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Quality of life support in advanced cancer – Web and technological interventions: systematic review and narrative synthesis

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ABSTRACT

Background As treatments continue to progress, patients with advanced cancer are living longer. However, ongoing physical side-effects and psychosocial concerns can compromise quality of life (QoL). Patients and physicians increasingly look to the internet and other technologies to address diverse supportive needs encountered across this evolving cancer trajectory.

Objectives 1. To examine the features and delivery of web and technological interventions supporting patients with advanced cancer. 2. To explore their efficacy relating to QoL and psychosocial well-being.

Methods Relevant studies were identified through electronic database searches (Medline, PsychINFO, Embase, CINAHL, CENTRAL, Web of Science and Proquest) and handsearching. Findings were collated and explored through narrative synthesis.

Results Of 5274 identified records, 37 articles were included. Interventions were evaluated within studies targeting advanced cancer (13) or encompassing all stages (24). Five subtypes emerged: Interactive Health Communication Applications (n=12), virtual programmes of support (n=11), symptom monitoring tools (n=8), communication conduits (n=3) and information websites (n=3). Modes of delivery ranged from self-management to clinically integrated. Support largely targeted psychosocial well-being, alongside symptom management and healthy living. Most studies (78%) evidenced varying degrees of efficacy through QoL and psychosocial measures. Intervention complexity made it challenging to distinguish the most effective components. Incomplete reporting limited risk of bias assessment.

Conclusion Whilst complex and varied in their content, features and delivery, most interventions led to improvements in QoL or psychosocial well-being across the cancer trajectory. Ongoing development and evaluation of such innovations should specifically target patients requiring longer-term support for later-stage cancer.

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KEY MESSAGES

What is already known?

- Use of the internet and other technologies to provide support across the cancer trajectory has proliferated in recent years.
- Reviews of evidence are limited by heterogeneity across studies and lack focus on advanced cancer.

What are the new findings?

- Diverse web and technological interventions, focused largely on psychosocial needs, provide self-management and expert-guided support in line with an identified model of delivery.
- The vast majority confer efficacy related to QoL and psychosocial well-being. Most encompass all stages of cancer; few are exclusive to advanced cancer.

What is their significance?

Clinical

- With ongoing progress in the treatment of advanced cancer, evidence-based interventions are needed to support patients' QoL. Viable designs and modes of delivery exist to deliver tailored, accessible support via the internet and other technologies.

Research

- The design and evaluation of future innovations must target advanced cancer more exclusively.

INTRODUCTION

The term 'advanced' describes the spread of cancer beyond the original tumour, either locally (stage III) or to distant regions of the body ('metastatic' or stage IV).[1] Though a cure is not usually attainable, treatment can slow the progression of disease and control symptoms. As therapies targeting these later stages continue to progress, patients are living longer with advanced cancer.[2] Yet, as the disease trajectory extends, supportive needs can become more complex and burdensome.[3] Around half of all patients with cancer are now estimated to survive 10 years beyond diagnosis, many living with advanced stage disease.[4] As such, cancer is increasingly conceptualised as a chronic disease, bringing distinct, long-term supportive care needs to those for whom it remains 'incurable but treatable'.[5][6] Physical symptoms of cancer progression are frequently experienced alongside diverse side-effects of treatments past and present. Furthermore, psychological, social and spiritual implications of ongoing disease and uncertain prognosis are far-reaching and greatly affect patients' quality of life (QoL).[7]

In 2007, the UK's Department of Health outlined services and support necessary for patients living with long-term conditions. Patient choice and collaboration were highlighted as key requirements within what was termed the 'Generic Choice Model'.[8] Harley et al. later applied qualitative research methods to tailor this model to the chronic cancer context.[6] Several of the overarching areas of support identified are increasingly delivered via the internet and technology. In particular, innovations supporting cancer patients' psychological well-being, self-care and self-management have proliferated over recent decades, from discussion forums and online support groups, to health information websites, mobile applications and platforms facilitating symptom monitoring.[9-11] With approximately 2.5 million people living with cancer in the UK, projected to rise to over 4 million by 2030,[12] cancer support services face ever-growing demand. Yet these technologies offer a viable alternative to in-person support, connecting patients to one another, as well as to clinical services and sources of expert support. For patients with advanced cancer, less frequent follow up and home-based treatments may limit contact with health services and professionals. Timely and accessible information and support, delivered via the internet and other technologies, has the potential to bridge this gap and to address what are widely reported to be unmet holistic support needs in this growing patient group.[7][13][14] Indeed, the need for such remote technologies has been further heightened by the COVID-19 pandemic and its impact on cancer care delivery.[15]

Previous reviews have explored web and technological innovations in the field of cancer support yet have generally lacked focus on the distinct supportive needs encountered in the advanced stages of disease. Insight is limited by heterogeneous evidence and populations, with calls for further research

in order to more clearly ascertain the efficacy of these interventions across the cancer survivorship trajectory.[16-19]

AIM & OBJECTIVES

Our aim is to address the overall research question, *'Does the use of web and technological supportive interventions in advanced and metastatic cancer improve quality of life?'*

The objectives of this systematic review are therefore to:

1. Examine the design and delivery of web and technological interventions in the context of advanced cancer.
2. Explore their efficacy in relation to patients' QoL and other psychosocial outcomes, evaluated within randomised and non-randomised trials.

METHODS

The study protocol was registered with PROSPERO (reference: CRD42018089153). Methodology followed Preferred Reporting Items for Systematic reviews and Meta Analyses (PRISMA) guidelines[20] and the Cochrane Handbook for Systematic Reviews of Interventions.[21]

Search strategy

Electronic database search

A search for randomised and non-randomised controlled trials evaluating web and technological interventions in patients with advanced cancer was conducted in April 2018. Database specific searches were performed in MEDLINE, Embase, PsycInfo, CINAHL, Web of Science, Cochrane Register of Controlled Trials and ProQuest. Search terms combined medical subject headings (MeSH) and keywords relating to advanced cancer (e.g. *advanced*, *stage III/IV*, *metastatic*), web and technological platforms (e.g. *internet*, *electronic*, *mobile*) and types of intervention (e.g. *programme*, *application*,

tool). Restrictions on language or year of publication were not applied. An updated database search was conducted in February 2019.

The full search strategy is available in the online supplementary file.

Hand-searching

Electronic searches were supplemented by hand searching key journals in the field (Journal of Clinical Oncology and Psycho-Oncology, from 2016 onwards) and reference lists of related systematic reviews.[16-19]

Eligibility criteria

The following inclusion criteria were developed using the 'PICOS' framework.[22]

- P̲opulation: inclusive of adults (≥ 18 years) diagnosed with any advanced or metastatic cancer (stage III or IV).
- I̲ntervention: web or technological interventions designed to support patients with cancer. The term 'technological' refers to interventions harnessing technologies which may not necessarily be web-based. Symptom monitoring interventions needed to include some form of feedback to be regarded as supportive.
- C̲omparison: between interventions (e.g. web-based versus face-to-face) or with usual care.
- O̲utcome: efficacy of the intervention assessed (as a primary or secondary outcome) through measures relating to QoL (validated QoL measures, e.g. EORTC QLQ-C30, or other QoL-related psychosocial constructs, e.g. anxiety, distress, functional status etc.)
- S̲tudy design: randomised controlled trials (RCTs) and non-randomised controlled trials.

Studies exclusively targeting early stage cancers or patients receiving treatment with curative intent were ineligible. Furthermore, articles which did not report primary data were excluded.

Data selection and extraction

Preliminary screening of titles and abstracts was performed (stage one), followed by full-text review (stage two). A random sample (20%) was screened by the wider research team (F.K, C.H, K.A). Concordance was high, with over 98% agreement between reviewers. Differing decisions were discussed until consensus was reached. Papers with titles and abstracts referring to 'cancer survivors', with no further details of staging, were reviewed in full to determine participant eligibility.

A data collection form was adapted and piloted in Microsoft Excel, following guidance for the process of data extraction.[21] This gathered data relating to study author, year & country of publication, study design, objective, sample size, study population, intervention period, description and delivery of the intervention, relevant outcome measures and results.

Risk of bias

Studies were critically appraised using a modified version of the Cochrane Collaboration's risk of bias assessment tool for RCTs.[23] This encompasses five domains of bias: selection, performance, detection, attrition and reporting. Each study was assessed for 'high', 'low' or 'unclear' risk of bias for each individual domain.

Narrative synthesis

Significant heterogeneity across interventions, study methods and outcome measures precluded meta-analysis. A narrative synthesis was therefore conducted, guided by methods outlined by Popay et al.[24] The first stage involved gathering commonalities and distinctions across interventions. This allowed for the development of theory and categorisations relating to their features and delivery. A preliminary synthesis of interventions within their emerging subtypes then allowed us to explore patterns and relationships across the data.

RESULTS

Electronic database searches identified 5194 articles, with an additional 80 identified through hand-searching. Following removal of duplicates, titles and abstracts of 3883 records were screened, with 112 full text articles subsequently retrieved.

In total, 37 studies (of 35 original interventions and 2 intervention adaptations) met the inclusion criteria. Figure 1 outlines the screening process in full.

[Figure 1 here]

Study characteristics

Of the 37 included studies, 30 were full-scale RCTs and 7 were pilot or feasibility studies. The majority were conducted in the USA (54%) and Europe (35%). Results were illustrative of a rapidly emerging field, with 42% published between 2017 and 2019. Thirteen studies specifically evaluated interventions in patients with advanced cancer, whilst the remaining 24 were inclusive of early and late stage disease. Most studies included either breast cancer at all stages (n=10) or a mixed population of many disease sites (n=15). Others targeted lung (n=3), ovarian (n=2), prostate (n=1), neurological (n=1), haematological (n=1), colorectal (n=1) and breast & prostate (n=1) cancers. The remaining (n=2) focused exclusively on metastatic breast cancer.

Online supplemental table S1 provides an overview of included studies and interventions evaluated.

Risk of bias assessment

Full results of the risk of bias assessment are detailed within online supplemental table S2. Pattern of risk varied across studies, though high risk of detection bias was widespread (78% of studies). This relates to the vast majority of QoL and psychosocial outcome measures in the trials evaluated being self-reported, as well as challenges relating to blinding in interventions of this nature. Lowest risk was observed for selection bias (86% of studies describing random sequence generation, 62% demonstrating allocation concealment). Crucially, risk of bias assessment was limited by the level of detail reported; insufficient information resulted in 'unclear' judgements. To provide a more complete overview of the evidence base, articles were not excluded from the review based on this assessment.

However, this risk (whether high or unclear) and associated study limitations must be considered when drawing inferences from their results.

Categorising interventions

Intervention subtypes

By collating descriptions of interventions' features and delivery, shared characteristics became apparent. Drawing on literature in the wider field, alongside the articles under review, definitions were assigned to five distinct intervention subtypes (table 1).

Some of these definitions mirror those used across the evidence base e.g. 'information websites' and 'symptom monitoring tools.'[25 26] The term 'Interactive Health Communication Applications' (IHCAs) was outlined by the Science Panel on Interactive Health Communication over two decades ago and has since proliferated across the field of chronic disease management.[27 28] Other definitions were developed to describe the shared purpose of related interventions, where appropriate terms had not yet been encountered.

Table 1: Web and technological intervention subtypes.

	Subtype	Definition	No. studies	No. studies evidencing QoL-related efficacy
Increasing complexity →	Interactive Health Communication Application (IHCA)[27]	Computer-based (usually web-enabled) package of information and support, bringing together health information with a range of other features, encompassing social support, behaviour change and decision making.	12	11
	Virtual programme of support	Structured programme of support (e.g. modular or a set number of sessions) providing education and/or training, delivered via an online platform or mobile application +/- expert facilitation.	11	9
	Symptom monitoring tool	Web based tool or mobile application allowing users to self-report occurrence and severity of symptoms, for the purposes of self and/or clinician monitoring, usually generating a written or graphical report of results.	8	7
	Communication conduit	Supportive resource acting as a channel for communication, allowing users to reach out and receive advice and guidance in the home setting from peers or from professionals such as clinical nurse specialists, counsellors etc.	3	1
	Information website	Web page(s) providing information/content and links on a single platform, in the absence of additional integrated components or tools.	3	1

Intervention focus

Further categories were assigned to describe the overarching focus of the interventions (identified in online supplemental table S1). These were defined by grouping together those targeting similar supportive needs, guided by areas of support discussed in the wider literature.[7 29]

➢ *'Psychosocial' (PS)*: Targeting psychological behaviours and symptoms or encouraging socio-emotional well-being through shared experience and communication. This was an overarching focus across all subtypes.

➢ *'Symptom management' (S)*: Focusing on the monitoring and management of predominantly physical symptoms and side-effects.

> *'Health & lifestyle' (H/L)*: Encompassing aspects of healthy living more generally, such as diet and exercise.

Many interventions encompassed more than one focus, most notably the IHCAs.

Mode of delivery

Interventions could also be distinguished according to aspects of their delivery:

(i) the level of patient versus health professional or other expert involvement;

(ii) the extent to which interventions were integrated within the patients' usual care pathway.

From these characteristics, various modes of delivery were described. 'Self-management' and 'clinically integrated' are terms used to describe what are often contrasting approaches to delivering patient support. However, approaches of the reviewed interventions were much more nuanced. Focusing on the patient and the professional (healthcare or otherwise) as key participators, their varying level of involvement was used as the basis for describing different modes of delivery. 'Supported self-management', a term increasingly encountered in cancer survivorship research,[30] was adopted to describe a 'middle ground' between patients independently self-managing and experts having a key role in facilitation. 'Professionally delivered' acknowledged significant expert input which was distinct from patients' usual care.

To illustrate our developing theory, we brought these modes together within a model of intervention delivery (figure 2). Level of patient independence in self-management increases with progression up the pyramid. Conversely, health professionals are more closely involved in the delivery of interventions further down the pyramid.

Some interventions traverse the pyramid, applying several modes of delivery in the support they provide.

[Figure 2 here]

Intervention features and delivery

Interactive health communication applications (IHCAs)

A wide range of IHCAs were evaluated across 12 RCTs. Half of these targeted patients with advanced cancer;[31-36] the remaining had diverse cancer patient populations. Their multi-faceted nature meant that most encompassed more than one focus. Psychosocial and symptom-management support were frequently integrated, with more general health and lifestyle support featuring to a lesser extent.

The majority included health information and signposting,[31-33 35-40] some providing self-management guidance as a separate focus (S).[31 33 35 38 39 41] One intervention presented topics at varying levels of detail, allowing users to access information according to their needs.[35] The 'Surviving and Thriving with Cancer' intervention delivered a weekly education course, encouraging both physical and psychological health behaviour change (H/L, PS).[42] In some cases, self-management information was accompanied by facilities for varying degrees of physical and psychological symptom and status monitoring (S/PS).[31-35 38-40] Uniquely, 'ILOVEBREAST' used a mobile gaming format to support chemotherapy side-effect self-management, integrating health information with features for social networking and self-assessment (S, H/L).[34]

Decision support was another key component of several IHCAs. These provided users with a range of holistic and disease-specific information, supporting them to make decisions about their care needs.[32 35 36 40]

The majority facilitated user-user communication via forums,[35 38 39 41] a chat room[31] and discussion groups.[32 36 37 40] Additionally, many permitted patients to communicate with and receive support from professionals.[32 33 35 38-41] Further interactive components included audio visual self-management resources[31 40] and online diaries.[31 35 38 39] The use of patient 'stories' to encourage learning through shared experience was also central to several interventions.[33 36]

Within the model of intervention delivery (figure 2), four IHCAs were classified as 'supported self-management', giving users the option to contact experts outside their healthcare team.[33 38 40 41] 'Supported self-management' and 'professional delivery' were combined in two IHCAs, both encouraging self-management with an element of expert guidance as a core feature.[37 42] Others represented purely self-management tools.[34-36 39] The remaining interventions incorporated clinical integration via follow-up with a care co-ordinator[31] and through an in-built symptom monitoring feature which sent reports and alerts to clinicians.[32]

Virtual programmes of support

Few of the virtual programmes of support (2/11) were specific to advanced cancer.[43 44] The majority applied cognitive behavioural therapy (CBT) principles, addressing symptoms such as stress, pain, insomnia and anxiety through guided online courses and exercises (PS).[43-49] Mindfulness and stress-management principles were also incorporated.[44 45 49 50] Another programme facilitated self-help through problem solving therapeutic principles.[51] Contrasting with the predominantly psychosocial focus, 'e-CUIDATE', a rehabilitative healthy lifestyle programme for breast cancer survivors, delivered online health information and tailored exercise sessions (H/L).[52] Another programme included physical symptom monitoring (S), with users self-reporting pain during self-guided CBT.[47]

Across programmes, patients were guided to work through modules[47-49 51], chapters[45] or sessions over a set number of weeks.[43 44 46 50 52 53] A range of modalities were used to deliver programmes via online platforms and mobile applications, including videos and graphics, [43 45 47-49 53] exercises and worksheets,[43-53] audio content[44 49 53] and vignettes.[45 46 48] Some offered elements of personalisation, tailoring content to users' responses and needs.[47 48 51 52] Several involved virtual group sessions, guiding development of self-management skills such as stress reduction, relaxation and mindfulness.[44 50] Numerous programmes included interactive elements, connecting users to professionals[44-46 49-52] and to each other[45] for support or feedback. Another applied an alternative approach, integrating videos displaying simulated patient-therapist interactions.[43]

The extent to which patients were supported to self-manage differed, with programmes incorporating various approaches outlined in the model of intervention delivery (figure 2). Some were professionally delivered[44-46 50 52] whilst others encouraged more independent self-management, either purely patient-led,[43 47 48 53] or with optional access to professional support.[49 51]

Symptom monitoring tools

The symptom monitoring tools supported patients to manage predominantly physical aspects of health and treatment (S), with 4/8 specific to advanced cancer.[54-57] The remaining encompassed all stages.[58-61]

Some used hand-held digital devices,[54 58] tablet computers[56 59] and web-applications[55 60] to enable at-home symptom reporting. Others harnessed similar technology to support shared symptom

monitoring during inpatient and outpatient clinical encounters.[57 60 61] Several tools combined self-reported symptoms with clinical data such as weight,[54 55] height, performance status and medications.[54] Two interventions supplemented objective self-report scores with additional patient input, in the form of free text comments [55] and a diary feature.[60]

There was significant variability in the depth of symptom monitoring permitted, in terms of number of symptoms and specified reporting frequency. Several involved weekly completions,[54 55 58] whilst others were aligned with clinical encounters.[56 57 59 61] One tool also encouraged patients to report symptoms in line with their needs.[60] Extent of monitoring ranged from between 9-24 specified symptoms or issues,[54-57 59] to full-length health/QoL questionnaires and inventories.[58 61] One tool generated additional questions based on patients' responses or severity grading.[59]

In all cases, symptom reports were generated for clinicians to review, some providing graphical overviews,[57 58 60 61] one ranking summarised symptoms in order of support need.[59] Notably, 'Choice Interactive Tailored Patient Assessment' (Choice ITPA) was used across intervention and control groups, with clinician review of symptom reports the intervention feature under evaluation.[59]

All symptom monitoring tools were clinically integrated (figure 2), though to varying extents. Some applied several approaches, whether encouraging patients to discuss symptoms at their next clinical encounter,[58-60] making reports available for clinicians to review[54 58-61] or using pre-defined thresholds to trigger alerts to clinicians, prompting urgent review outside of scheduled follow-up.[55 56] Several emphasised supporting[59] or 'coaching' patients to communicate symptoms with their clinician.[58 60] One tool stands out as being designed specifically for hospitalized patients.[57]

Communication conduits

Three interventions represented channels of communication for patients at home, providing predominantly psychosocial support by connecting them to experts or peers.[62-64] Two were advanced stage focused, [63 64] whilst the third targeted all stages of breast cancer.[62]

One study trialled the provision of individually tailored psychosocial counselling to patients with breast cancer, based on cognitive behavioural, rational emotive and solution-focused therapy, via email correspondence with a clinical psychologist.[62] Another had a dual physical and psychosocial focus (S/PS), providing tailored symptom management education and support through online message boards. This interactive platform facilitated communication and shared decision making between

patients and nurses.[64] The final intervention evaluated an unmoderated online support group which encouraged self-facilitation of peer support in women with metastatic breast cancer.[63]

A key feature of these interventions was the rapidity of support. Two were guided by health professionals, providing responses to patients within 24 hours, whilst remaining separate to the care pathway.[62][64] The patient-led social networking intervention, in contrast, was purely self-management, encouraging users to seek support through shared experiences.[63]

Information websites

Three studies evaluated the delivery of supportive information via websites of varying formats, targeting all cancer stages .[65-67] These supported physical[66] or psychosocial[65] aspects of health (S/PS); one encompassed both.[67]

One intervention involved patients' self-design of a personal website within a workshop setting, with a template comprising a blog, signposting, message board and 'how you can help' visitor information features.[65] Another used a diagrammatic format to present information relating to the care pathway of patients with breast cancer, with built-in signposting links.[66] The final website brought together patients' experiences of living with colorectal cancer, organised as themes and case studies.[67]

All three websites were self-management tools, delivered separately to patients' care pathway, without features for accessing expert support.

Efficacy relating to QoL and psychosocial domains

Considerable variation was observed within and across intervention subtypes in the QoL and psychosocial measures applied, as well as the methods used to evaluate these constructs. We were therefore unable to draw definitive conclusions regarding efficacy. However, the use of these measures, and indications of efficacy between and within studies, was explored.

Overall, 78% (29/37) of studies demonstrated efficacy, to varying degrees, through measures of QoL and related psychosocial constructs. These represented a primary outcome for 25 of the studies (four capturing them as primary and secondary outcomes), the remaining 12 capturing them as secondary outcomes alone. The studies which did not evidence efficacy in these areas (n=8) all reported limitations relating to small sample sizes and low statistical power.

Tables 2 & 3 provide an overview of the QoL and psychosocial outcome measures applied, their abbreviations and the constructs captured.

A summary of psychosocial and QoL-related results is provided in online supplemental table S1.

Table 2: Overview of QoL outcome measures.

		Outcome	Outcome measures
Type of outcome as measured by n= number of studies	**Quality of Life (QoL) (n=22)**	Quality of Life (QoL)/ Health Related Quality of life (HRQOL)[31, 33, 34, 38, 43, 44, 46, 48, 51, 52, 54, 56, 58, 59, 61]	- European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) - EuroQol 5-Dimensions (EQ-5D) - Functional Assessment of Cancer Therapy – General (FACT-G) - Short Form Health survey (SF-12, SF-36) - World Health Organisation Quality of Life abbreviated scale (WHOQOL-BREF) - 15-dimensional instrument for assessing HRQOL (15D)
		Cancer site specific QoL[40, 41, 45, 51-53, 55, 63, 66]	- EORTC-BN20 (Brain tumour module) - EORTC-QLQ-BR23 (Breast cancer module) - Functional Assessment of Cancer Therapy - Breast (FACT-B) - Functional Assessment of Cancer Therapy – Lung (FACT-L) - Quality of Life Instrument - Breast Cancer Patient Version (QOL-BC)
	Symptom related QoL (n= 19)	Chemotherapy induced peripheral neuropathy (CIPN)[47]	- European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire – CIPN20 (EORTC QLQ-CIPN20)
		Fatigue[31, 37, 42, 48-51, 58]	- Brief Fatigue Inventory (BFI) - Checklist Individual Strength (CIS) - Fatigue Symptom Inventory (FSI) - Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) - Functional Assessment of Cancer Therapy-Fatigue (FACT-Fatigue) - Multi-dimensional Fatigue Symptom Inventory - Short Form (MFSI- SF) - Profile of Moods States – Short Form (POMS-SF)
		Insomnia[42, 48]	- Insomnia Severity Index (ISI) - Women's Health Initiative Insomnia Rating Scale (WHIIRS)
		Symptom distress[32, 33, 38, 39, 41, 54, 59, 60, 64]	- Edmonton Symptom Assessment Scale (ESAS) - Memorial Symptom Assessment Scale (MSAS-SF) - MD Anderson Symptom Inventory (MDASI) - Modified Edmonton Symptom Assessment Scale (ESAS)[†] - Symptom Distress Scale (SDS-15, SDS-22) - Symptom Representational Questionnaire (SRQ) - Symptom scoring within intervention[59]
		Symptom severity, consequences & controllability[64]	- Symptom Representational Questionnaire (SRQ)
		Performance status/level of daily activity[33, 63]	- Eastern Co-operative Oncology Group (ECOG) Performance Status Scale

[†]Caregivers reported symptom distress of behalf of patient.[32]

Table 3: Overview of psychosocial outcome measures.

		Outcome	Outcome measures
Type of outcome as measured by n= number of studies	**Psychological & psychosocial constructs (n=26)**	Overall psychological functioning[37]	- Outcomes questionnaire (OQ-45)
		Depression[31, 34, 37-39, 41-44, 51, 58, 65] Depressed mood[36] Mood[48]	- Beck Depression Inventory (BDI) - Centre for Epidemiologic Studies Depression Scale (CES-D) - Hospital Anxiety and Depression Scale (HADS-D) - Patient Health Questionnaire (PHQ-8, PHQ-9) - Patient-Reported Outcomes Measurement Information System (PROMIS) – Depression item bank - Profile of Moods States – Short Form (POMS-SF)
		Stress[50]	- Calgary Symptoms of Stress Inventory (CSOSI)
		Anxiety/anxious mood[34, 36, 37, 39, 41, 43, 50, 66]	- Hospital Anxiety and Depression Scale (HADS-A) - Impact of Events Scale – Revised (IES-R) - Profile of Moods States – Short Form (POMS-SF) - Spielberger State-Trait Anxiety Inventory (STAI)
		Anger/angry mood[36, 50]	- Profile of Moods States – Short Form (POMS-SF)
		Positive/negative affect[45, 63]	- Negative Mood Regulation Scale (NMR) - Positive and Negative Affect Scale (PANAS)
		Positive mental health[46]	- Mental Health Continuum – Short Form
		Feelings over past week[65]	- Profile of Moods States – Short Form (POMS-SF)
		Cancer related intrusive thoughts & feelings/post-traumatic symptoms[45, 65] Rumination[46] Fear of cancer recurrence[46]	- Fear of Cancer Recurrence Inventory (FCRI) - Impact of Events Scale – Revised (IES-R) - Posttraumatic Growth Inventory (PTGI) - Rumination and Reflection Questionnaire (RRQ)
		Confusion[50]	- Profile of Moods States (POMS)
		Psychological distress[35, 37, 46, 49, 57, 62] Cancer related distress[44]	- Brief Symptom Inventory (BSI) - Distress Thermometer (DT) - Hospital Anxiety and Depression Scale (HADS) - Impact of Events Scale (IES)/Impact of Events Scale-Revised (IES-R) - Patient Health Questionnaire (PHQ-4)
		Self-efficacy for coping with cancer[38, 39, 41, 45, 67]	- Cancer Behaviour Inventory (CBI)/CBI-B (Brief version) - Stanford Inventory of Cancer Patient Adjustment (SICPA)
		Vigour/positive mood[37, 50, 65]	- Profile of Moods States (POMS, POMS-SF)
		Spirituality[50] Peace/meaning[36] Appreciation of life[65]	- Functional Assessment of Chronic Illness therapy - Spiritual well- being (FACIT-Sp) - Posttraumatic Growth Inventory (PTGI)
		Mindfulness[46, 50, 53]	- Five Facet Mindfulness Questionnaire (FFMQ) - Mindful Attention Awareness Scale (MAAS)
		Mental adjustment[62]	- Mental Adjustment to Cancer (MAC) scale
		Perception of positive changes after adversity[50, 65] Relating to others[65]	- Posttraumatic Growth Inventory (PTGI)
		Social & functional well-being[45]	- Functional Assessment of Cancer Therapy – Breast (FACT-B)
		Social support[38, 40, 41]	- Medical Outcomes Study Social Support Survey (MOS-SS) - Multi-dimensional Scale of Perceived Social Support (MSPSS) - Six-item Social Support scale (developed in a previous study.)[68]

Interactive health communication applications

Most IHCAs (11/12) demonstrated measurable improvements, to varying extents, in QoL and psychosocial constructs. These spanned the range of delivery modes (figure 2) and comprised vastly differing content (PS, S and H/L).

Five interventions demonstrated significant efficacy ($p≤0.05$) through direct measurement of QoL using FACT-G, FACT-B, WHOQOL-BREF and EORTC-QLQ-C30.[31 33 34 40 41] As well as supporting QoL, one intervention also resulted in less worsening of self-efficacy for users (following initiation of chemotherapy) compared to controls ($p=0.03$).[41] Another led to improvements in QoL alongside emotional function ($p<0.01$) and symptom distress ($p<0.01$).[33] Each of these interventions included features for symptom self-management, four also integrating some form of expert support.[31 33 40 41]

In the absence of direct QoL measurement, other IHCAs were found to support or improve diverse related constructs such as symptom distress, anxiety, depression and peace. Their content was equally diverse. Two were purely self-management,[36 39] though both featured user-user communication, and one included expert support through clinical integration.[32] For 'mi Living Story', an improved sense of peace was observed ($p=0.029$), alongside a 'trend' for improved depressed mood ($p=0.097$).[36] Breast cancer patients using the 'WebChoice' intervention reported significant improvements in symptom distress ($p=0.001$), anxiety ($p=0.03$) and depression ($p=0.03$) compared to those receiving usual care.[39] However, use of the same intervention in patients with breast and prostate cancers, with the addition of expert support, demonstrated limited efficacy (though contrasting outcome measures prevent direct comparisons between studies).[38] Use of the lung cancer (advanced stage) specific version of the 'Comprehensive Health Enhancement Support System' (CHESS) by patient-caregiver dyads resulted in lower physical symptom distress (measured using a modified ESAS) compared to internet use.[32] This was confined to measurements taken at 4 months ($p=0.031$) and 6 months ($p=0.004$) after initiating the intervention, however, and was not observed at earlier (2 months) or later (8 months) time points. The study evaluating the breast cancer specific version of CHESS[40] (compared to both controls and use of the internet) captured improvements in QoL (FACT-B) and social support (using a 6-item scale developed in a previous study),[68] this time confined to 4 months post-intervention ($p=0.018$ and $p=0.021$ respectively). Both versions included varying levels of expert support.

Users of 'Health Space', an IHCA focusing on user-user engagement with expert input, experienced significant improvement in fatigue (measured as a subscale of POMS-SF) relative to controls ($p=0.04$). However, improvements in other psychosocial domains (psychological functioning, depressive symptoms, anxiety and vigour) were not significant.[37] Similarly, the professionally delivered 'Surviving

and Thriving with Cancer' showed marginal efficacy, measuring a range of psychosocial variables (fatigue, insomnia and depression) and finding significant reductions for intervention users in insomnia alone (*p*=0.03).[42] The self-management 'Together' intervention also applied a range of psychological measures (HADS-A, DT and IES), though found no significant effects.[35]

Virtual programmes of support

Indications of QoL-related efficacy were also evident for diverse (predominantly PS) virtual programmes of support (9/11), delivered in numerous ways.

Three studies evidenced significant improvements in QoL scores (measured using FACIT-F, FACT-B, EORTC-QLQ-C30 and EORTC-QLQ-BR23),[49 52 53] though programme content and delivery contrasted significantly. 'Headspace' delivered mindfulness training through self-management, improving scores for both QoL (*p*<0.01) and mindfulness (*p*=0.04).[53] The others incorporated varying degrees of expert support. A supported self-management programme for coping with stress improved QoL relating to fatigue (*p*=0.007), as well as reducing distress (*p*=0.03),[49] and a professionally guided exercise (H/L) programme led to significantly improved QoL (*p*<0.01).[52]

Another online mindfulness programme, this time professionally delivered, assessed a host of psychosocial measures. These included total mood disturbance, stress, spirituality, post-traumatic growth (PTG) and mindfulness (captured using POMS, CSOSI, FACIT-Sp and FFMQ respectively). The study found significant improvements (*p*≤0.049), of moderate effect size, for all but PTG in intervention users versus controls.[50]

Five studies reported less definitive evidence of QoL-related efficacy. For some professionally delivered programmes, trends for improved scores in applied measures did not reach significance[44] or were confined to a specific subscale (e.g. mental health related QoL).[46] The professionally-delivered online CBT stress management (CBSM) intervention did not lead to a statistically significant improvement in QoL. However, mean difference in FACT-G scores between groups met the threshold for clinical significance (defined as a minimum difference of 4 points for the total scale and 2 points for subscales).[44] Whilst the electronic mindfulness-based cognitive therapy (eMBCT) improved mental health-related QoL, mindfulness skills and positive mental health, and reduced rumination and fear of recurrence (*p*<0.025), this was also true for the face-to-face equivalent, when compared to usual care.[46] Supported self-management did not lead to improved QoL for the 'Coping with Cancer Workbook', yet users demonstrated significant improvement in self-efficacy (*p*=0.019) and cancer

related post-traumatic symptoms (*p*=0.002).[45] Whilst participants trialling the self-management 'Sleep Healthy Using The Internet' (SHUTi) did not experience improvements in QoL, depression or anxiety, overall adjusted effect sizes for these constructs ranged from small to large (*d*=0.42-0.54).[48] Lack of significance may in part be explained by the underpowered analysis of a relatively small sample. Intervention use was, however, associated with significant improvements in fatigue, assessed using the MSFI-SF (*p*<0.01).[48] For the anxiety self-management mobile application, QoL, anxiety and depression improved for both intervention and control participants, yet there were no significant between group differences. Further analysis demonstrated efficacy for a distinct sub-group (severely anxious at baseline, *p*=0.010), though cautious interpretation is warranted due to small numbers.[43]

Two programmes were unable to evidence QoL-related efficacy, though both were evaluated within underpowered studies. These applied SF-36 to assess health-related QoL (HRQOL) with use of guided online self-help[51] and EORTC QLQ-CIPN20 to capture symptom-related QoL following online self-guided CBT pain management.[47] Notably, glioma patients using the online self-help (plus expert support) reported a post-treatment reduction in fatigue of borderline significance (*p*=0.054).[51]

Symptom monitoring tools

The symptom monitoring tools (all S and S/PS) demonstrated efficacy in 7/8 studies, across diverse QoL and psychosocial domains. Again, this was not confined to a particular style of intervention or mode of delivery.

Tools which alerted clinicians to serious reported symptoms demonstrated significant improvement in QoL scores using FACT-L (*p*=0.04)[55] and EuroQol EQ-5D (*p*=<0.001).[56] However, indications of efficacy were also reported for less intensive symptom monitoring approaches. Completion of touch screen QoL questionnaires in clinic, with subsequent clinician review, improved FACT-G scores for intervention versus control participants (*p*=0.006), though there was no significant difference between intervention users and the attention-control group (QoL questionnaire completion without clinician feedback).[61] For E-MOSAIC, direct integration of symptom reports completed in clinic did not result in a significant difference in global QoL (EORTC-QLQ-C30), though symptom distress (ESAS) was significantly less with intervention use (*p*=0.003).[54]

Tools coaching patients to communicate their symptoms to their healthcare team resulted in variable outcomes. Patients using the 'Communicating Health Assisted by Technology' (CHAT) intervention experienced worsening HRQOL, measured using SF-36.[58] Conversely, those using Choice ITPA were

significantly less distressed by their symptoms (specifically discomfort, eating/drinking, sleep/rest and sexuality, with significance set at $p \leq 0.10$) than control participants (Choice ITPA in absence of clinician review). Notably, the effect of Choice ITPA in comparison to care as usual (i.e. absence of symptom monitoring) was not assessed.[59]

Indeed, symptom monitoring plus clinician feedback resulted in reductions in symptom distress (p=0.003[54] and p=0.02[60]) and psychological distress (p=0.008)[57] across other interventions measuring this construct, using the ESAS[54][57] and the SDS-15.[60]

Communication conduits

The professionally guided (predominantly PS) communication conduits varied in efficacy. Participants receiving counselling via email experienced no significant improvement in distress or overall QoL, captured using the BSI and EORTC-QLQ-C30.[62] For patients using the message board based intervention (S/PS), there was no evidence of impact on consequences or controllability of symptoms between groups.[64] Yet, two weeks post intervention, users demonstrated significantly lower symptom distress (p=0.012), and a trend (though non-significant) for improved symptom severity, compared to controls (p=0.058). However, this effect, observed using the SRQ, was not maintained at six weeks.[64]

For the self-management peer-peer online support group, completion of QoL measures (ECOG and FACT-B) evidenced little difference between study arms, though definitive conclusions regarding efficacy were limited by a small study sample.[63]

Information websites

Within the studies evaluating self-management information websites, 2/3 did not demonstrate significant intervention effects in QoL-related outcomes (measured using the Quality of Life Instrument - Breast Cancer Patient Version,[66] the SAI[66] and the CBI-B[67]).

However, after six months, users creating their own personal (PS) website within a workshop setting ('Project Connect Online', which is likely to have involved some expert support), experienced significant improvements in broader psychosocial outcomes of depressive symptoms (p=0.009), positive mood (p=0.03) and life appreciation (p=0.03), applying the CES-D, POMS and PTGI respectively.[65]

DISCUSSION

This systematic review has identified a broad range of web and technological interventions delivering cancer support to patients living with advanced cancer. Based on shared features and functionality, and in consultation with the wider literature, five distinct subtypes emerged: IHCAs, virtual programmes of support, symptom monitoring tools, communication conduits and information websites. Distinct approaches to delivering support were identified and described within the model of web and technological intervention delivery (figure 2). These ranged from independent or supported self-management, to interventions with elements of professional facilitation and those integrated with usual care. Clinical integration was mostly observed in the symptom monitoring tools, with health professional involvement encouraged or directly facilitated, whilst the information websites guided independent self-management. For the most part, interventions could be placed between these two extremes, encouraging self-management whilst offering varying degrees of expert support. This model, and the definitions and categorisations described, could be used as a framework to guide future intervention development.

Interventions focussed on one or more of three key areas: psychosocial, symptom management and health & lifestyle. Psychosocial considerations were an overarching focus across the subtypes. For the virtual programmes of support, psychological behaviours or symptoms were targeted in almost all cases (10/11), most applying CBT techniques. Psychosocial needs were also a predominant focus for the IHCAs (11/12), incorporated through various forms of psychotherapy, psychoeducation or socioemotional support. The smaller number of information websites and communication conduits were also largely shaped by these considerations. Symptom monitoring tools, in contrast, mostly targeted patients' physical health through supported management of symptoms and side-effects. An underlying link to psychosocial well-being was recognised, however, with 6/8 of these studies assessing QoL or psychosocial constructs as primary study outcomes. The past decade has seen a breadth of research emphasising the need for psychosocial considerations as a core aspect of the care and support of patients with cancer.[69, 70] It is unsurprising, therefore, that such a large number of interventions are being developed with a focus on addressing these needs. However, whilst it is difficult to draw definitive conclusions, this review has highlighted wide-ranging efficacy across physical, psychosocial, and more general health & lifestyle support alike. A tendency for interventions to encompass patients across all stages of cancer makes it difficult to gauge their impact for those specifically in the advanced stages. Yet, these findings support research emphasising the sheer breadth of needs, often unmet, encountered right across the cancer trajectory.[7 71] Whilst psychosocial care and support is fundamental, it is one aspect of what is described as a 'spectrum' of patient

needs.[14] More complete support must also encompass the physical, functional and spiritual needs which collectively determine QoL.[72]

Furthermore, what is most evident from the significant variation in efficacy between studies, interventions, patient populations and modes of delivery, is that a standardised 'one size fits all' template for cancer support does not exist. IHCAs, in contrast, offer the possibility of meeting multiple supportive needs in a multitude of ways. This flexibility may explain why they were the most widely evaluated of the interventions. Though their focus was largely psychosocial, they brought together a range of other support and offer the scope to tailor to specific patient groups. Self-management and self-care were encouraged through integrated features such as educational exercises, forums and decision-making tools, delivered with varying levels of expert guidance. Most conferred some level of psychosocial or QoL-related benefit for users, albeit to varying extents and across heterogeneous populations.

Sheer complexity and variation within and across the intervention subtypes meant it was not possible to attribute efficacy in particular QoL/psychosocial domains to specific features or components. The relationship between mode of delivery and specific outcomes appeared equally complex. However, a potential relationship between QoL-related efficacy more generally and features for expert or health professional support, of varying intensity, appeared evident. Though not always the case, this was observed in interventions offering supported self-management, professionally delivered support or clinical integration of support as part of patients' usual care. Features for symptom monitoring and self-management were also frequently seen in interventions evidencing QoL-related efficacy. Indeed, these often incorporated some form of expert input, linking the two elements inextricably. However, the potential value of both is clear. Peer-peer communication, social networking or shared experiences were also features of multiple interventions evidencing QoL-related improvements. Whilst there is increasing emphasis on empowering patients with chronic diseases to self-manage and to have a central role in their care,[6] these findings remind us of the value of collaboration and shared input, engaging the patient, professionals and peers. Indeed, this lessens the burden of disease management at both an individual and a service level.[73] Crucially, the model of web and technological intervention delivery should not be seen as a hierarchy, rather as a group of potential approaches, any number of which may be harnessed to support diverse patient needs and preferences. This has been evidenced through widespread efficacy, with 78% of studies demonstrating measurable improvement in QoL and/or psychosocial well-being. Whilst this evidence guides us in supporting patients with cancer more generally, future interventions must target those with advanced cancer more specifically. This may be achieved through greater emphasis on patient and public involvement (PPI), integrating lived experiences in aspects of intervention development and evaluation. Indeed, Corbett et al

emphasised the potential value of patient involvement in intervention design, to ensure challenges specific to their stage of the cancer trajectory are addressed in a way which is both useful and acceptable.[17] Beyond the development phase, greater representation of patients with advanced cancer within larger scale intervention trials will strengthen the evidence base guiding their support.

Study limitations

Whilst this review aimed to evaluate support for those living with advanced cancer, just 13 of the 37 studies specifically targeted these patients. Across mixed populations, representation of advanced stage cancers was variable. Given the significant heterogeneity of study populations, it is hard to distinguish what works well for those with advanced cancer.

Further heterogeneity, related to interventions, study methods and outcome measures, meant we were unable to quantitatively determine intervention efficacy through meta-analysis. It was also difficult to ascertain whether studies were sufficiently powered to detect changes in the outcomes of interest, since this was not always reported for QoL and psychosocial measures. As risk of bias varied significantly across studies, with judgement limited by inadequate reporting, findings must also be interpreted cautiously.

Due to limited time and resources, data extraction and risk of bias assessment were performed by one reviewer (K.K). Furthermore, as indicated by the high proportion of recent publications, this field is fast moving and it is likely that relevant articles will have been published since our searches were conducted.

CONCLUSION

The evolving chronicity of cancer has significant implications on cancer services, not only in terms of growing demand but also in relation to changing patient needs. The internet and technology offer the possibility for more cost-effective, tailored and accessible monitoring and support, reducing the burden of follow-up on healthcare services and patients alike.[14 74] This review has identified a breadth of web and technological interventions designed to support patients across the cancer trajectory, the vast majority evidencing some degree of efficacy relating to QoL and psychosocial well-being. However, there is a pressing need for these innovations to more exclusively tailor their design and target their evaluation to the increasing number of patients living with advanced cancer. Involving

these patients in the development and larger-scale evaluation of future multi-faceted supportive interventions may ensure that their complex supportive needs are more holistically addressed. As cancer treatments continue to progress, so too should the evidence guiding us in how best to support the many patients who will, as a direct result, live longer in the advanced stages of disease.

Competing interests

None.

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Figure 1: PRIMSA flow diagram of study selection.

Figure 2: Model of web & technological intervention delivery.