Sexual Morbidity Assessment in Gyne-Oncology Follow-Up: Development of the Sexual Well-Being After Cervical or Endometrial Cancer (SWELL-CE) Patient-Reported Outcome Measure

Isabel Duncan White, PhD,¹ Alan Tennant, PhD,² and Cath Taylor, PhD³

ABSTRACT

Background: Clinical assessment and management of sexual difficulties after gynecological cancer remain a neglected aspect of women's rehabilitation.

Aim: To develop and validate a patient-reported outcome measure of sexual well-being for women experiencing sexual consequences of cervical and endometrial cancer treatment for use in routine follow-up.

Methods: This is a sequential mixed method study comprising (i) in-depth qualitative interviews (n=21 of 118) to generate items regarding sexual consequences of cervical or endometrial cancer and treatment; (ii) questionnaire construction with 51 core items (all respondents) and 4 subsections (18–58 items), depending on the relationship status and whether or not participants were sexually active (SA/NSA); (iii) item refinement following cognitive debriefing (n=13 of 21); (iv) validation of resultant items via postal survey (n=788 women) and Rasch analysis; and (v) creation of brief (14-item) clinical screener. Women attending routine follow-up (3 months to 5 years) at 6 English cancer centers and members of 3 UK cancer patient websites, who met the study inclusion criteria, were invited to participate.

Outcomes: The primary outcome of this study was the construction and initial psychometric testing of SWELL-CE short and long form versions.

Results: 21 women participated in interviews and 250 of 788 (32%) returned the postal survey (T1). 110 draft items were evaluated using cognitive testing (n=13) to refine instrument design and test face validity, comprehension, and acceptability. Exploratory factor analysis of survey data (n=250) produced an initial 6 domain structure as a guidance for the Rasch analysis. Subsequent Rasch analysis yielded a 3 domain structure: physical sexual function, sexual and relationship concerns, and sexual desire and sexual self-esteem, each satisfying Rasch model requirements within their respective SA (item pool =59) and NSA (item pool =53) categories, including the absence of local response dependency and all showing strict unidimensionality. The 3 subscales demonstrated good psychometric properties, external validity, and test-retest reliability. A valid Rasch short form of 14 items was created from the larger item pool.

Clinical Implications: This PROM may assist clinicians to improve identification, discussion, and management of women who could benefit from sexual rehabilitation.

Strengths & Limitations: Initial evaluation supports psychometric validity and reliability in the assessment of physical sexual function, sexual interest and sexual self-esteem, and sexual and relationship concerns in this study sample. However, given this study's modest response rate (32%, n=250), findings should be interpreted with caution. This PROM identifies sexual concerns in women who are sexually active or sexually non-active due to illness or treatment-associated sexual difficulties.

Conclusion: Sexual Well-being after Cervical or Endometrial Cancer is a novel and psychometrically valid sexual well-being measure for clinical assessment of female sexual difficulties after cervical or endometrial cancer treatment. **White ID, Tennant A, Taylor C, Sexual Morbidity Assessment in Gyne-Oncology Follow-Up: Development of the Sexual Well-Being After Cervical or Endometrial Cancer (SWELL-CE) Patient-Reported Outcome Measure. J Sex Med 2020;XX:XXX–XXX.**

Received March 13, 2020. Accepted June 25, 2020.

¹The Royal Marsden NHS Foundation Trust, Adult Psychological Support Service & Applied Health Research Group, London, UK;

²Leeds Institute of Rheumatic & Musculoskeletal Medicine, University of Leeds, Leeds, UK;

³School of Health Sciences, University of Surrey, Guildford, UK

Copyright © 2020, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.jsxm.2020.06.019>

Copyright © 2020, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

Key Words: Clinical Assessment; Sexual Well-Being; Cervical Cancer; Endometrial Cancer; Psychometric Evaluation; Patient-Reported Outcome Measure

INTRODUCTION

Despite improved survival rates for cervical and endometrial cancer, late treatment effects are under-recognized and reported in oncology follow-up.^{1–3} In many cancer centers, patient-clinician discussions about treatment-induced sexual concerns and the clinical use of patient-reported outcome measures (PROMS) to assess female sexual difficulties arising from cancer treatment remain infrequent.^{4–7} Physical treatment consequences include vaginal dryness, stenosis, shortening, bleeding, menopausal symptoms, urinary difficulties, bowel dysfunction, and infertility.^{8–10} Many women also experience negative psychological sequelae including anxiety, depression, fear of sexual pain, and altered femininity.^{4,5}

Treatment-induced changes in sexual function and well-being are important outcomes to measure from both a clinical and research perspective.^{3,4,11,12} However, if an assessment is performed to inform decisions about management and referral, it must be both psychometrically robust and without clinically important omissions.¹³ Furthermore, assessment content should incorporate contemporary definitions of female sexual (dys) function¹⁴ and sexual diversity, and capture physical, emotional, and relational elements of sexual well-being.¹⁵

A recent review of instruments that assess treatment-induced sexual difficulties among women with cervical or endometrial cancer included 2 quality of life (QOL) and 4 female sexual morbidity measures.¹³ Assessment of the quality of reporting (COnsensus-based Standards for the selection of health status Measurement INstruments checklist)¹⁶ revealed omission of measurement error (all 6 papers), responsiveness data (4 instruments), and criterion validity (3 instruments), and test-retest reliability reporting was inconsistent. Clinically, 5 instrument papers omitted at least 1 dimension of female sexual function, and only one explicitly measured distress associated with sexual changes.¹⁴ 4 papers included mediating treatment or illness effects (eg, vaginal changes, menopause, altered body image) and only one made explicit reference to solo or non-coital sexual expression and none had been validated for use in a non-heterosexual sample.

This review concluded that the Female Sexual Function Index is still the most robust research and clinical outcome measure for use in sexually active (SA) women treated for cervical or endometrial cancer.¹³ However, development of an instrument that can evaluate treatment-induced sexual difficulties and concerns in women who are infrequently/not sexually active (NSA) due to treatment consequences is still

required clinically to identify women in need of further support and sexual rehabilitation.^{12,13}

This article describes the development and validation of Sexual Well-being after Cervical or Endometrial Cancer (SWELL-CE), a new clinical PROM for SA and NSA women experiencing sexual difficulties of physical, emotional, or relational origin, after cervical or endometrial cancer and its treatment.

MATERIALS AND METHODS

This study is reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology cross-sectional study reporting guidelines.¹⁷

Patients

Participants were recruited from gynecology outpatient clinics at 4 English National Health Service cancer centers, 2 cancer units, and direct via 3 patient charity websites (Jo's Cervical Cancer Trust, Macmillan Cancer Support, and Womb Cancer UK) from 2011 to 2013. Women with a primary diagnosis of cervical or endometrial cancer, receiving routine medical follow-up from 3 months to 5 years post-treatment completion, were eligible to participate. Women were excluded from the study if they had limited understanding of English, a prognosis of less than 6 months, evidence of disease progression, were receiving treatment with palliative intent, or if their physical or emotional health was of concern to their treatment team.

Ethical approval was obtained from the London-Westminster Research Ethics Committee (Rec Ref: 10/H0802/50).

Design

The study design incorporated 4 stages (Figure 1).

Stages 1 and 2: Qualitative Interviews—Item Generation and Cognitive Debriefing

Instrument content was developed from semi-structured patient interviews and item statements derived from women's comments, often using their own words. This ensured instrument content (face) validity relevant to the target population and inclusion of issues considered important by women.¹⁸

The interview topic guide, derived from studies of sexual dysfunction after gynecological cancer and observational data from 33 gynecology follow-up consultations, explored women's

Figure 1. Outline of study stages. DASS-21 = Depression Anxiety Stress Scale; EFA = exploratory factor analysis; NSA = not sexually active; PSQ = Pelvic Symptoms Questionnaire; SA = sexually active; SVQ = Sexual Function Vaginal Changes Questionnaire; SWELL-CE = Sexual Well-being after Cervical or Endometrial Cancer; WEM = Warwick Edinburgh Mental Well-being Scale.

experience of sexual difficulties arising from their illness and treatment (please see [supplementary appendix 1](#) for further details).

Stage 1 transcripts were subjected to framework analysis.¹⁹ Following familiarization with the data and initial coding, data extracts were inserted into coding matrices (using Excel) which were examined to identify themes and sub-themes emergent from the data. Items generated from these themes and sub-themes fulfilled the following criteria:

- relevant to women experiencing treatment-associated sexual difficulties irrespective of relationship status or sexual orientation;
- relevant to women irrespective of current sexual activity (partnered/solo) or inactivity;
- used participants own words wherever possible;
- reflected a single idea and were unambiguous.

Cognitive Debriefing

Cognitive debriefing of the draft item set enabled participants to state their thought processes and observations about the questionnaire, as they answered individual items.²⁰ A structured interview schedule was used to ask participants about:

- appropriateness of questionnaire introduction and completion instructions;
- clarity of item wording and response format;
- omission identification;
- potentially offensive or embarrassing content; and
- overall ease of completion.

3 research interviewers discussed emergent themes and established a consensus regarding essential amendments to the draft instrument prior to production of the stage 3 survey.

Sampling

118 eligible women were invited to participate in stage 1 qualitative interviews. 21 women who participated in stage 1 interviews were also invited to participate in stage 2 cognitive debriefing interviews. Following written consent, most interviews took place in women's own homes or in an outpatient consultation room.

Stage 3: Postal Survey

The survey objective was to collect sufficient data from women in order to test the scaling properties of the item set by exploring the potential domains emerging via an exploratory factor analysis (EFA) and then, with this guidance, fitting the data to the Rasch model.

Survey Content

In addition to demographic details, draft items with binary "True"/"Not true" response options were included. Each participant was asked to complete a set of core items and 1 of 4 subsections depending on their relationship status and whether or not they were currently SA.

The questionnaire pack also included several comparator measures in order to examine the construct validity of the new scale. These included the Sexual Function Vaginal Changes Questionnaire (SVQ),²¹ Pelvic Symptoms Questionnaire (PSQ),^{22,23} Depression Anxiety Stress Scale (DASS-21),²⁴ and the Warwick Edinburgh Mental Well-being Scale (WEMWBS).²⁵ At the time of this study, the PSQ^{22,23} and SVQ²¹ were considered the best available PROMS for pelvic radiation and sexual morbidity assessment after gynecology radiotherapy, respectively.

Sample Size

As the number of items/domains was unknown at the study outset, a minimum sample size of 200 returned questionnaires was considered appropriate for EFA where only a crude structure was required prior to Rasch analysis.²⁶ Based on 30% survey completion rates derived from prior research,^{4,5} 788 Time 1 (T1) questionnaires were distributed.

Analytical Strategy

EFA was undertaken to identify the fewest domains that could adequately explain correlations between items.²⁶ This identified the potential dimensional structure of the item set suitable for subsequent Rasch analysis (a confirmatory procedure). The standardized root mean square residual was used as a guide to interpretation, with a value < 0.08 indicative of a working solution.²⁷ Thus, the EFA was used as an item screening procedure prior to Rasch analysis, where further post-hoc tests of unidimensionality would be implemented. Analysis was undertaken in MPlus (Muthén L.K. & Muthén B.O., Los Angeles, CA, USA) based upon a tetrachoric correlation matrix using the unweighted least squares estimation with a Promax rotation.²⁸

Rasch analysis is now widely used in the construction of PROMS.^{29,30} As Rasch analysis accommodates missing data points within the calibration process, the complete data set was used. Through an iterative process, it tests if data comply with requirements for a valid unidimensional scale where the raw score is a sufficient statistic, in this case for the level of sexual well-being. The Rasch model requires that an individual experiencing greater impact on sexual well-being would have a greater probability of affirming an item that reflects a higher impact. This was tested using the Chi-square test (which should be non-significant to indicate no deviation from the model expectations), and residual statistics for both persons and items should be in the range of ± 2.5 .

When developing a new scale from qualitative interviews it is not uncommon to find items which are similar. This breaches the local independence assumption, which means that the conditional association (ie, on the trait of sexual well-being) between 2 items should be zero. Residual correlations above 0.2 can indicate such a breach and thus potential redundancy in the item set.³¹ Unidimensionality was tested by grouping items based upon the loading of the first factor in the principal component of the residuals, and comparing estimates derived from these 2 sets of items. A t-test was undertaken for each respondent, comparing their estimates upon the 2 item sets, and no more than 5% of these estimates should be statistically different, or at least the lower binomial CI should fall below 5%.³² Finally, group invariance was tested through differential item functioning.³³ Group invariance was tested for age group, primary diagnosis, stage of disease (I, II, III, and IV), type of treatment (radiotherapy vs no radiotherapy), and time elapsed (months) post-treatment. That is, for example, *given the same level of sexual functioning*, there should be no difference in the probability of response to an item by group membership such as type of treatment.

When data are shown to fit the Rasch model, (i) the raw score is confirmed as a sufficient statistic and (ii) an interval scale transformation becomes available.³⁴ Rasch analysis was undertaken with the dichotomous Rasch model using RUMM2030 software (RUMM Laboratory, Perth, Australia).³⁵

Finally, a short-form screening instrument (SWELL-CE14) was developed from the full item set to be able to identify those patients who perceived that their treatment had led to problems with sexual functioning. Only those items which discriminated for a perceived problem were included in the item set. The data were again fit to the Rasch model, and sensitivity, specificity, and the positive and negative predictive values of the test calculated.

Once the new scales were derived from the Rasch analysis, construct validity was evaluated by assessing the correlation (Kendall's tau B) between SWELL-CE domains and the comparator measures. Known group validity was examined by differences in scores between subgroups of women that, based on

published literature and clinical practice, should theoretically differ in their levels of post-treatment sexual well-being.^{2,5,36,37}

Stage 4: Test-Retest Questionnaire

Participants returning a completed T1 questionnaire were asked if they would repeat the questionnaire 4 weeks later which, given the construct under investigation, was thought to offer a suitable stable period with minimum recall from the original questionnaire. The T2 survey contained an additional self-report item regarding whether there were factor(s) present in the past 4 weeks that could have impacted on sexual well-being to confirm stability. Mean scores for T1 and T2 responses were compared in women that confirmed that no factors that had an impact on stability had occurred, and the intraclass correlation coefficient (ICC (A) 2.1) was calculated.

RESULTS

Stage 1: Item Generation Qualitative Interviews

21 out of 118 (18%) eligible women aged between 30 and 70 years were interviewed: 11 received primary chemo-radiotherapy for cervical cancer, while 10 had radical hysterectomy, bilateral salpingo-oophorectomy, and adjuvant radiotherapy for endometrial cancer. Time post-treatment ranged from <12 months (n = 11) to 13–25 months (n = 10). 15 had a current partner and were SA. A total of 109 statements were derived from interview data.

Stage 2: Face and Content Validity: Cognitive Debriefing Interviews

Cognitive debriefing was undertaken with 13 out of 21 (62%) women who had participated in the stage 1 interviews. While women did not find the overall content of the instrument offensive or embarrassing, some considered specific items emotionally evocative. An additional 3 women who self-identified as lesbian or bisexual were purposively sampled to obtain feedback regarding content inclusivity regarding sexual orientation. This stage resulted in 5 amendments (Figure 1) and a final survey comprising 110 items.

Stage 3: Postal Survey

A total of 250 of 788 (32%) women completed the baseline survey (T1). Almost 2 in 5 (38%) were aged 50 years or less, 54% had a diagnosis of endometrial cancer, 62% were diagnosed at clinical stage 1, and 48% had received both surgery (hysterectomy + bilateral salpingo-oophorectomy) and pelvic radiotherapy (brachytherapy ± external beam radiotherapy). Just over four-fifth (82.7%) had a current partner, and almost 3 in 5 (59.2%) reported being currently SA. While 38% were premenopausal women, 61.2% were perimenopausal women.

Non-respondents comprised 538 women (68%), of whom 67 (12%) gave one or more reasons for refusal. The most common

reasons were no current partner (n = 23), NSA (n = 27), and older respondent or partner age (n = 13). Only 8 women refused participation due to sensitivity about sexual recovery as a topic.

EFA of the draft item set initially revealed 6 factors (standardized root mean square residual = 0.063), 5 of which were easily interpretable as “sexual concerns,” “physical sexual function,” “body image/femininity,” “sexual desire,” and “sexual fear,” reflecting key themes in prior qualitative analysis. The sixth factor contained a few cross-loading items.

Data were then entered into the Rasch model. Initially all domains misfit model expectations but after a modest iterative phase of removing items that had local dependency or misfit, 3 working Rasch domains emerged (Table 1).

The “sexual fear” and “body/image/femininity” domains were merged with the original “sexual desire” domain, as the former domains had relatively few remaining items and both conceptually and clinically these concepts were considered to directly impact upon sexual desire.

The final domains were *physical sexual function* (SA item pool = 18 items, NSA item pool = 16 items), *sexual and relationship concerns* (SA item pool = 16 items, NSA item pool = 17 items), and *sexual desire and sexual self-esteem* (SA item pool = 25 items, NSA item pool = 20 items).

Each domain satisfied Rasch model requirements within their respective SA and NSA categories, including the absence of local response dependency, and all items demonstrated strict unidimensionality (Table 1). Examples of items from each domain are provided in Table 2.

Levels of reliability were consistent with individual use (ie, $\alpha > 0.85$). Differential item functioning was largely absent, with just 3 items showing bias. Given the number of tests undertaken, this was deemed an acceptable level and no action was taken. Finally, a testlet-based bifactor solution was produced for a total score, the testlets being domain-based (ie, items from all 3 domains added together). This analysis indicated that 86% of the non-error variance in the total score was common, having shed 14% of unique variance, and consequently supporting a unidimensional latent estimate of the total score based upon this specific solution.

The data for the total score were reasonably targeted (Figure 2). Only 10% of women were at the floor of the scale, indicating no reported impact upon sexual well-being, and none were at the ceiling of the scale. Individual domains had different profiles; 16.8% of patients had no sexual and relationship concerns (ie, floor effect), 9.4% reported no physical sexual function problems, and 8.6% reported no impact on sexual desire or sexual self-esteem. Thus, 91.4% of women reported an adverse effect on sexual desire and sexual self-esteem, 90.6% reported an adverse effect on physical sexual function, and 83.2% of the women surveyed reported sexual and relationship

Table 1. Fit of data of the SWELL-CE scale to the Rasch measurement model

Analysis	Domain	Item residual		Person residual		Chi-square interaction			PSI		Unidimensionality		
		Mean	SD	Mean	SD	Value	DF	P	PSI α	PSI	% t-test	95% CI	
Sexually active													
1	Concerns	−0.0028	1.0816	−0.1674	0.7295	71.3	48	.016	0.59 0.87		7.6	4.3–10.8	
2	Physical	−0.3807	1.4170	−0.0860	0.7423	100.1	72	.016	0.77 0.93		4.6	1.4–7.8	
3	Desire	−0.1375	1.2713	−0.1739	0.8433	95.3	75	.057	0.83 0.93		6.8	3.8–9.8	
4	SWB †	−0.1385	0.8235	−0.4346	0.8929	11.5	12	.490	0.65 0.83		1.9	−2.3 to 6.0	
Sexually inactive													
5	Concerns	−0.1603	1.1287	−0.1438	0.7413	95.8	85	.198	0.52 0.83		5.2	2.0–8.5	
6	Physical	−0.2297	1.4286	−0.1321	0.7663	104.8	79	.028	0.71 0.88		1.7	−2.1 – 4.3	
7	Desire	−0.3281	0.9516	−0.1259	0.7477	71.2	80	.748	0.77 0.91		5.3	2.2–8.4	
8	SWB †	0.3010	0.22549	−0.1811	0.2692	5.8	6	.442	0.72 0.75		0.0	0.0–0.0	
Ideal values		0.0	1.0	0.0	1.0			>.05*	>0.7		<5.0	LCI <5.0	

DF = degrees of freedom; LCI = lower bound of the confidence interval; PSI = person separation index reliability; SWB = sexual well-being (total score); SWELL-CE = Sexual Well-being after Cervical or Endometrial Cancer.

*Bonferroni adjusted: † SWB is the testlet bifactor solution giving total score based upon first general "factor".

concerns. Among SA women, the concerns domain scores were found to vary according to age, with older women (>61 years) having less sexual and relationship concerns (F 7.03; $P = .001$). Physical domain scores (F 8.2; $P < .001$) varied, with older women reporting fewer problems in physical sexual function. In the case of the desire domain scores, the younger the woman, the greater was the negative impact on sexual desire and sexual self-esteem (F 4.3; $P = .015$). The exact same patterns were seen for those who were NSA.

SWELL-CE total scores also varied according to age for those that were SA: younger women reported better sexual well-being (F3.1; $P = .049$); however, age did not have an impact on total scores for those who were NSA.

Short Form

22 items were found to be sharply discriminating (>57% affirmation of an item for a reported perceived problem), and from these, after removal of local dependency and misfit, 14 items satisfied the Rasch model expectations. Item and person residuals were 0.955 and 0.801, respectively, and Chi-square value was 54.1 (degrees of freedom 56), $P = .547$, with alpha = 0.93, sensitivity = 90.9%, specificity = 84.7%, positive predictive value = 60.6%, and negative predictive value = 97.3%.

Convergent and Divergent Validity

Supplementary table 1 shows the correlations between the domain/total scores of the SWELL-CE and various comparator measures.

PSQ

There was a moderate positive correlation between the PSQ vagina domain and the SWELL-CE physical sexual function Rasch domain scores, particularly in the SA subgroup. However, the PSQ bladder and bowel domain scores were not correlated with SWELL-CE for the NSA subgroup and only weakly (positive) correlated for the SA subgroup.

SVQ

- There was a strong positive correlation between the SVQ vaginal changes and SWELL-CE physical (SA sample) domains. Given the relationship between physical sexual function and overall sexual satisfaction, there was also a strong correlation between the SVQ global sexual satisfaction and SWELL-CE physical domains for SA and NSA samples.
- There was a moderate positive correlation between the SVQ intimacy domain and SWELL-CE desire domains (SA sample).
- As hypothesized, a strong (positive) correlation between SVQ sexual functioning and SWELL-CE desire domain scores for SA women was found, but not for the NSA sample.

Table 2. Example of items from each instrument domain

Domain	Items
Sexual and relationship concerns	I am worried that if I have intercourse again it will bring my cancer back (SA/NSA) I find it hard to talk to my partner about changes in our relationship (SA/NSA) I do not know when it is ok to start having sex again (SA/NSA)
Physical sexual function	My vagina feels tight (SA) Intercourse is uncomfortable (SA) I am frightened to try to have intercourse (NSA)
Sexual desire and sexual self-esteem	Since my treatment I don't feel like having sex as often as before (SA) I do not feel like a woman anymore (SA/NSA) I don't feel as sexually attractive anymore (SA/NSA)

NSA = not sexually active; SA = sexually active.

(iv) There was a strong (positive) correlation between the SVQ global sexual satisfaction and SWELL-CE desire domain scores and a strong (positive) correlation between SVQ global sexual satisfaction and SWELL-CE concerns domain scores for both SA and NSA women.

DASS-21

As hypothesized, there was a moderate positive correlation for both SA and NSA subgroups between the DASS-21 and SWELL-CE total scores.

WEMWBS

As hypothesized, there was a weak to moderate negative correlation between the WEMWBS and SWELL-CE total scores for both SA and NSA subgroups.

Known Group Validity

As found clinically, and in published studies, younger (<60 years) premenopausal women with cervical cancer, treated by primary chemoradiotherapy, who were NSA at the time of study participation demonstrated higher (worse) mean domain scores across all 3 SWELL-CE domains (Table 3). While these group differences were not statistically significant for SA respondents, all mean Rasch domain scores demonstrated a trend in the same direction.

Furthermore, all 3 SWELL-CE domains discriminated between women with self-reported psychological comorbidities (low mood/depression and/or anxiety) and those without, among both SA and NSA respondents.

Test-Retest Reliability

Of 113 women who returned the T2 survey, 78 reported having stable sexual well-being over the past 3–4 weeks and had completed at least 80% of items. The intraclass correlation coefficients were 0.899 ($P < .001$), 0.917 ($P < .001$), and 0.852 ($P < .001$) for the physical, desire, and concerns domains, respectively. The mean Rasch scores for physical domain were 8.5 (SD 4.8) and 8.6 (SD 5.9) for T1 and T2, respectively, 7.6 (SD 5.7) and 7.8 (SD 5.4) for the desire domain, and 5.6 (SD 5.9) and 5.4 (SD 4.9) for the concerns domain. There was no significant difference between T1 and T2 domain Rasch scores, demonstrating excellent reliability over time.

DISCUSSION

The SWELL-CE is a novel and psychometrically valid sexual well-being PROM developed specifically for clinical assessment in women experiencing sexual difficulties arising from cervical or

Figure 2. SWELL-CE person-item threshold distribution. SWELL-CE = Sexual Well-being after Cervical or Endometrial Cancer.

Table 3. Known group comparisons across 3 domains of SWELL-CE for sexually active and non-active respondents (mean Rasch scores)

Attribute/status	Physical		Desire		Concerns	
	Active	Non-active	Active	Non-active	Active	Non-active
Age <60 years	9.9	13.9	8.5	12.8	6.3	10.0
Age ≥ 60 years	7.8	8.2	6.4	8.1	4.2	6.2
Premenopause	9.8	15.4	8.6	14.0	6.6	10.8
Postmenopause	8.7	10.1	7.2	9.6	4.8	7.6
Cervical	10.2	13.5	8.4	12.9	6.5	9.8
Endometrial	8.4	9.7	7.4	9.0	4.9	7.3
No previous sexual concerns*	8.8	10.8	7.5	10.2	5.5	7.8
Previous sexual concerns*	10.4	14.0	8.7	12.7	6.0	10.6
No physical comorbidities*	9.1	10.7	7.8	9.5	5.7	8.7
Physical comorbidities*	9.4	12.1	8.0	11.8	5.6	8.3
No psychological comorbidities*	8.5	10.4	7.0	9.5	5.1	7.8
Psychological comorbidities*	12.0	14.1	11.2	13.8	7.9	10.0

Contrasts are made vertically within sexually active and non-active status. Significant differences between Rasch mean scores are indicated by emboldened vertical pairs representing $P < .01$ (to account for multiple testing).

SWELL-CE = Sexual Well-being after Cervical or Endometrial Cancer.

*Pre-existing sexual, physical, and psychological comorbidities are self-reported in respondent demographic details and do not represent formal diagnostic categories.

endometrial cancer treatment. SWELL-CE convergent validity demonstrated relationships as hypothesized with selected comparator instruments, revealing moderate or strong positive domain score correlations where instruments were measuring similar or related concepts. The SWELL-CE also demonstrated good discriminant validity in differentiating between younger premenopausal women (cervical cancer), experiencing worse sexual well-being, and older postmenopausal women (endometrial cancer), particularly in the NSA subgroup. The SWELL-CE also discriminated between women with and without self-reported psychological comorbidities in both SA and NSA subgroups. This finding underlines the important contribution of emotional health to women's sexual well-being. Finally, test-retest reliability demonstrated excellent stability over time in all 3 domains for both the SA and NSA subgroups.

In contrast to some female sexual morbidity and QOL instruments, the domains and items of this instrument reflect all sexual response phases¹⁴ and extend beyond physical treatment effects to incorporate broader emotional (*altered femininity, sexual attractiveness, sexual anxiety*) and relational (*loss of intimacy, partner fears, sexual avoidance*) impacts on sexual well-being post-treatment.^{13–15} An instrument's ability to assess emotional and relationship aspects of sexual well-being is important clinically, particularly when irreversible anatomical or physiological changes (vaginal shortening, dryness) may require permanent adaptation of sexual behaviors and establishment of new norms, compared to the return to baseline sexual function commonly seen in non-organic sexual dysfunction. Another potential strength of the SWELL-CE is the use of dichotomous response options (“True” vs “Not true”), given the challenge some patients experience in completing more nuanced Likert scale response options found in many sexual and QOL questionnaires.¹³ Dichotomous response

options are associated with shorter completion times (important in clinical settings) and considered easier to use by older people and by those whose first language is not English.^{38,39} The SWELL-CE is methodologically robust and compliant with Food and Drug Administration guidelines on PROMS development⁴⁰ demonstrating strong face and content validity through derivation of its concepts, domains, and items from interviews with women experiencing disease and treatment impacts on sexual well-being and from published literature. Furthermore, the SWELL-CE has been scrutinized by women who self-identify as bisexual or lesbian to ensure this instrument is inclusive for women in both same sex and heterosexual partnerships. Finally, a key strength of this PROM, over many existing instruments, is that it identifies sexual concerns in both women who are SA or NSA due to illness or treatment-associated sexual difficulties. This is important clinically to identify women most in need of sexual rehabilitation.^{13,41}

There are several limitations to the study. While every attempt was made to recruit women from different ethnic and socioeconomic backgrounds, the majority of respondents (92%) were of white British descent. Similarly, regarding sexual diversity, 247 (98.8%) survey participants self-identified as heterosexual, 2 survey participants (0.8%) were bisexual, and no participant self-identified as lesbian in the stage 3 survey sample. This is comparable with UK Office for National Statistics data on sexual orientation,⁴² whereby 0.8% of the UK female population surveyed reported being bisexual and 0.7% lesbian/gay. Future psychometric testing of the SWELL-CE should aim to include women from ethnic minority backgrounds, those whose first language is not English, and women who self-identify as non-heterosexual to ensure the SWELL-CE is acceptable to the entire diversity of women affected.

With just 14 dichotomous items in the SWELL-CE14 short form, the power to detect multidimensionality was also low. The screening instrument was also based upon the patient's self-reported perceived problems, and thus a clinical validation will also need to be conducted in the future.

Most women reported adverse treatment effects on sexual desire and sexual self-esteem (91.4%), physical sexual function (90.6%), and sexual and relationship concerns (83.2%). The incidence of sexual difficulties in this survey is higher than the 30–63% after cervical cancer,⁴³ 67% (n = 688) of women experiencing long-term consequences >1 year after cervical cancer treatment,⁴⁴ or the 81% of endometrial patients experiencing sexual difficulties post-brachytherapy⁴⁵ cited previously. However, in light of this study's modest response rate (32%, n = 250) and selection bias in other sexual morbidity and QOL PROMS studies (high *sexuality* item non-response rates, inconsistently reported/low response rates), these findings should be interpreted with caution.^{21,46,47} Furthermore, SWELL-CE discriminant validity findings are considered exploratory at this stage of instrument development due to the number of potential confounding variables. Further analysis in a larger sample of women is required to enable a comprehensive examination of the moderating (interaction) effects of age, menopausal status, primary diagnosis, and treatment type upon these relationships.

Instrument Development: Next Steps

Clinical implementations of the 14-item short form (SWELL-CE14) and long form (SA/NSA) instrument versions are being evaluated in a feasibility study currently underway in gynecology follow-up clinics of 2 English cancer centers.

The study aims to pilot use and determine feasibility of the SWELL-CE14 (a brief screener) and SWELL-CE PROMS implementation to generate real-time patient self-report data that can inform clinical discussion and management decisions about sexual consequences of treatment for this group of women in gyne-oncology follow-up clinics.

This study explores the impact of implementation of these questionnaires on measurable clinical behaviors such as clinician enquiry/detection rates of sexual difficulties in routine follow-up consultations, together with rates and patterns of medical notes documentation and onward referral within/beyond the cancer center.

This study will also conduct further psychometric evaluation, including convergent validation of the new instruments against the Female Sexual Function Index⁴⁸ and new European Organisation for Research and Treatment of Cancer Sexual Health Questionnaire-22 sexual health module (recently completed phase 4 cross-cultural validation) as comparator instruments.¹⁵

Importantly, this study also evaluates feasibility and acceptability in the use of sexual morbidity PROMS in public health service gyne-oncology follow-up clinics where, understandably,

clinical emphasis is on disease surveillance and acute treatment toxicity. As many oncology colleagues lack confidence in discussing sexual morbidity with women, and are not usually familiar with female sexual morbidity PROMS emanating from sexual health/sexual medicine, this study also explores the content and utility of brief health professional training including local referral guidelines and sexual rehabilitation resource directory provision.

Assuming satisfactory demonstration of patient and clinician feasibility and acceptability, subsequent psychometric evaluation of the instrument's items and domains will include women treated for other types of gynecological or pelvic malignancies experiencing comparable treatment-induced sexual difficulties.

CONCLUSION

Initial evaluation of the SWELL-CE supports its psychometric validity and reliability in the assessment of physical sexual function, sexual interest and sexual self-esteem, and sexual and relationship concerns after cervical or endometrial cancer treatment.

Developed specifically for clinical use in both SA and NSA women after cervical or endometrial cancer, SWELL-CE and its short form screening version (SWELL-CE14) have the potential to assist clinicians to improve discussion, identification, and management of women who may benefit from sexual rehabilitation, the focus of a feasibility study currently underway.

ACKNOWLEDGMENTS

This post-doctoral research fellowship was funded by United Kingdom charities Remedi Rehabilitation Research and Macmillan Cancer Support; National Institute for Health Research Central Portfolio Management System (CPMS) Study ID 9620. The authors would like to thank the women for their willingness to take part in this study and study site collaborators for their assistance in data collection. The authors would also like to thank Jennifer Finnegan-John (Research Associate) for assistance in data acquisition and management and Dr Sam Norton and Dr Gill Gilworth (King's College London) for assistance with data analysis.

Corresponding Author: Isabel Duncan White, PhD, Adult Psychological Support Service & Applied Health Research Group, Royal Marsden NHS Foundation Trust, London, UK. Tel: +44 020 7811 8514; E-mail: drwhite@edinburghpractice.com or isabellawhite@btinternet.com.

Conflict of Interest: The authors report no conflicts of interest.

Funding: This work was supported by Remedi Rehabilitation Research and Macmillan Cancer Support UK charities. The study funders were not involved in any aspect of study design, conduct, report compilation, or subsequent publication.

STATEMENT OF AUTHORSHIP

Isabel Duncan White: Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Resources, Data Curation, Writing-Original Draft Preparation, Writing-Review & Editing, Visualization, Project Administration, Funding Acquisition; Alan Tennant: Conceptualization, Methodology, Validation, Formal Analysis, Resources, Writing-Original Draft Preparation, Writing-Review & Editing, Visualization, Supervision; Cath Taylor: Methodology, Validation, Formal Analysis, Resources, Data Curation, Writing-Review & Editing, Supervision, Project Administration.

REFERENCES

- Macmillan Cancer Support. Throwing light on the consequences of cancer and its treatment. London: Macmillan; 2013.
- Adams E, Boulton MG, Horne A, et al. The Effects of Pelvic Radiotherapy on Cancer Survivors: Symptom Profile, Psychological Morbidity and Quality of Life. *Clin Oncol* 2013; 26:10-17.
- Faithfull S, Lemanska A, Chen T. Patient-reported Outcome Measures in Radiotherapy: Clinical Advances and Research Opportunities in Measurement for Survivorship. *Clin Oncol* 2015;27:679-685.
- White ID, Allan H, Faithfull S. Assessment of treatment-induced female sexual morbidity in oncology: is this a part of routine medical follow-up after radical pelvic radiotherapy? *Br J Cancer* 2011;105:903-910.
- White ID, Faithfull S, Allan H. The re-construction of women's sexual lives after pelvic radiotherapy: A critique of social constructionist and biomedical perspectives on the study of female sexuality after cancer treatment. *Social Sci Med* 2013; 76:188-196.
- Chapman CH, Heath G, Fairchild P, et al. Gynecologic radiation oncology patients report unmet needs regarding sexual health communication with providers. *J Cancer Res Clin Oncol* 2019; 145:495-502.
- Gilbert A, Sebag-Montefiore D, Davidson S, et al. Use of patient-reported outcomes to measure symptoms and health related quality of life in the clinic. *Gynecol Oncol* 2015; 136:429-439.
- Maher EJ, Denton A. Survivorship, late effects and cancer of the cervix. *Clin Oncol* 2008;20:479-487.
- Incrocci L, Jensen P. Pelvic Radiotherapy and Sexual Function in Men and Women. *J Sex Med* 2013;10(suppl 1):53-64.
- Jensen PT, Froeding LP. Pelvic radiotherapy and sexual function in women. *Translational Androl Urol* 2015; 15:186-205.
- Daker-White G. Reliable and valid self-report outcome measures in sexual (dys)function: a systematic review. *Arch Sex Behav* 2002;31:197-209.
- Baser RE, Yuelin L, Carter J. Psychometric Validation of the Female Sexual Function Index (FSFI) in Cancer Survivors. *Cancer* 2012;118:4606-4618.
- White ID, Sangha A, Lucas G, et al. Assessment of Sexual Difficulties Associated with Multi-modal Treatment for Cervical or Endometrial Cancer: a systematic review of measurement instruments. *Gynecol Oncol* 2016;143:664-673.
- American Psychiatric Association. Diagnostic & Statistical Manual of Mental Disorders. Washington DC: USA: American Psychiatric Association; 2013.
- Oberguggenberger AS, Nagele E, Inwald EC, et al; Greimel E on behalf of the EORTC Quality of Life Group. Phase 1-3 of the cross-cultural development of an EORTC questionnaire for the assessment of sexual health in cancer patients: the EORTC SHQ-22. *Cancer Med* 2018;7:635-645.
- Terwee CB. Protocol for systematic reviews of measurement properties, Knowledge Center Measurement Instruments. Amsterdam, The Netherlands: Department of Epidemiology and Bio- statistics, EMGO Institute for Health and Care Research; 2011.
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453-1457.
- Patrick DL, Burke LB, Gwaltney CJ, et al. Content Validity – Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1 – Eliciting Concepts for a New PRO Instrument. *Value in Health* 2011;14:967-977.
- Ritchie J, Spencer L, O'Connor W. "Carrying out Qualitative Analysis". In: Ritchie J, Lewis J, eds. Qualitative Research Practice: a guide for social science students and researchers. London: Sage Publications Ltd; 2003.
- Patrick DL, Burke LB, Gwaltney CJ, et al. Content Validity – Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 2 – Assessing Respondent Understanding. *Value in Health* 2011;14:978-988.
- Jensen PT, Klee MC, Thranov I, et al. Validation of a Questionnaire for Self-Assessment of Sexual Function & Vaginal Changes after Gynaecological Cancer. *Psycho-oncology* 2004;13:577-592.
- Routledge JA, Burns MP, Swindell R, et al. Evaluation of the LENT SOMA scales for the prospective assessment of treatment morbidity in cervical carcinoma. *Int J Radiat Oncol Biol Phys* 2003;56:502-510.
- Barracough LH, Routledge JA, Farnell DJ, et al. Prospective analysis of patient-reported late toxicity following pelvic radiotherapy in patients with gynaecological cancer. *Radiother Oncol* 2012;103:327-332.
- Henry JD, Crawford JR. The 21-item version of the Depression Anxiety Stress Scales (DASS-21): Normative data and psychometric evaluation in a large non-clinical sample. *Br J Clin Psychol* 2005;44:227-239.
- Tennant R, Hiller L, Fishwick R, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes* 2007;5:63.

26. Henson RK, Roberts JK. Use of exploratory factor analysis in published research: Common errors and some comment on improved practice. *Educ Psychol Meas* 2006;66:393-416.
27. Asparouhov T, Muthén B. SRMR in Mplus; 2018. Available at: <https://www.statmodel.com/download/SRMR2.pdf>. [Accessed 14 May 2020].
28. Muthén LK, Muthén BO. Mplus User's Guide. Sixth Edition. Los Angeles, CA: Muthén & Muthén; 2007.
29. Tennant A, Conaghan PG. The Rasch measurement model in rheumatology: what is it and why use it? When should it be applied, and what should one look for in a Rasch paper? *Arthritis Rheum* 2007;57:1358-1362.
30. da Rocha NS, Chachamovich E, de Almeida Fleck MP, et al. An introduction to Rasch analysis for Psychiatric practice and research. *J Psychiatr Res* 2013;47:141-148.
31. Christensen K-B, Makransky G, Horton M. Critical Values for Yen's Q3: Identification of Local Dependence in the Rasch Model Using Residual Correlations. *Appl Psychol Meas* 2016;1-17.
32. Smith EV. Detecting and evaluating the impact of multidimensionality using item fit statistics and principal component analysis of residuals. *J Appl Meas* 2002;3:205-231.
33. Teresi JA, Kleinman M, Ocepek-Welikson K. Modern psychometric methods for detection of differential item functioning: application to cognitive assessment measures. *Stat Med* 2000;19:1651-1683.
34. Fischer GH, Molenaar IW, eds. Rasch models: foundations, recent developments, and applications. New York: Springer; 1995.
35. Andrich D, Sheridan BED, Luo G. RUMM2030: Rasch uni-dimensional models for measurement. Perth, Western Australia: RUMM Laboratory; 2009.
36. Kollberg KS, Waldenstrom A-C, Bergmark K, et al. Reduced vaginal elasticity, reduced lubrication and deep and superficial dyspareunia in irradiated gynaecological cancer survivors. *Acta Oncologica* 2015;54:772-779.
37. Carter J, Stabile C, Gunn A, et al. The Physical Consequences of Gynaecologic Cancer Surgery and Their Impact on Sexual, Emotional, and Quality of Life Issues. *The J Sex Med* 2013; 10:S1.
38. Grassi M, Nucera A, Zanolin E, et al. Performance comparison of Likert and Binary formats of SF-36 version 1.6 across ECRHS II adult populations. *Value in Health* 2007; 10:478-488.
39. Dolnicar S, Grün B, Leisch F. Quick, simple and reliable: forced binary survey questions. *Int J Market Res* 2011;53:231-252.
40. U.S. Department of Health and Human Services Food and Drug Administration (FDA). Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Maryland, USA: FDA; 2009.
41. Rosen RC, Revicki DA, Sand M. Commentary on "Critical Flaws in the FSFI and IIEF". *J Sex Res* 2014;51:492-497.
42. UK Office for National Statistics. 2015 Sexual Identity; 2016; <https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/sexuality/bulletins/sexualidentityuk/2015>. [Accessed 18 April 2017].
43. Sadovsky R, Basson R, Krychman M, et al. Cancer and Sexual Problems. *J Sex Med* 2010;7:349-373.
44. Jo's Cervical Cancer Trust. Long-term consequences of cervical cancer and its treatment. London: Jo's Cervical Cancer Trust; 2017.
45. Damast S, Alektiar KM, Goldfarb S, et al. Sexual Functioning Among Endometrial Cancer Patients Treated With Adjuvant High-Dose-Rate Intra-Vaginal Radiation Therapy. *Int J Radiat Oncol Biol Phys* 2012;84:e187-e193.
46. Greimel ER, Vlasic KK, Waldenstrom A-C, et al. The EORTC Quality of Life Questionnaire Cervical Cancer Module (EORTC QLQ-CX24). *Cancer* 2006;107:1812-1822.
47. Greimel E, Nordin A, Lanceley A, et al. Psychometric validation of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Endometrial Cancer Module (EORTC QLQ-EN24). *Eur J Cancer* 2011;47:183-190.
48. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multi-dimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000;26:191-208.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jsxm.2020.06.019>.