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The Fertility Quality of Life (FertiQoL) tool: development and general psychometric properties

Jacky Boivin, Ph.D., C.Psychol.,^a Janet Takefman, Ph.D.,^b and Andrea Braverman, Ph.D.^c

^a Cardiff Fertility Studies Research Group, School of Psychology, Cardiff University, Cardiff, Wales, United Kingdom;

^b Reproductive Centre, Department of Obstetrics and Gynecology, McGill University Health Centre, McGill University, Montreal, Quebec, Canada; and ^c Department of Obstetrics and Gynecology, University of Medicine and Dentistry of New Jersey, Newark, New Jersey

Objective: 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.

Design: Survey.

Setting: Online and fertility clinics in USA, Australia/New Zealand, Canada, and United Kingdom.

Participants: A total of 1,414 people with fertility problems.

Intervention(s): None.

Main Outcome Measure(s): FertiQoL.

Result(s): FertiQoL consists of 36 items that assess core (24 items) and treatment-related (10 items) quality of life as well as overall life and physical health (2 items). Cronbach reliability statistics for the Core and Treatment FertiQoL (and subscales) were satisfactory, in the range of 0.72 and 0.92. Sensitivity analyses showed that FertiQoL detected expected relations between quality of life 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.

Conclusion(s): FertiQoL is a reliable measure of the impact of fertility problems and its treatment on quality of life. Future research should establish its use in cross-cultural research and clinical work. (Fertil Steril® 2011;96:409–15. ©2011 by American Society for Reproductive Medicine.)

Key Words: Infertility, quality of life, psychology, treatment, assessment, burden, assisted reproductive technologies, in vitro fertilization

“Quality of life” (QoL) was defined by the World Health Organization (WHO) as “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” (1). The WHOQoL measure of quality of life broadly according to 29 facets (e.g., self-esteem, mobility, 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 (2).

Psychosocial studies convincingly demonstrate a high incidence of negative reactions to infertility and its treatment (3) which affect overall life satisfaction and well-being (4), success of treatment (5), willingness to continue with treatment (6), treatment evaluation (7), and the long-term satisfaction people can hope to achieve if treatment is unsuccessful and they remain childless (8). 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 presented in [Supplemental Table 1](#) (available online at www.fertstert.org) do not fulfill the need for a fertility-specific QoL assessment tool. The Fertility Problem Inventory (FPI) is the most frequently used distress measure (9). 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 (ART). Furthermore, 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 [Supplemental Table 1](#). The most frequently used QoL measure was developed for women suffering from polycystic ovarian syndrome (PCOSQ) (10). Several studies have examined its psychometric properties (11) 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 (12, 13). However, this and other fertility QoL measures were designed for specific subpopulations (e.g., endometriosis, male factor) and therefore cannot be used as generic measures for all people with fertility problems.

In summary, the need for a fertility QoL measure has not been fully met. Given the importance of addressing this need, the European

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Reprint requests: Jacky Boivin, Ph.D., C.Psychol., Cardiff Fertility Studies Research Group, School of Psychology, Cardiff University, Tower Building, Park Place, Cardiff, Wales CF10 3AT, UK (E-mail: boivin@cardiff.ac.uk).

Society of Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM) joined forces with Merck-Serono, Geneva, Switzerland (an affiliate of Merck, Darmstadt, Germany) to create FertiQoL (2002–2009). The overall aim of the FertiQoL project was to develop an international instrument to measure quality of life 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 WHO QoL measure (14) 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 each in Australia, Canada, New Zealand, and the United Kingdom and two clinics in the United States. 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 clinical sample consisted of 291 women and 75 men, and the online sample consisted of 1,014 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 clinical studies.

Materials

The Background Information Form covered sociodemographic 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 collectively could indicate the impact of fertility problems on QoL. Full details of item generation for the prototype are described in the [Supplemental Methods](#) (available online at www.fertstert.org) and briefly presented here. As shown in [Table 1](#), 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 14 areas (e.g., marriage/partnership, social network, emotions, cognitions, coping, treatment, physical health). 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 ([Table 1](#)). 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 (available online at www.fertiqol.org). At the time of writing, Korean and Hungarian versions were in progress. Cardiff University professional translators carried out the first translation, and two local fertility experts reviewed it to ensure it was appropriate to local customs and fertility references. 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 to 4, where higher scores indicated

more favorable QoL. The online survey (prototype FertiQoL and Background Information Form) was designed using SurveyTracker software (Training Technologies, 2008), 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, 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 <0.30 and eigenvalues <1 were eliminated. The FertiQoL total and subscale scores were computed and transformed to scaled scores and summary statistics (e.g., reliability coefficient, mean, SD) produced. Scaled scores were computed to achieve a range of 0 to 100, making comparisons between scales easier. For scaling, items were reverse scored where necessary and 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 comprised 24 core items, plus 10 optional treatment items. The final FertiQoL in all languages and with scoring instructions is available online at www.fertiqol.org.

RESULTS

Sample Characteristics

[Table 2](#) shows background characteristics, and these show that the clinical 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/suburban areas compared with the online sample. The clinical sample was more likely to have at least one child and 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 distribution, high intercorrelations (>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 comprised 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 they 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 intercorrelation among items to perform factor analyses. [Table 3](#) presents factor loadings for the online and (in parentheses) clinical samples for the Core FertiQoL and optional

TABLE 1

Steps in FertiQoL item generation, selection, and reduction carried out before this psychometric evaluation.

Task and aim	Participants	Materials	Outcome
Literature review and expert consultation to generate potential items	Psychosocial experts in reproductive health (n = 17) FertiQoL steering committee (n = 10) Groups included researchers, psychologists, social workers, counselors, patients, gynecologists, nurses, and 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, 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, be 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 (n = 136 participants): Canada, Germany, Mexico, USA, Italy ^a 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	n = 525 men and women in 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), UK (n = 79) and USA (n = 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 in 15–20 minutes Main problems: items that did not apply to all people (e.g., single or untreated) and time frame for “instructions” required

Note: FertiQoL technical working group involved in all aspects of project development. QoL = quality of life; WHO = World Health Organization.

^a Focus groups in Singapore canceled owing to the severe acute respiratory syndrome virus.

Boivin. *FertiQoL psychometric evaluation. Fertil Steril* 2011.

Treatment module. 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, Social) explained ≤ 10% of the item variance, but

all eigenvalues were >1. 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

TABLE 2

Demographic characteristics of the online and clinic samples.^a

Variable	Online (n = 1,048)	Clinic (n = 366)	Test statistic (χ^2 or <i>t</i>)
Demographics			
Age (y), mean (SD)	32.9 (4.9)	35.2 (4.0)	7.9 ^b
Women, % (n)	96.8 (1014)	79.5 (291)	113.4 ^b
Relationship status, % (n)			
Single	.2 (3)	4.0 (13)	49.4 ^b
In stable relationship			
Same-sex	1.7 (18)	6.2 (20)	
Heterosexual	98.0 (1027)	89.8 (289)	
Duration of partnership (y), mean (SD) ^d	6.85 (3.9)	7.0 (3.9)	.6
University education, % (n)	57.1 (598)	66.2 (139)	9.5 ^c
Residence, % (n)			
Urban	28.3 (296)	27.1 (95)	
Suburban	55.8 (584)	69.5 (244)	
Rural	15.9 (166)	3.4 (12)	
Country, % (n)			
Australia/NZ	14.5 (152)	25.1 (92)	243.4 ^b
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 ^b
Years infertile, mean (SD)	3.4 (2.9)	2.9 (2.0)	2.4 ^c
Know why infertile, % (n)	75.4 (790)	70.3 (225)	3.3
Perceived diagnosis, % (n)			
Unexplained	10.9 (86)	14.0 (38)	82.4 ^b
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 ^c
Years treated, mean (SD)	2.03 (2.4)	2.43 (1.8)	1.6

Note: 491 people did not provide data for years of treatment because of no treatment experience or missing data.

^a Sample size varies per variable.

^b $P < .001$.

^c $P < .05$.

^d For people in partnerships.

Boivin. FertiQoL psychometric evaluation. Fertil Steril 2011.

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 4 presents 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 Subscales 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 (mean 53.3, SD 16.2) than did men (mean 72.1, SD 14.7; $t(1,224) = 10.3$; $P < .001$). Core FertiQoL was significantly lower for participants without children

(mean 53.3, SD 16.3) than for participants with children (mean 59.5, SD 17.7; $t(1,217) = 5.27$; $P < .001$). Participants recruited from the online patient advocacy and support sites had significantly lower scores (mean 50.7, SD 15.1) than participants recruited from clinics (mean 67.8, SD 15.6; $t(1,224) = 16.6$; $P < .001$).

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 ($r(1,026) = 0.172$; $P < .001$), especially in the clinical sample ($r(206) = 0.289$; $P < .001$).

DISCUSSION

It is currently accepted that to effectively measure the impact of disease, one needs a disease-specific instrument (1). FertiQoL is a reliable and sensitive measurement tool for QoL in individuals with fertility problems. More than 2,000 people with fertility problems

TABLE 3

Factor loadings for online and clinical (in parenthesis) samples on FertiQoL items.

	Core FertiQoL				Optional FertiQoL Treatment module	
	Emotional	Relational	Mind/Body	Social	Treatment Environment	Treatment Tolerability
Angry	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)					
Affectionate		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)				
Fatigue			0.731 (0.745)			
Pain/discomfort			0.566 (0.663)			
Feel worn out ^b			0.620 (0.627)			
Disrupt activities			0.704 (0.625)			
Concentration	(0.634) ^a		0.554 (0.413)			
Life on hold ^b	(0.577) ^a		0.572 (0.355)			
Family understand				0.669 (0.669)		
Friend support				0.751 (0.649)		
Society expect				0.495 (0.446)		
Isolated		(0.558) ^a		0.509 (0.531)		
Handle/pregnant others ^b	0.538 ^a (0.589) ^a			0.306 (0.350)		
Shame, embarrassment ^b	0.527 ^a (0.580) ^a			0.319 (0.440)		
Interactions with staff					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)	
Quality emotional services					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)
Clinical 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)

Note: Some items reversed to avoid negative loadings. Only factor loadings >0.30 are shown. Factor loadings for Clinic sample in parentheses. Final FertiQoL item wording, response scale wording, and downloads in 20 languages are available at www.fertiqol.org.

^a Cross-loadings.

^b Wording for these items changed as a result of psychometric evaluation and participant feedback.

Boivin. *FertiQoL psychometric evaluation. Fertil Steril* 2011.

TABLE 4

Means and standard deviations for FertiQoL subscales and total scaled scores for the validation sample (online and clinical combined).

Scale	n	QoL domain	No. of items	Cronbach alpha	Mean (SD) scaled score 0–100
Core subscales					
Emotional	1,349	Impact on emotions (e.g., causes sadness, resentment, grief)	6	0.90	45.10 (23.2)
Mind-Body	1,338	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	1,330	Impact on partnership (e.g., sexuality, communication, commitment)	6	0.80	68.70 (19.2)
Social	1,343	Impact on social aspects (e.g., social inclusion, expectations, support)	6	0.75	51.10 (20.6)
Core FertiQoL	1,226	Overall core fertility quality of life	24	0.92	54.60 (16.8)
Treatment subscales					
Environment	1,072	Impacts related to treatment environment (e.g., access, quality, interactions with staff)	6	0.84	61.53 (19.6)
Treatment tolerability	1,093	Impacts due to consequences of treatment (e.g., physical and mode effects, daily disruptions)	4	0.72	58.81 (20.6)
Treatment FertiQoL	1,043	Overall treatment quality of life	10	0.81	60.43 (16.2)
Total FertiQoL	930	Overall fertility quality of life	34	0.92	55.43 (14.8)

Note: All items reversed or scored so that higher scores indicate more favorable quality of life. Final FertiQoL item wording, response scale wording, and downloads in 20 languages are available at www.fertiqol.org.

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contributed to the creation of FertiQoL, and it was developed by using an integrated mixed-methods 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 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, Geneva, Switzerland (an affiliate of Merck, Darmstadt, Germany). It is expected that FertiQoL will significantly contribute to future research and clinical endeavors aimed at investigating and ultimately improving quality of life in people with fertility problems.

Certain methodologic limitations need to be taken into account. First, despite the multidisciplinary contributions from experts worldwide, focus groups, and a feasibility and acceptability study in 10 countries, the final psychometric evaluation occurred in only five English-speaking countries. Second, targeted efforts to recruit a diverse group of people were not entirely successful for particular subgroups (namely, secondary infertility, 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 clinical samples were observed. Although data generated online has been

shown to be as valid as data collected through traditional methods (15, 16), one would need to determine whether the differences observed warrant more in-depth analysis, for example, a different set of norms for clinical 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. Because these associations were 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-methods approach and consultation with and evaluation from infertile people ensures 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 (17). The availability of FertiQoL in 20 languages will facilitate essential cross-cultural research particularly in

developing nations (18, 19). 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 terms 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 (7) and willingness to persist with treatment (20), the latter also shown in the present study. Furthermore, a recent large multicenter study showed a strong association between a high level of patient-centered care and favorable FertiQoL scores (21). 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.

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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-methods approach was used to generate the FertiQoL item pool for the evaluation phase, including: 1) expert consultation; 2) focus groups with patients; and 3) survey with people experiencing fertility problems who were/were not undergoing treatment. This process is summarized in Table 1 of the article.

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 (Supplemental Table 1) and treatment evaluation tools (1–14); 3) the World Health Organization (WHO) development manual (15) 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, UK, USA).

This process generated 302 items related to consequences of fertility problems on quality of life covering the following topics (numbers in parenthesis are numbers of items generated per topic): marriage/partnership ($n = 40$), social network ($n = 38$), emotions ($n = 30$), cognitions ($n = 30$), coping ($n = 29$), treatment ($n = 20$), self-esteem ($n = 18$), career and finances ($n = 18$), psychologic consequences ($n = 17$), optimism/pessimism ($n = 17$), reactions to alternative options to parenthood ($n = 16$), physical health ($n = 10$), importance of children ($n = 13$), and impact on lifestyle ($n = 6$). 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 regarding 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 WHO criteria to decide on wording and inclusion in the FertiQoL item pool presented to the focus groups (15). 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); and that items asked about single issues/facets and were free of ambiguity, could be phrased as short questions, omitted any reference to historical time frame, 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 by using the WHO response scales (15): 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 minimizes response sets (e.g., acquiescence) (16).

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 sociodemographic characteristics found to be relevant to reactions to infertility: age (i.e., $<$ or ≥ 35 years), gender, duration of infertility ($<$ or ≥ 2 years of infertility), and parenthood status (17). Four focus groups of eight people were conducted in Canada, Germany, and Mexico, two groups of eight people in the USA, and three groups of eight people in Italy (17 focus groups, 136 participants). Focus groups were also planned for Singapore,

but those were canceled owing to the severe acute respiratory syndrome epidemic in that region.

Psychosocial experts from each country facilitated the focus groups based on materials and guidance provided by the FertiQoL TWG. Materials were translated and back-translated to English by translators at Merck-Serono, Geneva, Switzerland (an affiliate of Merck, 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: 1) aim of FertiQoL; 2) its sponsors; 3) expected users; 4) objectives of focus groups; and 5) instructions to facilitators to guide participants through the FertiQoL questions and elicit feedback about these. The focus groups lasted between 1.5 and 2 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. People were also 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 as organized around the themes and items generated by the experts (e.g., emotions, partnership, social network) was discussed. For example, participants were asked to describe any physical consequences of 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 TWG.

Feedback from the focus group showed that participants appreciated the opportunity to provide their views and considered the FertiQoL project to be worthwhile. Based on their feedback we: 1) eliminated items endorsed by $< 50\%$ of the groups and incorporated new facets endorsed $\geq 50\%$ groups; 2) corrected wording issues (e.g., acceptable to both gender, improved clarity, and specificity of wording); 3) eliminated and/or combined redundant items; 4) improved facet validity to make clearer distinctions within and between facets; and 5) ensured that 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, health care) and eight domains with 23 facets linked to them: *affect* = infertility syndrome, positive feelings, hopefulness, coping effectiveness; *psychologic* = 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; and *psychoeducational* = interactions with medical team. Together these resulted in 102 items (e.g., Do you feel sexually attractive? rated on the 5-point intensity scale of not at all–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 include: 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, and randomizing 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.

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 per country regulations. The Core FertiQoL module and the optional FertiQoL Treatment module were translated from English into the target language by 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: 1) to indicate which questions, if any, were unclear and why; 2) to indicate whether there were other important areas of their life related to infertility that were not included in the questionnaire; and 3) to provide any other additional comments. Materials were translated and back-translated to English by translators at Merck-Serono, Geneva, Switzerland.

In total, 525 people participated in the acceptability phase of FertiQoL from ten 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), UK (n = 79) and USA (n = 43). The sample was 56.5% (n = 297) female, 45.5% (n = 239) were aged ≤ 35 years, and 60.7% were 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 that infertility and its treatment had on quality of life. Moreover, individuals felt satisfied that such a measure was being developed and felt that the time to complete it, 15–20 minutes,

was reasonable (men required longer time to complete). The problems reported concerned items that did not apply to all people, i.e., single women queried partnership items, untreated people queried items about interactions with the “fertility medical team,” and people with secondary infertility felt that items regarding life without children were not applicable. These issues were addressed, but few modifications to FertiQoL were necessary, with only 20 items altered. The other main comment concerned the “instructions” to FertiQoL and the fact that these had not provided the time frame for thinking about items. Respondents are now instructed to complete the FertiQoL regarding “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.

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SUPPLEMENTAL TABLE 1
Infertility-specific questionnaires.

Author	Name	Development sample	Content
Negative affect, distress and strain Bernstein et al., 1985, USA (1)	Infertility Questionnaire	Middle class, patients	Self-image, guilt/blame, sexuality, negative feelings, thoughts about infertility
Keye et al., 1984 (unpublished); Collins et al., 1992, USA (2)	Infertility Reaction Scale	Middle class, ART	Need for parenthood, social and work efficiency, social pressure to have a child
Newton et al., 1999, Canada (3)	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, The Netherlands (4)	SCREENIVF	Subsidized ART, women	Mood, helplessness, acceptance
Abbey et al., 1991, USA (5)	Fertility Problem Stress Inventory	Infertile couples	Infertility stress
Stanton et al., 1991, USA (6)	Infertility Feelings Questionnaire	Patients	Negative feelings in relation to infertility
Treatment-specific Boivin and Takefman, 1995, Canada (8)	Daily Record-Keeping Sheet	Middle class, ART patients	Negative (depression, anxiety, uncertainty) and positive affect and coping during treatment
Pook et al., 1999, Germany	Infertility Distress Scale	Andrology, men	Distress mainly due to infertility & childlessness
Franco et al., 2002, Brazil (9)	Psychologic evaluation test after ART	ART patients	Negative reactions to specific aspects of ART
Klonoff-Cohen and Natarajan, 2004, USA (10)	Concerns about reproductive technologies	Professional women, ART	Level of concern about different aspects of ART: procedural (e.g., side effects, anesthetics), treatment failure, disruption to work, financial considerations
Benyamini et al., 2005, Israel (11)	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)
Quality of life Cronin et al., 1998, USA (12)	Polycystic Ovary Syndrome Quality of Life	PCOS patients	Quality of life in five domains (emotions, body hair, weight, infertility, menstrual problems)
Jones et al., 2001, UK, (13)	Endometriosis Health Profile-30	Endometriosis, support group	Symptoms in five domains (pain, control and powerlessness, emotional well-being, social support, self-image)
Schanz et al., 2005, Germany (14)	Quality of life in infertile men	Men attending andrology clinic	Functioning in four domains (desire for a child, sexual relationship, gender identity, psychologic well-being)

Note: Measures of infertility cognitions and/or motivation not shown. ART = assisted reproductive technologies (ART); PCOS = polycystic ovary syndrome.

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