF: 33% (7/21)	RT/CT: 2% (1/58)	S & RT/CT no FF: 13% (9/68)	S & RT/CT & FF: 11% (5/46)
	Appearance	<0.001	S no FF: 3% (3/95)	S & FF: 33% (7/21)	RT/CT: 5% (3/58)	S & RT/CT no FF: 10% (7/68)	S & RT/CT & FF: 17% (8/46)
	Swallowing	<0.001	S no FF: 3% (3/95)	S & FF: 33% (7/21)	RT/CT: 24% (14/58)	S & RT/CT no FF: 7% (5/68)	S & RT/CT & FF: 28% (13/46)
	Chewing	<0.001	S no FF: 1% (1/95)	S & FF: 33% (7/21)	RT/CT: 16% (9/58)	S & RT/CT no FF: 6% (4/68)	S & RT/CT & FF: 37% (17/46)
	Taste	<0.001	S no FF: 6% (6/95)	S & FF: 19% (4/21)	RT/CT: 29% (17/58)	S & RT/CT no FF: 28% (19/68)	S & RT/CT & FF: 24% (11/46)
	Saliva	<0.001	S no FF: 15% (14/95)	S & FF: 24% (5/21)	RT/CT: 53% (31/58)	S & RT/CT no FF: 47% (32/68)	S & RT/CT & FF: 37% (17/46)
ACE27	Appearance	0.007	ACE 'None': 6% (8/137),	ACE 'mild': 8% (8/95)	ACE 'mod/severe': 21% (12/56)		
	Chewing	0.004	ACE 'None': 8% (11/137),	ACE 'mild': 13% (12/95)	ACE 'mod/severe': 27% (15/56)		
	Speech	0.003	ACE 'None': 3% (4/137),	ACE 'mild': 11% (10/95)	ACE 'mod/severe': 16% (9/56)		
IMD 2019Quintile (Q)	Mood	0.008	Q1 (worst): 25% (28/110),	Q2: 15% (6/40)	Q3: 10% (5/49)	Q4: 7% (4/55)	Q5 (best): 6% (2/34)
	Chewing	0.004	Q1 (worst): 21% (23/110),	Q2: 20% (8/40)	Q3: 4% (2/49)	Q4: 5% (3/55)	Q5 (best): 6% (2/34)
Currently working	Pain	0.003	Working: 17% (15/88),	Not working: 34% (66/192)			
	Recreation	<0.001	Working: 0% (0/88),	Not working: 12% (23/192)			
	Mood	0.001	Working: 5% (4/88),	Not working: 20% (39/192)			
	Swallowing	0.001	Working: 5% (4/88),	Not working: 20% (38/192)			
	Chewing	<0.001	Working: 2% (2/88),	Not working: 19% (36/192)			
Financial benefits	Pain	0.008	Benefits: 37% (40/107),	No: 22% (35/158)			
	Recreation	0.008	Benefits: 13% (14/107)	No Benefits: 4% (6/158)			
	Mood	<0.001	Benefits: 25% (27/107)	No Benefits: 8% (12/158)			
	Swallowing	<0.001	Benefits: 28% (30/107)	No Benefits: 6% (10/158)			
	Chewing	<0.001	Benefits: 25% (27/107)	No Benefits: 4% (7/158)			
	Speech	0.008	Benefits: 13% (14/107)	No Benefits: 4% (6/158)			
Total Household income	Mood	<0.001	<GBP 12,000: 35% (18/52)	GBP 12,000–22,999: 9% (4/47)	GBP 23,000–34,999: 11% (5/46)	≥GBP 35,000: 5% (3/56)	
	Swallowing	<0.001	<GBP 12,000: 35% (18/52)	GBP 12,000–22,999: 9% (4/47)	GBP 23,000–34,999: 9% (4/46)	≥GBP 35,000: 7% (4/56)	
	Chewing	<0.001	<GBP 12,000: 35% (18/52)	GBP 12,000–22,999: 11% (5/47)	GBP 23,000–34,999: 9% (4/46)	≥GBP 35,000: 2% (1/56)	
Tobacco user	Mood	<0.001	Current: 41% (15/37)	Former: 14% (23/163)	Never: 8% (6/80)		
	Fear of recurrence	0.009	Current: 24% (9/37)	Former: 12% (19/163)	Never: 5% (4/80)		
Alcohol user	Pain	0.004	Current: 25% (48/194)	Former: 42% (31/73)	Never: 8% (1/13)		
	Mood	0.004	Current: 12% (23/194)	Former: 29% (21/73)	Never: 8% (1/13)		
	Swallowing	0.003	Current: 10% (20/194)	Former: 25% (18/73)	Never: 31% (4/13)		

* Fishers exact test, with analyses using the variables of Table 1 but excluding not known categories. S = Surgery, RT = Radiotherapy, CT = Chemotherapy, FF = Free flap.

The number of PCI items selected by the 140 PCI patients varied significantly by overall clinical tumour clinical stage ($p < 0.001$) and by treatment ($p < 0.001$) but not by area IMD or patient-level deprivation indicators. For early-stage tumours, the median (IQR) number of items was 3 (2–6) while for advanced tumours, it was 7 (3–11). For patients having surgery without RT/CT or free-flap the number was 3 (1–5); otherwise, it was 7 (4–10). The most commonly selected PCI items were dry mouth (49%), dental health/teeth (34%), fear of recurrence (34%), chewing/eating (33%), salivation (33%), fatigue/tiredness (29%), swallowing (28%) and taste (27%). The 'financial benefits' item was selected by only 4% (6/140). Common patient selections were similar amongst selected subgroups relevant to area and patient-level deprivation (Table 5).

Table 5. Most commonly selected PCI items (≥20%) for some deprivation-related subgroups.

All Patients	Patient Living in Less Deprived 60% of IMD English Small Area Neighbourhoods	Patient Living in More Deprived 40% of IMD English Small Area Neighbourhoods	Patients in Households Receiving Financial Benefits	Patients in Households Not Receiving Financial Benefits
n = 288 (All in trial)	138	150	107	110
n = 140 (PCI group)	67	73	49	53
Dry mouth 49 Dental health/teeth 34 Fear of recurrence 34 Chewing/eating 33 Salivation 33 Fatigue/tiredness 29 Swallowing 28 Taste 27 Mucus 24 Sore mouth 24 Shoulder 22 Pain in head/neck 21 Cancer treatment 20	Dry mouth 55 Fear of recurrence 39 Dental health/teeth 36 Chewing/eating 31 Taste 31 Fatigue/tiredness 30 Salivation 30 Swallowing 30 Sore mouth 27 Mucus 25 Cancer treatment 24 Pain head& neck 24 Mouth opening 22 Weight 22 Appetite 21	Dry mouth 42 Salivation 36 Chewing/eating 34 Dental health/teeth 33 Fear of recurrence 30 Fatigue/tiredness 27 Swallowing 26 Shoulder 25 Taste 23 Mucus 22 Energy levels 21 Sore mouth 21	Dry mouth 53 Chewing/eating 39 Dental health/teeth 37 Taste 35 Fear of recurrence 33 Swallowing 33 Fatigue/tiredness 31 Salivation 31 Mucus 27 Appetite 22 Weight 22 Energy levels 20 Pain in head/neck 20 Shoulder 20	Dry mouth 47 Fear of recurrence 35 Salivation 35 Dental health/teeth 31 Chewing/eating 29 Sore mouth 28 Fatigue/tiredness 27 Taste26 Swallowing 23 Cancer treatment 22 Mucus 22 Mouth opening 21

5. Discussion

Socioeconomic factors have a strong influence on HRQOL following HNC, especially in patients with low SES who show the strongest impairment [27]. The detail on area-level and individual-level indicators of deprivation collected as part of this randomised trial has provided an unparalleled opportunity to assess the relationship between SES characteristics and both HRQOL and patient concerns. Although the IMD 2019 is a well recognised and up-to-date measure combining seven domains of deprivation (income, employment, education/skills/training, health/disability, crime, barriers to housing/services and living environment) within relatively focused postcode areas within England, the details asked of individual trial patients have considerably augmented the assessment of social determinants. In addition, the combination of HRQOL measures (DT, UW-QOL, EQ-5D and PCI) provides both a general and a head-and-neck-specific patient perspective. In terms of focusing on financial toxicity incurred during and after treatment, the trial predates a specific measure such as the Financial Index of Toxicity questionnaire [28], and this could be included in future studies. Another limitation of this study is that the data come from two areas in England (Liverpool and Leeds) and might not reflect other regions in the United Kingdom and internationally. However, although there will be differences between healthcare systems, any trends in the relationship between social determinants and HRQOL ought to apply.

Cancer-related financial hardship, or “financial toxicity” [29–31], is important as this has implications not only in terms of financial worries during treatment but also potentially in the longer term. Financial distress is a common concern with respect to quality of life, coping strategies and supportive care needs in head and neck cancer survivors [32,33]. There are out-of-pocket costs associated with treatment, and these have significant implications on quality of life and survival [34]. These costs are highest during treatment and gradually decrease over time. Finance is linked to the social determinants of health and the importance of this to HRQOL outcomes can be underestimated when considering other aspects such as cancer stage, site and treatment. Patients experiencing cancer-related financial hardship report worse quality of life, decreased psychosocial well-being and demonstrate lower treatment adherence [35].

As previously recognised in the literature, differences in HRQOL were seen by cancer stage and type of treatment; however, there were surprising associations with whether patients were currently not working, had ever been unemployed, financial benefits received and overall household income. The importance of these aspects in terms of HRQOL outcomes following HNC cannot be underestimated, with worse HRQOL scores being seen across all PRO measures, i.e., DT, UW-WOL subscales and EQ-5D. The relationship is not as clear regarding the area-level deprivation measure [19], hence the importance of considering individual indicators of SES.

Financial stability is linked to employment. In our sample, only one-third were aged 65 years or older, yet two-thirds overall were not currently working, and these reported a significantly worse overall QOL. The ability of patients to return to work is important [32]. Returning to work not only provides income but also adds to self-esteem and reduces social isolation. Baxi [36] found that in the long-term most survivors of HPV-related oropharyngeal cancer who were employed at baseline were able to return to work after taking a break from employment. However, side effects of treatment such as fatigue, pain, disfigurement, physical morbidity and depression can act as barriers to return to work. Following HNC, perhaps larynx/hypopharynx patients find a greater degree of workplace discrimination and inability to return to work [29]. Potentially there is value in improving HRQOL by a phased return to work and for a better understanding and support in the workplace of the challenges faced by HNC patients who wish to return to employment [37].

In addition, as a social determinant, just over half of those patients reported never having been unemployed, and this group had significantly better HRQOL scores. Currently in 2021, the UK unemployment rate is estimated at 4.8% [38].

HRQOL outcomes in this current study were worse for those with the lowest household incomes. Individuals with HNC are particularly vulnerable to financial strains given the established association with lower socioeconomic status [39]. For most patients, the cancer adds a substantial additional burden to an already financially strained population and happens disproportionately in the socioeconomically disenfranchised. In the UK, the government’s department of work and pensions defines low pay with any family earning less than 60% of the national median pay.

Patient concerns as measured by the PCI showed that the number of issues selected by patients was significantly associated with tumour stage and treatment but not noticeably with any of the deprivation indicators. Looking at the items most often selected in relation to area-level IMD area and patient-level financial benefits, there does not seem to be much difference. In addition, the PCI ‘financial benefits’ item was not selected that often, though this might relate more to the context of when the PCI is being used; for example in oncology, medical follow-up clinics patients might choose not to raise this issue as they might feel that the focus of the consultation is more about having a cancer disease-free check and about side effects of treatment and leave financial concerns to other healthcare professionals such as the Clinical Nurse Specialist. Holistic assessment tools such as the Patient Concerns Inventory are useful to help identify financially related concerns, particularly at the time of diagnosis.

The issue of benefits amongst patients with head and neck cancer has been previ-ously explored [40]. Over half the patients in that study said that they had suffered fi-nancially since diagnosis, and half the entire sample said that their financial burden was large or unbearable. The benefits system is complex, and the current COVID-19 pandemic has resulted in a large backlog of applications. In our experience from Liverpool and Leeds, patients often need support with general household bills, especially younger patients who must take time off work. Small grants are available from Macmillan (UK based cancer support charity), but patient experiences and needs do vary.

In conclusion, there is an inextricable interrelated relationship between socioeconomic factors and HNC, both in terms of relative risk for the disease itself and HRQOL outcomes. The aspect of financial 'toxicity' is important as relative poverty is associated with unemployment and depression. Not only should the history of a patient's employment, work status, income and reliance on financial benefits be included as case-mix information when a comprehensive assessment of HRQOL outcomes is being considered, but these aspects should also be considered as factors to help identify patients during and after treatment, as they will be at greater risk of having poor outcomes. Addressing the disparity caused by social determinants is a huge challenge, and innovative solutions are required to tackle this inequality.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsin-ki and approved given on 8 July 2016 by the North West-Liverpool Central Research Ethics Committee REC reference: IRAS 16/NW/0465, Project ID: 189554. It also has approval from the Health Research Authority (HRA) and the Research and Development Department at Aintree University Hospital National Health Service.

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