

# The fertility quality of life (FertiQoL) tool: development and general psychometric properties<sup>†</sup>

Jacky Boivin<sup>1,\*</sup>, Janet Takefman<sup>2</sup>, and Andrea Braverman<sup>3</sup>

<sup>1</sup>Cardiff Fertility Studies Research Group, School of Psychology, Cardiff University, Tower Building, Park Place, Cardiff Wales CF10 3AT, UK

<sup>2</sup>McGill University Health Centre, Reproductive Centre, Department of Obstetrics and Gynecology, McGill University, Montreal, Canada

<sup>3</sup>Department of Obstetrics and Gynecology, University of Medicine and Dentistry of New Jersey, Newark, NJ, USA

\*Correspondence address. E-mail: boivin@cardiff.ac.uk

Submitted on March 25, 2011; resubmitted on March 25, 2011; accepted on April 12, 2011

**BACKGROUND:** To develop the first international instrument to measure fertility quality of life (FertiQoL) in men and women experiencing fertility problems, to evaluate the preliminary psychometric properties of this new tool and to translate FertiQoL into multiple languages.

**METHOD:** We conducted a survey, both online and in fertility clinics in USA, Australia/New Zealand, Canada and UK. A total of 1414 people with fertility problems participated. The main outcome measure was the FertiQoL tool.

**RESULTS:** FertiQoL consists of 36 items that assess core (24 items) and treatment-related quality of life (QoL) (10 items) and overall life and physical health (2 items). Cronbach reliability statistics for the Core and Treatment FertiQoL (and subscales) were satisfactory and in the range of 0.72 and 0.92. Sensitivity analyses showed that FertiQoL detected expected relations between QoL and gender, parity and support-seeking. FertiQoL was translated into 20 languages by the same translation team with each translation verified by local bilingual fertility experts.

**CONCLUSIONS:** FertiQoL is a reliable measure of the impact of fertility problems and its treatment on QoL. Future research should establish its use in cross-cultural research and clinical work.

**Key words:** infertility / quality of life / psychology / treatment / assisted reproductive technologies

## Introduction

'Quality of life' (QoL) was defined by the World Health Organization (WHO) as an '... individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns...' (WHOQOL, 1995). The WHOQOL measures QoL broadly according to 29 facets (e.g. self-esteem, mobility and safety). QoL measurement is important to identify aspects of fertility problems associated with poor QoL and advance research in health service-evaluation, patient satisfaction and policy-making through the use of a standard measurement tool (Saxena *et al.*, 2001).

Psychosocial studies convincingly demonstrate a high incidence of negative reactions to infertility and its treatment (Verhaak *et al.*, 2007) that impact on overall life satisfaction and well-being (Greil, 1997), success of treatment (Boivin and Schmidt, 2005), willingness to continue with treatment (Smeenk *et al.*, 2004), treatment evaluation (Dancet *et al.*, 2010) and the long-term satisfaction people can

hope to achieve if treatment is unsuccessful and they remain childless (Daniluk, 2001). Therefore, the need to measure and take into account QoL in infertility is imperative and tackling this measurement hurdle could lead to improved patient outcomes.

The 14 existing self-report measures of infertility-specific distress, treatment reactions and QoL shown in Supplementary data, Table SI do not fulfill the need for a fertility specific QoL assessment tool (the table includes details of development sample, content and reference). The fertility problem inventory (FPI: Newton *et al.*, 1999) is the most frequently used distress measure. However, the items were developed without consultation with people experiencing fertility problems and the validation sample comprised primarily Caucasian patients from a homogeneous socioeconomic category using assisted reproductive techniques. Further, the FPI assesses level of strain rather than the broader construct of QoL and does not separate effects due to infertility treatment from those due to childlessness, which is important given the emotional challenges of each. These issues apply to most measures listed in Supplementary data, Table SI. The

<sup>†</sup>This manuscript is published simultaneously in Human Reproduction and Fertility and Sterility. The manuscript was peer-reviewed by F&S.

most frequently used QoL measure was developed for women suffering from polycystic ovarian syndrome (Cronin *et al.*, 1998). Several studies have examined its psychometric properties (Jones *et al.*, 2008) and used it to investigate moderators of QoL (e.g. obesity) and cross-cultural effects. Results confirm its reliability and the importance of cultural background as a moderator of QoL (Schmid *et al.*, 2004; Adamson, 2009). However, this and other quality of life measures for infertility were designed for specific sub-populations (e.g. endometriosis, male factor) and therefore cannot be used as generic measure for all people with fertility problems.

In summary, the need for a quality of life measure for infertility measure has not been fully met. Given the importance of addressing this need, the European Society of Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM) joined forces with Merck-Serono S.A. Geneva-Switzerland (an affiliate of Merck KGaA Darmstadt, Germany) to create the fertility quality of life (FertiQoL) measure (2002–2009). The overall aim of the FertiQoL project was to develop an international instrument to measure QoL in men and women experiencing fertility problems. Secondary aims were to evaluate the psychometric properties of the tool and to translate FertiQoL in multiple languages. The development phase was carried out according to the protocol used for the development of the WHOQOL measure (WHO, 1998) and is briefly described in the present article. However, the main focus of this report is on the psychometric evaluation.

## Methods

### Participants

Men and women experiencing fertility difficulties with and without medical experience were sampled from one fertility clinic in Australia, Canada, New Zealand, UK and two clinics from the USA. Patient advocacy websites in these countries (i.e. ACCESS, American Fertility Association, Resolve, Infertility Awareness Association of Canada, International Consumer Support for Infertility, Infertility Network UK) hosted the online survey. The clinic sample consisted of 291 women and 75 men, and the online sample consisted of 1014 women and 34 men. The Ethics Committee of the School of Psychology, Cardiff University approved the online study and the Internal Review Board of each clinic approved the clinic studies.

### Materials

The *Background Information Form* covered socio-demographic status (e.g. age, education), medical history (e.g. current illness) and fertility-related characteristics (e.g. duration of infertility).

*FertiQoL prototype:* The FertiQoL items were designed to translate abstract concepts (e.g. commitment, sense of belonging) into quantitative items that could collectively indicate the impact of fertility problems on QoL. Full details of item generation for the prototype are described in the Supplemental file and briefly presented here. As shown in Table I, item-generation involved four stages: generating potential items; eliminating redundant, irrelevant and outlier items; validation among people with fertility problems, and cross-cultural survey of acceptability and feasibility. A comprehensive literature review and consultation with psychosocial infertility experts generated an initial pool of 302 items on consequences of fertility problems on QoL in the following 14 areas (e.g. marriage/partnership, social network, emotions, cognitions,

coping, treatment, physical health etc.). The authors classified the 302 items into three levels of increasing concept specificity: dimensions (e.g. interpersonal), domains (e.g. partner relationship) and facets (e.g. intimacy) to form groups of items tapping into related aspects of QoL. Classification and subsequent focus groups reduced this pool to 102 items, which were submitted to the acceptability and feasibility study (see Table I). The prototype evaluated in the present study included these 102 Core items and 27 optional treatment items identified through the feasibility and acceptability phase.

### Translation

FertiQoL was produced in English and translated into 20 languages: Arabic, Chinese, Croatian, Danish, Dutch, English, Finnish, French, German, Greek, Hindi, Italian, Portuguese, Romanian, Russian, Serbian, Spanish, Swedish, Turkish and Vietnamese (see [www.fertiqol.org](http://www.fertiqol.org) to download FertiQoL; Korean and Hungarian versions in progress). Cardiff University professional translators carried out the first translation, and two local fertility experts reviewed it to ensure that it was appropriate to local customs and fertility word usage. Cross-cultural data will be presented in a separate paper.

### Procedure

The items in the prototype FertiQoL survey were randomly presented and rated on a scale of 0–4, where higher scores indicated more favorable QoL. The online survey (prototype FertiQoL and Background Information Form) was designed using SurveyTracker software for Training Technologies, inc and the paper version for clinic distribution was designed using InDesign. Webmasters were provided with a hyperlink to the survey. In clinics, FertiQoL coordinators at each site distributed the study pack to consecutive patients who returned completed surveys anonymously in a marked collection box in the patient waiting room.

### Statistical analysis

Data were screened and duplicate internet protocol (IP) addresses were eliminated unless of different gender and response pattern. Descriptive statistics and correlations were used to identify the best items for each *a priori* domain of QoL (e.g. emotional, mind/body, relational and social). This *a priori* work was done to ensure that conceptually similar groups of items were entered into the factor analysis. Factor analyses (orthogonal rotation) were computed (clinic, online) to ascertain relations among these items. Items with factor loadings less than 0.30 and eigenvalues less than one were eliminated. The FertiQoL total and subscale scores were computed and transformed to scaled scores and summary statistics (e.g. reliability coefficient, mean and standard deviation) produced. Scaled scores were computed to achieve a range of 0–100, making comparisons between scales easier. For scaling, items were reverse-scored (where necessary); all items then summed and multiplied by 25/k, where k was the number of items in the desired subscale or total scale. Higher scores mean better QoL. For the sake of brevity, only final analyses are shown here. These analyses generated the final FertiQoL, which composed 24 core items, plus 10 optional treatment items). See [www.fertiqol.org](http://www.fertiqol.org) for final FertiQoL in all languages and for scoring instructions.

## Results

### Sample characteristics

Table II shows background characteristics and these show that the Clinic group were older, and included more men, single women, same-sex couples and people with a university-education, but fewer American and UK residents and people living in rural/

**Table 1** FertiQoL item generation, selection and reduction.

Task and aims	Participants	Materials	Outcome
Literature review and expert consultation to generate potential items	Psychosocial experts in reproductive health ( <i>n</i> = 17)  FertiQoL Steering Committee ( <i>n</i> = 10) Groups included: researchers, psychologists, social workers, counselors, patients, gynecologists, nurses, clinicians in 11 countries: Australia, Canada, Denmark, France, Germany, Italy, New Zealand, Sweden, Switzerland, UK, USA	Psychosocial studies  Existing fertility-related tools Treatment evaluation tools  QoL measures WHO development manual	302 items in 14 domains (e.g. partnership, self-esteem and career)
Classification and reduction of item pool to eliminate redundant or irrelevant items or rare QoL effects	FertiQoL Technical Working Group (Boivin, Takefman, Braverman) and expert panel	WHO selection criteria: items should be revealing of QoL, cover key domains, use simple language, ask about single issues, free of ambiguity, etc	Item pool reduced to 116 items  WHO response scales matched to items
Focus groups with patients to validate the items generated by the experts and uncover any effects overlooked by the experts	17 focus groups ( <i>n</i> = 136 participants): Canada, Germany, Mexico, USA, Italy <sup>a</sup>  Purposive sampling for age (< or >35 years), gender, duration of infertility (< or >2 years) and parity (< or >1 child)  Psychosocial experts facilitated open, unstructured discussion groups followed by structured feedback exercise on FertiQoL item pool; duration 1.5–2 h	Structured interview guide (facilitators), workbooks (participants) and 116 item-pool FertiQoL	Item decrease from 116 to 102 (22 items eliminated and 8 added) based on > or <50% endorsement  Added 18 treatment items; Wording corrected; eliminated and/or combined redundant items; improved face validity; ensured items pertained to QoL and response scale appropriate
Survey to assess acceptability and feasibility of FertiQoL item style in different languages	<i>n</i> = 525 men and women in 10 countries: Argentina ( <i>n</i> = 48), Brazil ( <i>n</i> = 96), Canada ( <i>n</i> = 59), France ( <i>n</i> = 63), Germany ( <i>n</i> = 37), Greece ( <i>n</i> = 32), Italy ( <i>n</i> = 47), Mexico ( <i>n</i> = 46), New Zealand ( <i>n</i> = 11), Spain ( <i>n</i> = 43), UK ( <i>n</i> = 79) and the USA ( <i>n</i> = 43)	102 Core FertiQoL + 27 optional treatment items  Additional items inquired about clarity, coverage and problems with item pool  Material translated by experts	Final Core FertiQoL pool for psychometric phase was 102 items + 27 optional Treatment items  FertiQoL well accepted, perceived to be important and timely  Items easy to understand and relevant FertiQoL completing 15–20 min Main problems: items that did not apply to all people (e.g. single or untreated) and timeframe for 'Instructions' required

WHO, World Health Organization; TWG, technical working group (Boivin, Takefman, Braverman). FertiQoL TWG involved in all aspects of project development.

<sup>a</sup>Focus groups in Singapore cancelled due to the Severe Acute Respiratory Syndrome (SARS) virus.

suburban areas compared with the Online sample. The Clinic sample was more likely to have at least one child, a shorter duration of infertility but less likely to have other health problems.

### Item analyses

Descriptive and inferential statistics were used to screen for problematic items. Items were deleted for several reasons [i.e. highly skewed

**Table II** Demographic characteristics of the online and clinic samples<sup>a</sup>.

Variable	Online (n = 1048)	Clinic (n = 366)	Test statistic ( $\chi^2$ or t)
Demographic			
Age in years mean (SD)	32.9 (4.9)	35.2 (4.0)	7.9 <sup>b</sup>
Women % (n)	96.8 (1014)	79.5 (291)	113.4 <sup>b</sup>
Relationship status % (n)			49.4 <sup>b</sup>
Single	0.2 (3)	4.0 (13)	
In stable relationship			
Same-sex	1.7 (18)	6.2 (20)	
Heterosexual	98.0 (1027)	89.8 (289)	
Years in partnership mean (SD) <sup>d</sup>	6.85 (3.9)	7.0 (3.9)	0.6
University education (% yes, n)	57.1 (598)	66.2 (139)	9.5 <sup>c</sup>
Residence % (n)			40.4 <sup>b</sup>
Urban	28.3 (296)	27.1 (95)	
Suburban	55.8 (584)	69.5 (244)	
Rural	15.9 (166)	3.4 (12)	
Country % (n)			243.4 <sup>b</sup>
Australia/NZ	14.5 (152)	25.1 (92)	
Canada	10.3 (108)	42.0 (154)	
UK	8.7 (91)	2.7 (10)	
USA	64.1 (672)	30.2 (111)	
Other	2.4 (25)	—	
Reproductive characteristics			
Parenthood % (n)	18.9 (197)	30.1 (108)	19.8 <sup>b</sup>
Years infertile mean (SD)	3.4 (2.9)	2.9 (2.0)	2.4 <sup>c</sup>
Know why infertile, % (n)	75.4 (790)	70.3 (225)	3.3
Perceived diagnosis % (n)			82.4 <sup>b</sup>
Unexplained	10.9 (86)	14.0 (38)	
Female factor	44.5 (351)	18.0 (49)	
Male factor	19.9 (157)	21.7 (59)	
Mixed	11.9 (94)	14.7 (40)	
Same-sex	1.6 (13)	3.3 (9)	
Age-related	4.1 (32)	8.8 (24)	
Other	7.1 (56)	19.5 (53)	
Other health problems % (n)	30.8 (309)	24.0 (260)	5.8 <sup>c</sup>
Years treated mean (SD)	2.03 (2.4)	2.43 (1.8)	1.6

A total of 491 people did not provide data years of treatment due to no treatment experience or missing data.

<sup>a</sup>Sample size varies per variable.

<sup>b</sup> $P < 0.001$ .

<sup>c</sup> $P < 0.05$ .

<sup>d</sup>For people in partnerships.

distribution, high inter-correlations (of  $>0.80$  among item set), poor scale coherence, interpretive issues]. Other items were deleted because they measured broad constructs (e.g. self-esteem) that could be better captured by measures designed for that purpose and that, if retained, would confound associations with those measures in future research. The final FertiQoL item set submitted for exploratory factor analysis was comprised of 24 items from the core set of items and 10 items from the optional treatment module. The 24 core items were conceptualized as reflecting QoL in the emotional, mind-body (i.e. cognitive and physical), relational and social domains. The 10 optional treatment items were conceptualized as

indexing treatment environment and treatment tolerability. An additional two items measuring satisfaction with QoL and physical health were retained for the FertiQoL measure to indicate general physical and QoL satisfaction, but were not included in the factor analysis.

### Exploratory factor analyses and internal consistency

Kaiser-Meyer-Olkin measures of sampling adequacy were  $>0.80$  demonstrating sufficient inter-correlation among items to perform

**Table III** Factor loadings for online and clinic (in parenthesis) samples on FertiQoL items.

	Core FertiQoL				Optional Treatment FertiQoL module	
	Emotional	Relational	Mind/body	Social	Treatment environment	Treatment tolerability
<b>Angry</b>	0.752 (0.800)					
Grief/loss	0.763 (0.792)					
Sad/depressed	0.730 (0.772)					
Fluctuate hope/despair	0.643 (0.759)					
Jealousy and resentment	0.737 (0.634)					
Unable to cope	0.640 (0.594)					
<b>Affectionate</b>		0.749 (0.732)				
Difficult to talk		0.629 (0.696)				
Negative impact on relationship		0.707 (0.633)				
Content relationship		0.768 (0.616)				
Strengthen relationship		0.713 (0.603)				
Satisfied sexual relationship		0.575 (0.600)				
<b>Fatigue</b>			0.731 (0.745)			
Pain/discomfort			0.566 (0.663)			
Feel worn out <sup>b</sup>			0.620 (0.627)			
Disrupt activities			0.704 (0.625)			
Concentration	(0.634) <sup>a</sup>		0.554 (0.413)			
Life on hold <sup>b</sup>	(0.577) <sup>a</sup>		0.572 (0.355)			
<b>Family understand</b>				0.669 (0.669)		
Friend support				0.751 (0.649)		
Society expect				0.495 (0.446)		
Isolated	(0.558) <sup>a</sup>			0.509 (0.531)		
Handle/pregnant others <sup>b</sup>	0.538 <sup>a</sup> (0.589) <sup>a</sup>			0.306 (0.350)		
Shame, embarrassment <sup>b</sup>	0.527 <sup>a</sup> (0.580) <sup>a</sup>			0.319 (0.440)		
<b>Interactions with staff</b>					0.813 (0.784)	
Quality treatment information					0.802 (0.784)	
Quality surgery and medical treatment					0.780 (0.763)	
Fertility staff understand us					0.728 (0.750)	
<b>Quality emotional services</b>					0.632 (0.664)	
Medical services desired available					0.576 (0.585)	
Bothered effect daily activities and work						0.799 (0.790)
Bothered physical effects						0.792 (0.732)
Complicated medication and procedures						0.645 (0.715)
Treatment effects on mood						0.645 (0.681)
Online eigenvalue (% variance)	7.62 (31.8)	2.61 (10.9)	1.44 (6.0)	1.16 (4.8)	3.48 (34.9)	1.92 (19.3)
Clinic eigenvalue (% variance)	8.93 (37.8)	2.37 (9.9)	1.23 (5.1)	1.08 (4.5)	3.80 (38.0)	1.68 (16.8)

Bold indicates first item of each domain.

Some items reversed to avoid negative loadings. See [www.fertiqol.org](http://www.fertiqol.org) for final FertiQoL item wording, response scale wording and downloads in 20 languages. Only factor loadings >0.30 are shown. Factor loadings for Clinic sample in parenthesis.

<sup>a</sup>Indicates a cross-loadings.

<sup>b</sup>Wording for these items changed as a result of psychometric evaluation and participant feedback.

**Table IV** Means and standard deviations for FertiQoL subscales and total scaled scores for the validation sample (online, clinic combined).

Scale	<i>n</i>	QoL domain	Number of items	Cronbach alpha	Mean (SD) Scaled score 0–100
Core subscales					
Emotional	1349	Impact on emotions (e.g. causes sadness, resentment, grief)	6	0.90	45.10 (23.2)
Mind-body	1338	Impact on physical health (e.g. fatigue, pain), cognition (e.g. poor concentration) and behavior (e.g. disrupted daily activities)	6	0.84	54.86 (21.2)
Relational	1330	Impact on partnership (e.g. sexuality, communication and commitment)	6	0.80	68.70 (19.2)
Social	1343	Impact on social aspects (e.g. social inclusion, expectations and support)	6	0.75	51.10 (20.6)
<b>Core FertiQoL</b>	<b>1226</b>	<b>Average quality of life in all core domains</b>	<b>24</b>	<b>0.92</b>	<b>54.60 (16.8)</b>
Treatment subscales					
Environment	1072	Impacts related to treatment environment (e.g. access, quality, interactions with staff)	6	0.84	61.53 (19.6)
Treatment tolerability	1093	Impacts due to consequences of treatment (e.g. physical and mode effects, daily disruptions)	4	0.72	58.81 (20.6)
<b>Treatment FertiQoL</b>	<b>1043</b>	<b>Average quality of life for all treatment domains</b>	<b>10</b>	<b>0.81</b>	<b>60.43 (16.2)</b>
<b>Total FertiQoL</b>	<b>930</b>	<b>Average quality of life for all core and treatment domains</b>	<b>34</b>	<b>0.92</b>	<b>55.43 (14.8)</b>

All items reversed or scored so that higher scores indicate more favorable QoL. Core FertiQoL refers to see [www.fertiqol.org](http://www.fertiqol.org) for final FertiQoL items, response scale wording and downloads in 20 languages. Bold refers to total scores.

factor analyses. Table III shows factor loadings for the Online and (in parenthesis) Clinic samples for the Core FertiQoL and Optional Treatment Module domains. The first factor explaining item variance in the Core FertiQoL was the Emotional subscale explaining 31.8% (Online) and 37.8% (Clinic) of the item variability. Other factors (mind/body, relational and social) explained 10% or less of the item variance but all eigenvalues were above one. Loadings showed that items conceptualized to tap into the same concepts all had high factor loadings ( $>0.30$ ) on their designated factor. Cross-loadings were observed for items of the mind/body (i.e. concentration, life on hold) and social domains (i.e. isolation, shame) onto the emotional domains. For the Optional Treatment Module, the first factor was Treatment Environment, explaining 34.0% (Online) and 38.0% (Clinic) of item variance. There were no cross-loadings for the Treatment Quality and Treatment Tolerability subscales. Table IV shows summary information for all FertiQoL scales. Core FertiQoL and Treatment FertiQoL were normally distributed and individual subscales were normally distributed (data not shown), with only the relational subscale showing mild positive skew toward more favorable QoL in this domain.

### Sensitivity analyses for sub-scales and total scores

Potential moderators of QoL (gender, parenthood status and recruitment source) were examined in relation to FertiQoL scores. Women had a significantly lower Core FertiQoL ( $M = 53.3$ ,  $SD = 16.2$ ) than did men ( $M = 72.1$ ,  $SD = 14.7$ ) ( $t(1224) = 10.3$ ,  $P < 0.001$ ). Core FertiQoL was significantly lower for participants without children ( $M = 53.3$ ,  $SD = 16.3$ ) than participants with children ( $M = 59.5$ ,  $SD = 17.7$ ) ( $t(1217) = 5.27$ ,  $P < 0.001$ ). Participants recruited from

the online patient advocacy and support sites had significantly lower scores ( $M = 50.7$ ,  $SD = 15.1$ ) than did participants recruited from clinics ( $M = 67.8$ ,  $SD = 15.6$ ) ( $t(1224) = 16.6$ ,  $P < 0.001$ ).

The relationship between treatment subscales and six treatment persistence items (e.g. likelihood of trying further treatment, couple agreeing to persist, thinking of ending treatment) was also examined. Greater intention to persist with treatment was significantly associated with better Treatment FertiQoL ( $r(1026) = 0.172$ ,  $P < 0.001$ ), especially in the Clinic sample ( $r(206) = 0.289$ ,  $P < 0.001$ ).

## Discussion

It is currently accepted that to effectively measure the impact of disease, one needs a disease-specific instrument (WHOQOL, 1995). FertiQoL is a reliable and sensitive measurement tool for QoL in individuals with fertility problems. More than 2000 people with fertility problems contributed to the creation of FertiQoL, and it was developed using an integrated mixed-method approach that included literature reviews, international expert consultations, patient focus groups, a cross-cultural feasibility and acceptability survey, and a psychometric survey evaluation. FertiQoL comprises of a Core module evaluating the impact of fertility problems on emotional, mind-body, relational and social domains and an optional Treatment module evaluating treatment environment and tolerability. Subscales and total scales show mainly high reliability and sensitivity of FertiQoL to well-established moderators of QoL. FertiQoL is available in 20 languages with more translations in progress. This project was fully realized as a result of collaboration among ESHRE, ASRM and Merck S.A. Geneva-Switzerland (an affiliate of Merck KGaA Darmstadt, Germany). It is expected that FertiQoL will significantly

contribute to future research and clinical endeavors aimed at investigating and ultimately improving QoL in people with fertility problems.

Certain methodological limitations need to be taken into account. First, despite the multi-disciplinary contributions from experts worldwide, focus groups and a feasibility and acceptability study in 10 countries, the final psychometric evaluation only occurred in five English-speaking countries. Second, targeted efforts to recruit a diverse group of people were not entirely successful in recruiting particular subgroups (i.e. secondary infertile, men). Indeed, more psychometric research on men is required to fully establish reliability and validity. Third, the major proportion of the final sample was recruited online, and differences between the Online and Clinic sample were observed. Although, data generated online have been shown to be as valid as data collected through traditional methods (Bunting and Boivin, 2007; Lieberman, 2008), one would need to determine whether the differences observed warrant a more in-depth analysis—for example, a different set of norms for clinic samples. We eliminated records coming from the same IP address but it may be possible that the same person replied more than once to the survey. Finally, the subscales of the Core FertiQoL were not entirely orthogonal with cross-loadings on the social and mind/body domains. While these associations are expected, we have now modified the final wording of four FertiQoL items to reduce these cross-loadings. Further evaluation of these changes and FertiQoL as a whole on a new sample is required for final validation. These main limitations should be addressed in future psychometric research evaluating FertiQoL. However, the strengths of our mixed-method approach, and consultation and evaluation from infertile people ensure that FertiQoL captures the key life domains affected by fertility problems. It is hoped that FertiQoL will become a gold standard for the measurement of QoL for individuals experiencing fertility problems (whether in treatment or not).

FertiQoL will be useful to clinicians and researchers alike. FertiQoL can be used to identify people at risk of impaired QoL so that psychosocial resources can be offered and subscale scores could identify the specific domains where intervention might be most beneficial. Recent research has shown a close correspondence between Core FertiQoL and standardized measures of anxiety and depression in a Dutch sample (Aarts et al., 2011). The availability of FertiQoL in 20 languages will facilitate essential cross-cultural research, particularly in developing nations (Ombelet et al., 2008; van Balen and Bos, 2010). However, whether cross-cultural differences exist, whether different populations have different mean scores and whether separate cultural norms are needed are all important questions that need to be addressed in future research.

A unique aspect of FertiQoL compared with other QoL measures is the optional 10-item treatment module. This module measures QoL in respect of treatment quality (interactions with staff, quality of information), and treatment tolerability (effects on mood, disruptions daily life). These subscales can be used to assess effectiveness of new treatments/medications, to monitor quality of services and to optimize patient treatment experiences. Research has shown that quality of treatment and its tolerability are predictors of treatment satisfaction (Dancet et al., 2010) and willingness to persist with treatment (Olivius et al., 2004), the latter also shown in the present study. Further a recent large, multi-centered study showed a strong association between a high level of patient-centered care and favorable FertiQoL scores (Aarts et al., 2010). However, the sensitivity of

Treatment FertiQoL for these purposes needs to be investigated in clinical trials of new interventions.

In conclusion, the overall aim of the FertiQoL project was to develop an international instrument to measure QoL in men and women experiencing fertility problems, with the collaboration of individuals experiencing fertility problems and international experts in the field. This objective was accomplished and future use of FertiQoL will be essential to establish FertiQoL as an essential measurement tool for practice, research, health service-evaluation and policy-making.

## Supplementary data

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

## Authors' roles

All authors participated in the development of FertiQoL and its multiple studies. J.B. and J.T. wrote the manuscript, and A.B. reviewed it.

## Acknowledgments

Many people contributed to the development of FertiQoL. We wish to thank the sponsoring organizations European Society for Human Reproduction and Embryology, American Society for Reproductive Medicine and Merck-Serono S.A., the experts in fertility that contributed to item generation and/or verifications of translations, the organizations hosting the online survey, the translation team at Cardiff University and the researchers and students of the Cardiff Fertility Studies Research groups. Please see all contributors at [www.fertiqol.org](http://www.fertiqol.org). We particularly want to thank Robert Rebar for his efforts on this project. The European Society for Human Reproduction and Embryology, American Society for Reproductive Medicine, Merck-Serono S.A. Geneva-Switzerland (an affiliate of Merck KGaA Darmstadt, Germany) have reviewed this article but the views and opinions described in this publication do not necessarily reflect those of these organizations.

## Funding

The study was supported by European Society for Human Reproduction & Embryology, American Society for Reproductive Medicine and Merck-Serono S. A. Geneva-Switzerland (an affiliate of Merck KGaA Darmstadt, Germany). Funding to pay the Open Access publication charges for this article was provided by Merck Serono S.A. – Geneva, Switzerland (an affiliate of Merck KGaA, Darmstadt, Germany) one of the sponsors of the FertiQoL project.

## References

- Aarts JWM, van Empel IW, Boivin J, Kremer JAM, Verhaak CM. Quality of life measure as an extra tool for delivering patient-centred care. In: *Annual Meeting of the European Society for Human Reproduction & Embryology*, Rome, 2010.
- Aarts JWM, van Empel IWH, Boivin J, Nelen WK, Kremer JAM, Verhaak CM. Relationship between quality of life and distress in infertility: a validation study of the Dutch FertiQoL. *Human Reprod*, 2011;**26**:1112–1118.

- Adamson GD. Global cultural and socioeconomic factors that influence access to assisted reproductive technologies. *Womens' Health* 2009; **5**:351–358.
- Boivin J, Schmidt L. Infertility-related stress in men and women predicts treatment outcome one year later. *Fertil Steril* 2005; **83**:1745–1752.
- Bunting L, Boivin J. Decision-making about seeking medical advice in an internet sample of women trying to get pregnant. *Hum Reprod* 2007; **22**:1662–1668.
- Cronin L, Guyatt L, Griffiths E, Wong E, Azziz R, Futterweit W, Cook D, Dunaif A. Development of a health-related quality-of-life questionnaire (PCOSQ) for women with polycystic ovary syndrome (PCOS). *J Clin Endocrinol Metabol* 1998; **83**:1976–1987.
- Dancet EAF, Nelen WLD, Sermeus W, De Leeuw L, Kremer JAM, D'Hooghe TM. The patients' perspective on fertility care: a systematic review. *Hum Reprod Update* 2010; **16**:467–487.
- Daniluk JC. Reconstructing their lives: a longitudinal, qualitative analysis of the transition to biological childlessness for infertile couples. *J Couns Dev* 2001; **79**:439–449.
- Greil AL. Infertility and psychological distress: a critical review of the literature. *Soc Sci Med* 1997; **45**:1679–1704.
- Jones GL, Hall JM, Balen AH, Ledger WL. Health-related quality of life measurement in women with polycystic ovary syndrome: a systematic review. *Hum Reprod Update* 2008; **14**:15–25.
- Lieberman DZ. Evaluation of the stability and validity of participant samples recruited over the internet. *CyberPsychol Behav* 2008; **11**:743–745.
- Newton CR, Sherrard W, Glavac I. The fertility problem inventory: measuring perceived infertility-related stress. *Fertil Steril* 1999; **72**:54–62.
- Olivius C, Friden B, Borg G. Why do couples discontinue *in vitro* fertilization treatment? A cohort study. *Fertil Steril* 2004; **81**:258–261.
- Ombelet W, Cooke I, Dyer S, Serour G, Devroey P. Infertility and the provision of infertility medical services in developing countries. *Hum Reprod Update* 2008; **14**:605–621.
- Saxena S, Carlson D, Billington R. The WHO quality of life assessment instrument (WHOQOL-Bref): the importance of its items for cross-cultural research. *Qual Life Res* 2001; **10**:711–721.
- Schmid J, Kirchengast S, Vytiska-Binstorfer E, Huber J. Infertility caused by PCOS: health-related quality of life among Austrian and Moslem immigrant women in Austria. *Hum Reprod* 2004; **19**:2251–2257.
- Smeenk JM, Verhaak CM, Stolwijk AM, Kremer JAM, Braat DDM. Reasons for dropout in an *in vitro* fertilization/intracytoplasmic sperm injection program. *Fertil Steril* 2004; **81**:262–268.
- van Balen F, Bos HMW. The social and cultural consequences of being childless in poor-resource areas. Facts, views and vision in obstetrics and gynaecology, *Monograph* 2010; **2**:1–16.
- Verhaak CM, Smeenk JM, Evers AWM, Kremer JAM, Kraaijmaat FW, Braat DDM. Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Hum Reprod Update* 2007; **13**:27–36.
- World Health Organization. *World Health Organisation Quality of Life (WHO-QOL)*. User manual. Geneva: World Health Organization, 1998.
- World Health Organization Quality of Life assessment (WHOQOL): Position paper from the World Health Organisation. *Soc Sci Med* 1995; **41**:1403–1409.

## **SUPPLEMENTAL METHODS**

The FertiQoL Technical Working Group (TWG) managed the FertiQoL project and comprised as core investigators Jacky Boivin, Janet Takefman and Andrea Braverman with international collaborators joining the TWG as needed.

### Creation of FertiQoL item pool

A mixed method approach was used to generate the FertiQoL item pool for the evaluation phase including (a) expert consultation, (b) focus groups with patients, and (c) survey with people experiencing fertility problems who were/were not undergoing treatment. This process is summarized in Table 1 of the article.

#### a) Expert consultation

The initial item pool for the FertiQoL measure was generated from three sources to identify the life domains affected by fertility problems and childlessness: (1) reviews of psychosocial studies in infertility, (2) existing fertility-related assessment tools (see Supplemental Table 1), treatment evaluation tools, (3) the World Health Organization development manual (WHO, 1998) and related quality of life papers, and (4) input from psychosocial experts in reproductive health (n=17) and the FertiQoL Steering Committee (n=10) (i.e., and from various professions (researchers, psychologists, social workers, counsellors, patient user groups, gynecologists, nurses, fertility doctors) based in 11 countries (Australia, Canada, Denmark, France, Germany, Italy, New Zealand, Sweden, Switzerland, United Kingdom, United States).

This process generated 302 items related to consequences of fertility problems on quality of life covering the following topics (number in parenthesis is number of items generated per topic): marriage/partnership (40), social network (38), emotions (30), cognitions (30), coping (29), treatment (20), self-esteem (18), career and finances (18), psychological consequences (17), optimism/pessimism (17), reactions to alternative options to parenthood (16), physical health (10), importance of children (13) and impact on lifestyle (6). The FertiQoL technical working group classified the 302 items into three levels: dimensions (e.g., interpersonal), domains (e.g., partner relationship) and facets

(e.g., intimacy) to form groups of items tapping into aspects of quality of life. Each of the three levels of classification (dimensions, domains, facets) was seen to be increasingly more specific with regard to the particular aspect of quality of life being assessed. In total, 63 item-categories were generated.

This structured list was sent to the expert panel who were asked to use the World Health Organization (WHO) criteria to decide on wording and inclusion in the FertiQoL item pool presented to the focus groups (WHO, User manual, Appendix 2, p .60, 16). These criteria were that responses to items: would be revealing of quality of life, cover key domains affected by fertility problems, used simple language (e.g., avoiding double-negatives), items asked about single issue/facet and were free of ambiguity, could be phrased as short questions, omitted any reference to historical timeframe, and were worded to be applicable to infertile people in a range of situations. This process eliminated redundant, irrelevant and infrequent effects of infertility on quality of life and the item pool was reduced to 116 items. Response scales were then matched to item content using the WHO response scales (WHO, User manual, Appendix 1, 16): intensity (not at all – extremely); capacity (not at all – completely); frequency (never – always) and evaluation (very satisfied - very dissatisfied or very good - very poor). The reason for using multiple response scales is because not all items could be made to conform to the same scale and because diversity minimises response sets (e.g., acquiescence) (Robinson et al., 1991).

#### b) Focus groups

Focus groups were organized to validate the items generated by the experts against a patient's perspective. These groups were also used to uncover any important effects overlooked by the experts. Participants in the focus groups were recruited to ensure diversity according to socio-demographic characteristics found to be relevant to reactions to infertility: age (i.e., < or  $\geq$  35 years, gender, duration of infertility (< or  $\geq$  two years of infertility) and parenthood status (see for reviews Greil, 1997). Four focus groups of 8 people each were conducted in Canada, Germany and Mexico, two groups of 8 people in the United States and three groups of 8 people in Italy (17 focus groups, 136

participants). Focus groups were also planned for Singapore but these were cancelled due to the Severe Acute Respiratory Syndrome (SARS) epidemic in that region.

Psychosocial experts from each country facilitated the focus groups based on materials and guidance provided by the FertiQoL technical working group. Materials were translated and back-translated to English by translators at Merck-Serono S. A. Geneva-Switzerland (an affiliate of Merck KGaA Darmstadt, Germany). This guidance comprised a participant workbook that contained items culled from those generated by fertility experts as well as a leader topic guide. The topic guide for facilitators described: (a) aim of FertiQoL; (b) its sponsors; (c) expected users (d) objectives of focus groups, and (e) instructions to facilitators to guide participants through the FertiQoL questions and elicit feedback about these. The focus groups lasted between 1.5 and two hours. This information was also conveyed to participants at the start of each focus group in a separate information sheet. Because direct face-to-face personal questioning could be awkward for as personal a topic as infertility, participants were asked to indicate reactions in terms of “what you have experienced or heard others have experienced”. Participants were first asked to describe areas of their (or others’) life positively or negatively affected by fertility problems to generate consequences independent from concepts generated by experts. Further people were asked to discuss the importance of the consequences to quality of life. Only after this open-period of discussion was the structured content introduced in the focus group. The structured content was organized around the themes and items generated by the experts (e.g., emotions, partnership, social network) were discussed. For example, participants were asked to describe any physical consequences of their fertility problems and their effect on quality of life. Facilitators used a standard feedback form to report data from their focus groups to the FertiQoL technical working Group.

Feedback from the focus group showed that participants appreciated the opportunity to provide their views and thought the FertiQoL project worthwhile. Based on their feedback we (a) eliminated items endorsed by < 50% of groups and incorporated new

facets endorsed  $\geq 50\%$  groups. Based on general feedback we corrected wording issues (e.g., acceptable to both gender, improved clarity and specificity of wording); eliminated and/or combined redundant items; improved face validity to make clearer distinctions within and between facets; ensured all items pertained to quality of life and ensured response scale in line with items. The total number of items decreased from 116 to 102 (22 items eliminated and 8 added). The final structure included four dimensions (i.e., overall, personal, interpersonal, healthcare), eight domains (underlined below) and the 23 facets linked to them (i.e., [affect = infertility syndrome, positive feelings, hopefulness, coping effectiveness], [psychological=body image, self-perceptions, fertility fixation], [physical =health practices, somatic changes]; [spiritual=morals and beliefs, life meaning]; [partner relationship=intimacy, commitment, communication, discord, sexuality]; [social=expectations, belonging, support]; [occupation=interference]; [medical=accessibility and quality, burden of treatment]; [psychoeducational=interactions with medical team]. Together these resulted in 102 items (e.g., Do you feel sexually attractive? rated on the five-point intensity scale of not at all to extremely). The fertility experts panel further examined the items and structure (at the Annual Meeting of the American Society of Reproductive Medicine, 2003) and made minor revisions that included: fine-tuning the wording of some items (i.e., physical domain), grouping items according to response scale (e.g., capacity, intensity), reducing the number of response scales, randomising questions within response categories. The experts also decided that it would be best to extract treatment questions to create a separate and optional treatment module because not all people who would complete FertiQoL would have treatment experience. These amendments were made and the first FertiQoL prototype created.

### c) Acceptability and feasibility survey

In this phase the acceptability and feasibility of FertiQoL as an assessment tool for quality of life was investigated. Participants were recruited to ensure diversity for gender, age and education (none, primary, secondary, tertiary) but all were recruited from fertility clinics by the FertiQoL coordinator in that country. Country coordinators were responsible for ensuring that ethical approval was obtained as per country regulation. The core FertiQoL module and the optional FertiQoL treatment module were translated

from English into the target language using forward and backward process by skilled translators with a final check of the wording performed by the fertility expert coordinator from each country. Additional items at the end of the questionnaire asked participants to indicate (a) which questions, if any were unclear and why, (b) whether there were other important areas of their life related to infertility that were not included in this questionnaire and (c) to provide any other additional comments. Materials were translated and back-translated to English by translators at Merck-Serono S. A. Geneva-Switzerland (an affiliate of Merck KGaA Darmstadt, Germany).

In total 525 people participated in the acceptability phase of FertiQoL from 10 countries: Argentina (n=48), Brazil (n=96), Canada (n=59), France (n=63), Germany (n=37), Greece (n=32), Italy (n=47), Mexico (n=46), New Zealand (n=11), Spain (n=43), United Kingdom (n=79) and the United States (n=43). The sample was 56.5% (n=297) female, 45.5% (n=239) were aged 35 years or less and 60.7% educated to at least secondary level (n=319). Ten countries submitted acceptability reports. The results showed that FertiQoL was well accepted in all countries with positive comments indicating that items were easy to understand, relevant and indicative of the effect infertility and its treatment had had on their quality of life. Moreover, individuals felt satisfied that such a measure was being developed and felt the time to complete, 15-20 minutes, was reasonable (men required longer time to complete). The problems reported were in relation to items that did not apply to all people, that is, single women queried partnership items, untreated people queried items about interactions with the 'fertility medical team' and people with secondary infertility felt items concerning life without children were not applicable. These issues were addressed but overall few modifications to FertiQoL were necessary with only 20 items altered. The other main comment related to the "Instructions" to FertiQoL and the fact that these had not provided the timeframe for thinking about items. Respondents are now instructed to complete FertiQoL in relation to 'current thoughts and feelings'. Overall, couples attending fertility clinics provided support for the FertiQoL project.

FertiQoL was amended in light of these comments and the version for the prototype

psychometric phase was created. The item pool tested in the acceptability phase was retained despite redundancy because multiple items of each domain/facet were required to identify the best set of items in the psychometric evaluation phase. The core FertiQoL tested in the psychometric phase contained 102 items as well as the optional treatment FertiQoL module, which contained 27 items.

## References

- Abbey A, Andrews FM, Halman LJ. Gender's role in responses to infertility. *Psychol Women Quarterly* 1991;15:295-316.
- Benyamini Y, Gozlan M & Ehud Kokia E. Variability in the difficulties experienced by women undergoing infertility treatments. *Fertil Steril* 2005; 83:275– 83
- Bernstein J, Potts N, Mattox J. (1985). Assessment of psychological dysfunction associated with infertility. *J Obstet Gynaecol Neonatal Nurs (supplement)*, 1985;suppl:63-65.
- Boivin J, Takefman JE. Stress levels across stages of in vitro fertilization in subsequently pregnant and nonpregnant women. *Fertil Steril* 1995;64: 802-10.
- Collins A, Freeman EW, Boxer AS Tureck R. (1992). Perceptions of infertility and treatment stress in females as compared to males entering in vitro fertilization treatment. *Fertil Steril* 1992;57:350-56.
- Cronin L, Guyatt G, Griffith L, Wong E, Azziz R, Futterweit W, Cook D, Dunaif A. Development of a health-related quality-of-life questionnaire (PCOSQ) for women with polycystic ovary syndrome (PCOS). *J Clin Endo Metabol* 1998;83:1976-87.
- Franco JG, Baruffi RLR, Mauri AL, Petersen CG, Felipe V, Garbellini E. Psychological evaluation test after the use of assisted reproduction techniques. *J Assisted Reprod Genetics* 2002;19:274-78.
- Greil AL. Infertility and psychological distress: a critical review of the literature. *Soc. Sci. Med.* 1997;45:1679-1704.
- Jones G, Kennedy S, Barnard A, Wong J, Jenkinson C. Development of an endometriosis quality-of-life instrument: The Endometriosis Health Profile-30. *Obstet Gynecol* 2001;98:258-264.
- Klonoff-Cohen H, Natarajan L. (2004). The concerns during assisted reproductive technologies (CART) scale and pregnancy outcomes. *Fertil Steril* 2004;82: 982-88.
- Newton CR, Sherrard W, Glavac I. (1999). The Fertility Problem Inventory: Measuring perceived infertility stress. *Fertil Steril* 1999;72:54-62.
- Pook M, Rohrle B, Krause W. Individual prognosis for changes in sperm quality on the basis of perceived stress. *Psychother Psychosom* 1999;68:95-101.
- Robinson JP, Shaver PR, Wrightsman LS. Criteria for scale selection and evaluation. In: Robinson JP, Shaver PR, Wrightsman LS (eds) *Measures of Personality and Social Psychological Attitudes*. 1991. Academic Press, San Diego, CA.
- Schanz S, Baeckert-Sifeddine IT, Braeunlich C, Collins SE, Batra A, Gebert S, Hautzinger M, Fierlbeck G. A new quality-of-life measure for men experiencing involuntary childlessness. *Human Reprod* 2005;20:2858-65.

- Stanton A, Tennen H, Affleck G, Mendola R. Cognitive appraisal and adjustment to infertility. *Women and Health* 1991;17:1-15.
- Verhaak, CM, Lintsen AM, Evers AW, Braat DD. Who is at risk of emotional problems and how do you know? Screening of women going for IVF treatment. *Hum Reprod* 2010;25:1234-40.
- World Health Organization. World Health Organisation Quality of Life (WHO-QOL). User manual. World Health Organization, Geneva, 1998.

**Supplemental Table 1.** Infertility-specific questionnaires

<b>Author</b>	<b>Name</b>	<b>Development sample</b>	<b>Content</b>
<i>Negative affect, distress and strain</i>			
Bernstein, Potts & Mattox, 1985	Infertility Questionnaire	Middle-class, patients	Self-image, guilt/blame, sexuality, negative feelings and thoughts about infertility
Keye, Deneris & Sullivan, 1984, unpublished & Collins et al. 1992 - USA	Infertility Reaction Scale	Middle-class, ART	Need for parenthood, social and work efficiency and social pressure to have a child
Newton et al. 1999: Canada	Fertility Problem Inventory	Middle-class, patients	Strain or stress in social, sexual, relationship domain, need for parenthood, rejection of child-free living
Verhaak et al. 2010: Netherlands	SCREENIVF	Subsidised ART, women	Mood, helplessness, acceptance
Abbey et al., 1991: USA	Fertility Problem Stress Inventory	Infertile couples	Infertility stress
Stanton, 1991: USA	Infertility Feelings Questionnaire	Patients	Negative feelings in relation to infertility
<i>Treatment-specific</i>			
Boivin, J. & Takefman (1995): Canada	Daily Record-Keeping Sheet	Middle-class, ART patients	Negative (depression, anxiety, uncertainty), positive affect and coping during treatment
Franco et al. 2002: Brazil	Psychological evaluation test after ART	ART patients	Negative reactions to specific aspects of ART
Klonoff-Cohen & Natarajan, 2004: USA	Concerns about reproductive technologies	Professional women, ART	Level of concern about different aspects of ART technologies: procedural (e.g., side effects, anaesthetics), treatment failure, disruption to work and financial considerations
Pook et al. 1999	Infertility Distress Scale	Andrology, men	Distress due mainly to infertility and childlessness
Benyamini et al. 2005: Israel	Difficulty with infertility and its treatment	Patients (early stage)	Significance of 22 difficulties in four domains (uncertainty/lack of control, family and social pressures, impact on self-spouse, treatment-related problems)
<i>Quality of Life</i>			
Cronin et al. 1998: USA	Polycystic Ovary Syndrome Quality of life	PCOS patients	Quality of life in 5 domains (emotions, body hair, weight, infertility and menstrual problems)
Jones et al. 2001: United Kingdom	Endometriosis Health Profile-30	endometriosis, support group	Symptoms in 5 domains (pain, control and powerlessness, emotional well-being, social support and self-image)
Schanz et al. 2005: Germany	Quality of Life in infertile men	Men attending andrology clinic	Functioning in 4 domains (desire for a child, sexual relationship, gender identity, psychological well-being)

Note. Measures of infertility cognitions and/or motivation not shown