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Review

A systematic review of the use and validation of health-related quality of life instruments in older cancer patients ☆

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ABSTRACT

Aim: The aim of this paper is to systematically review the use and validation of HRQOL instruments in older cancer patients.

Method: A systematic review of 5 databases and 3 research registers identified studies reporting the use and validation of HRQOL instruments in cancer patients aged over 65 years from 1995 to mid 2007.

Results: Thirty-one studies reported the use of HRQOL measures in older people, using a range of generic and disease-specific instruments. Little work was reported in patients aged over 80 years. All studies exhibited methodological limitations. Fourteen studies were identified with variable evidence on the psychometric properties and clinical usefulness of identified instruments.

Conclusion: Our review identified that the development, validation and use of HRQOL instruments often ignore the specific needs of older people. This review highlights the need for a HRQOL instrument specifically designed to capture the issues and concerns most relevant to older cancer patients.

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1. Introduction

Although it is now recognised that elderly patients may be suitable for active cancer treatment, such therapies have thus

far had little effect on mortality rates in this age group.¹ Treatment efficacy therefore needs to be measured in other ways, and consideration of the impact of the disease and treatment on a patient's quality of life (QOL) becomes vital.

☆ On behalf of the EORTC Quality of Life Group and Task force for the Elderly

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Table 1 – Characteristics of papers reporting HRQOL in clinical trials and intervention studies of older cancer patients

Author	Year	Country	Disease site	Age	Study design	Intervention	Sample size
Allal et al. ¹⁹	1999	European	Anal	71 years and above <i>versus</i> <71 years	Cross-sectional	Radiotherapy +/- chemotherapy	41
Aapro et al. ²⁰	2006	USA and Switzerland	Mixed	65 years and above <i>versus</i> <65 years	Retrospective analysis of 3 non-randomised trials	Use of epoetin alfa treatment in anaemia following chemotherapy	3634 (pooled data of >65 years)
Blazeby et al. ²¹	2000	UK	Oesophageal	(SGA) 58–74 <i>versus</i> 51–79 <i>versus</i> 67–80	Prospective	Curative oesophagectomy or palliative treatment	92 (37 aged 65 years or above)
Buijt et al. ²²	2005	The Netherlands	Non-Hodgkins Lymphoma	65 years and above	RCT 2 ^o analysis	CHOP chemotherapy	132
Chen et al. ²³	2003	USA	Mixed	70 years and above	Prospective	Standard chemotherapy protocols	59
Crivellari et al. ²⁴	2000	International	Breast	65 years and above	RCT	CMF + tamoxifen <i>versus</i> tamoxifen alone	299
De Haes et al. ²⁵	2003	European	Breast (early stage)	70 years and above	RCT	Mastectomy <i>versus</i> tumour excision + tamoxifen	236
Demark-Wahnefried et al. ²⁶	2006	USA	Breast and prostate	65 years and over	RCT	Lifestyle interventions (exercise and diet)	182
Diaz de Liano et al. ²⁷	2003	Spain	Gastric	70 years and above <i>versus</i> <70 years	Prospective	R ⁰ resection	54
Elderly Lung cancer Vinorelbine Italian Study group ²⁸	1999	Italy	NSCL (advanced)	70 years and above	RCT	Vinorelbine <i>versus</i> supportive care alone	161
Esbensen et al. ²⁹	2004	Denmark and Sweden	Mixed	65 years and above	Cross-sectional	Newly diagnosed patients receiving supportive care	101
Giroto et al. ³⁰	2003	USA	Breast	65 years and above	Cross-sectional	Mastectomy + breast reconstruction	316 (24 aged 65 years or above)
Guner et al. ³¹	2006	Turkey	Mixed	65 years and above	Exploratory	Sociodemographic variables – gender, age, marital status, educational level, occupation and level of income	620
Hoffman et al. ³²	2006	USA	Prostate	75–84 years	Prospective Cohort	Standard treatment protocols (prostatectomy, radiotherapy, hormone treatment, no active treatment)	465

Hollenbeck et al. ³³	2002	USA	Prostate	(SGA) 69 years and above <i>versus</i> <69 years	Cross-sectional	Neo-adjuvant hormone therapy	114
Huguenin et al. ³⁴	1999	Switzerland	Prostate	74 years and above	Cross-sectional	Curative radiotherapy	59
Huguenin et al. ³⁵	1999	Switzerland	Endometrial	70 years and above	Prospective	Curative radiotherapy	49
Hurria et al. ³⁶	2006	USA	Breast	65 years and older	Prospective	Adjuvant chemotherapy	49
Langer et al. ³⁷	2002	USA	NSCL (advanced)	70 years and above <i>versus</i> <70 years	RCT	Cisplatin + etoposide <i>versus</i> cisplatin <i>versus</i> low or high dose paclitaxel	574 (86 aged 65 years and above)
Mainone et al. ³⁸	2005	Italy	NSCL (advanced)	70 years and older	RCT	Vinerolbine <i>versus</i> gemcitabine Gemcitabine + vinerolbine	566
Mantovani et al. ³⁹	1996	Italy	Mixed	65 years and above	RCT	Psychopharmacological (PP) treatment <i>versus</i> PP + social support <i>versus</i> PP + social support + structured psychotherapy for symptoms of anxiety and depression	74
Merli et al. ⁴⁰	2004	Italy	Non-Hodgkins lymphoma	65 years and above	RCT	Anthracycline regimens	91
Mohile et al. ⁴¹	2007	USA	Prostate	70 years and above	Prospective	Androgen Ablation treatments	50
Presant et al. ⁴²	2003	USA	Mixed	65 years and above	Prospective	Paclitaxel or paclitaxel + carboplatin for metastatic disease	26
Rao et al. ⁴³	2005	USA	Mixed	65 years and above	Randomised factorial trial (2 ⁰ analysis)	Geriatric evaluation and management unit or usual inpatient care + discharge to either a geriatric outpatient clinic or a usual outpatient care	99
Rogers et al. ⁴⁴	1998	UK	Oral/ oral pharyngeal	65 years and above	Prospective	Surgical resection	50
Sullivan et al. ⁴⁵	2006	USA	Metastatic Prostate	67–78 years	Prospective (2 ⁰ analysis)	Artrastentan <i>versus</i> placebo	809
Thome et al. ⁴⁶	2004	The Netherlands	Mixed	75 years and over	Cross-sectional	Comparison of QOL against matched population without cancer	150
Vansteenkiste et al. ⁴⁷	2004	Belgium	NSCL (advanced)	(SGA) 65 years and above <i>versus</i> <65 years	RCT (2 ⁰ analysis)	Gemcitabine <i>versus</i> cisplatin + vindesine	169
Wallace ⁴⁸	2003	USA	Prostate	65 years and above	Cross-sectional	Watchful waiting	21
Wu et al. ⁴⁹	2000	China	Gastric	65 years and above	Cross-sectional	Surgical resection	433

Abbreviations: SGA = Sub Group Analysis RCT = Randomised Controlled Trial CHOP Chemotherapy = Cyclophosphamide + Hydroxydoxorubicin + Oncovin + Prednisolone CMF Chemotherapy = Cyclophosphamide + Methotrxate + 5-Fluorouracil NSCL = Non Small Cell Lung Cancer.

Table 2 – Assessment methods of patient-reported outcome measures used in studies

Author (s)	Instruments used	End-point of concern	Definition provided	Rational for choice of instrument	Psychometric Properties reported	Cultural Validity reported	Adequacy of Domains	Instrument administration reported	Compliance reported	Timing of Assessment reported
Allal et al. ¹⁹	EORTC QLQ-C30 and QLQ-CR38	Primary	No	Yes	Part	Part	Yes	Yes	Yes	Not applicable
Aapro et al. ²⁰	LASA + FACT anaemia	Secondary	No	Yes	No	No	Yes	Yes	No	Yes
Blazeby et al. ²¹	EORTC QLQ-C30 + dysphagia scale of QLQ-OES24	Primary	No	Yes	Part	No	Yes	Yes	Yes	Yes
Buijt et al. ²²	EUROQOL 5D, EORTC QLQ-C30 and Multidimensional Fatigue Inventory (MFI-20)	Primary	No	Part	No	No	Yes	Yes	Yes	Yes
Chen et al. ²³	FACT-G, GDS	Secondary	No	Part	No	No	No	No	Yes	Yes
Crivellari et al. ²⁴	Perceived adjustment to chronic illness scale	Secondary	No	No	No	No	No	Part	Yes	Yes
De Haes et al. ²⁵	Ad hoc instrument based on EORTC QOL studies and short HADS and body image scale + social support	Secondary	No	No	Yes	No	Yes	Yes	Yes	Yes
Demark-Wahnefried et al. ²⁶	FACT-breast or prostate	Secondary	No	No	No	No	Part	No	Part	Yes
Diaz de Liano et al. ²⁷	EORTC QLQ-C30 + gastric module developed by Kuchler	Primary	No	Yes	Part	No	Yes	Yes	No	Not applicable
Elderly Lung cancer Vinorelbine Italian Study Group ²⁸	EORTC QLQ-C30 and QLQ-LC13	Primary	No	Yes	No	No	Yes	Yes	Yes	Yes
Esbensen et al. ²⁹	EORTC QLQ-C30	Primary	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not applicable
Giroto et al. ³⁰	SF-36	Primary	No	No	No	No	No	No	Yes	Not applicable
Guner et al. ³¹	Face to face interviews, Rolls-Royce QOL Scale.	Primary	No	Yes	Part	Part	Yes	Yes	Yes	Not applicable
Hoffman et al. ³²	SF-36 and ad hoc prostate specific instrument based on items from 3 other instruments	Secondary	No	No	No	No	Part	Yes	Part	Not applicable

Hollenbeck et al. ³³	13-item Prostate Cancer Index (EPIC)	Primary	No	Yes	No	No	No	Yes	Yes	Not applicable
Huguenin et al. ³⁴	EORTC QLQ-C30	Secondary	No	No	No	No	No	No	Yes	No
Huguenin et al. ³⁵	EORTC QLQ-C30	Secondary	No	No	No	No	No	No	Yes	No
Hurria et al. ³⁶	CGA developed incorporating OARS IADL scale, KPS (physician and self reported), BOMC, HADS, MOS Activity Limitations Measure (ALM) and Social Support Survey (SSS)	Primary	No	Yes	Yes	No	Yes	Yes	Yes	Not applicable
Langer et al. ³⁷	FACT-L	Secondary	No	No	No	No	Yes	Yes	Yes	Not applicable
Maione et al. ³⁸	EORTC QLQ-C30, ADL, IADL	Secondary	No	No	No	No	No	No	No	Not applicable
Mantovani et al. ³⁹	Spitzer QL index, Functional Living index-cancer	Primary	No	No	No	No	No	Yes	Yes	Part
Merli et al. ⁴⁰	EORTC QLQ-C30	Primary	No	Yes	Part	Part	Yes	Yes	Yes	Yes
Mohile et al. ⁴¹	VES-13 compared with validated CGA (including ADL, RAND MOS Social support scale and CALGB comorbidity scale)	Primary	No	No	No	No	Yes	Yes	Yes	Not applicable
Presant et al. ⁴²	Geriatric Oncology Module and IADL	Secondary	No	Yes	Part	No	Yes	Yes	No	Yes
Rao et al. ⁴³	SF-36 ADL Scale PPT	Primary	No	No	Part	Part	Yes	No	No	Yes
Rogers et al. ⁴⁴	SF-36, University of Washington Head and Neck Questionnaire (UW-QOL)	Primary	Yes	Yes	Part	No	No	Yes	Yes	Yes
Sullivan et al. ⁴⁵	EORTC QLQ-C30 and FACT-Prostate	Primary	No	Yes	Part	No	Yes	Yes	Yes	Yes
Thome et al. ⁴⁶	IADL scale SF-12 EORTC QLQ-C30	Primary	Yes	Yes	Yes	Part	Yes	Yes	Yes	Not applicable
Vansteenkiste et al. ⁴⁷	Visual analogue scales and patient diaries	Secondary	No	No	No	No	No	Yes	Yes	Yes
Wallace ⁴⁸	University of California Los Angeles Prostate Cancer Index (UCLA-PCI) and quality of life index	Secondary	Yes	Yes	Yes	No	Yes	Yes	Yes	Not applicable
Wu et al. ⁴⁹	Spitzer QL index	Not stated	No	No	Yes	No	No	Yes	No	Not applicable
Abbreviations are defined in the source references.										

There is considerable current interest in the treatment of cancer in the elderly.² Health-related quality of life (HRQOL) assessment in this patient group can complement the physician-based comprehensive geriatric assessment (CGA),² which is designed to assess the fitness for treatment, rather than the outcome of treatment. Outcome data incorporating HRQOL assessment are important to guide treatment decisions, and may require new measurement tools to capture the relevant data.

Although there have been previous reviews which have considered QOL as an outcome in the elderly patient,^{3–7} there has been relatively little attempt to assess the performance of existing HRQOL instruments in this specific demographic group. There is little evidence that current instruments have considered the specific needs and concerns of older people in their design, development and validation. A review across a wide range of older patient populations found that many established generic instruments are predominantly focused on physical functioning⁵ and may not reflect the complexity of the cancer experience in this population.⁸ There is some evidence that QOL in older people is affected less by the changes in physical, mental or social health than that in younger people.⁹ However, there is contradictory evidence on whether older people with cancer have better or worse QOL when compared to younger cancer patients¹⁰ and the general population of older people.¹¹ When specific evaluation of HRQOL instruments has occurred, instruments such as the EQOL-5D and SF-36 have demonstrated a heavy response burden and increased requirement for interview administration with advancing age.¹² In instruments specifically designed for cancer patient populations, poor compliance has also been demonstrated¹³ and there is a need to take age into account when interpreting data.¹⁴ One reason for this may be that in the development and validation of these instruments, little consideration was given to the distinctive needs and concerns of older people.

In order to provide a reasoned assessment of available tools for the investigation of HRQOL in older cancer patients, we have conducted a systematic review of the use of patient-reported HRQOL assessments in studies specifically addressing elderly cancer patients and have documented HRQOL instruments which have been specifically validated for use in this patient population.

2. Patients and methods

2.1. Literature search

We searched five databases (Medline, Embase, CINAHL, ISI Web of Knowledge, Cochrane) from January 1995 to April 2007, and 3 national (UK) trials registers. Search terms were refined through an initial scoping exercise¹⁵ using search terms relating to cancer (neoplasm, advanced cancer, palliative) in combination with elderly (aged, aged 80 and over, old*), health-related quality of life (QOL, subjective health status, patient based outcome) and assessment (measurement, instrument, questionnaire). Two reviewers (DF and SH or JG) screened abstracts and excluded citations which did not meet our inclusion criteria. Any disagreements were resolved by a

third reviewer (SG). Both sets of reviewers independently assessed all retrieved full papers for inclusion.

2.2. Inclusion and exclusion criteria

Our definition of a HRQOL assessment tool was a patient-reported outcome measure (PROM) which covers domain(s) of relevance to HRQOL, as identified through the initial scoping exercise.¹⁵ We defined 'older' as a person aged 65 years and above.¹⁶ Only studies which reported a total population aged 65 years and above or presented sufficient reporting of HRQOL data specific to a sub-population of patients aged 65 years and above were considered. We included all cancer diagnoses and interventions. Papers written in English were considered for inclusion; we excluded conference proceedings and abstracts. Papers that reported translation of an instrument were excluded. We also excluded phase II clinical trials in order to optimise the selection of studies with HRQOL as a primary objective and to limit studies with small samples.

2.3. Data extraction and quality assessment

Selected studies were primarily evaluated on the quality of HRQOL reporting and methodology rather than overall study quality. Five categories were compiled: patient population (including definition of older age group), study design (including whether QOL was a primary end-point), QOL instrument utilised (including domains covered), methodology of QOL assessment and statistical analysis. We employed the minimum data checklist developed by Efficace et al.¹⁷ to record methodology. Due to the lack of a gold standard at the time to evaluate the HRQOL analysis performed, we recorded whether tests of statistical significance, differences between treatment groups, clinical significance and discussion of missing data had been presented.

To document HRQOL instruments that had been specifically validated for use in older people with cancer, we assessed each instrument using a checklist to assess the psychometric properties of patient-reported outcome measures.¹⁸ A descriptive synthesis of data was undertaken.

3. Results

The searches yielded 4684 hits, of which all available abstracts were reviewed. After duplicate citations were removed, 870 papers were accessed and subjected to review, of which 45 papers met the inclusion criteria. The main reason for exclusion was the lack of specific focus on reporting HRQOL in older people in the analysis of the study findings. Twenty-seven studies were rejected because their definition of older people fell below our pre-specified criterion of aged 65 years and over.

3.1. The use of HRQOL instruments

Thirty-one studies reported HRQOL in older patients using one or more instrument (Table 1), as a primary or secondary outcome.^{19–49} A wide range of cancer diagnoses and treatment interventions were identified; the predominant focus

was on prostate, lung, breast and lymphoma patient populations. Only 13 (41%) reported HRQOL in older cancer patients within the context of a randomised controlled trial (RCT), with HRQOL a primary end-point in 5 studies. The number of patients recruited into studies varied from 74 patients³⁹ to 574 patients³⁷ for those papers reporting HRQOL as part of a RCT. The country with the largest number of studies was the United States of America (USA) ($n = 12$).

3.2. Age range of patients

Table 1 summarises the age ranges across the included studies, demonstrating the inconsistency of definitions of 'older' or an equivalent term in these specific cancer populations. Most studies focused on a population aged over 65 years; 7 studies reported extensive sub-group analysis, most of which compared those aged over 65 years with younger patients. Of studies that focused on older people only, the range of ages was variable, with the oldest patient included aged 89 years.²⁷ There was a dearth of information relating to HRQOL in the 'oldest-old' (aged 85 years or above), with only 7 studies reporting the inclusion of this age band in their range. Only 1 study reported a comparison of HRQOL between the youngest old and the oldest old age bands (e.g. aged 65–74 versus >85 years).

3.3. Measurement and analysis of HRQOL

Of the 31 studies selected for review, only 4 papers provided a definition for HRQOL; whilst 17 attempted to justify the use of their chosen instrument. The usual reason for instrument choice was for its psychometric properties ($n = 12$). No study presented a case for choice based on the specific needs and concerns of older people with cancer.

The type of PROMs used in the studies is reported in Table 2. In the studies published prior to 2004, the most reported approach was the use of a purely cancer-specific HRQOL assessment system (10/17). In contrast, 10/14 studies published from 2004 onwards also employed generic (i.e. non-cancer) assessment approaches, developed in general 'elderly' populations. The EORTC QLQ-C30 was the most frequently reported PROM across the whole review period (12/31 studies), whilst disease-site specific modules were used in 11 studies. Many papers reported a wide range of instruments and HRQOL domains, often at multiple assessment points.

The psychometric properties of selected instruments were fully reported by only 6 studies. There was little evidence to support the adequacy of domains covered or whether issues of cultural validity were considered (Table 2). Twenty-three studies reported the mode of PROM administration with most also reporting compliance and timing of assessment, where

Table 3 – Methods of analysis and presentation of outcome measures and results

Authors	Test of statistical significance applied	Difference between treatment/control group reported (RCT only)	Clinical significance addressed	Presentation of results	Missing data documented
Allal et al. ¹⁹	Yes	Not applicable	No	Yes	No
Aapro et al. ²⁰	Yes	Not applicable	Yes	Yes	Yes
Blazeby et al. ²¹	Part	Not applicable	No	Yes	No
Bujit et al. ²²	Yes	Yes	Yes	Yes	Yes
Chen et al. ²³	Yes	Not applicable	Yes	Yes	No
Crivellari et al. ²⁴	Yes	No	No	No	No
De Haes et al. ²⁵	Yes	Yes	No	Yes	No
Demark-Wahnefried et al. ²⁶	Part	Yes	Yes	Yes	No
Diaz de Liano et al. ²⁷	Part	Not applicable	No	Part	No
Elderly Lung Cancer Group ²⁸	Yes	Yes	Yes	Yes	Yes
Esbensen et al. ²⁹	Yes	Not applicable	No	Yes	No
Giroto et al. ³⁰	No	Not applicable	No	Part	No
Guner et al. ³¹	Yes	Not applicable	No	Yes	No
Hoffman et al. ³²	Yes	Yes	No	Yes	Yes
Hollenbeck et al. ³³	No	Not applicable	No	Part	No
Huguenin et al. ³⁴	No	Not applicable	No	Part	No
Huguenin et al. ³⁵	Yes	Not applicable	No	Yes	No
Hurria et al. ³⁶	No	Not applicable	No	No	Yes
Langer et al. ³⁷	Yes	No	No	Yes	Yes
Maione et al. ³⁸	Yes	Yes	No	Yes	No
Mantovani et al. ³⁹	Part	No	No	No	No
Merli et al. ⁴⁰	Yes	No	No	Yes	Part
Mohile et al. ⁴¹	Yes	Not applicable	No	Yes	No
Presant et al. ⁴²	No	No	No	Part	No
Rao et al. ⁴³	Yes	Yes	No	Yes	Yes
Rogers et al. ⁴⁴	Yes	Not applicable	Yes	Yes	Part
Sullivan et al. ⁴⁵	Yes	Not applicable	No	Yes	Part
Thome et al. ⁴⁶	Yes	Not applicable	No	Yes	Yes
Vansteenkiste et al. ⁴⁷	Part	No	No	Part	No
Wallace et al. ⁴⁸	Yes	Not applicable	No	Yes	No
Wu et al. ⁴⁹	Yes	Not applicable	No	No	No

Table 4 – Validation of patient reported outcome measures in older patients with cancer

Author and year	Country	Instrument	Sample characteristics	Reliability	Validity	Responsiveness	Precision	Acceptability	Authors' conclusions
Dale et al. ⁵⁰	USA	HRQOL questionnaire for patients with prostate cancer Dimensions covered: Daily living and relevant symptoms	150 patients –mean age 70 years Sub Group Analysis (SGA) presented <60 (8%); 60–64 (23%); 65–69 (23%); 60–74 (19%); 75–79 (17%) 80+ (10%)	Presented for total sample. Cronbach's alpha between 0.61 for impotence and 0.95 for sexual interest/satisfaction. Inter-scale correlations between 0.39 and 0.66	Factor analysis high for each dimension. Discriminant	Not assessed	Not assessed	Not assessed	A suitable tool for assessing HRQOL in three distinct dimensions for patients undergoing radiotherapy for prostate cancer
Di Mauro et al. ⁵¹	Italy	Interviewer based multidimensional assessment including ADL IADL and GDS	108 mixed cancer patients mean aged 71.4 (SD 5.5) years range 65–83. Control group 25 elderly patients without malignancy	Not assessed	Oncology patients' performance status correlated with ADL and IADL scores. Increased psychological vulnerability seen in oncology patients	Not assessed	Not assessed	Not assessed	Improvement in QOL should be principal goal of any intervention in the elderly cancer patient
Hamm-erlid and Taft ⁵²	Sweden	EORTC QLQ-C30 and QLQ-H and N35 + SF-36	135 Head and Neck Cancer survivors compared to general population norms SGA presented for SF-36 <65 years n = 73 > 65 years n = 56	Not assessed	Patients >65 years scored worse than population norm on 5/8 scales of SF-36 but only role, physical and social functioning significant QLQ-C30 score compared only to age group of 60–69	Not assessed	Not assessed	Not assessed	Factors relating to age appear to have a bearing on reported health status
Hurria et al. ⁵³	USA	CGA	Measure administered to 43 patients (Mean age = 74 Range = 65–87 year) with breast, lung or colorectal carcinoma or lymphoma, referred for chemotherapy	Individual components analysed: IADL subscale 5-week test-retest correlation 0.71 KPS (physician report) ratings: Pearson correlation of 0.69 ($p < 0.001$) BOMC Test-retest reliability Spearman rank correlation = 0.96 MOS ALM and SSS Cronbach's alpha coefficients = 0.77 and >0.90	Individual components show high validity. Correlation coefficients amongst the OARS IADL, physician-rated KPS and patient-rated KPS range from 0.52 to 0.67	Not assessed	Selection bias for healthier elderly patients (recruitment of those referred for chemotherapy). Relatively few patients with deficits severe enough to be detected by the tools used	Mean time to complete CGA = 27 min. 78% completed assessment without assistance. 83% said it was easy to understand, 90% were satisfied with the length. None found any items distressing. No association between age and ability to complete assessment without help	A brief but comprehensive CGA that is acceptable to patients and suitable for further trials of its reliability and validity
Ingram et al. ⁵⁴	USA	CGA incorporating the Gero-Oncology QOL assessment EORTC QLQ-C30, HADS, MOS Social support Scale, OARS IADL scale and exercise scale and Systems of Belief Inventory (SOBI)	261 male mixed cancer patients attending out-patient setting. 156 patients included in analysis Mean age 68 years, SGA performed. <65 year, n = 51, 65–74 year, n = 65 > 74 years, n = 38	Not assessed	Discriminant: No differences across age groups for each scale of the QLQ-C30 or HADS score. Patients <75 years had highest MOS scores and score higher on social support of SOBI ($p = 0.03$)	Not assessed	Not assessed	76% response rate noted	CGA can be conducted in an older out-patients community

Mandleblatt et al. ⁵⁵	USA	Measures of illness burden including physical function scale and global health scale of the SF-36	Aged 67 years and over (n = 718)	Not assessed	Discriminant: Women with higher scores more likely to receive breast conserving surgery and radiotherapy. Physical function score significantly lower with chemotherapy treatment	Not assessed	Not assessed	Not assessed	Although several measures of illness burden are associated with breast cancer therapy each measure only accounted for a small amount of variance. Further work is needed to develop and validate measures that are feasible, comprehensive and relevant
Monfardini et al. ⁵⁶	Italy	Interviewer administered multi-dimensional questionnaire (MACE) including IADL scale, short-form GDS + SIP	30 patients aged 65 years and above mean age 70.2	Inter-rater reliability: Kappa scores ranged 0.1–1.0 for each item in MACE. Test–retest reliability: Kappa values of 0–1.0. Internal consistency: Cronbach's alpha scores 0.42–0.94	Concurrent validity: Disability, cognitive status, depressive symptoms and number of days spent ill in bed sick correlated well with global, physical and social SIP scores	Not assessed	Not assessed	Mean time to administer MACE = 27.4 (SD 7.6, range 20–45) min	MACE is a clinical research tool which is structured, feasible and reliable to assess functional status
Over-cash et al. ⁵⁷	USA	FACT-G	Mixed cancer site patients aged 65 year and above attending out-patient Senior Adult Oncology Programme (n = 85) or community dwelling elderly without cancer (n = 27) Mean age 75 (65–90) year	Cronbach's alpha between 0.60 for emotional well-being to 0.85 for functional well-being scales, and 0.86 for total Fact G. Scores consistent with scores from original FACT validation study	Concurrent validity: (assessed with SF-36): Good correlations between total and sub-scores except for vitality on SF-36. Mean total scores amongst cancer patients 81.7 (SD 16.2) comparable to normative data mean score of 79.1 (15.4). Discriminant: Total FACT G scores unable to distinguish between those receiving and not receiving chemotherapy. Social well-being discriminates those with/without metastatic disease (p = 0.02). Total scores discriminated between those with cancer and without (p = 0.002)	Not assessed	Floor effects noted in relationship with medical doctor scale	Not assessed	The FACT-G is a valid and reliable instrument for use in older patients with cancer
Presant et al. ⁴¹	USA	Geriatric Oncology Module including three 5-point scales assessing pain, global QOL and functioning. IADL	26 patients aged 65 or over receiving chemotherapy for recurrent or metastatic cancer. Median (range) 75 (65–87) year	300 patients completed the measure; results compared with scale records. Consistency = >90%. (Descriptive analysis only)	Not assessed	Sensitivity analysis: Response rates showed some variance depending on the definition used. No statistical analysis	Not assessed	Evaluated by semi-structured interviews. Rates of evaluable responses compared: pain-83%; energy – 96%; QOL-91%; Longer IADL form – 52%	This GOM may be useful in the assessment of specific chemo-therapeutic interventions in elderly patients with cancer in community oncology practices

(continued on next page)

Table 4 – continued

Author and year	Country	Instrument	Sample characteristics	Reliability	Validity	Responsiveness	Precision	Acceptability	Authors' conclusions
Rao et al. ⁴²	USA	HR-QOL, Health Service Utilisation, Activities of Daily Living, Physical Performance	Secondary subset analysis from randomised factorial trial. 99 hospitalised patients aged 65 or over	PPT validated for the elderly. ADL scale not assessed	PPT validated for the elderly. SF-36 and ADL scale not assessed. Researchers unaware of SF-36 validity in assessing elderly cancer patients	Not assessed	Not assessed	Not assessed	Geriatric inpatient care specifically targeted to the elderly cancer patient may improve QOL
Repetto et al. ⁵⁸	Italy	CGA in elderly cancer patients including GDS, ADL, CGA functional scale (interviewer administrated)	363 mixed patients Median (range) 72.9 (65–92) year. SGA presented 65–74 years (n = 248) 75–84 years (n = 96) 85 + years (n = 19)	Not assessed	No significant differences in GDS and functional scores stratified by age groups	Not assessed	Not assessed	Not assessed	The CGA adds substantial information on the functional assessment of elderly cancer patients but longitudinal assessment required
Ringdal et al. ⁵⁹	Norway	EORTC QLQ-C30	1956 patients from seven mixed cancer samples <64 years n = 891 65 + years n = 883	Only minor variations seen in scale statistics (alpha coefficient) between two age groups. Violations noted in depression item	All scales exhibited satisfactory convergent and discriminant validity apart from role and cognitive functioning	Not assessed	Not assessed	Not assessed	Some refinement may be required to QLQ-C30. Mokken model well suited to examine the generalisability of HRQOL scales across sub-populations
Salmon et al. ⁶⁰	UK	Life Evaluation Questionnaire (LEQ) + RSCL and McAdam and Smith Scale	200 mixed advanced cancer patients. SGA presented <50 years (n = 33) 50–65 years (n = 89) > 65 years (n = 76)	Not age specific	Factor analysis on whole sample. Discriminant: significant difference in appreciation of life and resentment of LEQ comparing younger versus older patients No difference seen in RSCL	Not assessed	Floor effects demonstrated in Mac Adam and Smith Scales	Not assessed but LEQ derived from in-depth patient interviews	LEQ detect age effects – questionnaire can evaluate psychological needs of people with incurable cancer which are neglected by existing instruments
Tchen et al. ⁶¹	France	SF-20 and RSCL	89 patients aged 65 years and over with NHL. median (range) 74 (65–86) year	Internal consistency by Cronbach's alpha. SF-20: Physical 0.84 Role 0.86 Mental health 0.78 Health perception 0.84 RSCL Psychological 0.76 Pain 0.83 Fatigue 0.69 GI 0.60	Content validity: Full range of possible scores observed. Construct validity: Factor analysis performed using PCA; 2 factors extracted for each questionnaire explains 51% variance in SF-20 and 41% in RSCL Convergent validity: SF-20 items all significantly correlated. Item-scale discrimination observed for all items. RSCL items more independent	Not assessed	Time to complete 20 (10–>60) min. Most patients able to complete without assistance and welcome opportunity to report their experience. Frequency of contradiction between items assessed	No effect noted but RSCL physical and GI scores quite skewed towards healthy range	The data support use of a generic and specific questionnaire to assess QOL. QOL information can be obtained for elderly patients

relevant. However, important information regarding the number of patients completing baseline assessments and missing data at follow-up was not available in 23/31 studies reporting follow-up analysis (Table 3). The statistical analysis of HRQOL was variable, with few studies showing robust design (Table 3). In five studies, there was only descriptive presentation of data. Of the 13 RCTs, only 3 reported sufficient power to detect differences in HRQOL, and where tests of statistical significance had been undertaken, only 6 studies attempted to consider the clinical importance of findings. Of specific importance to our review, important issues to the choice of instrument in older people were not considered. For example, there was a lack of information on whether the instrument required adaptation (e.g. for those with sight difficulties), or in the cases where several instruments had been used, whether this was a burden to patients.

3.4. Validation of PROM in older patients with cancer

The second objective of our review was to examine the published evidence of the validation of instruments for use in older people. Fourteen papers met the review inclusion criteria^{50–63} (Table 4). There was a lack of comprehensive evidence on the psychometric properties of identified instruments, with no paper providing evidence of all criteria described by Fitzpatrick et al.¹⁸ on reliability, validity, responsiveness to change, applicability, precision and feasibility. Generic instruments demonstrated lack of precision and gave little information on the clinical responsiveness to change. Cancer-specific instruments such as the EORTC QLQ-C30 and FACT-G demonstrated clinical responsiveness to change along with some evidence of reliability and validity. The recent studies on the CGA as an approach to incorporate HRQOL assessment demonstrate early evidence of value in routine clinical practice and decision making.

However, the focus of reports of the use of the CGA has often been on prognosis and choice of treatment.¹⁰ Only one study⁶² specifically reported gathering prior in-depth information on older people's perceptions of HRQOL in order to inform the design or adaptation of the selected assessment approach. The majority of studies that reported any validation took an existing instrument and tested its performance on a population of older people. Little attempt was made to consider factors (e.g. education level, frailty) which may be important in assessing the usefulness of a HRQOL instrument in an older population.

4. Discussion

4.1. Main findings

The main aim of our review was to document the use of HRQOL in studies specifically reporting elderly cancer patients. Despite an increase in papers reporting HRQOL exclusively in older cancer patients, there remain some serious deficiencies in the quality of these reports, with conceptual, methodological and practical limitations identified. The failure to perform or refer to the validation of HRQOL measures specifically for older people suggests that many authors have simply not considered this aspect of their use.

The first important observation is the variation in definitions of the elderly population. For the purpose of this review, we defined the older person as aged 65 years or more, based upon the evidence from cancer trials.¹⁷ However, this can be considered an arbitrary cut-off. Our review found little comparison of HRQOL between the youngest old (65–75 or 80) and the oldest old (>75 or >80), therefore preventing an assessment of whether current instruments are suitable across the whole age range of elderly patients.

Another important observation is the lack of follow-up of the reported HRQOL data which may be due to the research questions asked in the individual studies. For example, the studies included in this review predominantly focused on the acute treatment phase, but many older people will live with cancer as a chronic illness,⁶⁴ alongside other biological, psychological and social consequences of ageing. Therefore, the long-term effects of cancer treatment and the interplay of other factors in relation to ageing upon HRQOL need careful assessment.

Similar to other reviews,^{17,63–69} we have demonstrated the variable quality in the analysis and interpretation of HRQOL data. One particular concern was the presentation of missing data, particularly in ascertaining whether data were missing at random. Information on whether research subjects complete instruments over time is critical to the quality of data derived from studies.⁶⁷

In contrast to other systematic reviews, we present a quality profile of studies. This profile is based on the strengths of the minimum checklist,¹⁷ but we have not attempted to assign scores, as our review includes reports that are very disparate in terms of population, research questions, study design and instruments reported. This descriptive approach enabled us to use the research team's experience of HRQOL design and validation to evaluate the importance to the reliability and validity of the PROM of the conceptual underpinnings of HRQOL (e.g. whether older people's perceptions of HRQOL were fully considered). All studies provided descriptions of how their instruments were assessed for reliability, but there were still several flaws in their methods. For example, two of the studies^{20,31} that looked at people aged both over and under 65 years presented the validity of their measures only in relation to the total sample. This means that it is not known whether the measures would be reliable when applied exclusively to older people with cancer. Others either assessed only some of the scales used or relied on the previous demonstrations of reliability in other medical populations. Again, this means it is difficult to ascertain how appropriate the PROMs are for older people with cancer.

4.2. The role of HRQOL in CGA

There is little doubt about the value and contribution made by CGA in assessing fitness for treatment in elderly cancer patients, and HRQOL assessment can make an important contribution alongside CGA by considering the wider impact of cancer and its treatment on an older person's life.⁷ The incorporation of HRQOL instruments in the CGA.⁵³ is a recent development and further work is needed to explore the value of this approach. The joint efforts of the EORTC Quality of Life Group and Cancer in the Elderly Task Force to develop HRQOL assessments specific for elderly cancer patients will contrib-

ute to the growing demand for this important area of geriatric oncology.⁶⁸

4.3. Limitations of the review

One of the main difficulties arose because we chose a wide search strategy to enhance sensitivity. This resulted in a large number of abstracts and papers related to HRQOL in older cancer patients to be reviewed for eligibility. We excluded studies that dealt with non-cancer patients in order to limit our findings to the cancer field. Our findings may have been affected by our not having pursued authors of individual studies for the clarification of points related to study population or methodology. Our decision to exclude conference abstracts and phase II studies may have missed important studies which are yet to be published in full. Nevertheless, we believe that this review provides an important assessment for the current status of published methods of HRQOL reporting in older cancer patient populations.

A second limitation is that we only included those studies that had at least a substantial element of HRQOL reporting focused on patients aged 65 years and over. This led us to exclude a large number of studies which combined data from older and younger people. Some of these studies may have provided important information to inform our review. Nevertheless, our hypothesis was that elderly cancer patients constitute a distinct population whose needs and concerns may be different compared to younger patients. There is now a need for further investigation into the complex interplay of ageing and cancer on patient interpretations of HRQOL. Until such information is available, we suggest that it would be inappropriate for any existing instrument to be simply applied to an elderly population without age-specific validation.

4.4. Assessing HRQOL in elderly people with cancer

Hjermstad et al.¹⁴ illustrated the specific nature of HRQOL in older patients by comparing older cancer patients' observed QOL scores with expected scores based on age equivalence calculated from a reference population. The two scores were significantly different, showing that age must be taken into consideration when interpreting HRQOL data for cancer patients. The context of the older person's cancer experience must be also taken into account, as an older person may have different expectations when compared to younger people.⁶⁹ In addition, expectations may change as experiences fluctuate over the course of treatment. This phenomenon, known as a 'response shift', should be taken into account when measuring QOL, as people may report similar levels of QOL even if their health has deteriorated.⁷⁰ This effect may be greater in older people as they may be more used to having to adapt to changes in health in order to successfully cope with ageing. For example, Bowman et al.⁷¹ reported that older patients with cancer appraised their experience as less stressful than younger patients. The importance of cultural aspects of ageing and cancer may also be important considerations if purporting to assess HRQOL across different languages and countries.

Although previous reviews have provided useful information on how HRQOL can be measured and have identified a range of challenges in this specific population,^{4–7,72–75} there

is an urgent need to ensure that the perspectives of older people themselves are considered. Our systematic review has demonstrated that this has not yet been achieved. Individual expectations have important bearings for any attempt to adapt or design an age-specific instrument for use in cancer trials and studies. As well as the requirement to meet established standards for instrument development and validation, researchers and clinicians should ensure that careful consideration is given to the perceptions of HRQOL in older people at different age points and also ensure that the need for such an 'elderly-specific HRQOL instrument' is justified by demonstrating what aspects of HRQOL are important to older people and different to younger patients.

4.5. Conclusions

There are a growing number of studies and reviews which have reported HRQOL specifically in elderly cancer patient populations, but our review highlights a number of conceptual, methodological and practical shortcomings. The future challenge is to improve HRQOL assessment in the design of trials and studies involving older patients. It is of paramount importance to ensure that the needs and concerns of older people are integrated into a HRQOL assessment which is appropriate, valid and reliable, and provides clinically important information on HRQOL outcomes in older patients with cancer.

Authors contributions

Conception and design: Deborah Fitzsimmons, Colin Johnson, Steve George.

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Data analysis and interpretation: Deborah Fitzsimmons, Jacqueline Gilbert, Sheila Hawker, Steve George, Matti Aapro and Colin Johnson.

Comment and discussion of data: All authors.

Manuscript writing: Deborah Fitzsimmons, Colin Johnson, Jacqueline Gilbert

Final approval of manuscript: all authors.

Conflict of interest statement

None declared.

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