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Extended Research Article

Digital intervention to support cancer survivors: the CLASP research programme

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Abstract

Background: There are increasing numbers of cancer survivors who have finished their primary treatment, but whose quality of life remains consistently poor over years. There is limited evidence for pragmatic, brief interventions to support cancer survivors in primary care, where most patients are managed.

Objective: To develop, trial and assess the effectiveness and cost-effectiveness of a digital intervention to support cancer survivors (named 'Renewed') designed to require minimal health service resources.

Design: Qualitative development of the intervention, then open randomised controlled trial, with a process analysis and health economic analysis.

Setting: United Kingdom primary care

Interventions:

Development of the intervention: We systematically reviewed the relevant qualitative and quantitative literature to inform initial intervention planning, intervention content and design features of a digital intervention. This was followed by iterative development and optimisation of intervention content and the human support component – in qualitative studies of the views of cancer survivor, and of National Health Service, volunteer and charity workers.

Main trial:

Participants: People who had finished primary treatment for colorectal, breast or prostate cancer with lower quality of life (European Organization for Research and Treatment of Cancer QLQ-C30 score < 85) within the last 10 years. Participants were randomised to one of three groups: (1) 'generic' advice: detailed digital National Health Service support for healthier living ('Living Well'), (2) a bespoke digital intervention ('Renewed') addressing symptom management, physical activity, diet, weight, distress and/or fear of recurrence, or (3) 'Renewed' plus support (additional brief support by e-mail, telephone, or face to face)

Main outcome measures: Primary outcome: European Organization for Research and Treatment of Cancer QLQ-C30 (overall score). Secondary outcomes: subscales of European Organization for Research and Treatment of Cancer QLQ-C30 (global self-rated health; functional subscales; symptom subscales), EuroQol-5 Dimensions, five-level version, psychological measures and costs.

Results: At the primary time point of 6 months, there were clinically important improvements in European Organization for Research and Treatment of Cancer QLQ-C30 score contrary to the expected trajectory of quality of life in this population, but with no evidence of differences between groups. By 12 months, the Renewed plus support group had continued to improve and was better than generic advice (1.42, 95% confidence intervals 0.33 to 2.51), with the largest differences in the prostate cancer subgroup. 13 of the 14 subscales also improved compared to generic advice, statistically significant for self-rated global health (Renewed: 3.06, 1.39 to 4.74; Renewed plus support: 2.78, 1.08 to 4.48), dyspnoea, constipation and enablement. For Renewed plus support, there were also statistically significant differences for physical, cognitive and emotional functioning and fatigue. Renewed and Renewed plus support were dominant given improved effectiveness combined with and lower mean primary care National Health Service costs per patient (respectively −£141, −153 to −128; −£77, −90 to −65).

Limitations: Of those sent invitation letters, 14% (7883/59,295) were assessed for eligibility and 35% (2732/7883) of those assessed were eligible and agreed to participate – which is normal with the 'cold calling' method of invitation. The digital intervention would not suit people who find technology or the internet difficult to access, but only 25% (2649/10,697) of those who gave reasons for declining did so due to lack of internet access. The extensive generic advice available to participants in the National Health Service limited the ability to assess the specific benefits of Renewed in the short term, but nevertheless longer-term benefit and lower National Health Service costs are likely to be achieved with the bespoke intervention.

Conclusions: Cancer survivors with lower quality of life given detailed generic online support improve significantly. Providing robustly developed, low-cost, bespoke digital support can provide further modest long-term improvements in enablement, symptom management and self-rated global health, with substantially lower National Health Service costs.

Future work: The cost-effectiveness and benefits for symptom management on self-rated health suggest a more widespread implementation study should be undertaken.

Trial registration: This trial is registered as Current Controlled Trials ISRCTN 96374224.

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Contents

List of tables

List of figures

List of boxes

List of supplementary material

Report Supplementary Material 1 TIDieR checklist

Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/PPLHG1141).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

The supplementary materials (which include but are not limited to related publications, patient information leaflets and questionnaires) are provided to support and contextualise the publication. Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately, and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

List of abbreviations

A&E	accident and emergency
BCTv1	Behaviour Change Techniques Taxonomy
BCW	Behaviour Change Wheel
CARE	Congratulate, Ask, Reassure, Encourage
CEAC	cost-effectiveness acceptability curve
CRN	Clinical Research Network
EORTCQLQ-C30	European Organization for Research and Treatment of Cancer QLQ-C30
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HCA	healthcare assistant
HCP	healthcare professional
HRG	Healthcare Resource Group
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio
INDEX	IdentifyiNg and assessing different approaches to DEveloping compleX interventions
ITT	intention to treat
NIHR	National Institute for Health and Care Research
NPT	Normalisation Process Theory
PCA	prescription cost analysis
PN	practice nurse
PPI	patient and public involvement
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life-year
RCT	randomised controlled trial
SAE	serious adverse event
SMD	standardised mean difference
TIDieR	Template for Intervention Description and Replication
WS	workstream

Plain language summary

We aimed to make and assess a website for use in general practices to support people who have poor quality of life after their initial cancer treatment. We made our website, called 'Renewed', based on the few studies about websites or apps. We tested 'Renewed' with people who had finished their initial treatment, National Health Service staff and others, and used their feedback to improve it.

Then we asked others to join a study to see how well 'Renewed' works. Each person invited to join the study had finished initial treatment for bowel, breast or prostate cancer but had poor quality of life. We placed them at random (by chance) into one of three groups:

1. given general advice from the NHS website for more healthy living ('Living Well')
2. given 'Renewed', with help designed for cancer survivors in managing symptoms, exercise, diet, weight, distress, and fear of cancer coming back
3. given 'Renewed', plus brief support by e-mail, telephone or face to face.

After 6 months, all groups reported better quality of life. After 12 months, the Renewed plus support group carried on improving and was a little better than general advice for quality of life. At this time both the Renewed groups had improved in their rating of their health, shortness of breath, constipation and feeling more able to manage their problems. People in the Renewed plus support group also had improved physical and emotional functioning and less fatigue. Both Renewed and Renewed plus support not only had improved outcomes but also lower costs for the NHS.

This study suggests that the online support provided by the Renewed website can help improve the quality of life of people who have finished initial cancer treatment, with both better outcomes and lower costs for the National Health Service.

Scientific summary

Background

There are increasing numbers of cancer survivors who have finished their primary treatment, but quality of life remains consistently poor over years for many patients. There is limited evidence for pragmatic, brief interventions to support cancer survivors in primary care, where most patients are managed.

Objective

To develop, trial and assess the effectiveness and cost-effectiveness of a digital intervention to support cancer survivors ('Renewed') designed to require minimal health service resources.

Methods

Intervention development

Collating the evidence

1. Rapid review of web-based interventions designed to improve quality of life in adults who have completed primary treatment for breast, prostate and colorectal cancer. A range of study designs were included, and information about intervention characteristics, experiences and outcomes was extracted. The data were analysed using thematic analysis.
2. Rapid scoping review of barriers and facilitators. A search identified studies during the past 20 years and further studies were identified by experts in the team and examination of reference lists.

Development of Guiding Principles

The rapid scoping review was used to identify key context-specific behavioural issues, and key intervention features were developed to meet each design objective. These Guiding Principles were improved in consultation with the development team and an expert stakeholder panel.

Behavioural analysis

A behavioural analysis table documented likely barriers for target behaviours, and for each barrier, interventions were described and coded according to three theoretical frameworks [Behaviour Change Techniques Taxonomy (BCTv1); Behaviour Change Wheel (BCW); Normalisation Process Theory (NPT)].

Logic model

Using Medical Research Council guidance, the behavioural analysis was used to develop the logic model – describing the problem, intervention targets/ingredients to resolve the problem, mechanisms of action, and outcomes.

Qualitative research: think-aloud interviews with cancer survivors

Think-aloud interviews were conducted with 32 cancer survivors. Positive and negative comments were then collated, modifications made, and further rounds of interviews conducted with the modified versions of the prototype until no important further changes were required.

Qualitative research: focus groups with National Health Service and cancer charity staff and volunteers

Seven focus groups were carried out with staff from five general practitioner practices, staff and volunteers from two cancer charities, addressing support and training materials, and the integration of the intervention in everyday practice.

Modifications were made and further rounds of focus groups were organised until no further improvements were identified.

Main trial

Participants
For the main trial, people who had finished primary treatment for colorectal, breast or prostate cancer up to 10 years previously, reporting suboptimal quality of life [European Organization for Research and Treatment of Cancer QLQ-C30 (EORTCQLQ-C30) score < 85].

Interventions
Participants were randomised to one of three groups: (1) 'Generic' advice: detailed digital NHS support for healthier living ('Living Well'), (2) a bespoke digital intervention ('Renewed') addressing symptom management, physical activity, diet, weight loss, distress management and/or fear of recurrence, or (3) 'Renewed' with additional brief support by e-mail, telephone, and face to face.

Automated randomisation with stratification was implemented using LifeGuide software (www.lifeguideonline.org) with a 1 : 1 allocation ratio stratified by:

- cancer type: breast/prostate/colorectal and
- EORTCQLQ-C30 score (64 or less/65 or more).

Main outcome measures
Primary outcome: EORTCQLQ-C30 (overall score). Secondary outcomes: subscales of EORTCQLQ-C30 (global self-rated health; functional subscales; symptom subscales), psychological measures, quality of life measured by EuroQol-5 Dimensions, five-level version (EQ-5D-5L) and costs.

Main statistical analysis
All participant data were analysed on an intention-to-treat basis, that is, as randomised. The primary analysis used imputed data, employing a chained equation multiple imputation model for missing data. A complete-case analysis was a sensitivity analysis. Generalised linear mixed regression models were used for continuous variables, controlling for baseline and stratification variables, including a random effect for practice. Pre-planned subgroup analyses were set out in the statistical analysis plan for age, gender and comorbidities. We also performed post hoc within-group analyses documenting the changes from baseline.

Health economic analysis
Cost per quality-adjusted life-year (QALY) was estimated. The base case took an NHS perspective using primary care consultation and medication costs, but with sensitivity analyses including secondary care costs. Resource use data were collected by a medical record review in primary care. Unit costs of primary care consultation, community services, outpatient visits and accident and emergency attendances were costed based on the Personal Social Services Research Unit. National reference costs were used to cost hospital stay based on corresponding diagnostic categories. Medications were priced based on the *British National Formulary*. All costs were based on 2019 prices. QALYs were estimated using the EQ-5D-5L and were based on the recommended national tariff.

Process analyses

Qualitative analysis
Forty-two patients were interviewed to explore their experiences of using the Renewed intervention and to understand the potential barriers and facilitators to using Renewed.

Quantitative analysis
Patients were included if they completed the 12-month follow-up measures and were classified according to how much of the intervention was accessed, and this was then related to the impact on outcomes.

Results

Intervention development

Rapid review
The database search identified 6327 papers, and 16 relevant papers relating to 9 interventions fulfilled eligibility criteria. Identified themes addressed aspects of intervention design (participant factors, characteristics of the online intervention, techniques used to change behaviour and preferred features of web-based interventions), including issues of uptake, adherence and attrition, engagement, feasibility, efficacy, positive behaviour change and acceptability of the interventions.

Scoping review
Facilitators and barriers were grouped according to key characteristics, including factors influencing participation; information included in the intervention; motivation/self-esteem/self-efficacy; self management/monitoring; emotions/mood; social support; intervention design/content; technical aspects and various practical issues.

Guiding principles
Target users did not see themselves as having health needs, so the content promoted well-being, rather than illness management. Cancer survivors felt that their usual behaviour in part caused their cancer, so suggestions for behavioural change did not stigmatise users' current behaviour. Target users form a heterogeneous group; hence the intervention provided tailored information to each user, based on answers to baseline questions. Participants wanted brief accessible information; hence short sessions on specific topics were provided and the intervention targeted behaviours which had the potential to improve multiple symptoms.

Behavioural analysis
Three target behaviours were identified (physical activity, diet and intervention engagement) and specific intervention components included to minimise barriers to each, mapped to elements of the BCTv1, BCW and NPT theoretical frameworks.

Qualitative research: think-aloud interview with cancer survivors
Participants found the intervention to be generally easy to navigate and the content being relevant and useful. Negative comments described barriers to engagement which resulted in modifications to the prototype; for example some were worried about overdoing physical activity, so changes emphasised that increasing physical activity should be done gradually.

Qualitative research: focus groups with National Health Service and cancer charity staff and volunteers
Several concerns were raised which led to further modifications; for example some questioned the use of the Congratulate, Ask, Reassure, Encourage approach, so additional information about how to provide support with patients who had not achieved their goals was added.

Main trial
At the primary time point of 6 months, there were clinically important improvements in EORTCQLQ-C30 score contrary to the expected trajectory of quality of life in this population, but with no evidence of differences between groups. By 12 months, the Renewed plus support group continued to improve and was better than generic advice (1.42, 95% confidence intervals 0.33 to 2.51), with the largest differences in the prostate cancer subgroup.

Thirteen of the 14 functional and symptom subscales also improved compared to generic advice, statistically significant for self-rated global health (Renewed: 3.06, 1.39 to 4.74; Renewed plus support: 2.78, 1.08 to 4.48), dyspnoea, constipation and enablement. For Renewed plus support, there were also significant differences for physical, cognitive and emotional functioning and fatigue.

Renewed and Renewed plus support demonstrated little or no change in QALY estimates using the EQ-5D-5L, but were dominant – with both a range of better health outcomes while incurring lower mean NHS primary care costs per patient (respectively −£141, −153 to −128; −£77, −90 to −65).

Process analyses

Qualitative process study

The results showed that even limited usage of Renewed Online may provide enough information to motivate behaviour change in those with less need for more tailored support. Novel information may need to be presented earlier in the intervention to motivate further engagement with Renewed in those who need more detailed and tailored information to make behaviour changes.

Quantitative process analysis

The majority of patients accessed the Core content of Renewed and completed the Core content. Approximately half of participants continued to use Renewed past the Homepage to access the Optional content. Those who used Optional content had higher quality of life (QoL) scores compared to those who only accessed the Core content.

Conclusions

Cancer survivors with lower quality of life given detailed generic online support improve significantly. Providing robustly developed, low cost, bespoke digital support can provide further modest long-term improvements in enablement, symptom management, and self-rated global health, with substantially lower primary care NHS costs.

Implications for health care

The current study provides reasonable evidence that a novel bespoke intervention to support cancer survivors could be integrated into current practice since there are both some longer-term benefits combined with lower costs to the NHS. However, all trial participants by definition had to engage with the trial and trial procedures, and so may not represent the wider patient population, and all were followed up with questionnaires and with phone calls where questionnaires were not returned. This could be mimicked in routine practice by brief follow-up contacts, which could be assessed in a larger implementation study.

Recommendations for research

The cost-effectiveness and benefits for symptom management self-rated health for both Renewed interventions suggest that an implementation study is the next step, including further assessment of the impact in different socio-economic groups and cancer types.

To consider using and/or developing more sensitive primary outcome measures among cancer survivors, particularly for briefer, low resource interventions – since the overall EORTCQLQ-C30 summary score is not sensitive to change, in contrast to both symptom subscales and self-rating of health.

To develop QALY measures that capture the benefit to QoL for low intensity, low resource interventions among cancer survivors given that neither the EQ-5D-5L or the EORTC-8d reflected important changes in patients' self-rating of health.

Further work is indicated to explore why people with some cancers may not be as willing to use the intervention as others and exploration of the key barriers for those from ethnic minority backgrounds to take part.

Trial registration

This trial is registered as Current Controlled Trials ISRCTN 96374224.

Funding

This award was funded by the National Institute for Health and Care Research (NIHR) Programme Grants for Applied Research programme (NIHR award ref: RP-PG-0514-20001) and is published in full in *Programme Grants for Applied Research*; Vol. 14, No. 4. See the NIHR Funding and Awards website for further award information.

Synopsis

Aims, overview and context of the research programme

Summary of aims and rationale

There are 2 million cancer survivors in the UK and this figure is expected to increase over time as the population ages and survival rates increase.[3] The UK also has one of the lowest cancer survival records among developed countries[4] and quality of life is poor,[5,6] with particularly high levels of psychological distress and fatigue.[6] There is evidence showing that both lifestyle and psychological well-being interventions are likely to significantly improve quality of life,[7–10] but most of these interventions have been intensive and impractical to implement in primary care, which is where most contact with cancer survivors takes place. It is plausible, based on our previous internet supported interventions, that relatively resource-light interventions using internet-based support in a primary care context could be effective and cost-effective.

The aim of this research programme was therefore to develop and evaluate an internet-supported intervention for lifestyle and well-being among cancer survivors in primary care, and to estimate its effectiveness and cost-effectiveness in enhancing quality of life in cancer survivors.

Summary of alterations to the programme's original aims/design

The planned feasibility trial was carried out, but it was later decided (in agreement with the funder) that it should be considered as an internal pilot study, as no changes were made to the intervention and study procedures between the feasibility and main trials. This allowed for data collected during the internal pilot to be used as part of the main trial.

The original intended plan had been to only use practice nurses (PNs) to provide support for the 'website plus human support' arm of the trial. In the early stages of the programme, we realised that for later dissemination, it might be wise to explore the potential for cancer charities to provide some of the human support during the feasibility trial. This was explored before the feasibility trial but proved to be unfeasible as cancer charities could only commit to supporting a small number of participants, which would not be adequate for the fully powered trial. In the end, PNs took on this role as planned, but with Clinical Research Network (CRN) nurses also providing support when Primary Care practices were unable to provide it.

During the main trial, a disparity in recruiting equal numbers to each cancer type (breast, prostate, colorectal) was noticed, with numbers for colorectal cancer participants being particularly low. This was attributed partly to the difference in prevalence of each cancer type, but also it appeared that colorectal cancer is often not well labelled in patient notes, so it was harder to identify these patients in primary care. The authors agreed with NIHR National Institute for Health and Care Research and the steering committee a plan to carry on recruiting to the 2500 participants target rather than trying to get equal numbers in each group. When the target was close to being reached, recruitment numbers showed an over recruitment of breast cancer participants, slight under-recruitment of prostate cancer participants, and low recruitment of colorectal cancer participants. We agreed with NIHR and the steering committee to continue recruiting prostate and colorectal cancer participants until the target for prostate cancer participants was reached. A no cost extension was granted by the NIHR to continue recruitment and the target for prostate cancer participants was subsequently reached in March 2020.

A final change was that we allowed eligible secondary care sites to participate. Only one secondary site was used (in Wales, which was experiencing slow recruitment at the time) as staff there were eager to participate and were able to carry out medical note reviews.

Although promised in the protocol, the societal health economic analysis was not proceeded with due to lack of any suggestions in the qualitative work that patients made use of non NHS services.

Summary of research

We proposed four workstreams (WSs) (see *Figure 1*).

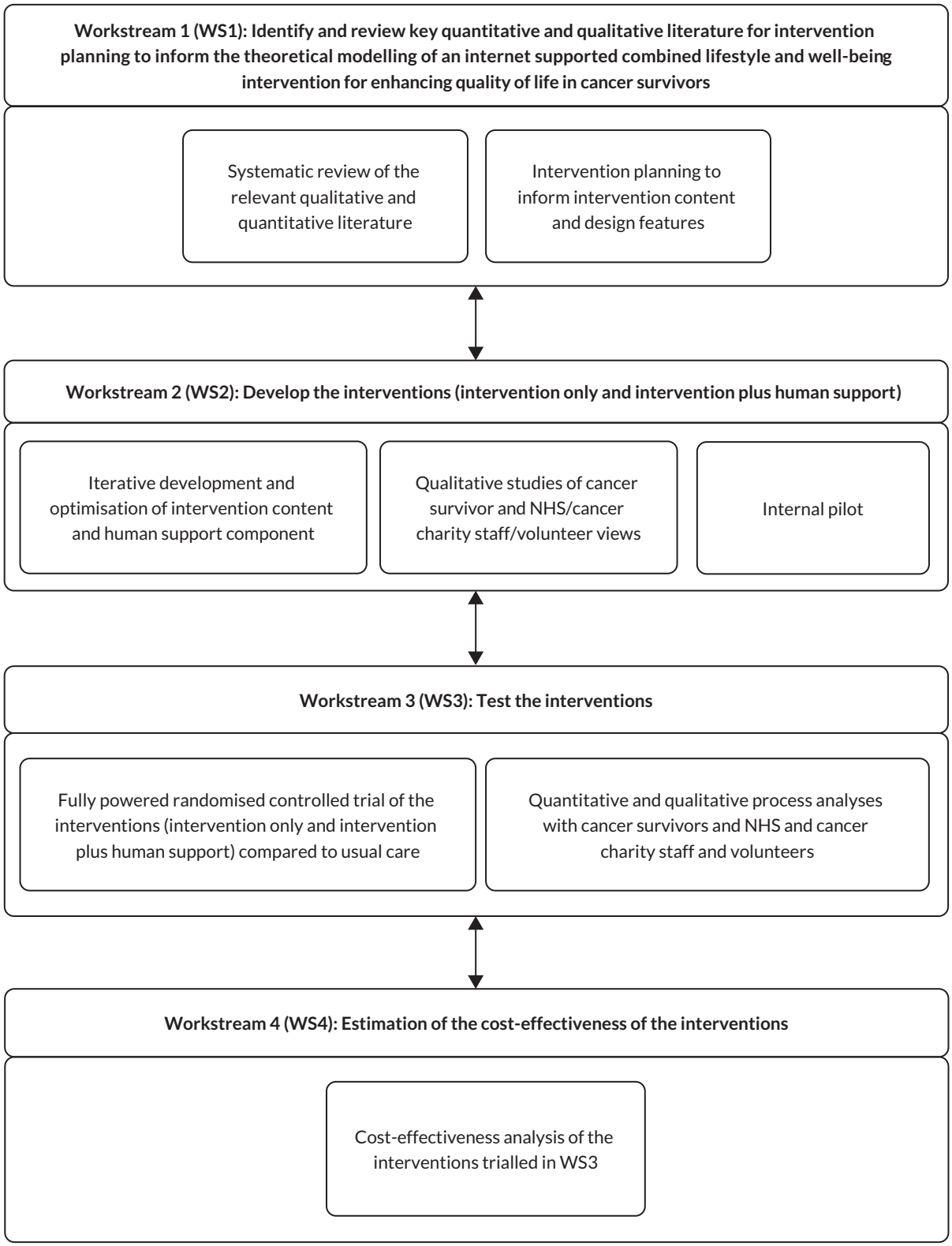

FIGURE 1 Research pathway diagram.

The first workstream (WS1) consisted of reviewing the literature and intervention planning, focusing on identifying intervention content and design features.

Workstream 2 developed the interventions (the website only and website plus human support), using iterative qualitative research to ensure that they were viewed as acceptable and useful by cancer survivors and those who provided human support (NHS and cancer charity staff and volunteers).

Workstream 3 and WS4 carried out a fully powered randomised controlled trial (RCT) of the cost-effectiveness for health-related quality of life (HRQoL) over 1 year of the optimum method(s) of delivering the intervention compared with usual care, with an embedded quantitative and qualitative process analysis.

Development of Renewed

Activities that have been carried out as part of the development of the Renewed intervention are reported in more detail in the following publications:

Corbett T, Singh K, Payne L, Bradbury K, Foster C, Watson E, *et al.* Understanding acceptability of and engagement with Web-based interventions aiming to improve quality of life in cancer survivors: a synthesis of current research. *Psycho-Oncology* 2018;**27**:22–33. https://eprints.soton.ac.uk/414881/

Bradbury K, Steele M, Corbett T, Geraghty AWA, Krusche A, Heber E, *et al.* Developing a digital intervention for cancer survivors: an evidence-, theory- and person-based approach. *NPJ Digit Med* 2019;**2**:85. https://doi.org/10.1038/s41746-019-0163-4

Corbett T, Cheetham T, Muller AM, Slodkowska-Barabasz J, Wilde L, Krusche A, *et al.* Exploring cancer survivors' views of health behaviour change: 'where do you start, where do you stop with everything?'. *Psychooncology* 2018;**27**:1816–24. https://eprints.soton.ac.uk/419278/

Introduction

The development process for creating the Renewed intervention was based on a combined evidence-, theory- and person-based approach.[11–13] The development work focused primarily on developing introductory content and two components to support physical activity ('Getting Active') and healthy eating ('Eat for Health'). In addition, two of our existing digital interventions (POWeR + for weight management[14] and Healthy Paths for distress management[15]) were adapted and included in the intervention.

Intervention development team and patient and public involvement

The intervention development team included patient and public involvement (PPI) representatives, clinicians with expertise in supporting those who have experienced cancer, general practitioners (GPs), behavioural scientists, experts in digital health, representatives of the charities Breast Cancer Now, Bowel Cancer UK and Prostate Cancer UK. Our PPI contributors comprised two patients who had experienced breast cancer (Tamsin Burford, Lesley Turner), two patients who had experienced bowel cancer (Peter Roberts, Kevin Summers) and two patients who had experienced prostate cancer (Geoffrey Sharman, Roger Bacon). Some of the PPI members were also involved in work with additional cancer charities (e.g. Macmillan, Prostate Cancer Support Organisation). All PPI members joined the project team and were invited to join monthly development group meetings to discuss the intervention development. They were also invited to quarterly management committee meetings to discuss important issues within the planning and development of the overall programme of research. Within the monthly development group meetings, PPI contributed to all discussions and decisions regarding the key intervention content. For example, PPI informed decisions about the frequency of human support that would be offered alongside the digital intervention and the key points at which this should be available. Within the quarterly management, meetings PPI contributed to decisions about the running of the research (such as how to optimise recruitment). PPI also commented on all patient facing recruitment materials to optimise the accessibility and persuasiveness of these materials.

The PPI group and clinicians commented on early versions of the written website content to ensure this was as accessible, feasible, motivating and persuasive as possible. PPI also each took part in three think-aloud interviews which helped to optimise this content further. For example, they suggested additional concerns about increasing physical activity that patients might have, which the research team were then able to address within the intervention. They also highlighted some areas of the digital intervention where navigation could be simplified to maximise accessibility.

Overall, PPI contributors promoted a focus on patent priorities throughout the intervention planning and optimisation. Their rapid feedback on early prototype intervention materials enabled the research team to make these as useful as possible before they were viewed by patients recruited from primary care in the qualitative think-aloud interviews.

Workstream 1 and workstream 2 objectives

This section describes the three phases within which activities were carried out to inform the planning and development of the Renewed intervention. Each activity is described, reporting on aims, methods used, results, and their practical implications for intervention development. The phases were:

Workstream 1 (phase 1): literature reviews

- Thematic synthesis of qualitative evidence
- Rapid scoping review

Workstream 1 (phase 2): intervention planning

- Guiding Principles
- Behavioural analysis
- Logic model

Workstream 2 (phase 3): intervention development and optimisation

- Qualitative research with cancer survivors
- Qualitative research with NHS and cancer charity staff and volunteers

This section ends with a description of how the recommended IdentifyiNg and assessing different approaches to DEveloping compleX interventions (INDEX) actions for developing complex interventions[16] were considered and addressed during the planning and development phases of the Renewed intervention.

Workstream 1 (phase 1): collating evidence from reviews of the literature

Thematic synthesis of the qualitative evidence for digital interventions for lifestyle and well-being support for cancer survivors (described in Corbett et al.[17])

Aims
To identify features and outcomes of web-based interventions which may be important to the quality of life of cancer survivors.

Methods
A rapid review was conducted to identify studies related to web-based interventions designed to improve quality of life in adults who have completed primary treatment for breast, prostate and colorectal cancer. A range of study designs were included (qualitative research, feasibility/pilot trials, randomised trials and process evaluations). All available information about intervention characteristics, experiences and outcomes was extracted. The data were treated as textual (qualitative) data and analysed using thematic analysis.

Results
The database search identified 6327 papers, of which 57 were assessed for eligibility through full-text screening. A total of 16 relevant papers relating to 9 interventions fulfilled all eligibility criteria for inclusion. Twenty-eight descriptive themes were identified and grouped into five analytical themes.[1] Four themes addressed aspects of intervention designs and implementation of web-based intervention.[18] The themes were: participant factors, characteristics of the online

intervention, techniques used to change behaviour and preferred features of web-based interventions. These themes were perceived as key factors that appeared to potentially influence a fifth analytical theme: the outcomes discussed in the papers including uptake, adherence and attrition, engagement, feasibility, efficacy, positive behaviour change and acceptability of the interventions. The results of this review have been published.[17]

Practical implications for intervention development

The findings highlight the importance of matching the intervention to the unique characteristics of the participants. The key findings suggest that survivors value interventions that consider their changing needs and are tailored to their stage of the cancer trajectory. Social networking features do not always provide added benefit and it is likely that web-based interventions will be effective without social networking features and with little input from clinical staff and researchers. Behavioural change techniques used in interventions need to be appropriate to the characteristics of the users and implemented carefully to avoid negative consequences. This information is vital in the development of successful interventions for cancer survivors.

Rapid scoping review to identify barriers and facilitators (described in Bradbury et al.[19])

Aims

To review existing evidence to identify facilitators and barriers to the success of interventions designed to improve the quality of life of cancer survivors, in order to inform the development of Guiding Principles,[11] theory-based behavioural analysis and logic modelling[20] for the Renewed intervention.

Methods

Five of the six core steps described by Arksey and O'Malley for carrying out scoping reviews were followed: identifying the research question, identifying relevant studies, study selection, charting the data, and collating, summarising and reporting the results.[21] The optional sixth step (a consultation exercise to seek expert consensus), was not carried out due to time constraints, although feedback from PPI representatives and members of the expert development group was sought.

A search was conducted using the Cochrane Library, Database of Abstracts of Reviews of Effects, Ovid MEDLINE and PsycInfo® (American Psychological Association, Washington, DC, USA), limiting the search to the past 20 years. Details of the inclusion criteria used for selection of studies have been published,[19] along with a Preferred Reporting Items for Systematic Reviews and Meta-Analyses[22] flow diagram, summarising the rapid scoping review, which also included further studies identified by experts in the team and through examination of reference lists of identified studies. This process yielded 49 studies to be retained for analysis, which resulted in a list of participant and intervention component characteristics for which potential facilitators and barriers were identified.

Results

Facilitators and barriers were grouped according to nine participant and intervention characteristics, namely, factors influencing participation (e.g. to protect against recurrence of cancer), information included in the intervention (e.g. including topics that are relevant to users), motivation/self-esteem/self-efficacy (e.g. lack of confidence or motivation to engage in suggested activities), self-management and self-monitoring methods (e.g. having a sense of having control over one's body), emotions/mood (e.g. fear of recurrence of cancer), social support (e.g. availability or lack of support, and its effect morale), intervention design/content (e.g. relatability, tailoring), technical aspects (e.g. navigation difficulties, ability to print information) and various practical issues (e.g. safety issues, time constraints, bad weather). The full list of facilitators and barriers was published.[19]

Practical implications for intervention development

This rapid scoping review highlighted several facilitators and barriers to take into consideration for the success of interventions aiming to improve quality of life in cancer survivors, which were then used to inform the guiding principles, behavioural analysis, and logic model, which in turn informed the design and content of the intervention. These are described in phase 2.

Workstream 1 (phase 2): intervention planning

Guiding Principles: identifying design objectives to meet target users' needs and maximise engagement (described in Bradbury *et al.*[19])

Aims
To develop Guiding Principles[11] which outline key behavioural issues and needs of target users, and how these will be addressed by the Renewed intervention in terms of design objectives and key intervention features.

Methods
Findings from the rapid scoping review (described in phase 1) were used to identify key context-specific behavioural issues, in terms of target user needs, issues, or challenges. For each of these, intervention design objectives were formulated, describing what the intervention will aim to do to address behavioural issues in order to maximise engagement with the intervention and the behavioural changes suggested. Finally, key intervention features were developed to describe how the intervention will achieve each design objective. These Guiding Principles were improved over time in consultation with members of the development team and of our stakeholder panel who have extensive expertise of cancer survivorship and knowledge of relevant literature.

Results
One key issue related to users not seeing themselves as having health needs or requiring health lifestyle changes after cancer, which could compromise engagement with the healthy lifestyle changes put forward by the intervention. To prevent this scenario, the preferred approach to presenting content would be to promote well-being, rather than suggesting ways to manage illness. Another issue related to a risk that cancer survivors could feel their usual behaviours, when compared with the intervention's proposed behaviours, were inappropriate, and that they may have even had a part to play in causing their cancer. The design objective for this issue consisted of ensuring that any suggestions for behavioural change did not stigmatise users' current behaviour, which could be achieved by avoiding using arguments or ways of presenting certain activities that could result in users feeling blamed for their cancer or for their poor mental health (e.g. overpromoting 'positive coping'). A third issue was that target users form a heterogeneous group in terms of the wide variety of symptoms and issues they experience, depending on cancer type, gender and individual circumstances. To address this, one of the key intervention features was to provide tailored information to each user, based on answers given as part of baseline quality of life measures, as well as gender and cancer type, so that it is as relevant as possible to them. Another issue related to the importance of information is being brief and easily accessible. Examples of intervention features for achieving this were to provide short sessions on specific topics that were also accessible via smartphones, with implications for the amount of text to be presented. The last Guiding Principle refers to the risk of the intervention being too large and complex as a result of trying to address multiple symptoms and proposing many behaviours to address them. To avoid this, an efficient design was used, for example by targeting behaviours which had the potential to improve multiple symptoms. The Guiding Principles were published.[19]

Practical implications for intervention development
The Guiding Principles provided a useful resource for development team members to refer to as a reminder of what challenges the intervention's target population face when engaging with its content, and how the intervention design, content, features, presentation approach, and tone, should address these challenges.

Behavioural analysis: identifying barriers, and how to address them (described in Bradbury et al.[19])

Aims
To describe the Renewed intervention and potential determinants of behaviour for each target behaviour, integrating theoretical frameworks from behavioural change and implementation sciences.

Methods
A behavioural analysis table was populated with likely barriers to achieving each target behaviour. These barriers were extracted from the scoping review findings described in phase 1, as well as from expert consultation. For each

barrier, intervention components designed to minimise them were described and coded according to three theoretical frameworks, namely, the Behaviour Change Techniques Taxonomy (BCTv1),[23] the Behaviour Change Wheel (BCW)[24] and Normalisation Process Theory (NPT).[25]

Results

Three target behaviours were identified: increase in physical activity, adopting a healthier diet and patient engagement with the intervention. For each of these behaviours, a range of barriers were listed, along with specific intervention components that would minimise them, as well as codes describing how these were mapped to elements of the BCTv1, BCW and NPT theoretical frameworks. For example, target users' concerns about being physically active were addressed by presenting success stories of other individuals like them, describing how they overcame concerns about being more active. This intervention component targeted three BCW constructs (psychological capability, reflective motivation and social opportunity), two BCW intervention functions (persuasion and modelling), one NPT construct (coherence) and three BCTv1 behaviour change techniques (9.1 credible source, 3.1 social support and 5.6 information about emotional consequences). The complete behavioural analysis table has been published.[19]

Practical implications for intervention development

The behavioural analysis was useful to ensure the intervention addressed as many known barriers as possible to achieve the intervention's key target behaviours. Although the mapping of barriers and intervention components to theoretical frameworks did not identify additional ones, it helped with ensuring none had been overlooked.

Logic model: outlining the proposed mechanism of action of the intervention (described in Bradbury et al.[19])

Aims

To outline a model of the hypothesised mechanisms of action of the Renewed intervention (how it is thought to work), which can then be later tested and refined during the process analysis.

Methods

Drawing on Medical Research Council guidance for process evaluation available at the time,[26] the behavioural analysis and findings from the rapid scoping review (described in phase 1) were used to develop the intervention's logic model,[20] which describes the problem the intervention addresses, intervention targets to resolve the problem, intervention ingredients, mechanisms of action, and outcomes the intervention is aiming to impact.

Results

All elements of the logic model were described, with poor quality of life in cancer survivors being the problem to be addressed by the intervention. Adopting healthy behaviours and improving mental health were identified as the intervention's targets. Intervention ingredients were defined, including, for each, details of the psychological constructs they target, as outlined in the behavioural analysis table. This is followed by a description of the proposed mechanisms of action and outcomes in a flow diagram format. For example, it is hypothesised that engagement with the intervention would result in the desired behaviour changes (increasing physical activity, improving dietary patterns), which would in turn improve quality of life (the primary outcome) and reduce anxiety and depression, fear of cancer recurrence and improvements in well-being and enablement (the secondary outcomes). The full logic model was published.[19]

Practical implications for intervention development

The logic model was useful for defining how the intervention is expected to lead to its effects and for providing a further check that the intervention design features and component are appropriate in terms of supporting the proposed mechanisms of action.

Workstream 2 (phase 3): intervention development and optimisation

Qualitative research: think-aloud interviews with cancer survivors (described in Bradbury et al.[19])

Aims
To explore target users' views on the prototype of the Renewed intervention, in order to identify modifications to be made to the intervention with a view to optimising user engagement with both the intervention and the behaviour changes it suggests.

Methods
Thirty-two cancer survivors who had completed treatment for breast, colorectal or prostate cancer in the past 10 years took part in the study by completing three separate think-aloud interviews each on different parts of the intervention. These interviews consisted of participants using the intervention for the first time and voicing their immediate reactions out loud in the presence of a trained interviewer who audio recorded the interview. This was followed by brief semi-structured interview questions to gain further insight into what they thought of the intervention as a whole, including what they thought about the behaviour changes it suggests. Positive and negative comments were then collated in a table, grouped by page, section or intervention feature. The table was then reviewed by the wider development team (including PPI representatives, clinical cancer experts and charity members), with potential modifications to the intervention discussed and agreed, especially if they related to comments that had been voiced by more than one participant, if they were critical to behaviour change, and were in line with the intervention's Guiding Principles. Further interviews were then conducted with a new modified version of the prototype. This iterative process continued until no important further changes were required.

Results
In terms of positive comments, participants found the intervention to be generally easy to navigate, also commenting on liking the look of the intervention. They mentioned valuing the fact that it was designed by experts in the field, and that this increased how much trust they could put in the information it provides. Most importantly, participants also commented on the content being relevant and useful to them.

Several negative comments describing barriers to engagement were also made, which resulted in modifications to be made to the intervention prototype. For example, some participants explained that they were worried about overdoing physical activity if they were to increase it. To address this concern, some changes were implemented. These included emphasising that this is a common concern, as well as suggesting that increasing physical activity should be done slowly and gradually, in order to avoid the more negative consequences of overdoing activity. The entire physical activity section was reviewed to ensure that all messages about increasing physical activity mentioned this should be done slowly.

Another example of an important barrier to behaviour change relates to the advice about reducing the consumption of meat in the healthy eating section of the intervention, which was perceived as promoting an inappropriately radical change in diet. This was not well received by all, with mentions of not liking the idea of having meat-free meals. This resulted in removing this suggestion and to instead encourage users to reduce the amount of red and processed meats they consume. Related to this, some participants found the argument about eating less meat benefiting the planet very off-putting. As a result of this finding, it was removed from the intervention. An overview of all the barriers and changes that have been made to the intervention to address them has been published, along with some examples of participant feedback.[19]

A thematic analysis of discussions on broader issues that took place during these interviews was also carried out. An important conclusion, which was published,[18] relates to whether this period of time after cancer treatment constitutes a 'teachable moment', a time during which individuals become motivated to make healthy lifestyle changes.[27] Most participants mentioned several general and cancer-specific barriers to making lifestyle changes after successful cancer treatment, which suggests that for the sample of participants we interviewed, this period of time did not appear to clearly constitute a teachable moment. This important question will be revisited as part of the qualitative process study to determine the reasons why the intervention may have not been effective for everyone.

Practical implications for intervention development

This qualitative research proved invaluable for understanding which aspects of the intervention target users liked and which potentially required modifications. This allowed the development team to optimise the intervention in order to maximise engagement and the behaviour changes it suggests.

Qualitative research: focus groups with National Health Service and cancer charity staff and volunteers (described in Bradbury et al.[19])

Aims

To explore potential supporters' views on the proposed support to be provided to users of the Renewed intervention, as well as the online training provided. To use findings to optimise the training material, the delivery of support, and to identify the most suitable supporters.

Methods

Seven focus groups were carried out with staff from five GP practices, as well as with staff and volunteers from two cancer charities. Topics for discussion included current support provisions, views on using an online tool for support, the online training material, the proposed CARE (Congratulate, Ask, Reassure, Encourage) approach (detailed elsewhere[28]), fitting in the intervention and supporter role in everyday practice and the use of e-mail to communicate with patients. The schedule that was used for these focus groups has been published.[19] Optimisation of the supporter aspect of the study was an iterative process whereby feedback was recorded in a table and discussed within the development team, after which agreed modifications to the training and support procedures were implemented. Additional focus groups were carried out until no further improvements were identified.

Results

Several concerns were raised which required modifications. For example, participants expressed unease with some of wording that was used in the online training, which discussed how the intervention aimed to improve quality of life and prevent cancer recurrence. Some NHS staff worried that as a result some supporters might give assurances to users of the intervention that they would not get cancer again if they followed all the advice. The development team agreed that this would pose a risk, and as a result rephrased 'prevent cancer recurrence' to 'lower chances of recurrence' in the supporter training material.

There were also some questions around the use of the CARE approach from some NHS staff. For example, how to apply the 'congratulate' part when providing support to a patient who is not achieving their goals. As a result, additional information about how to provide support with patients who are not successful was added to the guidelines on how to use the CARE approach.

Another concern related to ensuring that intervention users would not be left to feel abandoned should a supporter not respond to them due to being away because of unexpected long-term illness or holidays. As a result, the intervention was modified to enable GP practices to nominate a second supporter who could, if required, complete the training and take over as a supporter.

Discussions around which individuals would be suitable to take up the supporter role also took place. GP practice staff felt that healthcare assistants (HCAs) would be able to provide the support as no medical knowledge is required for this role. As a result, a decision was made to aim to recruit HCAs for the trial, and to also allow nurses to provide support as well as required.

An overview of the all the concerns and changes that have been made to the intervention to address them has been published, along with some examples of participant feedback.[19]

Practical implications for intervention development

Findings from these focus groups enabled the development team to refine the online training material (and therefore improving the quality of the support), practical aspects of the delivery of the support, as well as identifying suitable staff from GP practices who could conduct the role of supporter.

Mapping the Renewed planning and development process to the IdentifyiNg and assessing different approaches to DEveloping compleX interventions actions[16]

The INDEX actions provide guidance on the development of complex interventions to improve health and health care. The authors developed the INDEX actions based on a consensus exercise which was informed by reviews and qualitative interviews with developers and wider stakeholders. *Appendix 1* shows the retrospective mapping of the Renewed planning and development process to the 11 INDEX guidance actions.

A full description of the Renewed intervention using the Template for Intervention Description and Replication (TIDieR) checklist[29] is available in *Report Supplementary Material 1*.

Workstream 1 and workstream 2 limitations

Due to time constraints, the rapid scoping review was limited to literature published in the past 20 years in three databases. As such, the grey literature was not searched, potentially resulting in some literature findings being overlooked. The optional sixth step described by Arksey and O'Malley for carrying scoping reviews,[21] a consultation exercise to seek expert consensus, was not included. As we had consulted our expert and PPI development group, we did not feel that this step was sufficiently high priority to carry out within our limited time frame. This might have potentially resulted in more refined findings.

Men and ethnic minorities were underrepresented in the focus groups that took place with NHS and cancer charity staff and volunteers. As such, it is possible that their views were different to those included in our findings.

Finally, for both qualitative optimisation studies, it is possible that those who chose to not take part in them had different views to those expressed by those who did.

Workstream 1 and workstream 2 conclusions

The activities that have been carried out as part of the intervention development phase helped ensure that the Renewed intervention was accessible, acceptable, persuasive, motivating, and feasible to implement in practice for cancer survivors.

Workstream 3 evaluation of Renewed

Activities that have been carried out as part of the evaluation of the Renewed intervention are reported in more detail in the publications. The initial plan was for a feasibility trial followed by a main trial but we anticipated that there might be no changes from the initial feasibility phase which meant that the feasibility study became in effect an internal pilot for the main trial, and the approach was documented in advance in the ISRCTN registration and agreed with PGfAR.

Objectives

This section describes the evaluation of the Renewed intervention during a 30 month RCT. Aims, methods, results, and implications are described for each piece of research as follows:

- RCT to assess clinical and cost-effectiveness.
- Process evaluation exploring how patients and healthcare professionals (HCPs) experienced and implemented the intervention in practice:
  - Patient qualitative process study: perceptions of using the intervention for patients.
  - Patient quantitative process study: engagement and usage of the Renewed intervention by patients.
  - HCPs mixed methods process study: exploration of HCPs' experiences of and adherence to delivering the intervention within the supported arm of the trial.

The section finishes with a conclusions section which draws the findings together.

Randomised controlled trial to assess clinical and cost-effectiveness

Aims

To assess the effectiveness and cost-effectiveness of a digital intervention to support cancer survivors ('Renewed').

Methods

Overview

We evaluated an internet-based intervention (Renewed) to help support healthy behaviour changes and improve quality of life, psychological well-being and symptom management for breast, colorectal and prostate cancer survivors. Participants were randomly allocated to one of three arms: generic advice, access to Renewed or access to Renewed with brief support. All groups were assessed at follow up with patient reported outcome measures.

Inclusion criteria: we chose three contrasting common survivor groups to deal with the likely varying issues in needs and preferences across the gender and age spectrums: breast cancer survivors (younger and older women); prostate cancer survivors (predominantly older men); and colorectal cancer (a range of age and gender). Patients were: identifiable from GP case records; had completed primary treatment (e.g. chemotherapy/radiotherapy treatment) within the last 10 years; not receiving palliative care; had internet access; had poorer quality of life (scoring < 85 on the EORTCQLQ). Patients could be recruited opportunistically but mainly by written invitation.

Exclusion criteria: advanced cancer receiving palliative care; currently active cancer unless on active surveillance/watchful waiting for prostate cancer; another type of cancer (i.e. other than breast, prostate or colorectal) in the last 5 years; currently receiving any cancer treatment other than hormone therapy or finished treatment during the last month; expecting to start any cancer treatment during the study period; severe mental health problems and/or major uncontrolled depression, schizophrenia or dementia; sarcoma or lymphoma of the breast; living in the same household as another participant of the study.

Randomisation

Baseline measures were completed online immediately following eligibility screening and online consent. Automated randomisation (using a 1 : 1 allocation ratio) was then implemented using LifeGuide software (www.lifeguideonline.org; accessed 6 March 2025). Participant randomisation was stratified by:

- cancer type: breast/prostate/colorectal and
- EORTCQLQ-C30 score (64 or less/65 or more[30]).

Randomisation and follow-up were automated and conducted by software (i.e. keeping the research team blinded). Blinding of patients to the intervention was not possible. Participants were informed online as to which group they had been allocated to immediately via e-mail.

Trial arms:

1. **Control: Generic advice and follow-up.** All patients in the control and intervention groups had access to usual care (GPs and PNs for routine appointments), to manage any new symptoms, make further referrals and so on as appropriate. In addition, participants in this group received a link to the NHS LiveWell website to access evidence-based advice about living a healthier lifestyle, including detailed advice to support patients in their mental health, weight control, exercise, sleep, eating well, alcohol and smoking. All participants had the same structured questionnaire follow-up as in other trial groups, with telephone follow-up should questionnaires not be returned.
2. **Renewed: web only intervention.** This group had access to usual care as in (1) but were also given the Renewed intervention.

The initial core content of Renewed explained how key behaviour changes (physical activity, healthy eating, engagement with mood management strategies and weight loss support) would help reduce symptoms experienced after treatment for cancer. The answers previously supplied for the screening process generated personalised suggestions for modules to access; for example, if a participant indicated that they had been feeling tense or worried, a suggestion to look at the mood management section (Healthy Paths) would appear. In the first session of Renewed, there was also advice and information about active surveillance/watchful waiting for prostate cancer which was only available to participants who indicated that they were in that group. The core content also provided links to additional information and support available for topics not covered by Renewed (such as finances).

After participants completed the core content, they could access four additional optional sections of Renewed: Getting Active for increasing physical activity, Healthy Paths for stress reduction, Eat for Health for diet improvement and POWeR+ for weight loss. Once a participant had accessed each module, they were sent brief automated e-mails as reminders and for motivation with tips, interesting facts and brief information and advice. Participants were able to cancel e-mails at any time and there was a link in each e-mail with that provision.

1. **Renewed plus support: web-based intervention with additional guidance and support**. This group had access to usual care and the Renewed intervention as in (2) but were also given access to brief human support. This support was provided by a nurse or HCA at their surgery where possible, or else a research nurse employed by the NIHR CRN. The 'Supporters' received online training (approximately 15 minutes) to learn how to implement the previously validated CARE model[28] in order to provide support to their patients in using Renewed.

One to 2 weeks after initially logging on to Renewed, participants could have a face-to-face or phone appointment with their supporter. Where central CRN nurses provided support, sessions were held by phone. Follow-up support by phone or e-mail was then offered at 4 and 8 weeks, so three support sessions could be offered in total. Support sessions were brief (a maximum of 10 minutes) and comprised encouragement to use the website and patient-led discussion around the patient's goals, how patients had got on with the changes that they tried and how they overcame any barriers. Should further support be needed, participants could e-mail their supporter using the contact form on the Renewed website. All contact and support session details were logged on the 'Supporter's Log' kept in the surgery site-file.

Measures and outcomes

At baseline gender, age, marital status, years of education, ethnicity, height and weight were recorded.

Outcomes were patient self-reported and measured online using the LifeGuide system at baseline, 6 and 12 months (unless indicated), with two e-mail reminders, followed by two postal administrations for non-respondents (enclosing a £10 voucher at 6 months to reward participation and encourage completion), and a final telephone follow-up for those not responding to mail. Information from medical records was obtained by a blinded researcher.

Primary outcome

Health-related quality of life using the EORTC (European Organization for Research and Treatment of Cancer) Quality of Life Questionnaire C30 instrument[2] (version 3) summary score (https://qol.eortc.org/app/uploads/sites/2/2018/02/scoring_of_the_qlq-c30_summary_score.pdf; accessed 6 March 2025) measured at 6 and 12 months.

Secondary outcomes

- EORTCQLQ-C30 subscales (baseline, 6 and 12 months): Global self-rated Health, Symptom subscales, Functional subscales (e.g. Physical functioning, Social functioning, Emotional well-being).
- Quality of life [EuroQol-5 Dimensions, five-level version (EQ-5D-5L)][31] for health economic analysis (baseline, 6 and 12 months).
- Brief scales for Depression [Hospital Anxiety and Depression Scale (HADS)][32] Fear of Relapse[33] (modified to three items) and The Measure Yourself Concerns and Wellbeing questionnaire for Quality of Life[34] (baseline, 12 months).
- Modified enablement scale[35,36] (12 months).
- A website satisfaction measure modified for this study (12 months).
- Resource use data were collected through reviewing case notes and extracted from the electronic record at the end of the trial. Details of the information were extracted as follows:
  - Primary care, specifically consultations by type (face to face or telephone) and with who (GP, PN, HCA). Up to 12 visits were recorded.
  - Medications including both baseline and new medications with up to 15 medications, along with dose and if changed.
  - Other community-based services, including home visits, NHS calls, drop in centres, occupational therapy and others.
  - Inpatients, including for each admission, reason, disease and dates of admission and discharge.
  - Outpatients as for inpatients.
  - A&E attendance.

- Problematic Experiences of Therapy Scale with single item measures of self-reported adherence to website recommendations for physical activity, mental well-being, diet (12 months).
- Website usage and entries. With informed consent, this was unobtrusively automatically collected by the LifeGuide system, including time spent on each page and entries (e.g. goal setting and goal-related progress in physical activity, healthy eating, weight, fatigue and mood management).
- Adverse outcomes – serious adverse events (SAEs) were reported by both participants and practice staff, though it was anticipated that almost all of the SAEs would be unrelated to the research.

Sample size

Our aim was to encourage behaviour change, enable better management of symptoms, improve HRQoL, and improve self-rated health in each of the cancer types. We anticipated a long-term impact, but the sample size calculation, and therefore the timing of the primary analysis specified in the protocol was at 6 months (since 6 months was the main timescale of outcomes available in systematic reviews[37]). We anticipated that the web intervention, being very much briefer than the interventions previously described would be less effective than the more intensive face to face interventions used previously (we anticipated a standardised effect size of 0.15 to 0.30). We also wanted to demonstrate the effectiveness in each of the cancer clinical groups where possible. The Bonferroni correction has been criticised as being unduly conservative,[37] so in line with the rationale of Cook and Farewell,[38] we used $\alpha = 0.05$ since within each cancer subgroup there were independent pair-wise comparisons for the two intervention groups versus controls. To detect a difference

of 0.3 standardised mean difference (SMD) in any pairwise comparison between intervention subgroup and control for 80% power and α = 0.05, we required 176 intervention participants in each intervention subgroup and 176 controls, 1584 in total for the 3 clinical subgroups (breast, colorectal and prostate), or 1980 allowing for 20% loss to follow-up. We estimated that the total sample would allow us to detect overall differences between intervention groups of 0.15 SMDs. Despite the individually randomised design, cluster effects are possible: we assumed 8 patients per intervention group per practice, and an ICC of 0.03 with the inflation factor of 1.21 [1 + (8−1×0.03)], required 2396 participants. Allowing for some leeway in our assumptions, we aimed to recruit 2500 individuals.

Statistical analysis

All participant data were analysed (unless the participant/s specifically requested that their data be removed from the data set) on an intention to treat (ITT) basis, that is as randomised using Stata version 17 (StataCorp LP, College Station, TX, USA; www.stata.com/company). The primary analysis was with imputed data, using a chained equation multiple imputation model for missing data, including all outcomes as well as all variables included in the analysis model. A complete-case analysis was a sensitivity analysis. Generalised linear mixed regression models were used for the analysis of continuous variables, controlling for baseline values, stratification variables, and also controlling for potential confounding variables as appropriate, both for the overall trial sample and for each clinical subgroup (breast, prostate, colorectal). All models included a random effect for practice to allow for clustering of participants within practices, as per the sample size calculation. Pre-planned subgroup analyses were set out in the statistical analysis plan for age, gender and comorbidities. We also performed post hoc within-group analyses documenting the changes from baseline.

Workstream 4 health economic analyses

Detailed health economic analyses including design, data collection and methods were provided in *Appendix 2*.

In summary, we had hoped to perform a societal analysis but the data to do this was very incomplete, with low response rates. The study took an NHS and Personal Social Service (PSS) perspective, including all incurred costs in the cost-effectiveness analyses. However, as the intervention focused on self-management with in person or online support, the most likely to impact would be expected to be on primary care consultations and medication use (hence using primary care costs as our base case).

Itemised resource usage data were weighted by their corresponding unit costs hence accumulated costs were calculated for each patient. EQ-5D-5L scores were translated into utility scores based on the UK tariff, and quality-adjusted life-years (QALYs) were calculated using an area under the curve approach. Bootstrap methods based on 1000 replicates with replacement were employed to estimate means costs and QALYs, as well as the differences between groups with confidence intervals (CIs) associated with each estimate. Cost-effectiveness acceptability curves (CEACs) were produced based on the 1000 replicates.

The base-case analysis used NHS costs incurred in primary care. Sensitivity analyses included secondary service use [inpatient, outpatient and accident and emergency (A&E) attendances]. The primary care data are the most reliable, since it excludes those services least likely to have been influenced by the intervention, including inpatient services which were (except for emergencies) likely to have been planned before the intervention. Similarly, any emergency admissions were also unlikely to have been influenced by the intervention. The same arguments apply to outpatient attendances.

Role of funder: the funder, NIHR, had no role in data collection, analysis, interpretation, writing of the manuscript nor the decision to submit.

Results

Recruitment: 58,295 ‘cold calling’ invitations were sent by mail from 494 GP practices. Most people who did not wish to take part did not reply, but 10,840 people returned a reply slip to the study team. Of the 10,840, 143 did not give a reason, and the 10,697 gave one or more reasons, the most common being not wanting any help (5584), followed by not having or not wanting to use internet access (2649) (see *Table 1* for a full list of reasons). A total of 7883 individuals expressed interest in participating and were assessed for eligibility (*Figure 2*); 2732 patients were recruited from 494 practices, between 12 October 2017 and 2 April 2020). The main reason eligible participants were not recruited was that they already had good quality of life (see CONsolidated Standards Of Reporting Trials diagram; *Figure 1*). By 6 months 83% (2260/2712) and by 12 months 83% (2247/2712) of participants were followed up with complete

TABLE 1 Number of times reasons were given for not wanting to participate. Multiple options could be chosen

I don't have any problems that I want help with	5584
I don't feel well enough to take part at the moment	355
I don't have an e-mail address	2130
I'm not interested in taking part	875
I don't have time	323
I don't have internet access	2649
I don't want to use a website	1821
Other	2873
Total	16,610

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primary outcome data. The Programme Steering Committee advised stopping recruitment once the overall target was achieved and sufficient sample in prostate and breast subgroups.

Baseline characteristics. These were well balanced between groups (*Table 2*) and between cancers (*Table 3*) with the obvious exception of gender differences between prostate and breast. Only 430/2712 (16%) of participants were lost to follow-up at 6 months and 454/2712 (17%) at 12 months.

EORTCQLQ-30

There was improvement in both the generic advice groups and both the intervention groups (*Figure 3* and *Table 4*), with no statistically significant differences between groups overall at the primary time point of 6 months for the total score. However, the Renewed plus support group did experience higher quality of life at 6 months than the usual-care group in the prostate cancer subgroup by 2.03 points (95% CI 0.25 to 3.80). At 12 months, there was a statistically significant improvement in the Renewed plus support arm with QoL higher in this group than usual care by 1.42 points (95% CI 0.33 to 2.51). All cancer groups showed improved QoL over usual care but the results were only significant for prostate cancer (*Table 5*).

Results for subscales at 6 months

There was a significant difference in self-rated global health in both Renewed groups (*Table 6*). The Renewed plus support group also showed improvement in the physical function and cognitive function subscales.

Results for subscales at 12 months

The generic advice group remained stable by 12 months, but there were further improvements in both Renewed groups, with significant differences compared with generic advice in patients' perception of global heath, dyspnoea and constipation (*Table 7*). The Renewed plus support group also showed improvement in the physical, emotional, cognitive fatigue and dyspnoea subscales. All the other scales in the support group apart from financial difficulties improved compared to generic advice and this was significant for seven scales. A similar pattern was seen for the Renewed group without support: with significant changes in global health and improvement in dyspnoea and constipation. All but two of the sub-scales improved compared to generic advice.

Within-group analysis: improvement from baseline

The minimal clinically important difference for the EORTC questionnaire has not been robustly determined in our target population, but assuming a 6-point difference could be important,[39,40] more than 40% in each group achieved a 6-point improvement at 6 months with no difference between the groups. By 12 months there was continued improvement in both intervention groups (*Table 8*), but flattening off in the generic advice group.

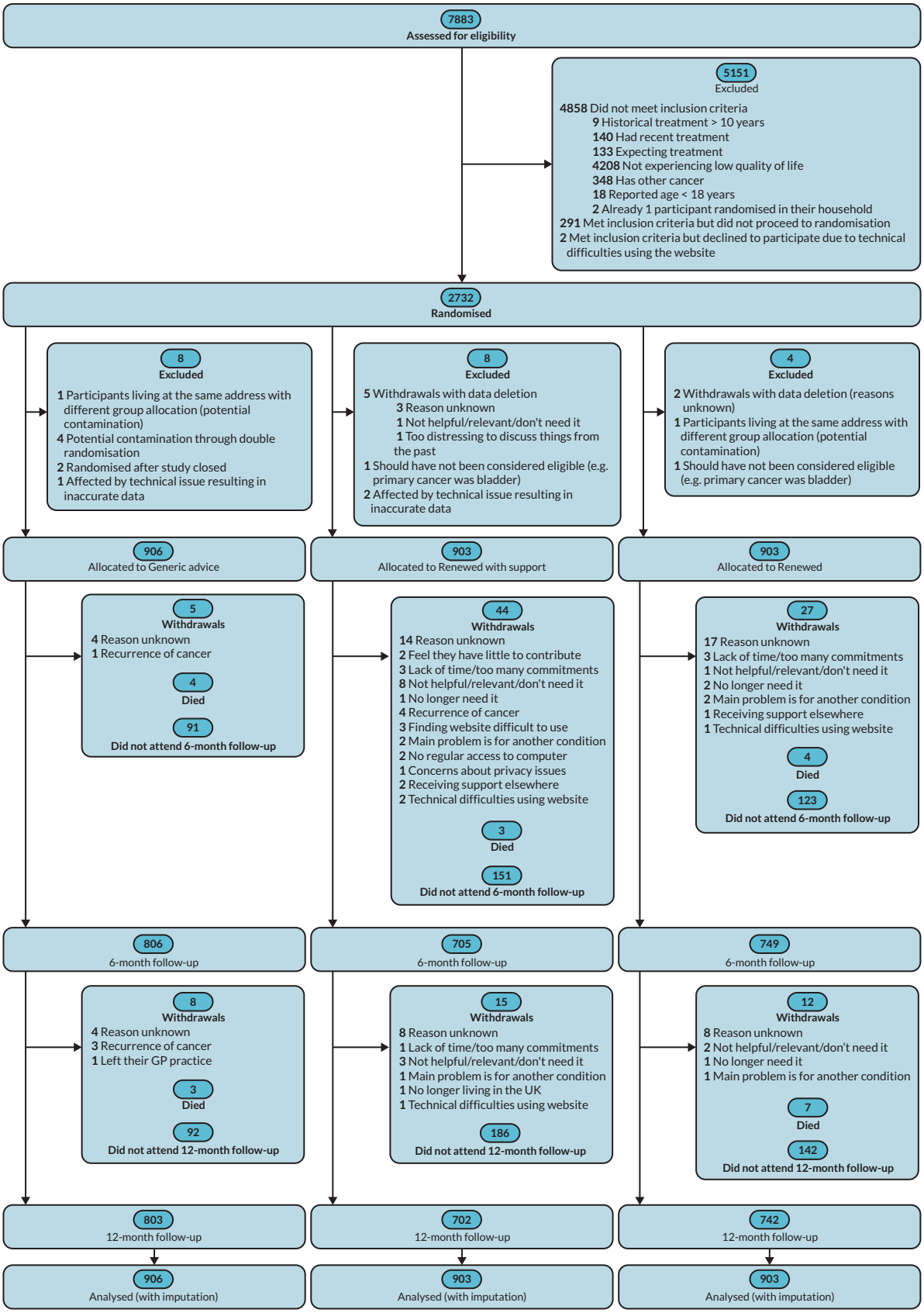

FIGURE 2 CONsolidated Standards Of Reporting Trials diagram. This figure has been reproduced from Little *et al.*[1] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

TABLE 2 Baseline characteristics by intervention group

	Generic advice (*n* = 906)	Renewed plus support (*n* = 903)	Renewed (*n* = 903)	Total (*n* = 2712)
Age (years)				
Mean (SD)	64.5 (10.9)	64.5 (11.2)	64.5 (10.7)	64.5 (10.9)
Baseline[a] EORTCQLQ-C30 score				
Mean (SD)	72.1 (12.2)	72.5 (11.8)	72.7 (11.7)	72.4 (11.9)
BMI				
Mean (SD)	28.0 (5.5)	28. 2 (5.5)	28.0 (5.4)	28.1 (5.5)
Ethnicity (non-White)				
	2/906 (2.4)	19/902 (2.1)	20/902 (2.2)	61/2710 (2.3)
Cancer group				
Bowel/colorectal	143/906 (15.8%)	143/903 (15.8%)	146/903 (16.2%)	432/2712 (15.9%)
Breast	474/906 (52.3%)	471/903 (52.3%)	471/903 (52.2%)	1416/2712 (52.2%)
Prostate	289/906 (31.9%)	289/903 (32.0%)	286/903 (31.7%)	864/2712 (31.9%)
Comorbidities				
Cardio	291/779 (37.4%)	325/787 (41.3%)	329/789 (41.7%)	945/2355 (40.1%)
Lung	130/779 (16.7%)	126/787 (16.0%)	149/789 (18.8%)	405/2355 (17.2%)
Other	548/779 (70.4%)	545/787 (69.3%)	563/789 (71.4%)	1656/2355 (70.3%)
Gender				
Male	379/906 (41.8%)	380/903 (42.1%)	368/903 (40.8%)	1127/2712 (41.6%)
Female	527/906 (58.2%)	523/903 (57.9%)	535/903 (59.3%)	1585/2712 (58.4%)
Time since last cancer treatment (years)				
Mean (SD)	4.0 (3.0)	4.1 (3.2)	3.9 (3.3)	4.0 (3.1)

BMI, body mass index; SD, standard deviation.
a Range 0–100, higher scores reflect higher quality of life.[1]

TABLE 3 Baseline characteristics by cancer type

	Bowel/colorectal (*n* = 432)	Breast (*n* = 1416)	Prostate (*n* = 864)	Total (*n* = 2712)
Age (years)				
Mean (SD)	67.0 (10.6)	59.4 (10.1)	71.6 (7.4)	64.5 (10.9)
Baseline[a] EORTCQLQ-C30 score				
Mean (SD)	72.1 (12.1)	71.6 (12.3)	73.8 (10.9)	72.4 (11.9)
BMI				
Mean (SD)	28.4 (5.7)	28.0 (6.0)	28.0 (4.3)	28.1 (5.5)

continued

TABLE 3 Baseline characteristics by cancer type (*continued*)

	Bowel/colorectal (*n* = 432)	Breast (*n* = 1416)	Prostate (*n* = 864)	Total (*n* = 2712)
Comorbidities				
Cardio	181/382 (47.4%)	349/1248 (28.0%)	415/725 (57.2%)	945/2355 (40.1%)
Lung	80/382 (20.9%)	206/1248 (16.5%)	119/725 (16.4%)	405/2355 (17.2%)
Other	280/382 (73.3%)	858/1248 (68.8%)	518/725 (71.5%)	1656/2355 (70.3%)
Gender				
Male	246/432 (56.9%)	17/1416 (1.2%)	864/864 (100.0%)	1127/2712 (41.6%)
Female	186/432 (43.1%)	1399/1416 (98.8%)	0 (0.0%)	1585/2712 (58.4%)
Time since last cancer treatment (years)				
Mean (SD)	4.1 (3.2)	4.0 (3.1)	3.8 (3.1)	4.0 (3.1)

BMI, body mass index; SD, standard deviation.
a Range 0–100, higher scores reflect improved health or functioning.

TABLE 4 Main results of EORTCQLQ-30 at 6 and 12 months

	All participants		
	Generic advice	Renewed plus support	Renewed
6 months			
Mean (SD)	76.0 (14.31)	76.7 (14.41)	76.1 (13.99)
Complete cases	806	705	749
Complete cases	REF	0.50 (−0.67, 1.66)	−0.42 (−1.57, 0.72)
Imputed (100 imputations)	REF	0.52 (−0.53, 1.57)	−0.20 (−1.23, 0.84)
12 months			
Mean (SD)	75.7 (15.13)	77.2 (14.07)	77.0 (14.42)
Complete cases	803	702	742
Complete cases	REF	1.11 (−0.10, 2.31)	0.72 (−0.46, 1.91)
Imputed (100 imputations)	REF	**1.42 (0.33, 2.51)**[a]	0.94 (−0.13, 2.01)

SD, standard deviation.
a Significant at the 5% level.

TABLE 5 Main results by cancer type

	Colorectal/bowel cancer			Breast cancer			Prostate cancer		
	Generic advice	Renewed + support	Renewed	Generic advice	Renewed + support	Renewed	Generic advice	Renewed + support	Renewed
6 months									
Mean (SD)[a]	75.4 (14.35)	75.1 (14.36)	75.2 (13.31)	75.8 (14.70)	76.3 (14.97)	75.9 (14.18)	76.4 (13.60)	78.3 (13.31)	77.0 (13.97)
Compete cases	REF	−2.23 (−4.97, 0.50)	−2.29 (−4.88, 0.31)	REF	−0.48 (−2.37, 1.41)	−1.01 (−2.85, 0.82)	REF	1.99 (−0.01, 3.99)	−0.06 (−2.09, 1.97)
Imputed (100 imputations)	REF	−1.56 (−1.21, 1.10)	−1.29 (−3.81, 1.22)	REF	0.27 (−1.21, 1.74)	−0.13 (−1.61, 1.36)	REF	**2.03 (0.25, 3.80)**	0.42 (−1.32, 2.16)
12 months									
Mean (SD)	74.1 (14.67)	76.4 (13.61)	77.0 (14.64)	76.0 (15.60)	76.9 (14.54)	77.2 (14.26)	75.8 (14.49)	78.3 (13.41)	76.7 (14.57)
Complete cases	REF	0.76 (−2.12, 3.64)	1.53 (−1.25, 4.33)	REF	−0.02 (−1.91, 1.88)	0.22 (−1.59, 2.04)	REF	2.00 (−0.13, 4.14)	−0.24 (−2.41, 1.94)
Imputed (100 imputations)	REF	1.04 (−1.68, 3.76)	1.74 (−1.03, 4.51)	REF	0.75 (−0.76, 2.27)	0.99 (−0.50, 2.47)	REF	**2.76 (0.87, 4.65)**	0.58 (−1.29, 2.45)

SD, standard deviation.

a Range 0–100, higher scores reflect improved health or functioning.

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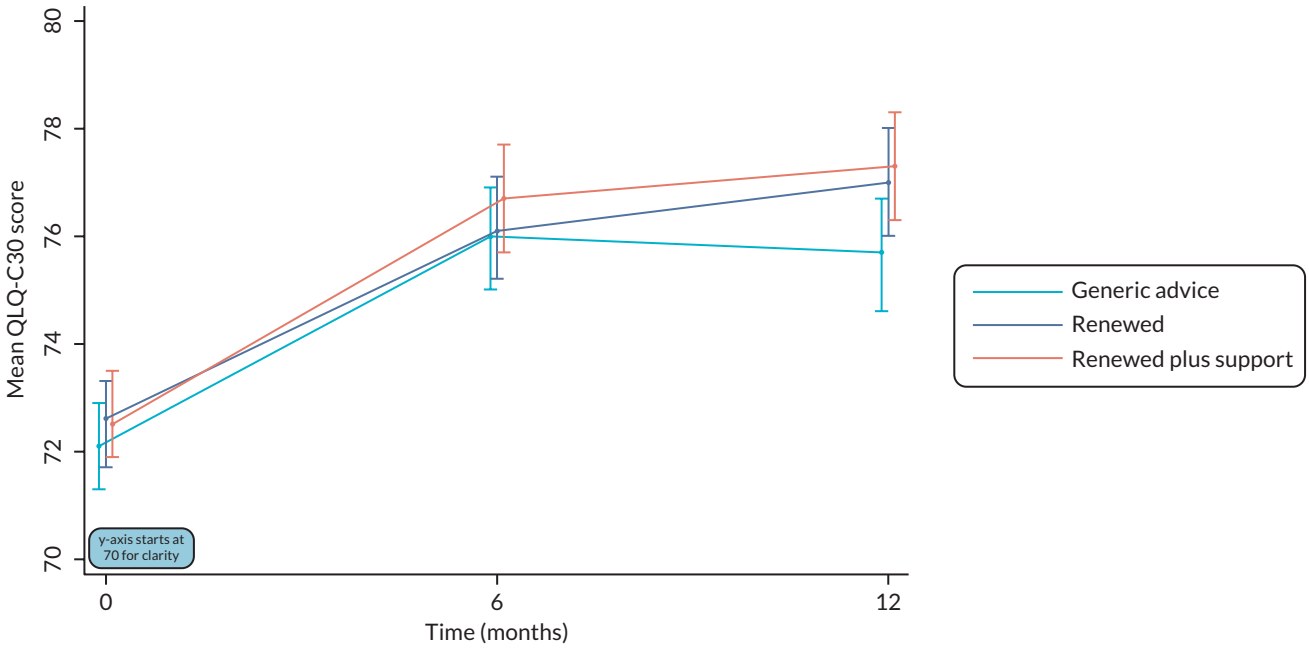

FIGURE 3 Graphical representation of improvement in EORTC QLQ-C30 over time. This figure has been reproduced from Little *et al.*[1] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure above includes minor additions and formatting changes to the original text.

TABLE 6 Means and mean differences between Renewed and Generic advice groups for EORTCQLC subscales (6 months)

	Generic advice	Renewed support		Renewed	
	Mean (SD)	Mean (SD)	Imputed (100 imputations)	Mean (SD)	Imputed (100 imputations)
Global health[a]	64.4 (19.89)	66.3 (18.54)	**1.82 (0.14, 3.52)**	65.9 (19.11)	**1.88 (0.18, 3.58)**
Functional subscales[a]					
Physical function	77.7 (20.68)	78.7 (19.88)	**2.00 (0.64, 3.36)**	78.2 (19.88)	0.50 (−0.82, 1.82)
Role function	71.9 (28.36)	71.3 (28.14)	−1.01 (−3.45, 1.42)	71.0 (27.49)	−1.06 (−3.44, 1.31)
Emotional function	69.8 (22.72)	70.5 (22.15)	0.79 (−1.01, 2.60)	70.0 (21.93)	−0.05 (−1.87, 1.76)
Cognitive function	73.5 (22.10)	76.5 (20.86)	**2.32 (0.52, 4.12)**	75.5 (21.33)	0.69 (−1.10, 2.48)
Social function	71.8 (27.55)	73.6 (27.46)	1.46 (−0.83, 3.75)	72.7 (26.68)	0.70 (−1.58, 2.97)
Symptom subscales[b]					
Fatigue	38.6 (22.60)	37.2 (22.75)	−1.18 (−3.08, 0.73)	38.7 (22.51)	0.20 (−1.72, 2.12)
Nausea and vomiting	5.5 (11.62)	6.0 (12.67)	0.55 (−0.59, 1.70)	5.8 (11.78)	0.26 (−0.85, 1.36)
Pain	31.5 (28.07)	31.8 (28.19)	0.43 (−1.89, 2.75)	32.2 (28.33)	0.81 (−1.49, 3.12)
Dyspnoea	20.8 (25.81)	19.0 (24.65)	−1.47 (−3.64, 0.70)	20.11 (26.41)	−0.92 (−3.00, 1.17)
Insomnia	41.5 (31.22)	41.5 (32.43)	0.001 (−2.81, 2.81)	42.0 (31.15)	0.39 (−2.38, 3.16)
Appetite loss	11.4 (21.37)	10.8 (20.83)	−0.36 (−2.28, 1.56)	11.1 (20.65)	0.07 (−1.81, 1.95)
Constipation	17.0 (25.79)	15.6 (24.86)	−1.51 (−3.75, 0.73)	15.8 (25.50)	−0.68 (−2.88, 1.52)
Diarrhoea	11.0 (20.62)	11.2 (22.66)	0.55 (−1.49, 2.58)	12.2 (23.06)	0.89 (−1.15, 2.92)

TABLE 6 Means and mean differences between Renewed and Generic advice groups for EORTCQLC subscales (6 months) (*continued*)

	Generic advice	Renewed support		Renewed	
	Mean (SD)	Mean (SD)	Imputed (100 imputations)	Mean (SD)	Imputed (100 imputations)
Financial difficulties	10.4 (23.42)	11.8 (23.82)	1.03 (−0.83, 2.89)	11.44 (23.02)	1.02 (−0.85, 2.89)

SD, standard deviation.
a Range 0–100, higher scores reflect improved health or functioning
b Range 0–100, lower scores reflect improved symptom control.
Bold values indicate statistically significant at the 5% level.

TABLE 7 Results for EORTCQLQ subscales at 12 months. Means for each group, and differences between Renewed groups and Generic advice

	Generic advice	Renewed support		Renewed group	
	Mean (SD)	Mean (SD)	Imputed (100 imputations)	Mean (SD)	Imputed (100 imputations)
Global health	63.8 (20.46)	66.6 (19.01)	**2.78 (1.08, 4.48)**	66.6 (18.68)	**3.06 (1.39, 4.74)**
Functional subscales[2]					
Physical function	78.3 (21.12)	79.6 (19.57)	**2.25 (0.88, 3.62)**	78.5 (20.54)	0.14 (−1.22, 1.50)
Role function	71.8 (28.63)	72.5 (27.57)	0.02 (−2.36,2.41)	73.2 (27.63)	0.89 (−1.50, 3.27)
Emotional function	68.9 (23.13)	71.5 (22.35)	**2.72 (0.84, 4.61)**	70.2 (22.82)	0.99 (−0.87, 2.84)
Cognitive function	73.6 (22.43)	76.3 (20.59)	**1.92 (0.13, 3.71)**	76.0 (21.33)	1.12 (−0.65, 2.89)
Social function	72.9 (28.45)	75.6 (27.62)	2.22 (−0.20, 4.64)	74.7 (27.83)	1.31 (−1.10, 3.72)
Symptom subscales[2]					
Fatigue	38.4 (22.91)	35.6 (22.50)	**−2.67 (−4.58, −0.75)**	37.0 (22.78)	−1.25 (−3.15, 0.66)
Nausea and vomiting	6.1 (12.58)	5.9 (12.58)	−0.24 (−1.41, 0.93)	5.2 (12.02)	−0.96 (−2.11, 0.20)
Pain	31.2 (28.32)	30.9 (27.08)	−0.22 (−2.53, 2.10)	31.8 (28.79)	0.86 (−1.48, 3.20)
Dyspnoea	22.2 (19.26)	19.3 (25.45)	**−2.73 (−4.92, −0.55)**	19.7 (25.31)	**−2.78 (−4.91, −0.64)**
Insomnia	42.5 (32.56)	41.2 (32.55)	−1.30 (−4.14, 1.55)	40.1 (30.84)	−2.27 (−5.08, 0.54)
Appetite loss	11.0 (20.46)	10.3 (20.15)	−0.68 (−2.53, 1.18)	10.5 (20.88)	−0.13 (−1.96, 1.69)
Constipation	18.9 (26.29)	16.6 (25.22)	**−2.36 (−4.62, −0.11)**	15.5 (24.95)	**−2.77 (−4.99, −0.55)**
Diarrhoea	11.8 (21.31)	11.2 (21.60)	−0.57 (−2.51, 1.37)	11.9 (21.40)	−0.42 (−2.38, 1.53)
Financial difficulties	9.2 (21.60)	9.8 (21.49)	0.28 (−1.49, 2.04)	9.5 (21.61)	0.36 (−1.40, 2.13)

SD, standard deviation.
Bold values indicate statistically significant at the 5% level.

TABLE 8 Within-group analysis of EORTCQLQ from baseline

	6 months			12 months		
EORTCQLQ	Generic advice	Renewed plus support	Renewed	Generic advice	Renewed plus support	Renewed
Mean at baseline (SD)[a]	72.0 (12.19)	72.0 (12.19)	72.4 (11.80)	72.6 (11.71)	72.4 (11.80)	72.6 (11.71)
Mean at follow-up (SD)[a]	76.0 (14.31)	76.0 (14.31)	76.7 (14.41)	75.7 (15.13)	77.2 (14.07)	77.0 (14.42)
Difference based on paired *t*-test (95% CI)	3.91 (3.16 to 4.66)	4.32 (3.52 to 5.11)	3.53 (2.76 to 4.29)	3.61 (2.81 to 4.40)	4.85 (4.04 to 5.67)	4.40 (3.60 to 5.19)
% achieving MCID improvement of 6 points	41.95%	44.68%	42.67%	41.97%	48.15%	45.46%

MCID, minimum/minimal(ly) clinically important difference; SD, standard deviation.
a Range 0–100, higher scores reflect improved health or functioning.

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Other secondary outcomes

This analysis relies heavily on imputation since we received only half of the HADS data and other 12-month secondary outcome questionnaire data. Therefore, we have also presented the crude means from the complete-case data. There was an improvement in both anxiety and depression in the Renewed plus support group at 12 months (as well as in the renewed group but this was not statistically significant) (*Table 9*). However, the improvement was modest at < 0.5 point. The bothersomeness on the MYCAW1 was lower in the support group, and the other MYCAW responses were in the same direction but not significant. The fear of recurrence scale showed no significant difference between the groups. The patient enablement instrument was significantly lower in both groups, which suggests higher enablement (these were coded 1 = strongly agree to 7 = strongly disagree) suggesting that on average one in three people said they agreed they felt enabled to manage their condition compared to those having generic advice (where on average people only slightly agreed). There were not enough events to look at survivorship but deaths across the three arms are summarised below.

Deaths: there were six deaths: one in the generic advice group, three in Renewed plus support and two in Renewed.

Health economics

Mean NHS primary care costs were lower in Renewed and Renewed plus support groups (–£141, –£77, respectively). There were very small differences in estimated quality of life based on the EQ-5D-5L. In addition, a substantial proportion of data in EQ-5D-5L were missing, leading to significant uncertainty in the estimates. Both interventions were likely to be cost-effective (incremental costs per QALY £11,281, –£7542, respectively) (*Table 10*); and the Renewed intervention is probably more cost-effective than Renewed plus support (see *Appendix 2* for the full Health Economic Analysis). Both intervention groups were dominant in term of the effectiveness measures – demonstrating improved outcomes with lower costs.

Results for cancer subgroups: There were no significant interaction terms and the subgroup results were generally in line with the main trial results (*Table 11*).[1] After controlling for cancer type, males did significantly better than females on the primary outcome at 6 months. There was also a suggestion that there could be more benefit among longer-term survivors.

Implications

Cancer survivors with lower quality of life given detailed generic online support improve significantly, including those where the primary course of treatment was several years previously – where improvement in quality of life would not be expected. Providing a robustly developed website to address peoples' support needs, with minimal additional resource implications, is likely to provide modest but significant further longer-term improvement in enablement, symptom management and most importantly self-rated global health, and with lower NHS costs in primary care.

TABLE 9 Secondary outcomes

	Generic advice	Renewed plus support		Renewed	
	Mean (SD)	Mean (SD)	Imputed (100 imputations)	Mean (SD)	Imputed (100 imputations)
HADS – Anxiety	7.54 (4.56)	7.14 (4.54)	**−0.43 (−0.77, −0.08)**	6.95 (4.27)	−0.35 (−0.71, 0.01)
HADS – Depression	5.76 (3.95)	5.28 (3.74)	**−0.40 (−0.70, −0.10)**	5.37 (3.81)	−0.26 (−0.59, 0.08)
PEI	3.22 (1.27)	2.91 (1.21)	**−0.30 (−0.44, −0.16)**	2.86 (1.23)	**−0.35 (−0.50, −0.21)**
MYCAW1	−0.73 (1.71)	−0.96 (1.73)	**−0.24 (−0.43, −0.05)**	−0.89 (1.71)	−0.15 (−0.37, 0.07)
MYCAW2	−0.68 (1.81)	−0.84 (1.75)	−0.15 (−0.38, 0.06)	−0.80 (1.78)	−0.11 (−0.35, 0.14)
FRRS1	3.37 (1.16)	3.43 (1.18)	0.05 (−0.07, 0.18)	3.38 (1.16)	0.01 (−0.13, 0.15)
FRRS2	3.42 (1.21)	3.49 (1.19)	0.05 (−0.07, 0.18)	3.43 (1.19)	0.002 (−0.13, 0.14)
FRRS3	2.52 (1.30)	2.58 (1.31)	0.06 (−0.07, 0.19)	2.53 (1.30)	0.02 (−0.12, 0.16)

HADS, Hospital Anxiety and Depression scale; MYCAW, Measure yourself concerns and well-being scale; 1 and 2 are the key problems identified by the participant FRRS: fear of relapse and recurrence scale; 1: cancer unpredictable so inability to plan future; 2 fear of cancer interfering with enjoying life; 3 afraid of recurrence PEI, patient enablement instrument; SD, standard deviation.
Bold values indicate statistically significant at the 5% level.

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TABLE 10 Cost–utility analyses (EQ-5D-5L) using bootstrap methods and based on imputed QoL data

Groups	Mean NHS primary care costs	Difference (compared with Generic advice)	
Generic advice	265 (254, 275)		
Renewed plus support	187 (180, 195)	−77 (−90, −65)	
Renewed	124 (118, 130)	−141 (−153, −128)	
Renewed vs. Renewed plus support		−63 (−73, −54)	
	QALYs (EQ-5D-5L)	**Difference (compared with Generic advice)**	**Incremental cost per QALY gained (ICER)**
Generic advice	0.7 (0.692, 0.709)		
Renewed plus support	0.699 (0.691, 0.707)	−0.001 (−0.013, 0.011)	11,281 (−76,949, 97,385)
Renewed	0.705 (0.696, 0.714)	0.005 (−0.007, 0.018)	−7542 (−116,829, 115,651)
Renewed vs. Renewed plus support		0.006 (−0.006, 0.018)	−6007 (−50,473, 46,389)

ICER, incremental cost-effectiveness ratio.

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TABLE 11 Results for pre-specified subgroups

		Generic advice	Renewed support		Renewed	
	N (%)	Mean (SD)	Mean (SD)	Difference (95% CI)	Mean (SD)	Difference (95% CI)
Primary outcome – total EORTCQLQ C30 score at 6 months						
Time since end of treatment						
Up to 1 year	427 (16%)	78.4 (12.87)	76.6 (14.81)	−0.84 (−3.60 to 1.93)	76.7 (13.66)	−2.14 (−4.80 to 0.52)
More than 1 year	2231 (84%)	75.5 (14.51)	76.8 (14.33)	0.78 (−0.96 to 1.37)	76.0 (14.06)	0.20 (−0.96 to 1.37)
Time since end of treatment (post hoc)						
Up to 3.5 years (median)	1311 (50.1%)	76.8 (13.6)	75.9 (15.45)	−0.67 (−2.23 to 0.90)	76.7 (13.90)	−1.43 (−2.95 to 0.09)
3.5 years	1307 (49.9%)	75.1 (14.91)	77.6 (13.26)	**1.75 (0.30 to 3.20)**	75.5 (14.06)	1.11 (−0.43 to 2.65)
Sex						
Male	1126 (42%)	76.1 (13.60)	78.3 (13.12)	**1.95 (0.39 to 3.51)**	76.9 (13.86)	0.48 (−1.03 to 1.99)
Female	1578 (58%)	75.8 (14.79)	75.6 (15.18)	−0.49 (−1.89 to 0.91)	75.6 (14.05)	−0.68 (−2.07 to 0.71)
Lung comorbidity						
No	2221 (83%)	76.9 (13.53)	77.9 (13.56)	0.99 (−0.16 to 2.14)	77.1 (13.65)	−0.13 (−1.26 to1.00)
Yes	452 (17%)	71.0 (16.90)	70.5 (16.86)	−1.81 (−4.75 to 1.14)	72.1 (14.72)	−0.32 (−3.14 to 2.50)
Other comorbidity						
No	786 (30%)	78.9 (12.50)	79.6 (13.75)	0.71 (−1.19, 2.61)	78.3 (13.33)	−0.47 (−2.34, 1.41)
Yes	1875 (70%)	74.7 (14.83)	75.5 (14.51)	0.46 (−0.83, 1.75)	75.2 (14.16)	−0.06 (−1.33, 1.21)

Bold values indicate statistically significant at the 5% level.

Process evaluations exploring how patients and healthcare professionals experienced and implemented the intervention in practice

Patient qualitative process study: experiences of using a supported digital intervention for cancer survivors in primary care

Please see *Appendix 4* for a full summary of this study.

Aims

To explore how cancer survivors used the Renewed intervention and to understand the potential barriers and facilitators to using Renewed and performing the recommended behaviours.

Methods

Forty-two patients took part in the interviews. Data were analysed using inductive thematic analysis.

Results

Three patients did not recall using Renewed and/or being in the study so their data were excluded from the analysis. Thematic analysis identified four themes: (1) The importance of motivation for using Renewed and performing behaviour changes, (2) Minimal usage of Renewed plus supported behaviour changes, (3) Supporter needs to add value and (4) Convenience of Renewed Online.

Practical implications

The results showed that even limited usage of Renewed Online may provide enough information to motivate behaviour change in those with less need for more tailored support. Novel information may need to be presented earlier in the

intervention to motivate further engagement with Renewed in those who need more detailed and tailored information to make behaviour changes. This has implications for the implementation of Renewed and similar interventions into clinical practice. Renewed may be implemented as stepped care approach for cancer survivors, where cost-effective support may be offered to many patients with less need for resource intensive and tailored support, and patients only 'step up' to more specialist support for more complex needs. In addition, adding support alongside digital interventions may motivate engagement, particularly for people who lack support elsewhere.

Patient quantitative process study: engagement and usage of the Renewed intervention by patients

Please see *Appendix 4* for a full summary of this study.

Aims

To evaluate how cancer survivors used Renewed. The specific research questions were: (1) How much did patients use Renewed? Which components of Renewed were most used? (2) Is there a difference in Renewed usage (i.e. frequency) based on patient characteristics? (3) Do patients who accessed human support use Renewed more compared to those who did not access human support or were without access to human support? (4) Do patients who accessed Renewed's Optional content have greater improvements in quality of life at 12 months?

Methods

This was a quantitative process study nested within the RCT of the Renewed intervention. Patients were sampled from all three arms of the Renewed trial: (1) Renewed Online, (2) Renewed Online with brief human support and (3) usual care. Data from patients from the Renewed Online and Renewed Online plus brief human support arms were analysed. This study was carried out 12 months after patients joined the Renewed study.

Patients completed questionnaires at baseline and 12 months post randomisation. The intervention software, LifeGuide, recorded their usage of Renewed. Patients were included in the analysis if they had completed the 12-month follow-up measures. Demographic and clinical characteristics were collected at baseline, and psychological characteristics were collected at 12 months.

Access to human support was characterised in three ways: (1) patients who accessed human support ('accessed support'), (2) patients who had the option to access human support but did not ('did not access support') and (3) patients who were in the Renewed Online only group who did not have access to human support ('without access to support').

Results

The sample consisted of the 1760 cancer survivors in the Renewed Online and Renewed Online with brief human support trial arms who completed follow-up measures at 12 months.

How much did participants use Renewed? Which components of Renewed were most used?

Patients accessed Renewed a median of 2 times, ranging from 0 to 268. The majority of patients (97%) accessed the Core content of Renewed, with 84% completing the Core content and reaching the Homepage where they could access the other components of Renewed. Slightly less than half (45%) of patients continued to use Renewed past the Homepage to access the Optional content of Renewed (Getting Active, Eat for Health, Healthy Paths, POWeR). After the Core content, Getting Active was the most used component of Renewed (30%), and least used was Healthy Paths (10%).

Is there a difference in Renewed usage (i.e. frequency) based on participant characteristics?

There were no significant associations between the overall number of times patients accessed Renewed and their characteristics (age, gender, cancer type, age when completed education and years since finishing treatment).

Do those who accessed support use Renewed more compared to those who did not access support or were without access to support?

At 12 months, the results showed a moderate significant difference in usage of Renewed based on access to support ($p < 0.001$). Those who accessed support used Renewed more than those who did not access support or were without

access to support (median number of times Renewed was accessed: 4, 1, 1, respectively). The approximate effect was greatest when comparing those who accessed support to those who chose not to access support (d = 0.37).

Do patients who accessed Renewed's Optional content have greater improvements in quality of life at 12 months?
At 12 months, those who used Optional content had higher EORTCQLQC30 scores compared to those who only accessed the Core content. The mean score was 2.15 (95% CI, 3.28 to 1.01; $p < 0.001$) points lower among those who only accessed the Core content compared to those who accessed the Optional content after adjusting for covariates ($p \leq 0.001$). There was a small standardised effect (d = 0.2).

Practical implications
These results suggest that motivating patients to engage more with Renewed Online is likely to lead to better outcomes. Renewed was largely used as intended, with usage of Optional content associated with greater improvements in QoL at 12 months. Patients who accessed human support engaged with Renewed more than patients who did not have human support or were without human support, suggesting that the brief support provided by HCPs encouraged engagement. However, as support was optional and had to be requested by patients, the patients who accessed human support may have already been more confident and motivated to engage with Renewed.

Healthcare professionals' qualitative process study: exploration of healthcare professionals' experiences of using the intervention

Aims
To explore Supporters' experiences of providing support to cancer survivors using the Renewed intervention to understand potential barriers and facilitators to the implementation of Renewed.

Methods
Twenty-eight semistructured telephone interviews were conducted with Supporters (practice-based nurses, practice-based HCAs and clinical research nurses). A semistructured interview schedule was developed, which explored: (1) Supporters' experiences of providing support, (2) perceptions of Supporter training, (3) experiences during support appointments, (4) perceptions of the CARE approach and (5) Supporters' perceptions of the Renewed programme. Interviews were audio-recorded and transcribed verbatim. Data were analysed using inductive thematic analysis.

Results
The final sample included 28 HCPs consisting of 16 PNs, 6 clinical research nurses, and 6 practice-based HCAs. They provided support for patients at a total of 45 GP practices. Twenty-seven HCPs were female; one was male.

Four themes were developed which reflected factors that Supporters identified as enabling or hindering them to support patients using Renewed. The themes were: confidence to enact the Supporter role, practicalities of delivering support alongside a digital intervention, managing a patient-led approach, and Renewed Online as an acceptable tool with some improvements. The results of this study have been published.[41]

Practical implications
Our results suggest that HCPs based in primary care found this type of digital intervention with a Support role acceptable and are amendable to contributing to the delivery of support to cancer survivors.

Healthcare professionals are central to providing support for cancer survivors, yet support is limited because of practitioners' perceived lack of time and expertise in how to help cancer survivors with symptoms after treatment, which are key barriers to providing this support. The results of this study show that these barriers could be overcome with a digital intervention such as Renewed, which provides the majority of support so HCPs only need to provide brief support to maximise engagement, with no need to develop cancer specific expertise or behaviour skills.

Key factors that may support the successful implementation of Renewed in practice include the increasing acceptability of phone support in primary care (particularly in the current climate of the coronavirus disease discovered in 2019 pandemic), and the utility and acceptability of the CARE approach among most HCPs. Ease of the Supporters' online

training and Renewed's perceived similarity to tools used in current practice also support successful implementation in practice.

Equality, diversity and inclusion

The population were reasonably well balanced for gender, with a good range of educational status, but only 2–3% of the study population compared with 6% from the 2021 census were from ethnic minorities, and which reflects the difficult of recruiting in ethnic minority areas.

Conclusions

Objectives

The aim of understanding the issues for cancer survivors and then iteratively developing an intervention requiring limited resources was achieved.

Implications of our findings for future research and practice in quality of life for cancer survivors

This is one of the few trials of brief multidimensional support for cancer survivors who are likely to have persistently lower quality of life in primary care and documents improvement in quality of life among participants given detailed evidence-based generic lifestyle advice. Comparing the Renewed interventions with generic advice there was limited evidence of between group differences in overall quality of life at 6 months. However, there were small differences between the supported Renewed intervention and the generic advice group by 12 months. Potentially more important and longer-term differences for both the Renewed groups compared with generic advice were found in global rating of health, symptom management, and enablement by 12 months.

Overall, quality of life improved both for participants encouraged to use a link to the NHS LiveWell website (Generic advice) and for participants given access to the Renewed interventions. The improvement in all groups is unlikely to be a reflection of the natural history in our sample (where the mean time since treatment was 4 years), since groups with poor HRQoL remain consistently poor in this population after 2 years,[42] and in particular groups with low quality of life do not improve. We anticipated a long-term impact, but the primary analysis time point was chosen as 6 months because that was the timescale previous systematic reviews had reported.[37] There were no significant differences between groups overall by 6 months, although participants with prostate cancer in the support group improved significantly more than those given the generic healthy lifestyle link.

By 12 months the generic advice group had stopped improving but improvement was maintained in the intervention groups, significantly so for participants in the support group. Most of the effect was seen in the subgroup with prostate cancer which may be important given the significant stigmatisation and need for support in this patient group.[43,44] The results for symptoms subscales demonstrated a small but significantly improved rating of global health at 6 months compared with the generic advice group, but limited evidence of between group differences in the other subscales. By 12 months both renewed groups continued significantly to improve ratings of global health compared to the generic advice group and there were also modest but significant between group differences in several other functional or symptom subscales, and enablement. Of the 14 subscales addressing function or symptoms (excluding the financial subscale which the intervention could not address), all but one subscale demonstrated improvement in the Renewed group compared to the generic advice group. Three out of the 14 were significantly different; for the Renewed plus support group all 14 subscales improved compared to the generic advice group and 7 of them were significant. This makes chance a very unlikely explanation. Most important of the subscales is arguably the improvement in self-rated global health, which improved significantly at 6 months and the effect was greater by 12 months. Self-rated global health is clinically important, since it has consistently been shown to be a strong predictor of mental health, physical health and mortality in the longer term.[45–51] The symptoms consistently improved compared to generic advice in both Renewed groups by 12 months were dyspnoea and constipation, also suggesting these were not chance findings. This is likely to be due to the development of specific, salient, advice tailored to address cancer survivors' issues[19] to better enable participants to manage their symptoms. The finding that enablement improved with Renewed (both with and without support), albeit with less complete data, is probably also important in its own right since in the ColoREctal Wellbeing colorectal cohort confidence to self-manage was highly predictive of subsequent health and well-being outcomes.[52] Mean NHS primary care costs were lower in Renewed and Renewed plus support groups (−£141, −£63, respectively) which resulted in both interventions being cost-effective based on standard National Institute for Health and Care Excellence thresholds. The modest longer-term improvement over and above the impact of detailed generic advice in most subscales particularly the global health subscales suggests that Renewed is a useful adjunct to generic advice, particularly given the primary care NHS cost savings.

There is some evidence from systematic reviews of trials that yoga, physical exercise more generally, cognitive–behavioural therapy, mindfulness-based stress reduction programmes, and dietary interventions can improve quality of life[37,53–59] but very little evidence of benefit at 6 months from multidimensional home-based interventions[59] and no evidence of benefit in the longer term. Although cohort studies suggest diet may impact recurrence and mortality,[60] the evidence from trials is less clear.[53,61] To our knowledge, there has been no trial with longer-term follow-up of robustly developed, brief multidimensional support for cancer survivors in primary care for pragmatic applicability in everyday practice.

Thus, the current study provides reasonable evidence that a novel bespoke intervention to support cancer survivors could be integrated into current practice since there are some longer-term benefits with lower costs to the NHS. However, all trial participants by definition had to engage with the trial and trial procedures, and so may not represent the wider patient population, and all were followed up with questionnaires and with phone calls where questionnaires were not returned. This could be mimicked in routine practice by brief follow-up contacts, but whether the effects in routine practice will turn out to be as useful as the current trial suggests requires a larger implementation study.

The contribution of patient and public involvement

The PPI involvement throughout this programme aimed to ensure that patients' needs and preferences were understood and accommodated wherever possible within the research. This included ensuring that the intervention itself was useful, reassuring, persuasive and motivating and that the research studies were accessible and feasible for people to participate in. The PPI group were an integral part of all stages of the research cycle. They helped design the research, optimise the research strategy (e.g. suggesting ways to optimise recruitment), helped with the interpretation of the study findings and with dissemination of these findings. PPI members contributed to larger meetings with the full research team, but also met with two researchers in smaller meetings to discuss issues in more depth. They also provided written input on the study documentation and intervention.

Our work with PPI contributors made a significant contribution to the CLASP research programme. *Box 1* provides specific examples of how our PPI group improved the research.

BOX 1 Specific examples of PPI contributions to Collaborative Labeling and Appliance Standards Program (CLASP)

1. Improving patient study documents to promote study engagement and patient experience.
   - Improving clarity of statements in the Participant Information Sheet for the RCT to make the description of the intervention groups and procedures involved easier to understand.
2. Intervention design.
   - Choosing the name of the intervention (Renewed).
   - Choosing between design mock ups for the look and feel of the Renewed website.
   - Suggesting the number of human support appointment contacts and frequency that would be most suitable.
   - Suggesting factors that might motivate patients to engage in behaviour change that were incorporated into the motivational quizzes (e.g. within Getting Active).
3. Intervention optimisation.
   - Testing the Renewed intervention and highlighting places that were confusing or harder to understand or navigate, enabling optimisation.
4. Providing a PPI perspective on findings.
   - The PPI group helped interpret the findings from the qualitative optimisation studies, main trial and process evaluation. For example, some highlighted that the intervention might have been more successful in those with prostate cancer because this group receive less support after discharge from primary treatment than those with bowel/breast cancer.
   - Suggesting additional questions to explore within the analyses – for example two PPI members suggested examining whether uptake of nurse support was different across cancer types within the process evaluation (it was not, but this was a useful avenue to explore).
5. Dissemination.
   - Inputting to discussions about how the intervention should best be disseminated to reach members of the public and those who have survived cancer.
   - Inputting into all of the academic publications resulting from this programme of research.
   - Volunteering to help disseminate the research findings within workshops for cancer survivors.

Strengths, successes, limitations and challenges

Strengths and successes

The complex intervention was developed robustly for a range of cancer survivors with a user centred approach, the Person-Based-Approach, which has been shown to be effective for the development of other complex behavioural interventions with brief support.[14,62,63] This is one of the largest trials to assess the impact of brief support to cancer survivors and addressed contrasting cancers. The method of invitation (a non-specific 'cold-calling' invitation to capture most potentially eligible patients) was largely successful, but inevitably resulted in a relatively low take up; reassuringly only 25% (2649/10,697) declined due to lack of internet access. This is similar to the national figure of 20% for 64–75 years old in 2018 (https://www.ons.gov.uk/businessindustryandtrade/itandinternetindustry/datasets/internetusers; accessed 6 March 2025). The sample had high levels of comorbidity as would be expected,[17,64,65] and among those assessed for eligibility only 6% (291/4858) of eligible participants declined which supports the generalisability of the trial.

Limitations and challenges

A small percentage of ethnic minority participants would be expected for the target population of patients; nevertheless, fewer were recruited than census data would suggest, which reflects the difficulty of recruiting in ethnic minority areas. Recruitment for participants with colorectal cancer was an unexpected challenge and for no clear reason that we could discern; hence we had limited power for the colorectal cancer subgroup. We also did not control for any variability in initial cancer treatment, but the size of the study means that that randomisation should have balanced out possible confounders. Developing a complex intervention suitable for supporting a variety of cancer survivors was certainly a challenge, but the flexibility in Person-Based Approach made this possible. A major challenge in designing the research was the choice of outcome measure – which needed to be validated and brief enough to make completion rates robust. For such a brief intervention the impact on quality of life would be expected to be small, so the subgroups overall are arguably underpowered, and the choice of overall EORTCQLQ score could be criticised as a blunt instrument for such low intensity interventions. In retrospect a measure more suited to cancer survivors in primary care settings would have been better or to consider using other measures of global health.

The sample only included those with lower quality of life scores initially, so regression to the mean is one possibility for the change in the generic advice group. However, in our sample, most of whom were beyond 2 years following primary treatment; quality of life would be expected to be stable[42] with low quality of life consistent over time.[52] We found that if anything the effect of intervention was more pronounced for those 4 years or more after finishing primary treatment. The 'generic' advice to the NHS website has a lot of click-throughs to more in-depth advice and support for people (e.g. physical activity programmes or mental health programmes that people can follow). This is more input than many cancer survivors would routinely receive in primary care and may be an important reason behind the useful improvement seen in the control group, and which would be expected to reduce any differences between groups. Two to three per cent of the study population compared with 6% from the 2021 census were non-White, and which reflects the difficult of recruiting in ethnic minority areas.

For the health economic analysis, although the first change in prescribed medications were costed and for subsequent changes the average cost per patient of the first change was used (due to the huge variability in recording of medication), this probably had little impact on overall cost per patient, as medications accounted for a low proportion of total costs. Inclusion of all service use during the trial led to possible overestimation of costs given that some such service use had no plausible connection to the intervention, and as expected the main reductions in cost were observed in primary care, but even using the total costs both interventions incurred lower costs than the control group. A societal analysis was not performed but since the NHS analysis suggested the interventions were cost-effective, it is likely that a societal analysis would provide even stronger evidence of cost-effectiveness.

Summary and recommendations for future research

Recommendations for future research

The cost-effectiveness and benefits for symptom management self-rated health for both Renewed interventions suggest that an implementation study is the next step.

To consider using and/or developing more sensitive primary outcome measures among cancer survivors, particularly for briefer, low resource interventions – since the overall EORTCQLQ-C30 summary score is not sensitive to change, in contrast to both symptom subscales and self-rating of health.

To develop QALY measures that capture the benefit to QoL for low-intensity, low-resource interventions among cancer survivors given that neither the EQ-5D-5L nor the EORTC-8d reflected important changes in patients' self-rating of health.

To explore possible barriers for ethnic minority groups, and individuals with different cancer types to participate

Implications for health care

Cancer survivors with lower quality of life given detailed generic online support improve significantly, including those where the primary course of treatment was several years previously – where improvement in quality of life would not be expected. Providing a robustly developed website to address peoples' support needs, with minimal additional resource implications, is likely to provide modest but significant further longer-term improvement in enablement, symptom management and most importantly self-rated global health, and with lower NHS costs, particularly costs in primary care.

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Data will be made available on request for data release to the corresponding author.

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Publications

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Appendix 1 INDEX actions report of the Renewed intervention

This section describes the development of the intervention using the INDEX guidance[16] and the description of the Renewed intervention using the TIDieR checklist.[29]

INDEX actions

The INDEX actions provide guidance for the development of complex interventions to improve health.[16] The authors completed reviews and qualitative interviews to present key principles and actions for consideration during intervention development. *Table 12* shows the retrospective mapping of the Renewed planning and development process to the INDEX guidance actions.

TABLE 12 Renewed intervention planning and development actions mapped to INDEX guidance actions

Action from INDEX guidance	How this action was addressed in the Renewed intervention
Plan the development process	The rationale for the development of the Renewed intervention was identified in the funding proposal, which was based on existing evidence: (a) The UK has over 2 million cancer survivors but one of the poorest cancer survival records among developed countries. Quality of life is poor with high levels of distress and fatigue. Lifestyle and psychological well-being interventions are likely to significantly improve quality of life. (b) Most previous interventions have been intensive and impractical to implement in primary care, which is where most contact with patients occurs. (c) It is plausible based on our previous internet supported interventions that relatively resource-light interventions using internet-based support in a primary care context are likely to be effective. The development process used a person, evidence and theory-based approach to intervention planning and optimisation. This approach combined input from PPI and a multidisciplinary team, literature reviews, theoretical modelling and in-depth qualitative research with cancer survivors and supporters. A protocol was created which outlined the processes to be carried out in the development of Renewed.
Involve stakeholders, including those who will deliver, use and benefit from the intervention	Relevant stakeholders were involved in the development of Renewed, including PPI, health psychologists, behaviour change specialists, intervention design specialists, clinicians, health economists, policy makers, statisticians and trial managers. The most effective ways of working with each stakeholder were identified and plans were put in place to give all stakeholders the opportunity to attend team meetings and contribute ideas.
Bring together a team and establish decision-making processes	Three groups were established to guide the development of Renewed. The management group comprised PPI, behaviour change specialists, clinicians, health economists, policy makers, statisticians, and trial managers. This group was established at the funding application stage and the group met every 3 months to oversee the project and discuss all important decisions. Members of the management group were invited to join the intervention development team which included PPI, health psychologists and clinicians who met monthly to guide intervention development. The core development team comprised health psychologists involved in developing the intervention. Key clinical academics were consulted when necessary. The team met weekly to discuss each part of intervention development.
Review published research evidence	A rapid scoping review identified cancer survivors' needs, including barriers and facilitators related to the success of interventions aiming to improve quality of life. The review informed the intervention's Guiding Principles, behaviour analysis and logic model. A review of the evidence suggested that a digital intervention could provide an efficient and effective way to provide support for lifestyle changes and improve psychological well-being for cancer survivors.
Draw on existing theories	The intervention was informed by three theoretical frameworks: BCTv1, the BCW and NPT.

TABLE 12 Renewed intervention planning and development actions mapped to INDEX guidance actions (*continued*)

Action from INDEX guidance	How this action was addressed in the Renewed intervention
Articulate programme theory	A logic model was developed which consisted of five parts: (1) The problem the intervention addresses (poor QoL in cancer survivors), (2) Intervention targets that would resolve the problem (healthy behaviours and mental health), (3) Intervention ingredients which incorporate behaviour change techniques, (4) Mechanisms of action which are expected to influence outcome measures through key target behaviours and (5) Intervention outcomes. The logic model was tested and refined during the process analysis.
Undertake primary data collection	In-depth qualitative research was carried out with the target population at every stage of development and evaluation. (a) One-to-one think-aloud interviews were conducted with cancer survivors who used the intervention with a researcher present and were asked to say their thoughts aloud to gauge their immediate reactions to the intervention. (b) Focus group discussions were used to elicit views of potential supporters (staff in the NHS and cancer charities) who had completed the online training. (c) Semistructured telephone interviews were conducted with supporters (PNs, practice-based HCAs and clinical nurses) to explore their experiences of providing support to cancer survivors using Renewed. An RCT compared a generic website (NHS-Livewell) with Renewed, and Renewed combined with human support. Data collected included: participant characteristics (age/gender/education/cancer), QoL and usage of the intervention.
Understand context	Context was considered throughout intervention development. The rapid scoping review that informed the intervention's Guiding Principles, behaviour analysis and logic model, enabled a deeper understanding of the perspectives and psychosocial context of users that appeared to influence target behaviours. Qualitative research with the target population (cancer survivors and supporters) showed that the intervention was acceptable, liked, and easy to use. Interviews with supporters provided data on how HCPs perceived the Renewed intervention within primary care settings.
Pay attention to future implementation of the intervention in the real world	The rationale for Renewed was to develop an effective and cost-effective digital intervention to enhance quality of life in cancer survivors. Therefore, Renewed was designed to be effective, simple to use for both patients and supporters, and efficient so that it could be implemented into health services at low cost. This was achieved in the following ways: Renewed is largely automated so requires little or no input from supporters; supporters can be HCAs (rather than nurses) as the role does not require medical knowledge; the online comprehensive training website can be easily disseminated; support calls are shorter than traditional support sessions; automated e-mails are used as prompts for actions. Implementation was discussed frequently with the management group with input from clinicians and PPI who contributed valuable knowledge on how to implement Renewed into health services.
Design and refine the intervention	Relevant stakeholders were involved in discussing ideas about the content, format and delivery of Renewed during the development process. Two optimisation studies were conducted, firstly think-aloud interviews with patients and then focus groups with healthcare practitioners and cancer charity workers. Minor changes to the intervention were made by core intervention developers, and the core development team were consulted about more significant changes. Examples of changes included: renaming the buttons from intervention names to a description of the intervention for clarity (e.g. 'Eat for Health' to 'Healthy eating') and adding a new page to address concerns about increasing physical activity because of health conditions. The mechanisms of actions, as outlined in the logic model were tested during the process analysis.
End the development phase	The TIDieR checklist was used to describe the intervention in detail (*Report Supplementary Material 1*) The content of the intervention is available here: https://renewedtau.lifeguidewebsites.org/player/play/renewedtau Online training provides Supporters with the information they need to support patients and this training can be disseminated directly. A demo of the Supporter's website is available here: https://lifeguidewebsites.org/player/play/renewedsupForKat In addition, Renewed has been described in several papers and will be disseminated through workshops.

Appendix 2 Health economic evaluation

Health economic analyses

The economic analyses adopted the NHS perspective and aimed to evaluate digital interventions (with and without support) compared with standard care for symptom management, well-being, and quality of life in patients survived from cancer treatment. Results were expressed as cost per QALY (cost–utility or £/QALY change) and as cost-effectiveness (£/clinical outcome change). The analyses were based on the ITT principle.

Data collection

Resource use and costing methods

Resource use data were collected by reviewing case notes and extracting from electronic record at the end of the trial. The Details of the information extracted were as follows:

- Primary care: primary care consultations were recorded by type (face to face or telephone) and by provider (GP, PN, HCA).
- Medications: data included both baseline and new medications, with up to 15 medications recorded, covering dosage, and any changed.
- Other community-based services: including home visits, NHS calls, walk-in-centres, occupational therapy, and other services.
- Inpatient admissions: recorded the reason, condition and dates for each admission,
- Outpatients attendances: recorded similar as inpatient admissions.

A standardised data extraction template was developed, and tested initially in a few practices before using it more widely. Practice staff conducted the extraction of data. In additional, patients completed online questionnaire to report personal costs, such as over-the-counter spending, time off work, informal care and physical activities.

Costing

The costing was based on 2020–21 prices with data on unit costs as necessary uprated using the gross domestic product deflator (reference 1)

Primary care

Six unit costs were employed (*Table 13*) based on the consultation data described above. The best and most widely used source, Personal Social Services Research Unit (PSSRU) (reference 2), provides estimates for GP face to face consultations, however, for those by PNs or assistants, it only provides cost estimates per hour. Therefore, assumptions were required to determinate the duration of these contacts. These were taken from a recent primary care trial, which recorded these (Thorn *et al.*, *BMJ Open*[66]) which also provided data on the time taken for telephone consultations. These show the cost for telephone consultations as less than for face to face for GP and PNs but not for HCAs.

Medications

The source of the unit costs was prescription cost analysis (PCA) – England 2020–1, Statistical Summary Tables – Calendar Year 2020 - National level (Publication date: 10 June 2021, reference 3) - which provides data at varying levels of detail. Since the data recorded in the trial was at varying levels of detail (chemical substance to brand name) with dosage largely missing, some assumptions were necessary. All medications recorded were assumed to have been funded by the NHS.

Key elements for costing were cost per item (pack size) and cost per quantity (based on the quantity in the pack). For tablets to be taken once a day, cost per quantity provides a useful measure but one which needs to be amended

TABLE 13 Unit costs for primary care consultations

PSSRU 2021	Face to face	Telephone
GP	39.23	31.33
PN (£44/hour)	11.07	4.33
HCA (£35/hour)	5.48	9.33

For GP face to face: PSSRU. Other unit costs based on duration of tasks by Thorn *et al.*[66]

Source
This table has been reproduced from Little *et al.*[1] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The table above includes minor additions and formatting changes to the original text.

for some items such as implants, inhalers and medicines recommended for less frequent use. For inhalers, 250 daily dosages were assumed based on the most used sizes.

As the data recorded on medications were poor due to multiple names (brand, generic, mis-spellings), missing elements (dose, duration, and so on) assumptions were necessary as follows:

- Only new medications were costed,
- The first new medication was linked to a prescription cost/item, which was taken as the most common of those recorded.
- If that medication was recorded as having stopped, only one item was assumed.
- But if that item did not have a stop date, then it was assumed that it continued to the end of the trial costed on the cost per quantity if tablets or as otherwise indicated.

The rationale for using the mean cost per new medication 1 was as follows: considerable work was required to code or classify different names; there was relatively low variation in cost between medicines; and the possibility of double counting due to the assumption above regarding medications that continued to the end of the trial. It was also known from previous work (PSSRU 2017) that use of a standard cost per medication was often unlikely to alter over cost differences due to the relatively small share of medications contributing to total NHS costs.

Up to 15 new medications were recorded. Given the time required to cost the first new medication, a single unit cost per medicine was applied to medications 2–15. This was the unit cost of the first new medication described above.

Other services

Other community-based services (NHS Call services, A&E, walk-in clinic, community nurse, OT, other) were recorded. These were costed using the unit costs in *Table 14*

Inpatients

For costing NHS hospital use, several approaches are possible depending on the data. Hospitals are paid on the basis of over 2000 Healthcare Resource Groups (HRGs), with spend data available at various levels of disaggregation in the National Schedule of NHS Costs (Year 2019–20 – All NHS trusts and NHS foundation trusts – HRG Data, reference 4). These divide HRGs between inpatient and day cases and distinguish basic types of inpatients: elective, non-elective, short stay and non-elective long stay.

Personal Social Services Research Unit, the key source for unit costs only provides limited data for hospital admissions. To allocate to HRGs, the data required must distinguish between elective and non-elective and also indicate day cases.

In the current study, data were collected on reasons of admission, specifics, date of admission, and date of discharge. The dates of hospital admission and discharge were used to derive whether an admission was a day case or an overnight

TABLE 14 Unit costs for community services

Service	Unit cost	Price of the year	In 2021 price (adjusted)	Unit £	Comments
GP visit face to face	39.23	2020–1	39.23	PSSRU	Adjusted
GP home	100.00	2015–6	115.00	PSSRU	
Primary nurse face to face	13.52	2020–1	13.52	PSSRU	
GP tel	31.33	2020–1	31.33	PSSRU	Adjusted re duration from Thorn *et al.*[66]
NHS call services	11.40	2018–9	12.37	Turner	
A&E attendance	97.95	2019–20	104.20	Reference costs	
Outpatient	149.00	2019–20	158.51	Reference costs	Av. C led
Walk in clinic	52.00	2019–20	55.32	Reference costs	
OT		2020–1		PSSRU	50/hour
NHS walk in clinic			41.74	Thorn *et al.*[66]	
NHS call			8.06	Thorn *et al.*[66]	
Community nurse	66/hour	2020–1		PSSRU	Band 7
Inpatient admission		2019–20		Reference costs	HRG
Medications: baseline and changes		2020–1		PCA	
New medications		2020–1		PCA	

stay and whether a short or long stay (over 30 days). Dates on A&E visits were also recorded, which combined with the dates of hospital admissions, allowed us to indicate whether an admission was elective or non-elective. If the date on both were the same, then the hospital admissions were non-elective; otherwise the episodes were assumed to be planned. Due to missing dates, HRGs unit costs were aggregated and averaged among elective, non-elective and day cases.

In the Collaborative Labeling and Appliance Standards Program data, the two most common diseases recorded were cancer (92) and heart disease (around 52) with the rest recorded as Other. HRGs for cancer were identified for two different cancer sites: breast and other cancer. A single unit cost was applied for heart disease and for all other HRGs. These were all based on the relevant averages from NHS reference costs.

These costs spanned a range from £1648 to £3827 (*Table 15*), with the lowest applying to all others and the highest for Breast Cancer.

Outpatients

Information was recorded whether patients had an outpatient attendance, the date and the reason of attendance. As with the inpatients, data were recorded on disease – with around half being cancer, followed by a smaller group with heart disease and a residual group labelled 'other'.

Unit costs for outpatients are included in the National Schedule of NHS Costs 2019–20. The data provide an average cost per attendance and distinguish between attendances that were consultant led and the rest. We used the former which was £149 per attendance 2019–20.

TABLE 15 Unit costs of hospital stay

Cancer types	Cancer	HRG £
Cancer breast	CaBr	3827
Cancer other	CaAv	3097
Heart disease	Heart disease	1811
Heart disease	Heart disease	1648

Intervention costing

Detailed information about the interventions was reported in previous chapters. Briefly, web-based interventions were implemented in two of three study groups: Access to Renewed or access to Renewed with brief support. In the Renewed group – web-based intervention: participants received brief automated e-mails as reminders and for motivation. In the Renewed group with brief support (web-based intervention with additional guidance and support) participants had access to usual care and the Renewed intervention (the automated e-mails) as stated above; additional support was provided by nurse or HCA either face to face, telephone, or by e-mail.

All information on the contact and support sessions were recorded in the supporter's log and kept in the surgery site-file. This recorded details of the date of support, type of the support (face to face, phone, or e-mails) and duration of the support. Automatic e-mail reminders and encouragement e-mails (to prompt completion of outcomes) were also recorded. As the latter were research related cost, we did not include those in the cost calculation of the intervention.

Costing the intervention was based on the time recorded in the database. Where the duration of the support data were missing, we assumed the following generic times: time on face-to-face support 10 minutes, time on phone support 10 minutes, and time with e-mail support 5 minutes.

The unit cost of nursing support for face-to-face, phone or e-mail services were considered the same at £44 per hour. The differences were reflected in the duration of such services received (i.e. cost of support = time of the service use*£44/60).

Costing digital interventions can be based on several approaches. McManus *et al.* (2021)[67] in the Home BP study estimated the costs of the digital intervention based on the cost related to digital intervention occurred during the trial, including staff costs (maintenance) and equipment costs (BP monitor), and then divided costs by number of participants in the trial. They estimated the cost of intervention at £39.72 per patient. Reed *et al.* (2010)[68] estimating the intervention cost including maintenance and delivery (staff cost, hosting website and security and so on shared among trial population) and estimated the cost of the digital intervention at £226 per patient. Both of those studies have overstated the costs of the digital intervention, as the capability of the any digital platform could be much higher than the limited number of patients that participated in those trials.

The principle for costing interventions is to include only the real cost that would occur when an intervention is being rolled out. Therefore, research cost or developing costs of a digital intervention should be excluded. One sound way to costing a digital intervention is to consider the licence fees of an online platform with full service support, then divide it by the maximum capability of the platform at one time. With rapid development of online technology and wide access of digital interventions, the cost per person is likely to diminish close to zero. Therefore, we did not include the cost of digital intervention in our base-case analyses. Similarly, the cost of using the internet or equipment will be spread over many other uses. Adding £10 pounds per patient in the two intervention groups could potentially be added, but this would have no impact on the directions of our results.

Key intervention costs and choice of perspective

We designed the study to include a societal perspective, but we received very few responses for the use of non NHS services (*Table 16*). It was unclear whether this reflected actual absence or simply missing data, so including this data would have potentially provide misleading inferences. Therefore, we did not perform a societal analysis. Given

TABLE 16 Personal spending – and whether reported less, more or the same being spent

	Less	More	The same	Unsure
Shopping				
Generic advice	3	13	160	11
Renewed plus support	4	7	113	7
Renewed	6	14	117	6
Physical activities				
Generic advice	18	20	122	26
Renewed plus support	9	11	98	12
Renewed	8	11	98	23
Informal care				
Generic advice	0	4	54	4
Renewed plus support	0	6	47	7
Renewed	2	4	47	8
Time off work				
Generic advice		20		
Renewed plus support		10		
Renewed		12		
Total		42		
Over the counter spending				
Generic advice		28		
Renewed plus support		11		
Renewed		15		
Total		54		
Other spending				
Generic advice		26		
Renewed plus support		22		
Renewed		26		
Total		74		

the practical challenges and usefulness of collecting PSS data (including our past experience e.g. PD-REHAB), we opted not to collect PSS usage explicitly. This approach ensured a focused, efficient analysis of the key relevant cost drivers. Instead, we used the NHS perspective including all incurred costs in the cost-effectiveness analyses. Since the intervention focused on self-management with in person or online support which would primarily impact primary care consultations and medication use, our primary analysis considered the primary care perspective – the most important driver of costs being the support sessions received (*Tables 17a* and *17b*). The frequency of other community resource usage is shown is *Table 18*. We have discussed the rationale for excluding the equipment and internet costs above.

Quality of life and calculation methods

Quality of life was measured by EQ-5D-5L and collected at baseline, 3, 6 and 12 months. EQ-5D-5L was translated into utility score based on the UK tariff (reference 5 and 6). QALYs were calculated based on area under the curve approach.

TABLE 17a Support usage (number of individuals receiving support sessions) by intervention groups

	Number of support sessions received	Renewed plus support	Renewed
Face-to-face support	1	98	1
	2	30	0
	3	13	1
	4	1	0
Phone support	1	83	3
	2	31	1
	3	5	0
E-mail support	1	30	0
	2	15	0
	3	1	0
	4	1	0

TABLE 17b Number of patients using support sessions and the mean cost per patient in each group

Group	Number of Patients	Number of Patient using supports	Mean cost (SD) per patient (£)
Generic advice	906	1	7.3 (7.3)
Renewed with support	903	270	16.6 (13.4)
Renewed	903	5	18.3 (19.0)

SD, standard deviation.

TABLE 18 Other community service usage itemised by group

Item of service usage	Generic advice	Renewed plus support	Renewed
Home visit	22	23	25
NHS call	3	8	2
Out-of-hour call	3	8	2
Walk-in visits	29	19	30
Adverse-event visits	93	123	127
Community nurse visits	5	4	8

Analyses

Accumulated costs were calculated for each patient. Bootstrap methods based on 1000 replicates with replacement were employed to estimate means costs and QALYs, and the differences between groups provided with CIs associated with each estimate. CEACs were produced based on the 1000 replicates. All analyses were conducted based on recommended methods and followed the Consolidated Health Economic Evaluation Reporting Standards checklist (references 7–9).

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Base case

Our proposed study was taken from the primary care NHS perspective in which all costs occurred in primary care (support, consultations and medication costs) were included in the cost-effectiveness analyses. Sensitivity analyses were conducted based on costs including secondary service use (inpatient, outpatient and A&E attendances). This is likely to be the most plausible costing approach since hospital services are unlikely to have been influenced by the intervention. The same argument applies to outpatient attendances.

Results

Costs

The mean costs for our base case, £Tot3 (Primary Care: Medication and consultation costs) was £226, £128 and £51, respectively, that is much lower in both renewed groups. The mean total NHS cost per patient by group (£Tot), that is, including hospital and community services (*Table 19*), shows Renewed as the highest total NHS cost at £924 followed by Renewed plus support and generic advice at £811 and £828, respectively. When hospital services were excluded from total NHS costs (£Tot2 community Services), the pattern remained similar (with both Renewed groups having lower costs) but at much lower levels – £310 for Generic advice, £212 for Renewed plus support and £144 for Renewed. This indicates the importance of hospital services for the total cost results, which realistically are much less likely to reflect costs be affected by the interventions.

Cost of interventions

A total of 276 patients received nurse support (face-to-face, phone or e-mail), in total 438 sessions (*Table 20*). The mean times for support were 11.6, 11.5 and 17.9 minutes for phone, e-mail and face to face, respectively (see *Table 20*). The mean cost per patient for those received services was £14.8 [standard deviation (SD) 12.1].

Quality of life

The completion rate of EQ-5D-5L fell from 2688 (100%) at baseline to 1227 (46%) at 6 months to 1457 (54%) at 12 months (*Table 21*).

The mean utility scores together with completion rate by time point and study groups are shown in *Table 22*.

TABLE 19 Mean NHS cost per person by group, total all services, and by service

Results	*N*	£Tot3 (primary care: medication and consultation costs)	£Tot2 (community services and primary care)	£Tot (total NHS cost including hospital services)
Generic advice	776	226	310	924
Renewed plus support	788	128	212	811
Renewed	787	51	144	828

TABLE 20 Mean recorded time (in minutes) receiving support across all study groups by support categories

Support	Number of supports	Number with recorded time	Min (minutes)	Max (minutes)	Mean (minutes)	Std (minutes)
Phone	166	119	0	56	11.61	7.14
E-mail	67	46	5	30	11.46	5.34
Face to face	205	137	5	70	17.87	11.08
Total	438	302				

TABLE 21 Completion rate of the EQ-5D-5L

Time points	EQ-5D-5L (%)
Baseline	2688 (100%)
6 month	1227 (46%)
12 month	1457 (54%)

TABLE 22 EuroQol-5 Dimensions scores at baseline and follow-up by group

Group	Follow-up time	EQ-5D-5L score	
		Completion (%)	Mean (SD)
Generic advice *N* = 903	Baseline	903 (100%)	0.686 (0.169)
	6 months	498 (55%)	0.711 (0.183)
	12 months	589 (65%)	0.708 (0.193)
Renewed plus support *N* = 892	Baseline	891 (100%)	0.676 (0.174)
	6 months	353 (40%)	0.714 (0.181)
	12 months	407 (46%)	0.711 (0.188)
Renewed *N* = 894	Baseline	894 (100%)	0.684 (0.171)
	6 months	376 (42%)	0.71 (0.202)
	12 months	461 (52%)	0.739 (0.169)

Cost-effectiveness analyses

In the base care scenario, in which costs only included medication, primary care and intervention costs and missing date were imputed, cost and effectiveness analyses based on bootstrapping with resampling 1000 replacement are reported in *Table 23*. The mean costs per patient were £265 (95% CI 254 to 275), £187 (95% CI 180 to 195) and £124 (95% CI 118 to 130) for Generic advice, Renewed plus support and Renewed, respectively. The Generic group incurred higher

TABLE 23 Base-case cost–utility analysis using bootstrap methods using imputed QoL data (quality of life measured by EQ-5D-5L) and costs based on primary care, medication and intervention costs AQ7

Groups	Mean costs	Difference (compared with Generic advice)	
Generic advice	265 (254, 275)		
Renewed plus support	187 (180, 195)	−77 (−90, −65)	
Renewed	124 (118, 130)	−141 (−153, −128)	
Renewed vs. Renewed plus support		−63 (−73, −54)	
	QALYs (EQ-5D-5L)	Difference (compared with Generic advice)	Incremental cost per QALY gained (ICER)
Generic advice	0.7 (0.692, 0.709)		
Renewed plus support	0.699 (0.691, 0.707)	−0.001 (−0.013, 0.011)	11,281 (−76,949, 97,385)
Renewed	0.705 (0.696, 0.714)	0.005 (−0.007, 0.018)	−7542 (−116,829, 115,651)
Renewed vs. Renewed plus support		0.006 (−0.006, 0.018)	−6007 (−50,473, 46,389)

health resource use cost compared with both Renewed with Support and Renewed. Compared with the Generic advice group, the difference is −£77 (95% CI −90 to −65) and −£141 (95% CI −153 to −128) for Renewed plus support and Renewed, respectively. QALYs based on EQ-5D-5L were 0.7 (95% CI 0.692 to 0.709), 0.699 (95% CI 0.691 to 0.707), and 0.705 (95% CI 0.696 to 0.714) for Generic, Renewed plus support and Renewed group, respectively. Compared with Generic, the differences in QALYs were −0.001 (−0.013, 0.011) and 0.005 (−0.007, 0.018) for Renewed Plus and Renewed group, respectively.

The incremental cost-effectiveness ratio (ICER) was £11,281 (95% CI −76,949 to 97,385) and −£7542 (95% −116,829 to 115,651) per QALYs gained, respectively for Renew with Support and Renewed compared with Generic advice. The cost-effectiveness ratios could potentially indicate dominance for Renew intervention groups and cost-effectiveness for the Renew with Support group but the ratios are very sensitive to the very small differences in the QALY denominator, which in turn are not likely to be sensitive to, or representative of, the benefits observed in the main results.

Sensitivity analyses

Two sensitivity analyses were conducted: first, as in the base case, but with no imputation, that is a complete-case analysis (*Table 24*); secondly, as in the base case but including secondary care costs (*Table 25*). Both analyses were based on bootstrapping methods with 1000 replicates.

The differences in QALYs were close to zero for both intervention groups. The cost-effectiveness ratio in both sensitivity analyses is similar to our base-case analyses, but the magnitude of the difference changed slightly due to the denominator being close to zero.

The CEAC curves demonstrate that both Renewed with support (*Figure 4*) and Renewed (*Figure 5*) or both interventions together (*Figure 6*) are likely to be cost-effective at a threshold of £20,000 per QALY.

TABLE 24 Cost–utility analyses using bootstrap methods based on complete data for primary care and medication costs

	QALYs (EQ-5D-5L)	Difference (vs. usual care)	Incremental cost per QALY gained (ICER)
Generic	0.711 (0.7, 0.723)		
Renewed plus support	0.71 (0.694, 0.725)	−0.001 (−0.02, 0.018)	4407 (−50,260, 61,605)
Renewed	0.707 (0.691, 0.723)	−0.004 (−0.025, 0.016)	7979 (−103,152, 96,438)

TABLE 25 Cost–utility analyses based on all costs including secondary care costs

Groups	Main costs (£)	Difference (vs. usual care)	
Usual care	783 (725, 847)		
Support	679 (630, 729)	−105 (−186, −24)	
Intervention	713 (657, 768)	−70 (−155, 14)	
Intervention vs. Support		34 (−40, 107)	
	QALYs (EQ-5D-5L)	**Difference (vs. usual care)**	**Incremental cost per QALY gained (ICER)**
Usual care	0.7 (0.692, 0.709)		
Support	0.699 (0.691, 0.707)	−0.001 (−0.013, 0.011)	6444 (−115,312, 148,914)
Intervention	0.705 (0.696, 0.714)	0.005 (−0.007, 0.018)	−10,907 (−64,117, 54,736)

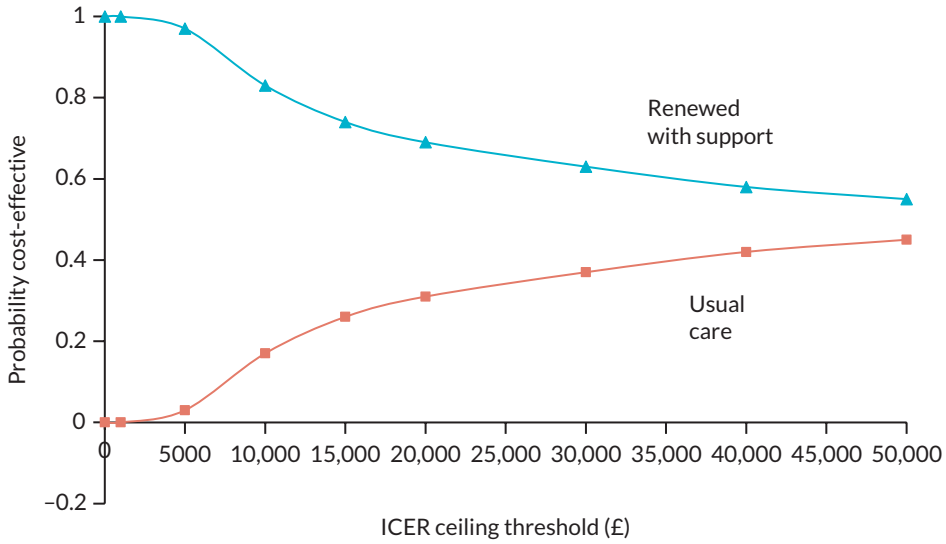

FIGURE 4 Cost-effectiveness acceptability curve of the Renewed with support and usual-care groups based on QALY measured by EQ-5D-5L over 1 year.

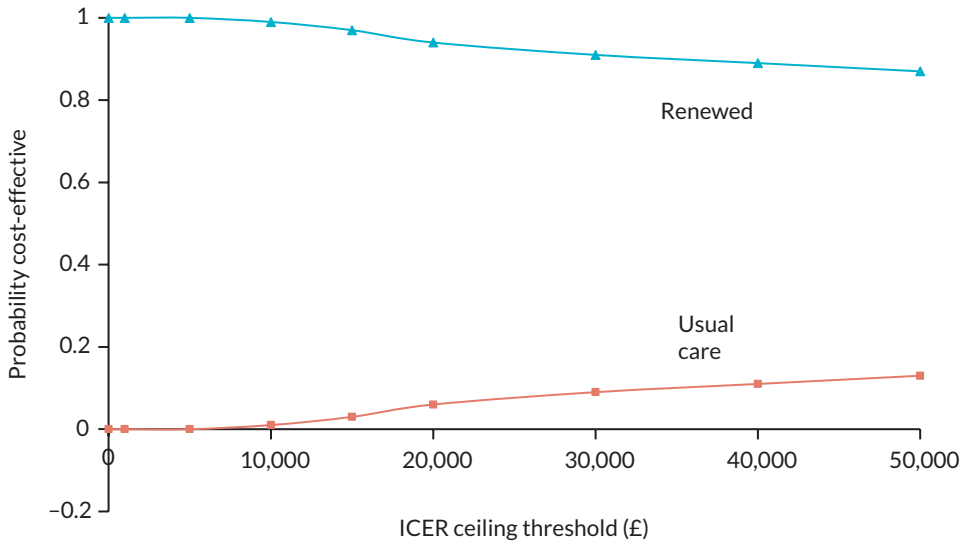

FIGURE 5 Cost-effectiveness acceptability curve of the Renewed Intervention and usual-care groups based on QALYs measured by EQ-5D-5L over 1 year.

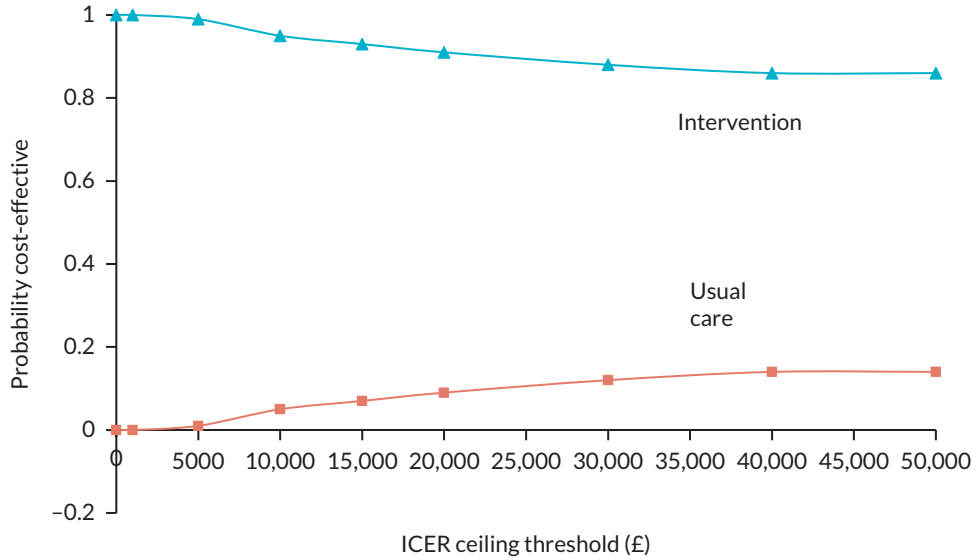

FIGURE 6 Cost-effectiveness acceptability curve for both interventions (Renewed and Renewed with support) based on QALY measured by EQ-5D-5L over 1 year.

Conclusions for the economic analysis

In summary, on balance the trial showed improvement in outcomes and moderate, statistically significant reductions in cost per patient for each of the interventions compared to the control arm. Very small changes were observed in QALYs, which, by contrast with the primary or secondary outcomes, were not statistically significant and not consistent in direction of change. These results can be interpreted as cost saving and QALY neutral. The incremental cost per QALY ratios, which span infinity in their credible intervals, are difficult to interpret but broadly meet conventional levels regarded as value for money in the UK's NHS.

Limitations

Several assumptions and restrictions were made in costing. We did not perform a societal perspective analysis due to significant uncertainty about the quality of the data as discussed above. Given the practical challenges and usefulness of collecting PSS data (including our past experience, e.g. PD-REHAB), we opted not to collect PSS usage explicitly. This approach ensured a focused, efficient analysis of the key relevant cost drivers. However, we collected informal care/homecare from persona perspective, a community nurse care from the NHS perspective. The costs of development were not included since these are not normally included in economic analyses of interventions. We have also assumed that the digital cost element of the intervention was assumed to fall to zero if rolled out, but even if the digital rollout costs were much larger, they are unlikely to exceed £77 per person, so still very likely to be cost saving. Only changes in prescribed medications were costed and within these only the first change with subsequent changes costed at the average cost per patient of the first change. This was due to the medications being recorded in many ways (generics, brands, misspellings). This has little impact on overall cost per patient as medications, as in other studies, accounted for a low proportion of total cost. Some underestimation of medication cost is however possible. Furthermore, only 12 consultations were included, again to make data collection manageable; the implication is likely to be, given the direction of differences in costs from what was collected, that if anything we have underestimated the likely cost differences between intervention groups and usual care. Given some errors are possible in data extraction we are also likely to have underestimated the precision of the costing data. EQ-5D-5L data were commonly missing but the inferences from the imputed and compete analyses were similar.

Inclusion of all service use during the trial led to possible overestimation of costs, again a limitation as some such service use had no plausible connection to the interventions.

The costing of telephone consultations in primary care relied on data on the duration of such calls by GPs and others from a different study (due to the lack of such data in the current data files), and unit costs of health and Social Care (PSSRU). Further, the cost of web access was not included in the costs. The latter is a burden borne by patients and hence excluded by the NHS perspective taken in this study.

In terms of implications for policy, the main reductions in cost were observed in primary care as might be expected given the types of interventions. This suggests that the web service to some extent either substituted for face to face and telephone contacts with practices, and/or provided improved symptom management and self-rated health so that consultations were needed less.

The overall conclusion is that these interventions reduced costs to the NHS and had modest beneficial effect on outcomes that were not captured in the QALY measures, and that both interventions – particularly the Renewed intervention without support – are likely to be cost-effective.

Appendix 3 Summary of patient qualitative process study: experiences of using a supported digital intervention for cancer survivors in primary care

Aims

To explore how patients used the Renewed intervention and which factors may serve as potential barriers and facilitators to using Renewed and performing the recommended behaviours.

Methods

Patients were sampled from all three arms of the Renewed trial: (1) Renewed Online, (2) Renewed Online with brief human support and (3) usual-care group. They were sampled purposively to achieve the maximum variation in the sample with respect to sociodemographic factors that may influence Renewed's delivery, acceptability or effectiveness. These sociodemographic factors were: cancer type, gender, age, educational level, QoL scores, time since completion of treatment and Renewed usage. Most interviews were conducted within the first 3 months of patients using Renewed, as these interviews were richer.

Usage was categorised into three groups: (1) not completing Core content (2) completing only the Core content, and (3) completing the Core content and using the optional content.

Semistructured interview schedules were developed with open-ended questions to allow patients to describe their experiences in their own words and focus on what was important to them. The topics covered for the two groups that used Renewed Online were: experiences of using Renewed, behavioural changes made while being in the Renewed study, and experiences of HCP support received within Renewed. The interviews were audio-recorded and transcribed verbatim. Data were analysed using inductive thematic analysis.

Results

Forty-two patients took part in the interviews. Three patients did not recall using Renewed and/or being in the study so their data were excluded from the analysis. Data from 39 patients were analysed, of which 17 were in the 'Renewed Online' group, 16 were in the 'Renewed Online with brief human support' group, and six were in the usual-care group. The demographic and clinical characteristics of the 39 patients are reported in *Table 26*.

Thematic analysis identified four themes: (1) The importance of motivation for using Renewed and performing behaviour changes, (2) minimal usage of Renewed plus supported behaviour changes, (3) supporter needs to add value and (4) convenience of Renewed Online. These themes gave insight into the factors that may serve as potential barriers and facilitators to patients' engagement with Renewed and performing the recommended behaviours. No patterns were found in the themes relating to gender, age, time since treatment was completed, QoL scores and education level.

The results are shown below and include quotations to illustrate the different experiences of patients within the four themes, with cancer type and use of Renewed.

The importance of motivation for using Renewed and performing behaviour changes

The Renewed content sometimes increased patients' motivation to use the programme. If patients perceived the content to be novel and informative, it was thought to be motivating, for example the Eat for Health traffic light system.

TABLE 26 Participant characteristics

Baseline characteristics	*n*	%	Median	Mean	SD	Range
Age				64	10.69	36–83
Sex						
Male	17	44				
Female	22	56				
Cancer type						
Colorectal	12	31				
Breast	16	41				
Prostate	9	23				
Prostate active surveillance	2	5				
EORTC score				71	12.03	42–83
Years since completed treatment			4			0–9
Age when left education				18	3.45	15–30
Renewed RCT group						
Renewed Online	17	44				
Renewed Online with brief human support	16	41				
Usual care	6	15				
Usage (n = 33)						
Those that did not complete Session One	6	18				
Those that completed Session One	13	39				
Those that completed Session One and used at least one other component of Renewed	14	42				
Support sessions (n = 16)						
Had support sessions	9	56				
Did not have support sessions	7	44				

> *The [Eat for Health] traffic lights [information] has been very helpful 'cause I know really know which ones I'm supposed to dodge … it's kind of exciting because I think well, I haven't really thought thoroughly the things before. I thought, 'well, no, just go and have a look at what they offer'*
>
> *Participant 16, used optional content, 56 years old, female, breast cancer, Renewed Online group*

The majority of patients perceived Renewed to be valuable for people experiencing difficulties with recovery and treatment, however, the majority also commented that the content was basic and they already knew most of the information or were already performing the behaviours.

> *I would say I'm actually quite well informed but for a lot of people that aren't, it's very useful. I thought I knew enough about my dietary stuff.*
>
> *Participant 27, did not complete Core content, 64, female, breast cancer, Renewed group*

Minimal usage of Renewed plus supported behaviour changes

Some patients who only completed the Core content did not make any or made very few changes to their behaviour.

> *Looked around it, but haven't really taken up on any of the suggestions it makes.*
>
> *Participant 22, did not complete Core content, colorectal cancer, Renewed Online group*

However, other patients who only completed the Core content reported making changes to their behaviour.

> *I followed some of the diet advice. And taking yourself off out for a walk and things like that, which I did try. Just to make my lifestyle a bit healthier.*
>
> *Participant 35, did not complete Core content, Renewed Online group*

Some patients who used some of the optional content started making behaviour changes and stopped using Renewed when they perceived that they had sufficient information to implement changes. They also used their own tools, such as Fitbit and calendars.

> *Trying to get my weight down, that sort of thing. I found that all that very useful and I made up the little calendar thing but, because, once you referred to these, all the suggestions on the site, I didn't really feel a great deal of need to go back to them, because I put what I could into action, and did it.*
>
> *Participant 6, used optional content, prostate cancer, Renewed Online with human support group*

Supporter needs to add value

Most patients saw the value in support after completing their cancer treatment.

> *I've spoken to lots of people who do find that when they're in remission after cancer, it's almost as if everybody thinks, 'Oh, that's it', you know, 'You're cured, you don't need help anymore'. but I do, I know a lot of people who do feel that people are not interested in how they're getting on and whether they're doing very well.*
>
> *Participant 11, used optional content, colorectal cancer, Renewed Online with brief human support group*

A few patients in the Renewed Online group (who did not have access to Supporter sessions) wanted HCP support offered with Renewed. They wanted to be able to discuss their problems with someone and they thought this would have made Renewed more personal.

> *You can't pick up the phone and then talk to somebody about a specific problem … So I suppose that is where I fall down a bit with it … the ability perhaps to email somebody to discuss, might be something that ought to be considered added on.*
>
> *Participant 12, used optional content, colorectal cancer, Renewed Online group*

Perceived value and need for support seemed to depend on patient's existing social support. Most patients who did not take up Supporter sessions appeared to already have social support from other medical professionals, charities, community support groups, or friends and family. As they already had social support in place, they did not feel the need for support from Renewed.

> *I'm very lucky, I've got an excellent key, key worker at the hospital, yeah, and she's been brilliant. So, she's the one I've tended to go to.*
>
> *Participant 11, used optional content, colorectal cancer, Renewed Online with brief human support group*

Across different types of cancers, patients reported various levels of pre-existing social support available to them. Prostate cancer survivors reported considerably less social support than breast or colorectal cancer survivors. This may be why some prostate cancer survivors in the Renewed Online group stated that some human support in Renewed would have been appreciated.

> *I feel that it [Renewed Online] can make you feel that you're not completely on your own … it's just having somewhere where some people who may be having this they don't have any contact with other people … But also from that, I feel*

> *that it could be improved if somebody in the background within Renewed maybe should be contacting them [those using Renewed], maybe a health professional, because a lot of the time I find that I can go to a, my GP or whatever and I can write all my concerns or my questions down, but sometimes there's no time to actually talk to them about problems.*
>
> *Participant 24, completed Core content, prostate cancer, Renewed Online group*

Convenience of Renewed Online

Many patients expressed liking that they could use Renewed at a time and location convenient to them and go through the programme at their own pace. Being able to review information and activities again and change plans were seen to be useful features of Renewed.

> *You can take whatever you want … choose and change, you don't have to keep to one plan. If you've got more confident you think 'oh well, I've done this but, later on I can do a bit of this also' … it always reminds you also that if you don't have time now you can go back on the home page, so it doesn't put pressure on you.*
>
> *Participant 16, used optional content, 56 years old, female, breast cancer, Renewed Online group*

A few patients experienced technical issues with Renewed (e.g. navigation problems, seeing error pages), however this only appeared to be a barrier when the issue persisted and led to the patient not being able to use the programme effectively. For example, POWeR is a large standalone programme which Renewed Online linked to but some patients found it frustrating to switch between Renewed Online and POWeR.

> *I did find most of the navigation was really good but I did find sometimes that when you went to an external site, like the POWeR, it was quite difficult to get back because there's, there's the button that says 'take me back to Renewed Online' I was hoping it'd take me back to the login page of Renewed Online but it didn't. It took me back to the page I'd just visited which was the POWeR website. So there were some funny little, you know, blips like that.*
>
> *Participant 15, used optional content, 65 years old, female, breast cancer, Renewed group*

Implications

The usage analysis supports a theory of effective engagement as some users who did not use Renewed beyond the Core content, still made changes to their behaviour. This suggests that patients started making changes to their behaviour when using Renewed and once they had established a habit or gained confidence in these behaviours, they stopped using Renewed. Using the first session of Renewed may prepare patients for behaviour change and mediate the start of behaviour changes.

Although many patients stated a perceived value in being supported by a HCP, this perceived value was not sufficient to motivate them to take up support. Only a third of patients in the Renewed Online with brief human support group participated in Supporter sessions. A reason for this may be that the patients who did not take up support may have already had social support and did not feel the need for additional support. In addition, the support in Renewed was pulled, meaning that patients had to initiate support (rather than supporters initiating support) so support sessions may have been under-utilised. Although participating in supporter sessions was related to increased usage of Renewed Online and higher adherence to behavioural recommendations, the RCT trial data suggest that participating in supporter sessions did not relate to outcomes in QoL at 6- or 12-month follow-up.

Appendix 4 Summary of patient quantitative process study: engagement and usage of the renewed intervention by patients

Aims

To evaluate how cancer survivors used Renewed. The specific research questions were: (1) How much did patients use Renewed? Which components of Renewed were most used?, (2) Is there a difference in Renewed usage (i.e. frequency) based on patient characteristics?, (3) Do patients who accessed human support use Renewed more compared to those who did not access human support or were without access to human support? and (4) Do patients who accessed Renewed's Optional content have greater improvements in quality of life at 12 months?

Methods

This was a quantitative process study nested within the RCT of the Renewed intervention. Patients were sampled from all three arms of the Renewed trial: (1) Renewed Online, (2) Renewed Online with brief human support and (3) usual care. Data from patients from the Renewed Online and Renewed Online with brief human support groups were analysed. Patients randomised to the Renewed Online with brief human support group were able to access support sessions provided by a HCP. This study was carried out 12 months after patients joined the Renewed study.

Patients completed questionnaires at baseline and 12 months post randomisation. The intervention software, LifeGuide, recorded their usage of Renewed. Patients were included in the analysis if they had completed the 12-month follow-up measures. Demographic and clinical characteristics were collected at baseline, and psychological characteristics were collected at 12 months.

Demographic and clinical characteristics

Patients were asked to self-report their age, gender, ethnicity and cancer type. In addition, patients reported the age they finished education and the year they finished cancer treatment.

Psychological characteristics

Data on Renewed Online usage, including pages accessed and the number of times each page was accessed, were accessible to researchers from LifeGuide through encrypted Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA) files. Usage was defined as the overall number of times patients accessed Renewed and its components. This was considered a good representation of usage because it provides an objective measure of the extent of usage over time.

Quality of life was measured with the EORTIC measure. The EORTC QLQ-30 assessed functional domains (i.e. physical, emotional, role and cognitive and social) and common cancer symptoms (i.e. pain, fatigue, nausea/vomiting, dyspnoea, sleep problems, loss of appetite). The questionnaire included 30 items, each with a four-point response scale from 'not at all' to 'very much'. Scores were calculated using a linear conversion to create a score from 0 to 100. In this sample Cronbach's alpha was $\alpha = 0.88$ at 12 months, indicating high level of reliability at both time points. EORTC is a widely used questionnaire for HRQoL in cancer research.

Statistical analysis

Data were analysed using SPSS version 27 (IBM Corporation, Armonk, NY, USA). All data were examined for deviations from normality. The distributions of the measures for usage analysis were not normally distributed and were therefore analysed using non-parametric tests. For regression models and partial correlations, the models controlled for baseline quality of life scores, baseline anxiety and depression scores, baseline fear or cancer relapse/recurrence, body mass

index, age, time since end of treatment, gender and cancer type. It was not possible to control for covariates in the non-parametric tests (Mann–Whiney U and Kruskall–Wallace) and therefore unadjusted results are reported.

Access to human support was characterised in three ways: (1) patients who accessed human support ('accessed support'), (2) patients who had the option to access human support but did not ('did not access support'), and (3) patients who were in the Renewed Online only group who did not have access to human support ('without access to support').

Usage outcomes

Spearman's partial correlations were used to examine relationships between patients' characteristics and usage, controlling for potential confounding variables. Kruskal–Wallis tests were used to analyse differences between the type of cancer patients had and their usage of Renewed. Kruskal–Wallis was also used to examine the differences in usage of Renewed based on whether patients accessed support, did not access support, or were without access to support. A Mann–Whitney U test was used to examine the relationship between patients' gender and their use of Renewed. While the Mann–Whitney U test does not directly allow the calculation of effect sizes, approximate effect sizes which may be interpreted in a similar way to Cohen's *d* have been calculated using the methods set out in Rosenthal *et al.* (1994).

12-month quality-of-life outcome

To examine the relationship between whether or not patients accessed the Optional content of Renewed and 12-month QoL, analysis of covariance was used. The independent variable was whether patients accessed the Core or Optional content, the dependent variable was QoL and other potentially confounding variables were added as covariates.

Results

Participant characteristics

The sample consisted of the 1760 cancer survivors in the Renewed Online and Renewed Online with brief human support trial arms who completed follow-up measures at 12 months. The majority of patients were female (58%), had breast cancer (52%), and were White (97.8%). The QoL scores ranged from 13 to 85 (cut-off scores above 85), with a mean of 72.39, indicating a relatively high quality of life within this sample.

Usage outcomes

1. How much did participants use Renewed? Which components of Renewed were most used?

Patients accessed Renewed a median of 2 times, ranging from 0 to 268. The majority of patients (97%) accessed the Core content of Renewed, with 84% completing the Core content and reaching the Homepage where they could access the other components of Renewed. Slightly less than half (45%) of patients continued to use Renewed past the Homepage to access the Optional content of Renewed (Getting Active, Eat for Health, Healthy Paths, POWeR). After the Core content, Getting Active was the most used component of Renewed (30%), and least used was Healthy Paths (10%). Of those who continued beyond the Core content, the majority (56%) accessed just one additional component of Renewed, with 26% accessing two, 13% accessing three, and 5% patients accessing all four optional sections. Among patients given the option to access support sessions (the Renewed Online with brief human support arm), the majority (69%) of patients chose not to access this support. An overview of Renewed usage data is provided in *Table 27*.

2. Is there a difference in Renewed usage (i.e. frequency) based on participant characteristics?

There were no significant associations between the overall number of times patients accessed Renewed and their characteristics (age, gender, cancer type, age when completed education and years since finishing treatment).

3. Do those who accessed human support use Renewed more compared to those who did not access human support or were without access to human support?

TABLE 27 How patients used Renewed

Component of Renewed	*n* (%)	Median number of times accessed	Quartiles (First, Third)	Range number of times accessed
Overall number of times accessed		2	1, 3	0–268
Core content				
Accessed Core content	1703/1760 (97%)			
Did not access Core content	55/1760 (3%)			
Homepage				
Accessed homepage	1487/1760 (84.4%)	2	1, 3	0–268
Did not access homepage	273/1760 (15.5%)			
Getting Active				
Accessed Getting Active	524/1760 (29.7%)	0	0, 1	0–106
Did not access Getting Active	1236/1760 (70.2%)			
Eat for Health				
Accessed Eat for Health	485/1760 (27.5%)	0	0, 1	0–103
Did not access Eat for Health	1275/1760 (72.4%)			
Healthy Paths				
Accessed Healthy Paths	179/1760 (10.2%)	0	0, 0	0–123
Did not access Healthy Paths	1581/1760 (89.8%)			
Power				
Accessed Power	137/1231 (11.1%)	0	0, 0	0–125
Did not access Power	1094/1231 (88.8%)			
Accessed Core content plus one component	440/790 (55.7%)			
Accessed Core content plus two components	207/790 (26.2%)			
Accessed Core content plus three components	103/790 (13%)			
Accessed Core content plus four components	40/790 (5%)			
Support sessions				
Accessed support	235/756 (31%)	1	1, 2	1–4
Did not access support	521/756 (68.9%)			

At 12 months, the results showed a moderate significant difference in usage of Renewed based on access to human support ($p < 0.001$). Those who accessed human support used Renewed more than those who did not access human support or were without access to human support (median number of times Renewed was accessed: 4, 1, 1, respectively). The approximate effect was greatest when comparing those who accessed support to those who chose not to access support ($d = 0.37$), see *Table 28*.

4. Do patients who accessed Renewed's Optional content have greater improvements in quality of life at 12 months?

TABLE 28 Number of times patients used Renewed and support accessed

	Accessed support	Did not access support	Without access to support
Median number of times accessed Renewed. Quartiles (lower, upper)	4 (2, 9)	1 (1, 3)	1 (1, 3)
Approximate effect size	Ref	0.37	0.31
Test statistic (Mann–Whitney *U*: *U*)	Ref	33,484	59,206.5
Significance	Ref	< 0.001	< 0.001

At 12 months, those who used Optional content had higher QoL scores compared to those who only accessed the Core content. The mean QoL score was 2.15 points lower among those who only accessed the Core content compared to those who accessed the Optional content after adjusting for covariates [$F(1, 1410)= 13.81$, $p \leq 0.001$] (*Table 29*). There was a small but meaningful standardised effect ($d = 0.2$).

TABLE 29 Quality of life scores at 12 months for patients who accessed the Core plus Optional content, and Core content

	Accessed Core content plus Optional content	Accessed up to the Core content
Mean EORTC score at 12 months (SD)	79.11 (13.37)	75.68 (14.52)
Difference between means [*B* (95% CI)]	Ref	−2.15 (−3.28 to −1.01)
Standardised effect size	Ref	0.2
Significance	Ref	< 0.001

Practical implications

These results suggest that motivating patients to engage more with Renewed Online is likely to lead to better outcomes. Renewed was largely used as intended, with usage of Optional content associated with greater improvements in QoL at 12 months. Patients who accessed human support engaged with Renewed more than patients who did not have human support or were without support, suggesting that the brief support provided by HCPs encouraged engagement. However, as human support was optional and had to be requested by patients, the patients who accessed support may have already been more confident and motivated to engage with Renewed.

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