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

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 $\geq 4$ 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  |
| $\geq$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-SD-SL VAS | EQ-SD-SL TTO |
|-----------------------------|-------------------------------------|---------------------------------------|----------------------------------------|--------------|--------------|
| **Patients %** | **n** | **p-Value** | **Median** | **IQR** | **Median** | **IQR** | **Median** | **IQR** | **Median** | **IQR** | **p-Value** |
| **Total** | 288 | 31 | 89 | | | | | | | | 0.77 | 0.64–0.88 |
| **Location** | | | | | | | | | | | | | |
| Aintree | 178 | 26 | 47 | 0.05 | | | | | | | 0.05 | 0.58–0.88 |
| Leeds | 110 | 38 | 42 | 45 | 49 | | | | | | 0.74 | 0.63–0.88 |
| **Age** | | | | | | | | | | | | | |
| <55 | 71 | 37 | 26 | 0.13 | | | | | | | 0.02 | 0.58–0.88 |
| 55–64 | 116 | 33 | 38 | 47 | 55 | | | | | | 0.02 | 0.58–0.88 |
| ≥75 | 34 | 15 | 5 | 21 | 7 | | | | | | 0.15 | 0.58–0.88 |
| **Gender** | | | | | | | | | | | | | |
| Male | 198 | 30 | 60 | 0.78 | | | | | | | 0.15 | 0.58–0.88 |
| Female | 90 | 32 | 29 | 46 | 41 | | | | | | 0.43 | 0.74–0.88 |
| **Tumour site** | | | | | | | | | | | | | |
| Oral cavity | 134 | 37 | 49 | 0.27 | | | | | | | 0.15 | 0.58–0.88 |
| Oropharynx | 91 | 25 | 23 | 47 | 56 | | | | | | 0.15 | 0.58–0.88 |
| Larynx | 41 | 29 | 12 | 34 | 14 | | | | | | 0.15 | 0.58–0.88 |
| Other | 22 | 23 | 5 | 27 | 6 | | | | | | 0.15 | 0.58–0.88 |
| **Overall stage** | | | | | | | | | | | | | |
| Early 0-2 | 124 | 38 | 47 | 0.04 | | | | | | | 0.01 | 0.58–0.88 |
| Advanced 3-4 | 164 | 33 | 54 | 50 | 82 | | | | | | 0.15 | 0.58–0.88 |
| **Treatment** | | | | | | | | | | | | | |
| Surgery only, no FF | 95 | 19 | 18 | 0.01 | | | | | | | 0.01 | 0.58–0.88 |
| Surgery only, & FF | 21 | 33 | 7 | 67 | 14 | | | | | | 0.15 | 0.58–0.88 |
| RT/CT only | 58 | 38 | 22 | 50 | 29 | | | | | | 0.15 | 0.58–0.88 |
| Surgery & RT/CT, no FF | 68 | 31 | 21 | 47 | 32 | | | | | | 0.15 | 0.58–0.88 |
| Surgery & RT/CT, & FF | 46 | 46 | 23 | 50 | 23 | | | | | | 0.15 | 0.58–0.88 |
| **ACE27 comorbidity** | | | | | | | | | | | | | |
| None | 137 | 24 | 33 | 0.02 | | | | | | | 0.02 | 0.58–0.88 |
| Mild | 95 | 33 | 31 | 49 | 47 | | | | | | 0.02 | 0.58–0.88 |
| Mod/severe | 56 | 45 | 25 | 48 | 27 | | | | | | 0.02 | 0.58–0.88 |
| **Ethnic group** | | | | | | | | | | | | | |
| White British | 279 | 30 | 84 | 0.14 | | | | | | | 0.02 | 0.58–0.88 |
| Other | 9 | 56 | 5 | 79 | 7 | | | | | | 0.02 | 0.58–0.88 |
| **IMD 2019 quintile** | | | | | | | | | | | | | |
| 1 worst | 110 | 37 | 41 | 0.19 | | | | | | | 0.02 | 0.58–0.88 |
| 2 | 40 | 35 | 14 | 53 | 21 | | | | | | 0.15 | 0.58–0.88 |
| 3 | 49 | 29 | 14 | 41 | 20 | | | | | | 0.15 | 0.58–0.88 |
| 4 | 55 | 25 | 14 | 35 | 19 | | | | | | 0.15 | 0.58–0.88 |
| 5 best | 34 | 18 | 6 | 41 | 14 | | | | | | 0.15 | 0.58–0.88 |
| **Currently living in house or flat** | | | | | | | | | | | | | |
| With other | 220 | 31 | 69 | 0.88 | | | | | | | 0.02 | 0.58–0.88 |
| Alone | 65 | 29 | 19 | 34 | 22 | | | | | | 0.15 | 0.58–0.88 |
| Not known | 3 | 1 | 2 | 55 | na | | | | | | 0.15 | 0.58–0.88 |
| **Currently working** | | | | | | | | | | | | | |
| Yes | 88 | 20 | 18 | 0.008 | | | | | | | 0.02 | 0.58–0.88 |
| No | 192 | 36 | 70 | 47 | 91 | | | | | | 0.02 | 0.58–0.88 |
| Not known | 8 | 1 | 3 | 77 | na | | | | | | 0.15 | 0.58–0.88 |
## Table 2. Cont.

| Overall QOL: Less Than Good | Distress Thermometer (DT) Score ≥ 4 | UWQOL Social–Emotional Subscale Score | UWQOL Physical Function Subscale Score | EQ-SD-5L VAS | EQ-SD-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 | | | 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 | 0.66–1.00 | |
| ≥ £23,000–34,999 | 46 | 20 | 9 | | 39 | 18 | | 82 | 61–91 | | 73 | 63–88 | | 80 | 70–90 | | 0.77 | 0.70–1.00 | |
| > £35,000–54,000 | 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 | | 72 | 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 | 0.66–0.88 | 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 ($p = 0.002$).
| Variables Associated | p Value * | Observed Nature of Dysfunction |
|----------------------|-----------|-------------------------------|
| **Casemix Dysfunction** | | |
| Age                  | 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               | 0.011     | Male: 7% (13/198) Female: 21% (19/90) |
| Tumour site          | 0.003     | Oral: 24% (32/134) Oropharynx: 7% (6/91) Larynx: 10% (4/41) Other: 14% (5/22) |
| Saliva               | 0.002     | Oral: 28% (28/134) Oropharynx: 48% (44/91) Larynx: 17% (7/41) Other: 41% (9/22) |
| Overall stage        | 0.005     | Taste: 12% (15/124) Saliva: 21% (26/124) |
| Treatment *          | 0.003     | Shoulder: 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) |
|                      | <0.001    | Appearance: 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) |
|                      | <0.001    | Swallowing: 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) |
|                      | <0.001    | Chewing: 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) |
|                      | <0.001    | Taste: 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) |
|                      | <0.001    | Saliva: 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                | 0.007     | Appearance: ACE 'None': 6% (8/137), ACE 'mild': 8% (9/95), ACE 'mod/severe': 21% (12/56) |
|                      | 0.004     | Chewing: ACE 'None': 8% (11/137), ACE 'mild': 13% (12/95), ACE 'mod/severe': 27% (15/56) |
|                      | 0.003     | Speech: ACE 'None': 3% (4/137), ACE 'mild': 11% (10/95), ACE 'mod/severe': 16% (9/56) |
| IMD 2019Quintile (Q) | 0.008     | Mood: Q1: 25% (28/110), Q2: 15% (8/50), Q3: 10% (5/50), Q4: 7% (4/55), Q5: 6% (2/34) |
|                      | 0.004     | Chewing: Q1: 21% (26/124), Q2: 20% (8/40), Q3: 4% (2/49), Q4: 3% (1/35), Q5: 6% (2/34) |
| Currently working    | 0.008     | Pain: Working: 17% (15/88), Not working: 34% (66/192) |
|                      | <0.001    | Recreational: Working: 0% (0/88), Not working: 100% (0/88) |
|                      | <0.001    | Mood: Working: 17% (15/88), Not working: 34% (66/192) |
|                      | <0.001    | Swallowing: Working: 5% (4/88), Not working: 95% (8/17) |
|                      | <0.001    | Chewing: Working: 2% (2/88), Not working: 98% (15/15) |
| Financial benefits   | 0.008     | Pain: Benefits: 37% (40/107), No Benefits: 63% (57/90) |
|                      | 0.008     | Recreational: Benefits: 13% (14/107), No Benefits: 86% (93/109) |
|                      | <0.001    | Mood: Benefits: 37% (40/107), No Benefits: 63% (57/90) |
|                      | <0.001    | Swallowing: Benefits: 28% (30/107), No Benefits: 72% (87/121) |
|                      | <0.001    | Chewing: Benefits: 25% (27/107), No Benefits: 75% (80/107) |
|                      | 0.008     | Speech: Benefits: 13% (14/107), No Benefits: 86% (93/109) |
| Total Household income | <0.001   | Mood: <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% (2/36) |
|                      | <0.001    | Swallowing: <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% (2/36) |
|                      | <0.001    | Chewing: <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% (2/36) |
| Tobacco user         | <0.001    | Mood: Current: 41% (15/37), Former: 14% (23/163), Never: 8% (6/80) |
|                      | 0.009     | Fear of recurrence: Current: 24% (9/37), Former: 12% (19/163), Never: 5% (4/80) |
| Alcohol user         | 0.004     | Mood: Current: 25% (18/73), Former: 29% (21/73), Never: 8% (1/13) |
|                      | 0.003     | Swallowing: 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 \((\geq 20\%)\) 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 | Dry mouth 55 | Dry mouth 53 | Dry mouth 47 | Fear of recurrence 35 |
| Dental health/teeth 34 | Dental health/teeth 36 | Salivation 36 | Salivation 35 | Dental health/teeth 31 |
| Fear of recurrence 34 | Chewing/eating 31 | Dental health/teeth 33 | Dental health/teeth 31 | Chewing/eating 29 |
| Chewing/eating 33 | Fear of recurrence 30 | Fatigue/tiredness 30 | Fatigue/tiredness 30 | Sore mouth 28 |
| Salivation 33 | Salivation 30 | Fatigue/tiredness 30 | Swallowing 33 | Fatigue/tiredness 27 |
| Fatigue/tiredness 29 | Swallowing 30 | Swallowing 26 | Swallowing 31 | Salivation 21 |
| Swallowing 28 | Sore mouth 27 | Shoulder 25 | Mucus 27 | Mucus 27 |
| Taste 27 | Mucus 25 | Taste 23 | Appetite 22 | Appetite 22 |
| Mucus 24 | Cancer treatment 24 | Mucus 22 | Weight 22 | Weight 22 |
| Sore mouth 24 | Pain head& neck 24 | Energy levels 21 | Energy levels 20 | Energy levels 20 |
| Shoulder 22 | Mouth opening 22 | Sore mouth 21 | Pain in head/neck 20 | Pain in head/neck 20 |
| Pain in head/neck 21 | Weight 22 | | Shoulder 20 | Shoulder 20 |
| Cancer treatment 20 | Appetite 21 | | Mucosal 20 | Mucosal 20 |

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 previously explored [40]. Over half the patients in that study said that they had suffered financially 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 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.

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