Health-related quality of life at 3 months following head and neck cancer treatment is a key predictor of longer-term outcome and of benefit from using the patient concerns inventory

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Abstract

Introduction: During clinical follow-up it can be difficult to identify those head and neck cancer (HNC) patients who are coping poorly and could benefit from additional support. Health-related quality of life (HRQOL) questionnaires and prompt lists provide a means by which patients can express their perceived outcomes and raise concerns. The first aim of this secondary analysis following a randomized trial was to explore which patient characteristics, at around 3 months following treatment completion (baseline), best predict HRQOL 12 months later. The second aim was to attempt to ascertain which patients were most likely to benefit from using prompt list.

Methods: Cluster-controlled pragmatic trial data were analyzed. HRQOL was measured by the University of Washington Quality of Life questionnaire (UW-QOLv4). The prompt list was the Patient Concerns Inventory (PCI-HN).

Results: The trial involved 15 eligible consultants and a median (inter-quartile range) of 16 (13–26) primary HNC patients per consultant, with 140 PCI patients and 148 controls. Baseline HRQOL was the dominant predictor of 12-month HRQOL with other predictors related to social, financial, and lifestyle characteristics as well as clinical stage and treatment. Although formal statistical tests for interaction were non-significant the trend in analyses over a range of outcomes suggested that patients with worse baseline HRQOL could benefit more from the PCI-HN.

Discussion: HRQOL early post-treatment is a key predictor of longer-term outcome. Measuring and using HRQOL and the PCI-HN are not only surrogates for predicting HRQOL at 15 months post-treatment, but also tools to help guide interventions.

Keywords

health-related quality of life, patient concerns inventory, head and neck cancer
1 | INTRODUCTION

Health-related quality of life (HRQOL) is an established key outcome after treating patients for head and neck cancer (HNC), not only in the short term, but also long term.\(^6\) There is now more understanding of the cancer journey long after treatment completion and we are starting to appreciate the variations at the individual-patient level and their effect on HRQOL.

The Patient Concerns Inventory (PCI-HN) prompt list is specific to HNC,\(^2\) that was designed to fit into routine clinic consultations. It is freely available and consists of 56 clinical items which patients select from prior to their appointment, to help guide their outpatient consultation through the symptoms and problems that they experience following treatment for HNC. It helps to direct the consultation and can trigger targeted onward referral for clinical areas of need and helps signpost patients for any advice and support they may need. It has been implemented in clinical care over the last 14 years and has undergone extensive development and validation. A systematic review of 14 self-report measures recommended the use of the PCI-HN to measure unmet needs, regarding content validity as being more important than quantitative psychometric properties.\(^3\) International data from 19 units provided an opportunity to reflect and supports the PCI approach in populations with different characteristics.\(^4\) The PCI-HN prompt list allows HNC patients to discuss issues that might otherwise be overlooked.

A recent intervention trial evaluated the use of the PCI-HN at routine outpatient clinics for 1 year after treatment on HRQOL.\(^5\) This trial integrated the PCI-HN and the University of Washington Quality of life questionnaire (UW-QOLv4) into routine consultations as a simple low-cost means to benefit HNC patients. The UW-QOL questionnaire is well established and has often been used in the last 20 years in HNC patients at different times after primary diagnosis. The UW-QOLv4 and PCI-HN can be used together in digital format in routine clinical practice with algorithms that can quickly identify patients doing badly, thus facilitating an immediate intervention from the clinical team.\(^6\) Published work indicated relationships between number of symptoms, functional status, physical status, and overall HRQOL.\(^7\) Previous work suggested that the number of PCI-HN items were associated with overall HRQOL more strongly than with case-mix variables\(^4\) of age, gender, tumor stage, site, and treatment.

There are many available studies looking at longitudinal changes in QOL, or trying to determine factors predictive of poor long-term QOL, from pretreatment to 1 year, cross-sectional to 5 years, even 10 years with a diverse use of instruments (EORTC, UW-WOL).\(^1,7-9\) With the introduction of the PCI in this study clinicians can evaluate patient needs in a longitudinal design, rather than looking at absolute scores.

We have reported previously\(^9\) that the HRQOL changes from 2 years to 10 years are minimal. There is flattening regarding change after 6 months-to a year, that continues in long-term survivorship.\(^9\) Regarding the population of patients included in this study we are not aware of any other randomized trials comparing HRQOL at different points within 2 years of diagnosis. Data from our recent trial\(^5,10\) gave us the opportunity to look at the relevance of baseline patient baseline characteristics and their effect on HRQOL.

The first aim was to explore which baseline patient characteristics best predicted HRQOL outcome 12 months after being in the trial. The second aim was to explore which types of patients responded best to being in the PCI intervention arm of the trial and after completing the PCI prompt list at routine clinics throughout their trial follow-up.

2 | METHODS

A pragmatic cluster-controlled trial was conducted at Aintree and Leeds cancer centres in the United Kingdom. Fifteen consultants (trial clusters) were randomized to “using” or “not using” the PCI prompt list intervention at all their routine outpatient clinics within the trial. The methods were detailed previously.\(^11\) Eligible patients were treated with curative intent for primary HNC, including all sites, stages, and treatments. Patients treated with palliative intent or those with recurrence were excluded as were patients with psychoses, cognitive impairment, or dementia. There was no limitation by age or histology. The PCI lists 56 clinical items\(^2\) and patients can select from these just before seeing their consultant, to help steer the outpatient consultation through a range of issues experienced after their treatment for HNC. MDT discussions about trial patients first took place meetings between January 2017 and December 2018, and the trial baseline clinics were from April 2017 to October 2019.

A baseline clinic questionnaire collected information as to whether patients lived alone or with others, whether they were working, had ever been unemployed, lived in a household receiving financial benefits, and the total household income before tax. Lifestyle factors about tobacco and alcohol use were also collected, as was patient ethnicity, gender, and age. Clinical details about primary tumor site, grade, treatment, and ACE27 comorbidity were obtained from clinical records. Index of multiple deprivation (IMD 2019) ranks were derived from patient postcodes using publicly available data and were analyzed as IMD quintile categories ranging from patients living in...
the 20% of most deprived small areas in England to pa-
tients in the 20% least deprived.

The UW-QOLv4 contains 12 single question domains, with 3–5 evenly scaled responses scored from 0 (worst) to 100 (best).12 Regarding overall QOL, patients were asked to consider not only mental and physical health, but also other factors, such as family, friends, spirituality, or per-
sonal leisure activities important to their enjoyment of
life. Subscale composite scores have been developed13 as
have domain algorithms to screen for significant problems
or dysfunction.14 Intimacy and fears of recurrence domain
questions have also been developed using a similar con-
cept of response hierarchy.15,16 HRQOL data also included
the Distress Thermometer (DT),17 where a score of 4 or
greater reflects moderate to severe distress.

2.1 Statistical methods

The prespecified primary outcome measure of the trial
was the percentage with less than good overall QOL
(UWQOLv4) at 12 months. Two prespecified second-
ary outcomes at 12 months were the percentage with a
DT score ≥4 and the mean social–emotional subscale
score of the UWQOLv4. Other outcomes analyzed at
12 months were the mean physical functioning subscale
of the UWQOLv4 and also whether there was dysfunc-
tion indicated specifically in each of the 12 UWQOL
domains. HRQOL status at baseline clinic was analyzed as a
predictor of status at 12 months alongside other baseline
patient characteristics. The Mann–Whitney (2 compari-
sion groups) or Kruskal–Wallis (>2 comparison groups)
tests were used to compare patient groups for numeri-
cal outcomes and Fishers exact test was used for binary
outcomes. Tests for interaction between baseline predic-
tors and trial arm on 12-month outcome were performed
using logistic regression (binary outcomes) or linear re-
gression (numerical outcomes). R² statistics estimating
how much variation in an outcome was explained by a
predictor variable, were obtained either from logistic
regression (Nagelkerke pseudo R²) for binary outcomes or
from linear regression for numerical outcomes. The dis-
tribution of the number of UWQOL domains indicating
dysfunction at 12 months (range 0–14) was skewed and
regression methods incorporating bootstrapping methods
(5000 replications) were used to estimate the significance
of trial arm after adjusting for the baseline number of do-
main dysfunctions. Stepwise regression methods were
used to select predictors of each outcome, and these al-
lowed predicted probabilities (of binary outcomes, logistic
regression) or expected scores (of numerical outcomes,
linear regression) to be used to estimate the significance
of trial arm after adjustment for the predictors. SPSSv25
and Statav13 were used for data analysis. In these explora-
tory analyses no allowance was made for clustering effects
of the 15 consultants. Also, many statistical tests were per-
formed and in general the more inferences being made,
the more likely that erroneous inferences will occur.
However, in the spirit of being exploratory and with the
intent to be as inclusive of trends as possible we have re-
tained our significance criteria at p < 0.05. Exploratory
findings require confirmation by others.

3 RESULTS

There were 15 trial consultants and they saw a median
(inter-quartile range [IQR]) of 16 (13–26) patients, with
140 PCI-HN patients and 148 controls. Patient flow charts
from MDT to trial baseline clinic10 and from baseline to
final trial clinic5 have been published. Baseline clinics took
place a median (IQR) of 194 (125–249) days after diagno-
sis and 103 (71–162) days after patients ended their treat-
ment. Baseline characteristics have been described.5,10

Final clinic data were available for 71% in each group
(PCI 100/140, non-PCI 105/148), with 46% (38/83) lost due
to cancer recurrence, palliation, 2nd primary, and death
(PCI 45%, 18/40; non-PCI 47%, 20/43) and 27% (22/83)
due to early trial closure because of the COVID-19 pan-
demic (PCI 28%,11/40; non-PCI 26%, 11/43).

Final trial clinics (referred to as being at 12 months) for
100 PCI-HN patients were a median (IQR) of 357 (329–380)
days after trial baseline clinics, 364 (322–396) days for 105 controls. They were also a median (IQR) of 15.5
(13.8–17.2) months after the end of treatment. The me-
dian (IQR) number of PCI-HN items selected were five (2–9) at the baseline clinic and two (0–4) at 12 months. The
two trial groups were broadly similar in demographic and
clinical characteristics apart from differences in tumor lo-
cation and mode of treatment (Table 1) which were cluster
(consultant) related with MFU and ENT consultants seeing
different types of cases.

At 12 months, 23% (48/205) reported less than good
overall (UWQOL) quality of life, 32% (65/205) a DT score
of 4 or more, social–emotional median (IQR) subscale
scores of 87 (71–96), mean 81, and physical function
median (IQR) subscale scores of 80 (66–95), mean 78.
Significant associations of baseline casemix character-
istics (Table 1) with main trial outcomes are shown in
Table 2, with results stratified by trial arm. Baseline
HRQOL was the dominant predictor of 12-month HRQOL
with PCI patients tending to have better outcomes than
controls when baseline HRQOL was worst. Formal tests
for interaction between trial arm and baseline HRQOL
on 12-month outcomes were all non-significant. Worse
outcomes were noted for those in households receiving
TABLE 1 Baseline demographic, lifestyle and clinical characteristics

|                           | All patients | PCI patients | Non-PCI patients |
|---------------------------|--------------|--------------|------------------|
|                           | No. %        | No. %        | No. %            |
| Total                     | 205 100      | 100 100      | 105 100          |
| Location                  |              |              |                  |
| Aintree                   | 119 58       | 55 55        | 64 61            |
| Leeds                     | 86 42        | 45 45        | 41 39            |
| Age                       |              |              |                  |
| <55                       | 49 24        | 20 20        | 29 28            |
| 55–64                     | 87 42        | 45 45        | 42 40            |
| 65–74                     | 46 22        | 23 23        | 23 22            |
| ≥75                       | 23 12        | 12 12        | 11 10            |
| Gender                    |              |              |                  |
| Male                      | 143 70       | 65 65        | 78 74            |
| Female                    | 62 30        | 35 35        | 27 26            |
| Tumour site               |              |              |                  |
| Oral cavity               | 91 44        | 38 38        | 53 50            |
| Oropharynx                | 70 34        | 33 33        | 37 35            |
| Larynx                    | 25 12        | 17 17        | 8 8              |
| Other                     | 19 9         | 12 12        | 7 7              |
| Overall stage             |              |              |                  |
| Early 0–2                 | 89 43        | 40 40        | 49 47            |
| Advanced 3–4              | 116 57       | 60 60        | 56 53            |
| Treatment                 |              |              |                  |
| S only, no FF             | 73 36        | 36 36        | 37 35            |
| S only, & FF              | 17 8         | 5 5          | 12 11            |
| RT/CT only                | 39 19        | 26 26        | 13 12            |
| S & RT/CT, no FF          | 51 25        | 24 24        | 27 26            |
| S & RT/CT, & FF           | 25 12        | 9 9          | 16 15            |
| ACE27 comorbidity         |              |              |                  |
| None                      | 107 52       | 58 58        | 49 47            |
| Mild                      | 61 30        | 26 26        | 35 33            |
| Mod/severe                | 37 18        | 16 16        | 21 20            |
| Ethnic group              |              |              |                  |
| White British             | 198 97       | 98 98        | 100 95           |
| Other                     | 7 3          | 2 2          | 5 5              |
| IMD 2019 (quintile)       |              |              |                  |
| 1 worst                   | 72 35        | 35 35        | 37 35            |
| 2                         | 22 11        | 12 12        | 10 10            |
| 3                         | 40 20        | 18 18        | 22 21            |
| 4                         | 45 22        | 23 23        | 22 21            |
| 5 best                    | 26 13        | 12 12        | 14 13            |
| Currently living in house |              |              |                  |
| or flat                   |              |              |                  |
| With other                | 165 81       | 82 82        | 83 80            |
| Alone                     | 39 19        | 18 18        | 21 20            |
| Not known                 | 1 1          |              |                  |

Currently working

|                      | All patients | PCI patients | Non-PCI patients |
|----------------------|--------------|--------------|------------------|
| Yes                  | 72 36        | 41 43        | 31 30            |
| No                   | 128 64       | 55 57        | 73 70            |
| Not known            | 5 4          | 1            |                  |

Ever been unemployed

|                      | All patients | PCI patients | Non-PCI patients |
|----------------------|--------------|--------------|------------------|
| Yes                  | 69 35        | 32 34        | 37 36            |
| No                   | 129 65       | 63 66        | 66 64            |
| Not known            | 7 5          | 2            |                  |

Household receives financial benefits

|                      | All patients | PCI patients | Non-PCI patients |
|----------------------|--------------|--------------|------------------|
| None                 | 125 65       | 64 68        | 61 62            |
| Yes                  | 68 35        | 30 32        | 38 38            |
| Not known            | 12 6         | 6            |                  |

Total household income from all sources before tax

|                      | All patients | PCI patients | Non-PCI patients |
|----------------------|--------------|--------------|------------------|
| <£12,000             | 35 17        | 14 14        | 21 20            |
| £12,000–22,999       | 31 15        | 16 16        | 15 14            |
| £23,000–34,999       | 37 18        | 19 19        | 18 17            |
| ≥£35,000             | 46 22        | 21 21        | 25 24            |
| Not known            | 56 27        | 30 30        | 26 25            |

Tobacco user

|                      | All patients | PCI patients | Non-PCI patients |
|----------------------|--------------|--------------|------------------|
| Current              | 24 12        | 12 12        | 12 12            |
| Former               | 117 59       | 60 61        | 57 56            |
| Never                | 59 30        | 26 27        | 33 32            |
| Not known            | 5 2          | 3            |                  |

Alcohol user

|                      | All patients | PCI patients | Non-PCI patients |
|----------------------|--------------|--------------|------------------|
| Current              | 146 73       | 80 81        | 66 65            |
| Former               | 45 22        | 15 15        | 30 29            |
| Never                | 10 5         | 4 4          | 6 6              |
| Not known            | 4 1          | 3            |                  |

Abbreviations: CT, chemotherapy; FF, free-flap; RT, radiotherapy; S, surgery.

benefits, currently not working, or with household incomes under £12,000. Clinical stage and treatment associated with physical function scores. Across Table 2 there were no significant interactions between baseline predictors and trial arm on outcome apart from patients ever having been unemployed (yes/No) in regard to less than good overall QOL ($p = 0.03$). Table 2 predictors were entered into stepwise regression models ($p < 0.05$ entry) and from final models predicted probabilities (of overall QOL less than good and DT score ≥ 4) and predicted scores (of UWQOL subscale scores) were obtained for each patient. These 12-month outcome predictions were plotted against actual outcome for each arm of the trial (Figure 1) to assess the trial arm effect after adjusting for the regression
| 12 month outcome | Baseline predictor variable | Trial arm | Observed nature of association, with 12 month outcomes reported |
|------------------|-----------------------------|-----------|--------------------------------------------------------------|
| Overall QOL less than good: % (n) | IMD 2019 | Worst 2 quintiles<sup>a</sup> | Best 3 quintiles |
| | p = 0.01 | PCI | 26% (12/47) | 19% (10/53) |
| | R² = 0.05 | No PCI | 38% (18/47) | 14% (8/58) |
| Currently working | PCI | 7% (3/41) | 35% (19/55) |
| | No PCI | 16% (5/31) | 29% (21/73) |
| Ever unemployed | PCI | 22% (7/32) | 24% (15/63) |
| | No PCI | 43% (16/37) | 15% (10/66) |
| Financial benefits | No PCI | 40% (12/30) | 16% (10/64) |
| Household income | PCI | 57% (8/14) | 19% (3/16) |
| | No PCI | 48% (10/21) | 13% (2/15) |
| Overall QOL | PCI | 67% (6/9) | 38% (8/21) |
| | No PCI | 83% (5/6) | 46% (10/22) |
| DT score ≥4: % (n) | Male | 28% (18/65) | 43% (15/35) |
| | Female | 26% (20/78) | 44% (12/27) |
| Tumour site | Oral cavity | 42% (16/38) | 33% (11/33) |
| | Oropharynx | 38% (20/53) | 30% (11/37) |
| | Larynx | 4% (1/25) | 13% (1/8) |
| | Other | 3% (1/25) | 33% (7/22) |
| IMD 2019 | Worst 2 quintiles<sup>a</sup> | Best 3 quintiles |
| | p = 0.02 | PCI | 36% (17/47) | 30% (16/53) |
| | R² = 0.04 | No PCI | 45% (21/47) | 19% (11/58) |
| Financial benefits | PCI | 40% (12/30) | 28% (18/64) |
| | No PCI | 47% (18/38) | 18% (11/61) |
| Household income | PCI | 38% (5/14) | 25% (4/16) |
| | No PCI | 57% (12/21) | 20% (3/15) |
| DT score (0–10) | Zero | 13% (1/8) | 33% (7/22) |
| | 1–3 | 4% (1/25) | 20% (5/25) |
| | 4–5 | 6% (1/16) | 43% (10/23) |
| | ≥6 | 1% (1/100) | 38% (10/26) |

(Continues)
| 12 month outcome | Baseline predictor variable | Trial arm | Observed nature of association, with 12 month outcomes reported |
|------------------|-----------------------------|-----------|---------------------------------------------------------------|
| UWQOL social-emotional subscale score: median (IQR), mean, n | Currently working | Working | Not working |
| p = 0.006 | PCI | 90 (80–98), 86.8, n = 41 | 87 (73–96), 81.8, n = 55 |
| $R^2 = 0.05$ | No PCI | 86 (72–96), 84.3, n = 31 | 78 (62–91), 74.8, n = 73 |
| Financial benefits | Benefits | PCI | 78 (70–91), 78.5, n = 30 | 90 (79–96), 86.4, n = 64 |
| $p < 0.001$ | No PCI | 67 (51–84), 67.6, n = 38 | 87 (73–95), 83.8, n = 61 |
| $R^2 = 0.14$ | Household income | ≤£12,000 | £12,000–22,999 | £23,000–34,999 | ≥£35,000 | Not known |
| p = 0.002 | PCI | 73 (53–82), 70.9, n = 14 | 93 (75–100), 87.9, n = 16 | 88 (83–95), 85.4, n = 19 | 87 (78–100), 85.1, n = 21 | 88 (78–96), 86, n = 30 |
| $R^2 = 0.11$ | No PCI | 71 (57–88), 69.7, n = 21 | 83 (74–95), 80.8, n = 15 | 76 (70–96), 78.3, n = 18 | 91 (76–96), 84.0, n = 25 | 78 (65–91), 76, n = 26 |
| Alcohol use | Current | PCI | 88 (78–96), 85.1, n = 80 | 74 (67–92), 77.6, n = 15 | 95 (na), 85.4, n = 4 |
| p = 0.005 | No PCI | 83 (71–95), 79.8, n = 66 | 72 (61–87), 72.5, n = 30 | 88 (na), 80.8, n = 6 |
| $R^2 = 0.06$ | UWQOL Social-emotional subscale score quintile | ≤55.8 | 55.9–70.0 | 70.1–81.7 | 81.8–90.8 | ≥90.9 |
| PCI | 65 (45–74), 58.8, n = 10 | 83 (69–87), 78.2, n = 21 | 91 (77–98), 87.7, n = 25 | 91 (87–97), 89.8, n = 18 | 94 (87–100), 90.3, n = 26 |
| $p < 0.001$ $R^2 = 0.46$ | No PCI | 57 (46–70), 53.7, n = 19 | 73 (63–84), 72.0, n = 22 | 78 (71–90), 79.0, n = 20 | 87 (76–95), 85.7, n = 16 | 96 (88–100), 93.4, n = 28 |
| 12 month outcome | Baseline predictor variable | Trial arm | Observed nature of association, with 12 month outcomes reported |
|------------------|-----------------------------|-----------|---------------------------------------------------------------|
| **UWQOL physical function subscale score: median (IQR), mean, n** | Overall stage | Early 0–2 | Advanced 3–4 |
| | $p = 0.002$ | PCI | 90 (78–96), 87.3, $n = 40$ | 78 (65–91), 77.4, $n = 60$ |
| | $R^2 = 0.07$ | No PCI | 86 (68–96), 81.1, $n = 49$ | 73 (60–83), 70.9, $n = 56$ |
| Treatment | | PCI | 93 (79–100), 89.4, $n = 36$ | 71 (na), 75.5, $n = 5$ |
| | $p < 0.001$ | No PCI | 90 (73–100), 83.6, $n = 37$ | 83 (67–94), 78.5, $n = 12$ |
| | $R^2 = 0.16$ | PCI | 93 (79–100), 89.4, $n = 36$ | 71 (na), 75.5, $n = 5$ |
| | No PCI | PCI | 78 (66–95), 78.8, $n = 30$ | 85 (73–95), 82.9, $n = 64$ |
| | $p = 0.005$ | No PCI | 67 (58–79), 67.0, $n = 38$ | 86 (70–95), 80.7, $n = 61$ |
| Household income | | PCI | 77 (55–95), 74.5, $n = 14$ | 82 (72–94), 82.6, $n = 16$ |
| | $p = 0.03$ | No PCI | 66 (58–78), 67.3, $n = 21$ | 79 (61–100), 79.3, $n = 15$ |
| | $R^2 = 0.07$ | PCI | 50 (50–60), $n = 12$ | 74 (59–83), 71.8, $n = 23$ |
| | No PCI | PCI | 58 (38–73), 56.5, $n = 19$ | 68 (57–80), 68.9, $n = 20$ |
| | $p < 0.001$ | PCI | 58 (38–73), 56.5, $n = 19$ | 68 (57–80), 68.9, $n = 20$ |

**Note:** The baseline predictor variable $p$ values (2nd column) came from Fishers Exact test in regard to overall QOL and DT outcomes, or from Mann-Whitney (2 group comparison) or Kruskal-Wallis (>2 groups) tests regarding the subscale score outcomes. The $R^2$ statistics (also 2nd column) were derived from logistic regression (Nagelkerke pseudo $R^2$) in regard to overall QOL and DT and from linear regression for the subscale scores.

**Abbreviations:** CT, chemotherapy; na, IQR was not computed for denominators <10; RT, radiotherapy; S, surgery.

*IMD 2019: ’Worst 2 quintiles’ indicates those patients living in the most deprived 40% of English small area neighbourhoods; ’Best 3 quintiles’ indicate patients living in other less deprived small area neighbourhoods.

*Quintiles derived from baseline sample of 288.
After such adjustment, PCI-HN patients tended to have better outcome results at 12 months for the UWQOL subscale outcomes while differences regarding overall QOL were weaker and inconsistent for DT. UWQOL domain dysfunction at 12 months ranged from 22% (saliva), 13% (anxiety), and 12% (pain) to 3% (recreation and speech) and 2% (appearance and intimacy). Nearly half (48%, 98/205) had at least one domain dysfunction while 24% (49/205) had two or more dysfunctions and 9% (19/205) had four or more. When results for the number of domain dysfunctions at 12 months were stratified by the number of domain dysfunctions at baseline the tendency was for PCI-HN patients on average to have less 12-month dysfunction than control patients (Figure 2), the independent effect of PCI-HN being \( p = 0.01 \) after adjusting for baseline number of dysfunctions. Stepwise logistic regressions \( (p < 0.05 \) for entry) of 12-month dysfunction for each domain always selected baseline domain status as the first predictor and additional predictors were selected for anxiety (+benefits), speech (+ever unemployed), taste (+tumor stage), and saliva (+benefits). For each situation the extra independent effect of PCI-HN was assessed and this was significant for swallowing \( (p = 0.01) \) and chewing \( (p = 0.04) \).

For PCI-HN patients the more PCI-HN items they selected at baseline the greater the number likely to be selected at 12 months: 52 patients selecting 0–5 items at baseline selected a median of 1 (mean 1.7) items at 12 months, 26 patients selecting 6–9 at baseline selected a median of 2 (mean 3.4) items at 12 months, while 22 patients selecting 10–28 items at baseline selected a median of 5 (mean 7.1) items at 12 months. Also, the more PCI-HN items selected at baseline the greater the percentage of
patients at 12 months having less than good overall QOL and the worse the scores for the two UWQOL subscales (Figure 3); no trend was seen for DT scores of 4 and above.

4 | DISCUSSION

A strength of this study is the details collected at baseline and the prospective collection of HRQOL and PCI-HN data. To our knowledge this is the only randomized trial that evaluates the HRQOL at 3 months (post treatment end) and 12 months later within the stated patient group. This paper highlights patient characteristics that predict HRQOL outcomes at around 15 months following treatment. Prominent among these, is the starting (posttreatment) HRQOL level.

Previous retrospective cohort studies have suggested that baseline (pre-treatment) HRQOL strongly influences posttreatment HRQOL with greater impact than treatment modality. The importance of early HRQOL measurement, just after treatment completion, is highlighted by our intervention trial. It is known from already published work that the patients’ HRQOL deteriorates just after treatment and subsequently improves, slowly toward pretreatment scores, after 1 year. Furthermore,

![FIGURE 2](image)

**FIGURE 2** Number of 12-month UWQOL dysfunction outcomes by baseline status and trial arm. From linear regression analysis using bootstrapping methods (5000 replications) the PCI effect was significant ($p = 0.013$) on the number of dysfunctional domains per patient at 12 months after adjusting for baseline number of dysfunctional domains (0, 1, 2, 3–4, 5–12). 95% CI: approximate 95% confidence interval number of patients at baseline with: 0 dysfunctional domains (27 PCI, 30 no PCI), 1 dysfunction (33 PCI, 33 no PCI), 2 dysfunctions (18 PCI, 17 no PCI), 3–4 dysfunctions (15 PCI, 12 no PCI), and 5–12 dysfunctions (7 PCI, 13 no PCI). PCI, Patient Concerns Inventory; UW-QOLv4, University of Washington Quality of Life questionnaire

| TABLE 3 | Notable associations ($p < 0.05$) between baseline status and UWQOL dysfunction at 12 months |
|---|---|---|---|---|
| 12 month UWQOL outcome | Overall result ($n = 205$) | Baseline status and 12 month outcome result: % ($n$) | Baseline status | Best baseline score | In-between baseline status | Baseline dysfunction |
| Dysfunction in UWQOL social-emotional subscale domains | | | | |
| Pain | 12% (24) | $p = 0.001, R^2 = 0.14$ | 4% (3/80) | 10% (7/71) | 26% (14/54) |
| Activity | 6% (12) | $p < 0.001, R^2 = 0.25$ | 2% (1/65) | 3% (4/119) | 33% (7/21) |
| Recreation | 3% (7) | $p < 0.001, R^2 = 0.36$ | 1% (1/89) | 1% (1/101) | 33% (5/15) |
| Shoulder | 6% (13) | $p = 0.001, R^2 = 0.16$ | 2% (2/119) | 10% (6/61) | 20% (5/25) |
| Mood | 9% (18) | $p < 0.001, R^2 = 0.32$ | 1% (1/75) | 6% (6/106) | 46% (11/24) |
| Anxiety | 13% (27) | $p < 0.001, R^2 = 0.13$ | 6% (5/83) | 12% (11/92) | 37% (11/30) |
| Dysfunction in UWQOL physical function subscale domains | | | | |
| Appearance | 2% (5) | $p = 0.002, R^2 = 0.24$ | 2% (1/55) | 1% (1/136) | 21% (3/14) |
| Swallowing | 6% (12) | $p < 0.001, R^2 = 0.33$ | 1% (1/78) | 3% (3/106) | 38% (8/21) |
| Chewing | 5% (10) | $p < 0.001, R^2 = 0.27$ | 1% (1/84) | 3% (3/103) | 33% (6/18) |
| Speech | 3% (7) | $p < 0.001, R^2 = 0.63$ | 0% (0/90) | 1% (1/105) | 60% (6/10) |
| Taste | 9% (19) | $p < 0.001, R^2 = 0.32$ | 3% (2/68) | 3% (3/100) | 38% (14/37) |
| Saliva | 22% (46) | $p < 0.001, R^2 = 0.13$ | 8% (5/59) | 18% (14/77) | 39% (27/69) |
| Dysfunction in extra UWQOL domains | | | | |
| Intimacy | 2% (5) | $p < 0.001, R^2 = 0.37$ | 0% (0/158) | 8% (3/37) | 20% (2/10) |
| Fears of recurrence | 6% (13) | $p = 0.002, R^2 = 0.28$ | 0% (0/36) | 5% (8/152) | 29% (5/17) |

Note: $p$ values came from Fishers Exact test while the $R^2$ statistics (Nagelkerke pseudo $R^2$) were estimated from using logistic regression.
patient concerns decrease as these patients progressed in their recovery.20 The study by Aminnudin et al. (2020) revealed a significant association between the number of PCI-HN items selected and the “time after treatment completed” (p < 0.001). They20 observed that a high number of concerns were strongly associated with patients in the “1-month to 1-year post-treatment”. The same study also suggested an association between the number of concerns and the patients’ HRQOL, and although they did not specifically look at the HRQOL at 3 months (posttreatment end) and 12 months later, their results are indirectly supporting the data presented in this paper.

Recommendations regarding the frequency of HRQOL measurement have been published as early as 2003 and may include collection of data at multiple points in the cancer journey.21 The vast majority of oncological studies that report on HRQOL include measurements during or shortly after treatment.22 Recommendations include the frequent use of different outcome measures for evaluating patient well-being.23 In an ideal setting policy recommendation and the evaluation of different treatment modalities on HRQOL, should be based on QOL outcomes throughout the patients’ cancer care; however, taking into account the available resources this may not be possible. The analyses suggested that the PCI-HN intervention impacts on the social emotional and physical function subscales, and this also showed through in the analyses of domain dysfunction. The evidence regarding overall HRQOL and DT appears weak, as already inferred from the primary outcomes paper. The trial effect on the social emotional and physical function subscale scores at 12 months seems small in absolute terms when compared to the relationship noted for other predictors, especially baseline HRQOL—but this is often the case with randomized trial effects—a series of small gains. Although tabulated results might suggest variation in how patients in
different baseline subgroups respond to using the PCI, there was little formal statistical test evidence of interaction. The resulting logic is that any observed variation in results regarding the trial effect in different patient subgroups is consistent with chance/random variation.

4.1 Study limitations

The trial ended up being underpowered generally, partly because of early termination due to the COVID-12 pandemic but also the greater than expected loss in the time lag between the multidisciplinary team meeting and trial posttreatment baseline clinics. The analyses were deliberately exploratory, the prespecified main analyses having already been reported. The intention was to be inclusive of trends and impressions rather than be parsimonious, but in so doing it is accepted that the more inferences that are made the more likely that erroneous inferences will occur. By definition exploratory findings require confirmatory analyses from other researchers. However, the results do offer more clarity as to predictors of 12-month outcome than about which groups of patients benefit most from using the PCI-HN. Baseline HRQOL status looks to be the dominant predictor of 12-month outcomes and the trend in analyses over a range of outcomes suggests that patients with worse baseline HRQOL could benefit more from the PCI-HN. The findings from this work are applicable to any population with similar ethnic and socioeconomic characteristics.

4.2 Clinical implications

The explanation for why 3 month posttreatment scores may be predictive of 1 year scores need further research. Many factors will contribute to this and not only include treatment effects, but also included other psychosocial factors such as resilience, coping mechanisms, personality, as well as the interactions between patients and family members or carers. Further explanatory and intervention studies are required to explain how the PCI prompt list aids adaptation following HNC.

From the results of this work the starting HRQOL (just after treatment) measurement with the concurrent use of the PCI-HN, could be the foundation for treatment assessment and target early interventions, with long-term benefits. Other notable predictors were individual social, financial, and lifestyle factors as well as characteristics of the area in which patients lived; also, clinical stage and treatment predicted physical function. The financial burden of cancer was highlighted in a previous cross-sectional study several years ago. Despite that, almost 10 years later this is still an issue that multidisciplinary teams need to do more about, by signposting early, appropriate available benefits for patients and carers. In conclusion, measuring the HRQOL early after the completion of treatment provides an indication of the likely HRQOL at 12 months later. By acting on both HRQOL scores and PCI-HN concerns, clinicians can make a valuable contribution to improve outcomes for their patients. Further research is needed to develop suitable and effective interventions to improve the long-term HRQOL.

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CONFLICT OF INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AUTHOR CONTRIBUTIONS

This study could not have taken place without the valued contribution and support of the 15 consultants who participated in this trial. Anastasios Kanatas contributed to the design, delivery of trial and collection of data, and writing the manuscript, Derek Lowe contributed to the design and methodology of the trial, data analysis, and the writing of the manuscript and Simon N. Rogers contributed the design, delivery of trial and collection of data, and writing the manuscript. Simon N. Rogers was the chief investigator of the trial. The final manuscript was approved by all authors.

ETHICAL APPROVAL STATEMENT

The study complied with all aspects of ethical standards of clinical research. Ethical approval from North West-Liverpool Central Research Ethics Committee REC reference: IRAS 16/NW/0465, Project ID: 189554. The PCI trial has approval from the Health Research Authority (HRA). The Research and Development Department at Aintree University Hospital NHS Trust (AUH) is coordinating the trial and AUH is the sponsor for the trial. Trial registration: 32,382. Clinical Trials Identifier, NCT03086629.
**PATIENT CONSENT STATEMENT**

Participants provided written informed consent. A patient information leaflet was provided and the patients had an opportunity to decide if they would like to take part in the trial, after a period of 2 weeks.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**REFERENCES**

1. Singer S, Langendijk J, Yarom N. Assessing and improving quality of life in patients with head and neck cancer. *Am Soc Clin Oncol Educ Book*. 2013. doi:10.1200/EdBook_AM.2013.33.e230

2. Rogers SN, El-Sheikha J, Lowe D. The development of a Patients Concerns Inventory (PCI) to help reveal patients concerns in the head and neck clinic. *Oral Oncol*. 2009;45:555-561.

3. Shunmugasundaram C, Rutherford C, Butow PN, Sundaresan P, Dhillon HM. Content comparison of unmet needs self-report measures used in patients with head and neck cancer: a systematic review. *Psychooncology*. 2019;28(12):2295-2306.

4. Rogers SN, Alvear A, Anesi A, et al. Variations in concerns reported on the patient concerns inventory in patients with head and neck cancer from different health settings across the world. *Head Neck*. 2020;42(3):498-512.

5. Rogers SN, Allmark C, Bekiroglu F, et al. Improving quality of life through the routine use of the patient concerns inventory for head and neck cancer patients: main results of a cluster preference randomised controlled trial. *Eur Arch Otorhinolaryngol*. 2021;278(9):3435-3449.

6. http://www.hancsupport.com/professionals/patient-concerns-inventory. Accessed September 4, 2021.

7. Astrup GL, Hofso K, Bjordal K, et al. Patient factors and quality of life outcomes differ among four subgroups of oncology patients based on symptom occurrence. *Acta Oncol*. 2017;56(3):462-470.

8. Wells M, Swartzman S, Lang H, et al. Predictors of quality of life in head and neck cancer survivors up to 5 years after end of treatment: a cross-sectional survey. *Support Care Cancer*. 2016;24(6):2463-2472.

9. Rogers SN, Lowe D. Health-related quality of life after oral cancer treatment: 10-year outcomes. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2020;130(2):144-149.

10. Rogers SN, Allmark C, Bekiroglu F, et al. Improving quality of life through the routine use of the patient concerns inventory for head and neck cancer patients: baseline results in a cluster preference randomised controlled trial. *Eur Arch Otorhinolaryngol*. 2020;277(12):3435-3447.

11. Rogers SN, Lowe D, Lowies C, et al. Improving quality of life through the routine use of the patient concerns inventory for head and neck cancer patients: a cluster preference randomized controlled trial. *BMC Cancer*. 2018;18(1):444.

12. Rogers SN, Gwanne S, Lowe D, Humphris G, Yueh B, Weymuller EA Jr. The addition of mood and anxiety domains to the University of Washington quality of life scale. *Head Neck*. 2002;24(6):521-529.

13. Rogers SN, Lowe D, Yueh B, Weymuller EA Jr. The physical function and social–emotional function subscales of the University of Washington Quality of Life Questionnaire. *Arch Otolaryngol Head Neck Surg*. 2010;136:352-357.

14. Rogers SN, Lowe D. Screening for dysfunction to promote multidisciplinary intervention by using the University of Washington Quality of Life Questionnaire. *Arch Otolaryngol Head Neck Surg*. 2009;135:369-375.

15. Low C, Fullarton M, Parkinson E, et al. Issues of intimacy and sexual dysfunction following major head and neck cancer treatment. *Oral Oncol*. 2009;45:898-903.

16. Rogers SN, Cross B, Talwar C, Lowe D, Humphris G. A single-item screening question for fear of recurrence in head and neck cancer. *Eur Arch Otorhinolaryngol*. 2016;273:1235-1242.

17. Hegel MT, Collins ED, Kearing S, Gillock KL, Moore CP, Ashles TA. Sensitivity and specificity of the Distress Thermometer for depression in newly diagnosed breast cancer patients. *Psychooncology*. 2008;17:556-560.

18. El-Deiry MW, Putran ND, McDowell JA, Weymuller EA, Yueh B. Influences and predictors of long-term quality of life in head and neck cancer survivors. *Arch Otolaryngol Head Neck Surg*. 2009;135(4):380-384.

19. Doss J, Ghati W, Razak I, et al. Changes in health-related quality of life of oral cancer patients treated with curative intent: experience of a developing country. *Int J Oral Max Surg*. 2017;46(6):687-698.

20. Aminnudin AN, Doss JG, Ismail SM, et al. Can post-treatment oral cancer patients’ concerns reflect their cancer characteristics, HRQoL, psychological distress level and satisfaction with consultation? *Ecancermedicalscience*. 2020;14:1118.

21. Movsas B. Quality of life in oncology trials: a clinical guide. *Semin Radiat Oncol*. 2003;13(3):235-247.

22. Haslam A, Herrera-Perez D, Gill J, Prasad V. Patient experience captured by quality-of-life measurement in oncology clinical trials. *JAMA*. 2020;3(3):e200363.

23. Buiting H, Olthuis G. Importance of quality-of-life measurement in oncology clinical trials. *BMC Cancer*. 2015;15:922.

24. Rogers SN, Harvey-Woodworth CN, Hare J, Leong P, Lowe D, Humphris G. The development of a Patients Concerns Inventory (PCI) to help reveal patients concerns in the head and neck clinic. *Head Neck*. 2020;42(3):498-512.

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