

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/122192/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Koert, Emily, Takefman, Janet and Boivin, Jacky 2021. Fertility quality of life tool: update on research and practice considerations. *Human Fertility* 24 (4) , pp. 236-248. 10.1080/14647273.2019.1648887

Publishers page: <https://doi.org/10.1080/14647273.2019.1648887>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21

Fertility Quality of Life Tool: Update on Research and Practice Considerations

E. Koert^{a1}, J. Takefman^b, J. Boivin^{*c}

^aVisiting Researcher, Cardiff Fertility Studies Research Group, School of Psychology, Cardiff University, Tower Building, Park Place, CF10 3AT, Cardiff, United Kingdom, e-mail: fertiQoL@cardiff.ac.uk

^bAssistant Professor, Departments of Obstetrics/Gynecology and Psychology, Director of Psychological Services, McGill University Health Centre Reproductive Centre, 888 de Maisonneuve Blvd E, Suite 200, Montreal, Canada, H2L 4S8, e-mail: janet.takefman@muhc.mcgill.ca

^{c*}Professor, Cardiff Fertility Studies Research Group, School of Psychology, Cardiff University, Tower Building, Park Place, CF10 3AT, Cardiff, United Kingdom, e-mail: boivin@cardiff.ac.uk. Phone: +44 029 208 75289.

[*Corresponding author: Professor Jacky Boivin](#)

¹ Present address: University of British Columbia, Department of Educational and Counselling Psychology and Special Education, 2125 Main Mall, Vancouver, British Columbia, Canada, V6T1Z4. email: emily.koert@ubc.ca

22 Abstract

23 The 36-item Fertility Quality of Life (FertiQoL) tool is increasingly used in research and practice. It
24 measures quality of life in four personal domains (emotional, social, relational, mind/body) and two
25 treatment domains (tolerability, environment). A literature review of published empirical research using
26 FertiQoL was undertaken to provide an overview of this research base. Five databases were searched
27 using ~~“the key word-FertiQoL”~~ and its variant. In total, 41 published articles from 35 independent
28 samples in 23 countries involving 16,315 participants, mainly in clinical settings, were reviewed.
29 FertiQoL was used for three main purposes. First, to assess quality of life and FertiQoL measurement
30 properties (especially Core FertiQoL) ~~)-in new populations-using cross-sectional designs~~. Second, to
31 identify correlates, predictors and consequences of fertility quality of life. ~~These also-Some~~ included
32 international comparisons. Finally, to assess the effect of psychological interventions on fertility quality
33 of life. The range of median FertiQoL Core, Treatment and subscale (scaled) scores in 31 samples was
34 between 60 and 75. Poorer fertility quality of life was ~~most~~ consistently associated with being a woman,
35 longer duration of infertility, poorer psychological functioning and lower patient-centered care. Some
36 FertiQoL subscale scores ~~were shown to improved~~ after psychological interventions. Future research
37 should address measurement issues and ~~provide more in-depth understanding of~~ examine reported
38 associations with fertility quality of life.

39
40 **Keywords:** infertility; fertility

41

42

Introduction

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

FertiQoL is an international instrument to measure quality of life in individuals experiencing fertility problems (Boivin, Takefman, & Braverman, 2011). As defined by the World Health Organization, quality of life encompasses: "...individuals' perception 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." (World Health Organization, p. 1403). It is important to measure quality of life (QoL) of individuals experiencing fertility problems because infertility and fertility care have an impact on it (Aarts et al., 2011; Boivin et al., 2011; Huppelschoten et al., 2013b; Kitchen, Aldhouse, Trigg, Palencia, & Mitchell, 2017), and, conversely, QoL is linked to patient behaviour and clinical outcomes (Domar, Gross, Rooney, & Boivin, 2015; Gameiro, Canavarro, & Boivin 2013; Kitchen et al., 2017). The measurement structure of FertiQoL was proposed to include a Core FertiQoL component with subscales that measure the impact of fertility problems on emotional (e.g., 'Do you feel able to cope with your fertility problems?'), mind-body (e.g., 'Are you bothered by fatigue because of fertility problems?'), relational (e.g., 'Do you find it difficult to talk to your partner about your feelings related to infertility?'), and social (e.g., 'Are you socially isolated because of fertility problems?') domains of quality of life. The FertiQoL structure also includes the Treatment FertiQoL that measures treatment quality of life via the treatment environment (e.g., 'Do you feel the fertility staff understand what you are going through?') and tolerability (e.g., 'Are you bothered by the physical side effects of fertility medication and treatment?') subscales. A higher score on all subscales (and total scores) means more quality of life. The FertiQoL was a collaborative effort among the European Society of Human Reproduction and Embryology (ESHRE), American Society for Reproductive Medicine (ASRM), Merck-Serono, Geneva Switzerland (part of Merck, Darmstadt Germany) and Cardiff University to address the unmet need for a more standardised approach to fertility specific quality of life measurement for patient understanding, service evaluation, and research.

FertiQoL added to existing fertility distress tools by measuring the broader concept of quality of life, involving fertility patients in its development and validating it with a large international sample.

68 FertiQoL has now been translated into 48 languages and used extensively (see Boivin et al., 2011 and
 69 www.fertiqol.com for more detailed information about the tool, available translations, scoring methods).

70 Potential users must strictly adhere to the Terms of Reference. Items should not be altered. FertiQoL is
 71 judged to perform well in reviews of patient reported outcomes (Kitchen et al. 2017; Pedro et al. 2016)
 72 but findings using FertiQoL have not yet been reviewed in depth despite a large number of studies using
 73 FertiQoL. The purpose of the literature review was to identify all research using FertiQoL to date, to
 74 consolidate and summarize what has currently been reported using it, and to identify areas for future
 75 study. A review of this nature would enable us to show progress in understanding of fertility quality of
 76 life, how FertiQoL has been (and could be) used in patient-oriented work (clinical care or research-
 77 based), and identify potential directions for future research about fertility quality of life (e.g., causes and
 78 consequences of poor fertility quality of life, the effectiveness of clinical care strategies and psychological
 79 interventions in improving fertility quality of life, and the effect of fertility quality of life on treatment
 80 trajectories) or on FertiQoL itself. This paper presents the characteristics of the studies reviewed, a
 81 thematic summary of what the results show about fertility quality of life, and offers suggestions for future
 82 directions for research.

83

84 **Material and Methods**

85 **Search Procedure and Study Selection**

86 The search strategy covered FertiQoL studies to November 4, 2017. Online databases including
 87 Ovid Medline, EMBASE, PsychINFO, CINAHL, and Cochrane were searched between 2002 (the year
 88 FertiQoL was released) and November 2017 (see Supplementary Table 1). Search terms included
 89 ‘Fertility OR Infertility’ and ‘FertiQoL OR Fertility quality of life’. The search strategy was crosschecked
 90 with three key studies (Aarts et al., 2011; Boivin et al., 2011; Gameiro et al., 2013). Reference lists of
 91 included articles were manually searched. Studies identified in all searches were included if they were
 92 published empirical research collecting FertiQoL data. Review papers, study protocols, studies not using
 93 FertiQoL, conference abstracts, non-English articles and duplicates were excluded. Two researchers

94 screened the titles, abstracts, and full-text articles independently and any disagreements were resolved
95 with discussion. Overlapping studies using a portion or all of same sample were accepted if the article
96 reported on different outcomes (von Elm, Poggia, Walder, & Tramer, 2004). For these studies,
97 psychometric properties on the largest sample with available data for subscales (i.e., mean, standard
98 deviation, reliability) were reported. Studies were identified as overlapping in Tables and in text where
99 relevant. No ethics approval was sought.

100

101 *Data Extraction and Synthesis*

102 EK extracted the following from the included studies: authors; publication date; country; study
103 design; purpose; sample size; population (gender) and treatment (i.e., type of treatment); recruitment
104 source (in clinic, online); when FertiQoL measured (e.g., pre-treatment, during treatment, post-treatment);
105 response rate; and results (scaled scores, effect sizes or p-values). In the present study we report FertiQoL
106 scaled scores, which range from 0 to 100 with higher scores indicating higher quality of life (see
107 <http://sites.cardiff.ac.uk/fertiqol/scoring/> for more details about scoring). Each study's purpose and results
108 were reviewed and grouped into themes according to commonalities across studies. A summary for each
109 theme and subthemes was developed.

110

111 *Quality Appraisal*

112 EK assessed study quality of articles available in English using an adapted Newcastle-Ottawa
113 quality assessment scale (Wells, 2010) and the Critical Appraisal Skills Program checklist (CASP, 2016).
114 Quality criteria included the representativeness of the sample, comparability based on control of
115 confounders, validity of aims, hypotheses, and methods, adequacy of outcome measures, and quality of
116 outcome reporting. The overall quality was the sum of all points where 1-2 points was considered low
117 quality; 3-5 points moderate quality; and 6-7 points high quality scores. Intervention studies were
118 evaluated based on the Specialist Unit for Review Evidence (SURE, 2013) criteria for experimental
119 studies with and without control groups. These studies could receive up to 8 points. Only one quality

120 assessment was done per sample. In overlapping studies, quality assessment was informed by all reports
121 where relevant (e.g., when an outcome was reported in a later article). Supplementary Tables 2 to 4
122 provide detail of the quality appraisal and point system.

123

124

Results

125 Figure 1 shows the flowchart for study selection. After exclusion, 41 included studies were reviewed and
126 critically appraised (from 35 independent samples).

127

128 Characteristics of Included Studies

129 The 41 included studies were drawn from 35 independent samples (16,315 participants) in 23
130 countries. Five clusters of studies using overlapping samples were identified (characteristics of largest
131 sample reported in this section: Aarts et al., 2011; Gameiro et al., 2013; Huppelschoten et al., 2013b;
132 Maroufizadeh, Ghaheeri, Amini, Omani Smani, 2017a; Sexty et al., 2016).

133 Overall the majority of included studies were cross-sectional (26 studies, 74.3%), with remaining
134 studies being pre to post designs (4 studies, 11.4%) or prospective or longitudinal designs (5 studies,
135 14.3%). The largest number of studies pooled participants at different treatment stages (13 studies,
136 37.1%) but some sampled patients exclusively pre-treatment (7 studies, 20%), during treatment (8 studies,
137 19.4%), or post treatment (4 studies, 11.4%). Overall 21 studies recruited individuals (60%) and 14
138 (40%) couples. The majority of included studies (28, 80%) used non-systematic methods of recruitment
139 in clinics (e.g., convenience sampling) with few studies recruiting consecutive patients (4 studies, 11.4%),
140 or using random sampling (3 studies, 8.6%). All but one study sampled patients in treatment (97.1%),
141 most commonly undergoing assisted reproductive technology (ART) treatment cycles (28 studies, 80%).
142 The median sample size across included studies was 301 participants (range 18 to 3,088), and the female
143 to male ratio was close to 4:1 in individual, non-couple studies. The participation rate averaged across
144 included studies was 70% (range 41 to 92.5%). Quality assessment of included papers (overlapping

145 samples included once) indicated 11 studies were of high quality (31.4%), 23 of moderate quality (65.7%)
 146 and one low-quality (2.9%),

147 We grouped the results of the included studies into the three broad themes their data addressed
 148 (see Supplementary Tables 5 to 10 for study details). A summary of what the results show about fertility
 149 quality of life is provided for each theme. One included study was not considered further (Hsu, Lin,
 150 Hwang, Lee, & Wu, 2013) because several subscales showed a likely error in scoring that had previously
 151 been communicated to the authors (personal communication via email from J Boivin, 6 August 2013).

152

153 **1. What are the psychometric properties of FertiQoL as a measure of fertility quality of life?**

154 *a) Confirmatory factor analysis of FertiQoL measurement structure*

155 As noted, FertiQoL was conceptualised as measuring quality of life in four Core personal
 156 domains (Emotional, Mind/Body, Relational, Social) and two Treatment domains (Environment,
 157 Tolerability). Donarelli et al. (2016) and Maroufizadeh et al. (2017a) both reported best-fit indices that
 158 were within satisfactory standards indicating observed data in Italy and Iran (respectively) with the
 159 proposed FertiQoL Core conceptual model, and Treatment (Maroufizadeh et al., 2017a) only.

160

161 *b) Internal consistency of FertiQoL*

162 See Supplementary Table 11 for summary of Cronbach coefficient alpha for each study providing
 163 these data and Supplementary Table 12 for specific details of each subscale. Reliability is generally
 164 considered satisfactory when $\geq .70$ (Peterson, 1994). For all studies, reliability for the Core FertiQoL was
 165 $> .80$. Further, satisfactory reliability was reported for the Emotional, Mind/Body and Social subscales ($>$
 166 $.70$) with one exception for social domain (Sexty et al., 2016). In contrast, the Relational subscale
 167 generally showed unsatisfactory reliability with most studies reporting alpha coefficients between $.60$ and
 168 $.70$. The Treatment Module reliability was $> .70$ as was its two subscales (Environment and Tolerability)
 169 in all but one study from Iran (Maroufizadeh et al., 2017a) and one study from Turkey (Kahyaoglu Sut &

170 Balkanli Kaplan, 2015). The Total FertiQoL reliability coefficient was > .90 in all five studies reporting
 171 it.

172

173 *c) Construct validity of FertiQoL*

174 In all cases, construct validity was measured by correlating FertiQoL scores with cognate
 175 measures in which scores should be associated in predictable ways (i.e., convergent validity; e.g.,
 176 depression scale and FertiQoL Emotional subscale should be positively correlated). Results suggested
 177 convergent validity. For example, lower FertiQoL scores were associated with higher anxiety and
 178 depression scores in a sample of Dutch women accessing fertility treatment (Aarts et al., 2011) and in
 179 Turkish infertility patients (Kahyaoglu Sut & Balkanli Kaplan, 2015). The FertiQoL Relational subscale
 180 and scores on a relationship adjustment scale were positively correlated in an Italian sample of couples
 181 awaiting a first ART cycle (Donarelli et al., 2016). Women with a high level of marital distress reported
 182 significantly lower relational quality of life than women not distressed (Chan, Lau, Tam, & Ng, 2016).
 183 Similarly, in a Hong Kong study the Relational subscale showed the highest correlation with sexual
 184 dysfunction and those experiencing sexual dysfunction had significantly lower Relational FertiQoL scores
 185 than those without such problems (Lo & Kok, 2016). Higher Treatment FertiQoL scores were associated
 186 with measures of better patient centered care in cross-sectional studies (Aarts et al., 2012; Pedro,
 187 Canavarro, Boivin, & Gameiro, 2013; Holter et al., 2014). Finally, the disease-specific FertiQoL was
 188 compared to a global quality of life tool (Short Form-36; SF-36) in a prospective study of 41 Spanish
 189 women undergoing fertility treatment (Heredia et al., 2013). Results showed positive and significant
 190 correlations between FertiQoL scores and the majority of SF-36 mental dimensions (vitality, social
 191 functioning, mental health and emotional role functioning). See Supplementary Table 11 for summary of
 192 studies measuring construct validity.

193

194 **2. What has been learnt about fertility quality of life from using FertiQoL?**

195 *a) Average fertility quality of life scores (including International Comparisons)*

196 Figure 2 shows that median scores across FertiQoL subscales, Core, Treatment and Total were in
 197 the range of 60 to 75 (n=31 independent samples, overlapping samples counted once, Hsu et al. (2013)
 198 not included). Figure 3 shows Core FertiQoL mean scores across country. Supplementary Table 13
 199 presents descriptive data (means and standard deviations) for included studies. Core and Treatment
 200 FertiQoL scores were moderately correlated within included studies ($r(22) = .574, p \leq .011$).

201 Four cross-sectional studies (moderate quality) did comparative analyses. Jordanian couples were
 202 shown to have poorer emotional, relational and mind-body quality of life than did German and Hungarian
 203 couples (Cserepes et al., 2014; Sexty et al., 2016) but after controlling for group differences on socio-
 204 demographic and fertility variables the Jordanian group differed only on emotional quality of life. Chi et
 205 al. (2016) found lower Core subscale scores in a Korean sample compared to the FertiQoL development
 206 sample (i.e., Boivin et al. 2011). Valsangkar, Bodhare, Bele, and Sai (2011) found similar results in
 207 comparison between the FertiQoL development sample and an Indian sample. Madero and colleagues
 208 (2017) compared FertiQoL scores in men and women from Germany, Italy and France undergoing cross-
 209 border oocyte donation in Spain. French patients showed poorer emotional and mind-body quality of life
 210 than Italians, whereas both French and German patients showed lower relational quality of life than
 211 Italian patients. However, Italian patients had lower social quality of life than Germans.

212 FertiQoL was used to examine the QoL of specific infertile populations. The studies were of
 213 moderate quality. In one prospective, controlled cohort study, infertile women with and without
 214 endometriosis were found to have similar FertiQoL scores except that women with endometriosis had
 215 lower QoL in the Mind-Body domain (Santulli et al., 2015). In a longitudinal study (Jarvholm,
 216 Johannesson, Clarke, & Brannstrom, 2015), nine women undergoing uterine transplant were shown to
 217 have higher FertiQoL scores than that reported for general infertile populations (e.g., Aarts et al., 2011).
 218 In another prospective study, Santoro and colleagues (2016) reported that women with polycystic ovary
 219 syndrome (PCOS) had lower FertiQoL scores than women with unexplained infertility (except for
 220 Relational domain). However, additional analyses showed that this difference was explained by
 221 differences in features of disease (i.e., greater weight and hirsutism in PCOS group). Partners of these

222 women showed a reverse pattern namely, men partnered with women having PCOS had higher QoL
 223 (except relational) than partners of women with unexplained infertility (Santoro et al., 2016).

224

225 *b) Clinically important thresholds*

226 To identify level of quality of life associated with distress three studies determined the FertiQoL
 227 scores corresponding to cut-offs for depression and anxiety on validated measures (no corresponding
 228 Supplementary Table as studies reported in other sections). In a Dutch sample, the total FertiQoL scores
 229 that corresponded to the clinical cut off for anxiety and depression were 59 and 52, respectively (Aarts et
 230 al., 2011). Using similar methodology, cut offs of 55 and 52, respectively, were reported for women in
 231 Turkey (Dural et al., 2016) whereas another study of Turkish women found the same cut offs as the Dutch
 232 sample (Kahyaoglu Sut & Balkanli Kaplan, 2015). In an Italian study, FertiQoL Relational scores below
 233 around 74 corresponded to marital dysfunction on dyadic adjustment questionnaire (range 74 to 84,
 234 depending on measure, Donarelli et al., 2016).

235

236 *c) Variables that co-vary with fertility quality of life*

237 Eighteen cross-sectional studies (moderate to high quality) investigated correlates of fertility
 238 quality of life (see Supplementary Table 7). This research was primarily conducted using convenience
 239 samples with women recruited through infertility clinics completing FertiQoL prior to or during
 240 treatment. There were mixed results for demographic variables. Gender was the strongest predictor
 241 across studies, with women consistently showing poorer quality of life than men. Huppelschoten et al.
 242 (2013b) reported that 28% of variability in Core FertiQoL was due to gender. Unemployment was
 243 associated with lower FertiQoL scores in one study (Keramat et al., 2014) but not in two others (Goker,
 244 Yanikkerem, Birge, & Kuscu 2017; Heredia et al., 2013). Higher income level was associated with better
 245 quality of life in five studies (Karaca et al., 2016; Keramat et al., 2014; Namavar, Mansouri, Forouhari,
 246 Poordast, & Salehi, 2018; Steuber and High, 2015; Santoro et al., 2016), but not in three others (Hasson et
 247 al., 2017; Karabulut, Ozkan, & Oguz, 2013; Karabulut, Demirtas, Sonmez, Karaca, & Gok, 2017). Higher

248 education was associated with better quality of life in three studies (Karabulut et al., 2013; Keramat et al.,
 249 2014; Namavar et al., 2018), and lower quality of life in two studies (Hasson et al., 2017; Porat-Katz,
 250 Paltiel, Kahane, Eldar-Geva, 2016) and no association in four others (Kahyaoglu Sut & Balkanli Kaplan,
 251 2015; Karabulut et al., 2017; Maroufizadeh, Ghaheeri, & Omani Samani, 2017b; Santoro et al., 2016).
 252 Older age was correlated to higher FertiQoL scores in five studies (Asazawa & Mori, 2015; Goker et al.,
 253 2017; Karabulut et al., 2013; Porat-Katz et al., 2016; Santoro et al., 2016) but not in five others (Heredia
 254 et al., 2013; Kahyaoglu Sut & Balkanli Kaplan, 2015; Karabulut et al., 2017; Keramat et al., 2014;
 255 Maroufizadeh et al., 2017b). Marital status was not associated with quality of life in two studies (Hasson
 256 et al., 2017; Porat-Katz et al., 2016). Longer marital duration was associated with higher quality of life in
 257 one study (Goker et al., 2017) but not in another (Keramat et al., 2014).

258 Characteristics of the infertility or treatment experience were also associated with fertility quality
 259 of life, but not consistently. Time trying to conceive was associated with lower FertiQoL scores in one
 260 study (Kahyaoglu Sut & Balkanli Kaplan, 2015). A longer duration of infertility was associated with
 261 poorer quality of life in five of seven studies (Karabulut et al., 2013; Karaca et al., 2016; Keramat et al.,
 262 2014; Namavar et al., 2018; Santoro et al., 2016) as was unexplained infertility (Heredia et al., 2013;
 263 Maroufizadeh et al., 2017b). In contrast secondary infertility was associated with better quality of life
 264 than primary infertility (Karabulut et al., 2013). Being in treatment or having had a consultation for
 265 infertility was associated with lower quality of life in one study (Namavar et al., 2018). A greater number
 266 of treatment attempts was associated with lower quality of life in one study (Kahyaoglu Sut & Balkanli
 267 Kaplan, 2015) but not in two others (Heredia et al., 2013; Smith, Madeira, & Millard, 2015). Cycle
 268 cancellation in ART was associated with lower FertiQoL scores compared to a completion cycle (whether
 269 pregnant or not; Heredia et al., 2013). The partner accompanying the patient at clinic was associated with
 270 higher quality of life (Heredia et al., 2013). Use of complementary medicine was associated with higher
 271 Relational quality of life and lower Social quality of life in one study (Porat-Katz et al., 2016). One study
 272 reported that higher BMI and more hirsutism were associated with lower FertiQoL scores (Santoro et al.,
 273 2016).

274 Indicators of psychological vulnerability were more consistently associated with poorer quality of
275 life. Specifically, higher depression (Chan et al., 2016; Kahyaoglu Sut & Balkanli Kaplan, 2015;
276 Maroufizadeh et al., 2017b), anxiety (Chan et al., 2016; Kahyaoglu Sut & Balkanli Kaplan, 2015;
277 Maroufizadeh et al., 2017b), desire for psychological support (Karabulut et al., 2013), lower marital and
278 sexual satisfaction (Keramat et al., 2014), lower sexual functioning (Lo & Kok, 2016; Smith et al., 2015)
279 decisional conflict (Chan et al., 2016), and use of indirect forms of communication to disclose fertility
280 problems (e.g., email or jokes; Steuber & High, 2014) were all related to poorer quality of life.

281 FertiQoL subscales were correlated with cognate measures of psychological and interpersonal
282 functioning. For example, three showed that higher depression and anxiety were related to lower
283 FertiQoL scores (Aarts et al., 2011; Chi et al., 2016; Dural et al., 2016). Some of the associations between
284 psychological vulnerability and FertiQoL were mediated by other variables. For example, in a cross-
285 sectional American sample perceived social support accounted for the benefit of direct forms of
286 disclosing fertility problems (e.g., face-to-face) on quality of life (Steuber & High, 2014). One cross-
287 sectional study tested a ‘partnership causal model’ for couples undergoing fertility treatment in Japan
288 (Asazawa & Mori, 2015) and showed that higher emotional support from partner was positively
289 associated with higher FertiQoL scores for both genders. Importantly, support from medical professionals
290 (e.g., doctors and nurses) at the clinic was associated with better quality of life through strengthening the
291 partner relationship during treatment (Asazawa & Mori, 2015).

292 Only three studies examined correlates of fertility quality of life for men and women separately
293 (Goker et al., 2017; Karabulut et al., 2017; Namavar et al., 2018). Two studies found shorter duration of
294 education was associated with lower FertiQoL scores in men (Goker et al., 2017; Namavar et al., 2018)
295 but only one of the studies found this association in women (Namavar et al., 2018). Unemployment was
296 associated with poorer quality of life for men but not women in one study (Karabulut et al., 2017). One
297 cross-sectional study examining FertiQoL in Turkish couples found that lower education, living in a
298 town/village, and having primary infertility was associated with poorer QoL for men but correlates of low
299 FertiQoL in women were being of middle/lower income and having undergone previous treatment. Being

300 younger, in their first marriage, in an arranged marriage, having a shorter duration of marriage (under 10
 301 years), and being childless for more than 5 years was associated with poor QoL for both sexes (Goker et
 302 al., 2017).

303 There is evidence that correlates may differ according to FertiQoL domain scores. For example,
 304 Goker et al. (2017) found that for men education predicted lower Emotional, Mind-body and Tolerability
 305 domains, shorter marriages additionally predicted Social domains whereas being in an arranged marriage
 306 predicted Relational and Environment domains. Similarly, Hasson et al. (2017) found immigration status
 307 predicted all FertiQoL domains except Relational and Treatment Tolerability domains.

308

309 *d) Associations with fertility quality of life over time*

310 Of the studies reviewed, six provided longitudinal or prospective data about fertility quality of
 311 life over time. Jarvholm et al. (2015) assessed FertiQoL prior to and 3, 6 and 12 months after uterine
 312 transplant in nine Swedish women and their partners. Scores were stable over time for women and men.
 313 Chan et al. (2016) assessed FertiQoL (Core, Treatment) immediately after learning of ART treatment
 314 failure, two to three weeks later when couples decided about further treatment, and three months hence
 315 (Hong Kong sample). Descriptive statistics were reported showing little change over time in FertiQoL.
 316 Correlations showed that FertiQoL scores at each assessment were highly predictive of scores at the next
 317 assessment ($r > .70$). Chan et al. (2016) also found that Core and Treatment FertiQoL were predictive of
 318 each other across time (correlations .30 to .50).

319 A few studies explored whether FertiQoL scores could predict future outcomes. In the Chan et al.
 320 (2016) study lower Core and Treatment FertiQoL immediately after a failed cycle predicted higher
 321 decisional conflict at post-treatment consultation two to three weeks later (regardless of decision).
 322 Additionally, Treatment quality of life predicted decisional regret three months later. Three studies
 323 predicted dropout from pre-treatment scores. Huppelschoten et al. (2013a) assessed Core FertiQoL within
 324 three months of a treatment cycle and found it did not predict treatment discontinuation at 12-month
 325 follow-up. Domar et al. (2015) reported that Emotional FertiQoL assessed within a month of the start of

326 an ART cycle did not predict dropout at 12 months, and this lack of association was observed in patients
 327 randomised and not randomised to a coping intervention. Finally, Santoro et al. (2015) reported that pre-
 328 treatment FertiQoL scores did not predict dropout over a five-month treatment protocol. Santoro et al.
 329 (2015) also reported on pregnancy rates. It was found that lower pre-treatment Emotional FertiQoL
 330 predicted lower pregnancy and live-birth rate in women with PCOS whereas lower Mind-Body FertiQoL
 331 predicted higher pregnancy in women with unexplained infertility. The authors argued that results in
 332 PCOS were due to confounding effects of BMI that were related to both Emotional FertiQoL and treatment
 333 outcomes.

334 Heredia et al. (2013), Li, Long, Liu, He, and Li (2016), and Oron et al. (2015) also had a
 335 prospective design but none of the analyses provided data on FertiQoL associations over time.

336

337 **3. Is fertility quality of life responsive to psychological interventions?**

338 *a) Intervention Studies*

339 Four intervention studies (moderate to high quality) used FertiQoL as an outcome measure to
 340 determine whether fertility quality of life was responsive to psychological interventions. A partnership
 341 program in Japan did not affect FertiQoL scores compared to controls, except for improved Mind-Body
 342 scores (Asazawa, 2015). In the United States, a cognitive behavioural intervention (coping and relaxation)
 343 administered for the two-week waiting period was associated with increased FertiQoL Core scores
 344 especially in the Emotional domain compared to a routine care control group (Domar et al., 2015). In
 345 China, an increase in all FertiQoL subscales and Total score was observed for women randomised to a
 346 mindfulness intervention group versus control (Li et al., 2016). Finally, improvement in the Emotional
 347 and Mind-Body subscales was found after a 6-week yoga program in Canada (pre to post design without
 348 control group, Oron et al., 2016).

349

350 *b) Evaluations of Treatment Service*

351 Three cross-sectional studies in Portugal (using overlapping samples, Gameiro et al., 2013;
 352 Lopes, Canavarro, Verhaak, Boivin, & Gameiro, 2014; Pedro et al., 2013) found that higher scores on the
 353 Patient-Centredness Questionnaire (PCQ) (communication, competence, accessibility and continuity of
 354 care) were indirectly associated to patient wellbeing via increased treatment tolerability as measured by
 355 FertiQoL Tolerability subscale (n= 433; Gameiro et al., 2013). Higher Tolerability for treatment was
 356 associated to increased likelihood of persisting with treatment (n=348; Pedro et al., 2013). Aarts and
 357 colleagues (2012) showed that higher perceived patient centered care was correlated with higher FertiQoL
 358 subscale scores in a Dutch sample.

359 Discussion

360 The studies reviewed sampled more than 16,000 men and women in 23 countries. Results of the
 361 literature review provide evidence that FertiQoL is useful in understanding fertility quality of life. It
 362 shows the general psychometric soundness of the FertiQoL in measuring fertility quality of life
 363 (satisfactory internal consistency, model fit, and correlation with cognate measures) but also demonstrates
 364 that many factors (e.g., gender, culture, psychological vulnerability) are likely to be causes, consequences,
 365 mediators or moderators of fertility quality of life. The goal of future research should be to better
 366 understand these associations in order to identify those at risk of poorer fertility quality of life. Some
 367 additional challenges in FertiQoL's use need to be addressed, namely the lower reliability of the
 368 Relational subscale, ~~and~~ the lack of clinically meaningful thresholds (and critical differences between
 369 groups) and, robustness of translations and invariance across groups. The evidence reviewed supports
 370 continued international efforts to understand fertility quality of life and the use of FertiQoL in research
 371 and practice.

372 Results of this literature review should be examined in light of strengths and limitations in the
 373 literature review process and included studies. We excluded conference abstracts and non-English studies
 374 and only reported on main study findings due to resource considerations (e.g., searching grey literature,
 375 cost of translations). These decisions were motivated by the fact that conference abstracts often did not
 376 include complete data (e.g., all subscales, population characteristics, study design) and few sub-analyses

377 were theoretically motivated. Further, data extraction and study selection was performed by one person,
 378 but discussed with other authors when uncertainty arose. These decisions mean that our literature review
 379 may lack the rigor associated with systematic reviews. Limitations in primary studies were over-reliance
 380 on convenience sampling, cross-sectional studies, bivariate tests that rarely took account of confounders.
 381 The studies that did carry out confounder analyses showed that quality of life has multiple determinants
 382 best understood using multifactorial models (e.g., see model testing; Asazawa & Mori, 2015). As the
 383 FertiQoL research base gains momentum we expect methodological rigour to improve both for the review
 384 process and primary research.

385 FertiQoL has largely satisfactory psychometric properties at the subscale and summed score level
 386 (Core, Treatment) for the measurement of multi-dimensional construct of fertility quality of life. This
 387 conclusion is consistent with recent reviews of patient-reported outcomes in infertility (Kitchen et al.,
 388 2017; Pedro et al. 2016) and other studies examining the factor structure of FertiQoL (Pedro et al. 2016;
 389 Melo et al. unpublished results). There was also evidence of construct validity because of correlations
 390 between FertiQoL subscales and cognate measures of psychological and interpersonal functioning.
 391 However, there is a need for further investigation of measurement properties [and users are urged to](#)
 392 [consider the following in using FertiQoL](#). The Relational subscale has poorer reliability than other
 393 subscales. Similar relational scales in other quality of life measures also show less reliability (e.g., World
 394 Health Organization quality of life, reliability coefficients .60 to .70, factor loadings < .50, see
 395 Skevington, Lotfy, & O'Connell, 2004). These measurement issues are often attributed to clinical
 396 characteristics, for example functional status (Schuler et al., 2016). Our analysis suggests, however,
 397 potential conceptual and cultural underpinnings. For example, the items with lowest factor loadings on
 398 the social subscale required the individual to have informed others of their fertility problems (i.e., 'Are
 399 you satisfied with support you receive from friends...', 'Do you feel your family can understand what you
 400 are going through?'). Many infertile people do not disclose their infertility to others. In-depth multi-
 401 country analyses would help determine best course of action to address these measurement issues (e.g.,
 402 re-word item, remove item, use total scores, drop subscale). [The Core and Treatment subscales should be](#)

403 [reported separately and not combined into a Total score because the reliabilities of the Core and](#)
 404 [Treatment FertiQoL is better as individual totals. Finally, studies on the factorial validity of the FertiQoL](#)
 405 [though promising are scarce as is the test of measurement invariance. As such caution should be exercised](#)
 406 [in using FertiQoL until further psychometric studies have been carried out.](#)

407 The median subscale scores indicate that fertility problems have a moderate impact on quality of
 408 life, with some domains impacted more than others. The lack of a clinically meaningful threshold is an
 409 issue for the interpretation of FertiQoL scores, as has been noted in another review (Kitchen et al., 2017).
 410 Determining what is an [sub-] optimal FertiQoL score is a challenge (e.g., Aarts et al. 2011; Donarelli et
 411 al. 2016), and in particular what score is indicative of individuals needing additional support. One
 412 approach would be to use the median scores obtained thus far in published studies (see Figure 2 median
 413 FertiQoL scores in the range of 60 to 75 across 31 independent samples) or to use reports of the FertiQoL
 414 scores that correspond to cut-off scores for clinical levels of depression and anxiety on validated ‘gold
 415 standard’ measures such as the HADS (FertiQoL Core scores below 52 to 59, see Aarts et al., 2011, Dural
 416 et al., 2016, Kahyaoglu Sut & Balkanli Kaplan, 2015). However, comparisons to median scores or
 417 HADS scores must be made with caution because the studies reviewed were not designed to establish
 418 normative or reference scores (Kendall, Marrs-Garcia, Nath, & Sheldrick, 1999; Kendall & Sheldrick,
 419 2000). Derivation of reference values requires a standardised protocol (e.g., population, recruitment)
 420 applied consistently across [the](#) settings contributing to norms, which has not yet been done but could be a
 421 next step in FertiQoL development. Such data would facilitate comparisons of FertiQoL across person,
 422 place and time and would facilitate translating research findings into clinical application. [It is also](#)
 423 [possible that FertiQoL scores are used purely descriptively for profiling individual patients for clinical](#)
 424 [meetings, case histories, discussions with patients themselves and so on. However, based on the medians](#)
 425 [\(see Figure 2\), w](#)~~We~~ offer an illustrative description of a typical research (patient) participant willing to
 426 complete FertiQoL during treatment [based on results from Figure 2. This illustrative profile was derived](#)
 427 [\(using by using the](#) median scores [to pinpoint the median of the response scale for each item in the](#)
 428 [FertiQoL subscales](#)~~median scores, response scale, and item content.~~ Note this profile is illustrative only),

429 with the caveat that there may be differences in how these issues manifest or are described according to
 430 gender and culture. If the Figure 2 medians were scores from a n the typical patientpatient then the profile
 431 could be described as participant:

432 Emotional quality of life appears to be impacted the most with individuals often
 433 experiencing feelings of grief and loss, jealousy and resentment and occasionally feeling sad,
 434 depressed and angry. They often fluctuate between hope and despair however they generally feel
 435 able to cope with their fertility problems. There is less impact on the cognitive and physical
 436 quality of life. Individuals generally experience a small amount of fatigue, pain and discomfort,
 437 and their attention and concentration, energy level and ability to meet their day-to-day obligations
 438 rarely impacted. They occasionally feel their fertility problems make them inferior to others with
 439 children and experience some pressure to have children. However, they generally feel understood
 440 and satisfied with the support they receive from family and friends and feel comfortable attending
 441 social situations that could involve families and children. The relational quality of life domain
 442 appears to be impacted the least with individuals feeling satisfied with their relationship and
 443 believing that their fertility problems have strengthened their commitment to each other. They
 444 may find it difficult at times to talk to their partner about their fertility problems. In terms of the
 445 treatment experience, the median scores suggest that individuals feel understood by fertility staff
 446 and feel satisfied with the quality of services, treatment and information they receive and their
 447 interactions with fertility staff while in treatment. They are seldom bothered by the physical side
 448 effects or the impact of treatment on their lives in general and do not find the procedures or
 449 details required by treatment to be very complicated.

451 The included research showed that fertility quality of life could be predicted with women, those
 452 with psychological vulnerability and those with longer duration of infertility reporting poorer quality of
 453 life. These findings are consistent with previous research in infertile populations showing these to be risks
 454 for depression and anxiety (e.g., Verhaak et al., 2007) and poorer quality of life using other measures
 455 (e.g., Chachamovich et al., 2010). Separate gender analyses suggest men from lower socioeconomic
 456 backgrounds (less education, unemployed) may also be at greater risk for poor quality of life. As many
 457 studies were cross-sectional the direction of causation remains to be established. However, the literature
 458 review also provides promising evidence that fertility quality of life could be improved through targeting
 459 modifiable risk factors for poor FertiQoL or enhancing protective factors (e.g., through interventions such
 460 as a cognitive behavioural intervention; Domar et al., 2015).

461 There is evidence that FertiQoL could be useful in practice. Poorer quality of life of some patient
462 groups could be better understood (e.g., patients with endometriosis, PCOS). Treatment quality of life
463 predicted decisional conflict and regret and intentions to persist with treatment (Gameiro et al., 2013)
464 though not actual dropout (Huppelschoten et al., 2013a). Pre-treatment FertiQoL scores also predicted
465 pregnancy and live birth in some groups (Santoro et al., 2016). More studies are needed to clarify these
466 relationships because confounder analyses and prospective studies suggested such prediction could be due
467 to the multiple determinants of quality of life (e.g., obesity, longer duration of infertility, greater treatment
468 attempts) that could also impact on treatment outcomes. FertiQoL could also be useful in practice to
469 identify aspects of treatment that could improve quality of life. For example, the review suggested that
470 patient centered care was associated with better quality of life, as was support from medical professionals
471 (e.g., doctors and nurses) in strengthening the partner relationship (Asazawa & Mori, 2015).

472 To date very few of the FertiQoL studies examined how quality of life predictors differed across
473 groups (e.g., gender, treatment status, country). Understanding more deeply international variations in
474 FertiQoL scores is an important future research goal. FertiQoL has been translated (see
475 www.fertiqol.com for translations) using a consistently applied process (see Boivin et al., 2011) that
476 involves a cooperative exchange between a professional translator and bilingual fertility experts in
477 psychology and medicine in the country requesting the translation. This co-production is important
478 because it helps ensure that the translation has high fidelity to the English version but is also culturally
479 tailored (Kreuter, Lukwago, Bucholtz, & Clark, 2003). This quality control does not necessarily prevent
480 threats to validity. According to Herdman, Fox-Rushby, and Badia (1998) a true translation also implies
481 that the meaning of FertiQoL items is equivalent across translations. As noted, we lack at present in-
482 depth cross-cultural psychometric and qualitative studies to confirm validation in the ‘meaning’ of items.
483 Continued research could help disentangle cultural from methodological difference. The use of the
484 COSMIN checklist (COnsensus-based Standards for the selection of health Measurement Instruments;
485 Mokkink et al., 2010) and qualitative research into item meaning can help in this endeavour.

486

487 Conclusion

488 This literature review presented a consolidation and summary of research using the FertiQoL to date and
489 presented considerations for future research. The review showed FertiQoL is a reliable and valid
490 measurement tool for quality of life among people with fertility problems showing promise in multiple
491 settings for a range of research and practical goals. Methodological and conceptual challenges remain, but
492 these are being addressed. Future efforts with FertiQoL should aim to better understand some
493 measurement issues (e.g., reliability of relational subscale, invariance of FertiQoL across samples),
494 generate valid population normative scores, extend clinical application (e.g., identify clinically
495 meaningful thresholds) and extend understanding of reported associations with fertility quality of life
496 through more rigorous research designs (e.g., prospective studies).

497

498 Acknowledgements

499 The authors thank Toni Harris and Dr. Rasha Bayoumi for assistance with an early review and Dr. China
500 Harrison with check of final review.

501

502 Disclosure of Interest

503 EK and JT report no conflict of interest. JB has received funding from Merck Norway (Merck AB NUF)
504 for the Norwegian translation of the Fertility Quality of Life (FertiQoL) tool and funding from Ferring
505 International Center S.A. for the Czech translation of the FertiQoL scale. The employer of JB (Cardiff
506 University) could one day receive royalties from the commercial use of Fertility Quality of Life
507 (FertiQoL).

508

509 Study Funding

510 No funding was received for this manuscript. The Fertility Quality of Life (FertiQoL) tool was developed
511 in collaboration with the European Society of Human Reproduction (ESHRE) and the American Society

512 of Reproductive Medicine (ASRM) with funding from Merck-Serono, Geneva Switzerland (part of
513 Merck, Darmstadt Germany) and Cardiff University.

514

515

516 **References**

517 Aarts, J. W. M., Huppelschoten, A. G., van Empel, I. W. H., Boivin, J., Verhaak, C. M., Kremer, J. A. M.,
518 & Verhaak, C. M. (2012). How patient-centred care relates to patients' quality of life and distress: a study
519 in 427 women experiencing infertility. *Human Reproduction*, 27, 488-495.

520 Asazawa, K (2015). Effects of a partnership support program for couples undergoing fertility treatment.
521 *Japan Journal of Nursing Science*, 12, 354-366.

522 Asazawa, K., & Mori, A. (2015). Development of a partnership causal model for couples undergoing
523 fertility treatment. *Japan Journal of Nursing Science*, 12, 208-221.

524 Boivin, J., Takefman, J., & Braverman, A. (2011). The fertility quality of life (FertiQoL) tool:
525 Development and general psychometric properties. *Fertility & Sterility*, 96, 409–415.

526 Chachamovich, J. R., Chachamovich, E., Ezer, H., Fleck, M.P., Knauth, D., & Passos, E. P. (2010).
527 Investigating quality of life and health-related quality of life in infertility: a systematic review. *Journal of*
528 *Psychosomatic Obstetrics & Gynecology*, 31, 101-110.

529 Chan, C.H., Lau, H.P., Tam, M.Y., & Ng, E. H. (2016). A longitudinal study investigating the role of
530 decisional conflicts and regret and short-term psychological adjustment after IVF treatment failure.
531 *Human Reproduction*, 31, 2772-2780.

532 Chi, H.-J., Park, I.-H., Sun, H.-G., Kim, J.-W., & Lee K.-H. (2016). Psychological distress and fertility
533 quality of life (FertiQoL) in infertile Korean women: The first validation study of Korean
534 FertiQoL. *Clinical and Experimental Reproductive Medicine*, 43, 174-180.

535 Critical Appraisal Skills Programme. (2016). CASP Cohort Study Checklist. Retrieved from
536 http://media.wix.com/ugd/dded87_5ad0ece77a3f4fc9bcd3665a7d1fa91f.pdf.

537 Cserepes, R. E., Bagan, A., Korosi, T., Toth, B., Rosner, S., Strowitzki, T., & Wischmann, T. (2014).

- 538 Infertility specific quality of life and gender role attitudes in German and Hungarian involuntary childless
 539 couples. *Geburtsh Frauenheilk*, 74, 1009-1015.
- 540 Domar, A. D., Gross, J., Rooney, K., & Boivin, J. (2015). Exploratory randomized trial on the effect of a
 541 brief psychological intervention on emotions, quality of life, discontinuation, and pregnancy rates in in
 542 vitro fertilization patients. *Fertility & Sterility*, 104, 440–451 e447.
- 543 Donarelli, Z., Lo Coco, G., Gullo, S., Salerno, L., Marino, A., Sammartano, F., & Allegra, A. (2016). The
 544 Fertility Quality of Life Questionnaire (FertiQoL) Relational subscale: psychometric properties and
 545 discriminant validity across gender. *Human Reproduction*, 31, 2061-2071.
- 546 Dural, O., Yasa, C., Keyif, B., Celiksoy, H., Demiral, I., Yuksel Ozgor, B., ... Bastu, E. (2016). Effect of
 547 infertility on quality of life of women a validation study of the Turkish FertiQoL. *Human Fertility*, 19,
 548 186-191.
- 549 Gameiro, S., Canavarro, M. C., & Boivin, J. (2013). Patient centred care in infertility health care: Direct
 550 and indirect associations with wellbeing during treatment. *Patient Education and Counseling*, 93, 646-
 551 654.
- 552 Goker, A., Yanikkerem, E., Birge, O., & Kuscu, N. K. (2017). Quality of life in Turkish infertile couples
 553 and related factors. *Human Fertility*. Advance online publication. doi: 10.1080/14647273.2017.1322223.
- 554 Hasson, J., Tulandi, T., Shavit, T., Shaulov, T., Seccareccia, E., & Takefman, J. (2017). Quality of life of
 555 immigrant and non-immigrant infertile patients in a publicly funded invitro fertilisation program: a cross-
 556 sectional study. *British Journal of Obstetrics and Gynaecology*, 124, 1841-1847.
- 557 Herdman, M., Fox-Rushby, J., & Badia, X. (1998). A model of equivalence in the cultural adaptation of
 558 HRQoL instruments: the universalist approach. *Quality of Life Research*, 7, 323-325.
- 559 Heredia, M., Tenais, J. M., Rocio, R., Amparo, F., Calleja, M. A., & Valenzuela, J. C. (2013). Quality of
 560 life and predictive factors in patients undergoing assisted reproduction techniques. *European Journal of*
 561 *Obstetrics, Gynecology and Reproductive Biology*, 167, 176-180.

- 562 Holter, H., Sandin-Bojo, A.-K., Gejervall, A.-L., Wikland, M., Wilde-Larsson B., & Bergh, C. (2014).
 563 Quality of care in an IVF programme from a patient's perspective. Development of a validated instrument.
 564 *Human Reproduction*, 29, 534-547.
- 565 Hsu, P. Y., Lin, M. W., Hwang, J. L., Lee, M.S., & Wu, M. H. (2013). The fertility quality of life
 566 (FertiQoL) questionnaire in Taiwanese infertile couples. *Taiwan Journal of Obstetrics and Gynecology*,
 567 52, 204–209.
- 568 Huppelschoten. A. G., van Dongen, A. J., Philipse, I. C, Hamilton, C. J., Verhaak, C. M., Nelen, W. L., &
 569 Kremer, J. A. (2013a). Predicting dropout in fertility care: A longitudinal study on patient centredness.
 570 *Human Reproduction*, 28, 2177-2186.
- 571 Huppelschoten, A. G., van Dongen, A. J., Verhaak, C. M., Smeenk, J. M., Kremer, J. A., & Nelen, W.L.
 572 (2013b). Differences in quality of life and emotional status between infertile women and their partners.
 573 *Human Reproduction*, 28, 2168–2176.
- 574 Jarvholm, S., Johannesson, L., Clarke, A., & Brannstrom, M. (2015). Uterus transplantation trial:
 575 Psychological evaluation of recipients and partners during the post-transplantation year. *Fertility &*
 576 *Sterility*, 104, 1010-1015.
- 577 Kahyaoglu Sut, H., & Balkanli Kaplan, P. (2015). Quality of life in women with infertility via the
 578 FertiQoL and the Hospital Anxiety and Depression Scales. *Nursing & Health Sciences*, 17, 84–89.
- 579 Karabulut, A., Demirtas, O., Sonmez, S., Karaca, N., & Gok, S. (2017). Assessing factors associated with
 580 infertility using a couple-based approach. *International Journal of Gynecology & Obstetrics*, 137, 96-98.
- 581 Karabulut, A., Ozkan, S., & Oguz, N. (2013). Predictors of fertility quality of life (FertiQoL) in infertile
 582 women: analysis of confounding factors. *European Journal of Obstetrics, Gynecology and Reproductive*
 583 *Biology*, 170, 193–197.
- 584 Karaca, N., Karabulut, A., Ozkan, S., Aktun, H., Oregul, F., Yilmaz, R., ... Batmaz, G. (2016). Effect of
 585 IVF failure on quality of life and emotional status in infertile couples. *European Journal of Obstetrics,*
 586 *Gynecology and Reproductive Biology*, 206, 158-163.
- 587 Kendall, P. C., Marrs-Garcia, A., Nath, S. R., & Sheldrick, R.C. (1999). Normative comparisons for the

- 588 evaluation of clinical significance. *Journal of Consulting and Clinical Psychology*, 67, 285-299.
- 589 Kendall, P. C., & Sheldrick, R. C. (2000). Normative data for normative comparisons. *Journal of*
590 *Consulting and Clinical Psychology*, 68, 767-773.
- 591 Keramat, A., Masoumi, S. Z., Mousavi, S. A., Poorolajal, J., Shobeiri, F., & Hazavehie, S. M. M. (2014).
592 Quality of life and its related factors in infertile couples. *Journal of Research in Health Sciences*, 14, 57-
593 64.
- 594 Kitchen, H., Aldhouse, N., Trigg, A., Palencia, R., & Mitchell, S. (2017). A review of patient-reported
595 outcome measures to assess female infertility-related quality of life. *Health and Quality of Life Outcomes*,
596 15, 86.
- 597 Kreuter, M., Lukwago, S., Bucholtz, D., & Clark, E. (2003). Achieving cultural appropriateness in health
598 promotion programs: targeted and tailored approaches. *Health Education & Behavior*, 30, 133-146.
- 599 Li, J., Long, L., Liu, Y., He, W., & Li, M. (2016). Effects of a mindfulness-based intervention on fertility
600 quality of life and pregnancy rates among women subjected to first in vitro fertilization treatment.
601 *Behaviour Research and Therapy*, 77, 96-104.
- 602 Lo, S. S. -T., & Kok, W.-M. (2016). Sexual functioning and quality of life of Hong Kong Chinese women
603 with infertility problem. *Human Fertility*, 19, 268-274.
- 604 Lopes, V., Canavarro, M.C., Verhaak, C. M., Boivin, J., & Gameiro, S. (2014). Are patients at risk for
605 psychological maladjustment during fertility treatment less willing to comply with treatment? Results
606 from the Portuguese validation of the SCREENIVF. *Human Reproduction* 29, 293-302.
- 607 Madero, S., Gameiro, S., Garcia, D., Cirera, D., Vassena, R., & Rodriguez, A. (2017). Quality of life,
608 anxiety and depression of German, Italian and French couples undergoing cross-border oocyte donation in
609 Spain. *Human Reproduction*, 32, 1862-1870.
- 610 Maroufizadeh, S., Ghaheri, A., Amini, P., & Omani Samani, R. (2017a). Psychometric properties of the
611 fertility quality of life instrument in Iranian women. *International Journal of Fertility & Sterility*, 10, 371-
612 379.

- 613 Maroufizadeh, S., Ghaheri, A., & Omani Samani, R. (2017b). Factors associated with poor quality of life
 614 among Iranian infertile women undergoing IVF. *Psychology, Health & Medicine*, 22, 145-151.
- 615 Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & The PRISMA Group. (2009).
 616 Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS*
 617 *Medicine*, 6, e1000097.
- 618 Mokkink, L. B., Terwee, C. B., Patrick, D. L., Alonso, J., Stratford, P. W., Knol, D. L., ... de Vet, H. C.
 619 (2010). The COSMIN study reached international consensus on taxonomy, terminology, and definitions
 620 of measurement properties for health-related patient reported outcomes. *Journal of Clinical*
 621 *Epidemiology*, 63, 737-745.
- 622 Namavar, J. B., Mansouri, M., Forouhari, S., Poordast, T., & Salehi, A. (2018). Quality of life and its
 623 influencing factors of couples referred to an infertility center in Shiraz, Iran. *International Journal of*
 624 *Fertility & Sterility*, 11, 293-297.
- 625 Oron, G., Allnutt, E., Lackman, T., Sokal-Arnon, T., Holzer, H., & Takefman, J. (2015). A prospective
 626 study using Hatha Yoga for stress reduction among women waiting for IVF treatment. *Reproductive*
 627 *BioMedicine Online*, 30, 542-548.
- 628 Pedro, J., Canavarro, M. C., Boivin, J., & Gameiro, S. (2013). Positive experiences of patient-centred care
 629 are associated with intentions to comply with fertility treatment: findings from the validation of the
 630 Portuguese version of the PCQ-Infertility tool. *Human Reproduction*, 28, 2462-2472.
- 631 Pedro, J., Frederiksen, Y., Schmidt, L., Ingerslev, H. J., Zachariae, R., & Martins, M. V. (2016)
 632 Comparison of three infertility-specific measures in women and women going through assisted
 633 reproductive technology treatment. *Journal of Health Psychology*. Advance online publication.
 634 <https://doi.org/10.1177/1359105316678669>
- 635 Peterson, R. A. (1994). A meta-analysis of Cronbach's coefficient alpha. *Journal of Consumer Research*,
 636 21, 381-391.
- 637 Porat-Katz, A., Paltiel, O., Kahane, A., & Eldar-Geva, T. (2016). The effect of using complementary

- 638 medicine on the infertility-specific quality of life of women undergoing in vitro fertilization. *International*
639 *Journal of Gynecology & Obstetrics*, 135, 163-167.
- 640 Santoro, N., Eisenberg, E., Trussell, J. C., Craig, L. B., Gracia, C., Huang, H., ... Zhang, H. (2016).
641 Fertility-related quality of life from two RCT cohorts with infertility: Unexplained infertility and
642 polycystic ovary syndrome. *Human Reproduction*, 31, 2268-2279.
- 643 Santulli, P., Bourdon, M., Presse, M., Gayet, V., Marcellin, L., Prunet, C., ... Chapron, C. (2015).
644 Endometriosis-related infertility: assisted reproductive technology has no adverse impact on pain or
645 quality-of-life scores. *Fertility & Sterility*, 105, 978-987.
- 646 Schuler, M., Musekamp, G., Bengel, J., Nolte, S., Osborne, R. H., & Faller, H. (2014). Measurement
647 invariance across chronic conditions: a systematic review and an empirical investigation of the Health
648 Education Impact Questionnaire (heiQ™). *Health and Quality of Life Outcomes*, 12, 56.
- 649 Sexty, R. E., Hamadneh, J., Rosner, S., Strowitzki, T., Ditzen, B., Toth, B., & Wischmann, T. (2016).
650 Cross-cultural comparison of fertility specific quality of life in German, Hungarian and Jordanian couples
651 attending a fertility center. *Health and Quality of Life Outcomes*, 14, 1-8.
- 652 Skevington, S., Lotfy, M., & O'Connell, K. (2004). The World Health Organization's WHOQOL-BREF
653 quality of life assessment: Psychometric properties and results of the international field trial. A report
654 from the WHOQOL Group. *Quality of Life Research*, 13, 299-310.
- 655 Smith, N. K., Madeira, J., & Millard, H.R. (2015). Sexual function and fertility quality of life in women
656 using in vitro fertilization. *Journal of Sexual Medicine*, 12, 985-993.
- 657 Steuber, K. R., & High, A. (2015). Disclosure strategies, social support, and quality of life in infertile
658 women. *Human Reproduction*, 30, 1635-1642.
- 659 Specialist Unit for Review Evidence. (2013). Questions to assist with the critical appraisal of randomized
660 controlled trials and other experimental studies. 2013. Retrieved from
661 http://www.cardiff.ac.uk/insrv/libraries/sure/doc/SURE_RCT_Checklist_2013.pdf.
- 662 Valsangkar, A., Bodhare, T., Bele, S., & Sai, S. (2011). An evaluation of the effect of infertility on
663 marital, sexual satisfaction indices and health-related quality of life in women. *Journal of Human*

- 664 *Reproductive Sciences*, 4, 80-85.
- 665 van Balen F., & Bos, H. M. W. (2009). The social and cultural consequences of being childless in poor-
666 resource areas. *Facts, Views & Visions in Obgyn*, 1, 106-121.
- 667 van Balen, F., & Gerrits, T. (2001). Quality of infertility care in poor-resource areas and the introduction
668 of new reproductive technologies. *Human Reproduction*, 16, 215-219.
- 669 Verhaak, C. M., Smeenk, J. M., Evers, A. W., Kremer, J. A., Kraaimaat, F.W., & Braat, D. D. (2007).
670 Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Human*
671 *Reproduction Update*, 13, 27-36.
- 672 von Elm, E., Poglia, G., Walder, B., & Tramer, M. R. (2004). Different patterns of duplicate publication.
673 An analysis of articles used in systematic reviews. *Journal of the American Medical Association*, 291,
674 974-980.
- 675 Wells, G. A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2010). The
676 Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis.
677 Retrieved from http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
- 678 World Health Organization. (1995). The World Health Organization Quality of Life Assessment
679 (WHOQOL): position paper from the World Health Organization. *Social Science & Medicine*, 41, 1403-
680 1409.
- 681
- 682

683 **Biographical Notes:**

684 **Dr. Emily Koert:**

685 Dr. Emily Koert is a Registered Psychologist and Adjunct Professor at the University of British
686 Columbia, Vancouver, British Columbia, Canada. Her research and clinical work focuses on fertility-
687 related issues such as consequences of delayed childbearing, the psychosocial impact of recurrent
688 pregnancy loss and infertility, and fertility awareness and decision-making.

689

690

691 **Dr. Janet Takefman:**

692

693 Dr. Janet Takefman is a reproductive health and clinical psychologist. She is the coordinator of
694 psychological services & research at the MUHC Reproductive Centre and holds joint assistant
695 professorships at the Departments of Obstetrics & Gynecology and Psychology at McGill University,
696 Montreal, Canada.

697

698 She is considered a leader in her field and has co-authored over 100 monographs, grants, book chapters,
699 research studies and peer review articles and has been an invited speaker more than 50 times for medical
700 conferences around the world. She is the co-creator of the FertiQoL the only international validated
701 quality of life measure for the infertile population. She provides counselling and therapy.

702

703 **Professor Jacky Boivin:**

704 Professor Jacky Boivin is a Professor of Health Psychology and Chartered Health Psychologist in the
705 School of Psychology, Cardiff University.

706 Prof. Boivin's most important contribution to the field of reproductive health has been to bring about a
707 more systematic and research oriented perspective to the investigation of psychosocial issues in
708 reproductive health. She is the co-creator of the FertiQoL.

709 **Figure 1: Flowchart for study selection**

710

711

712

713

714

715

716

717

718

719

720

721

722

723

724

725

726

727

728

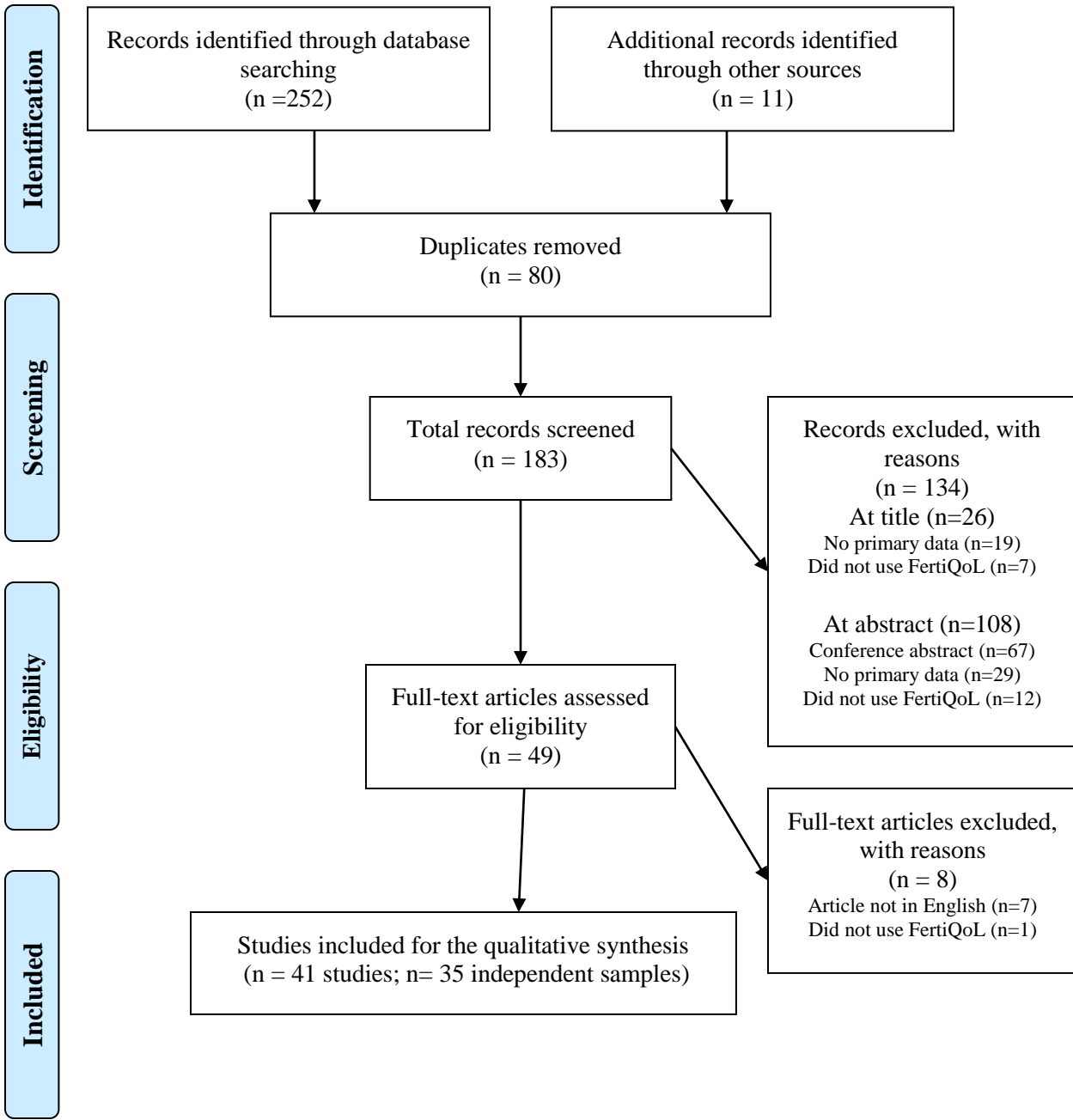
729

730

731

732

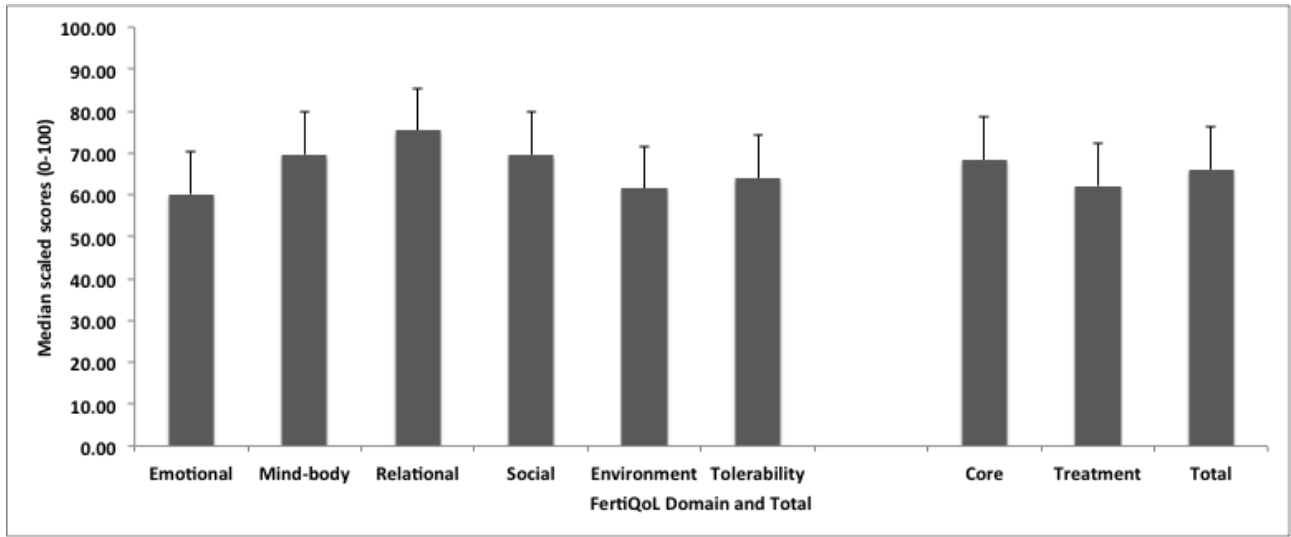
733



Note: PRISMA Diagram from reference Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.

PLoS Medicine, 6, e1000097.

734 **Figure 2: Average FertiQoL median scores (and standard deviations) from selected studies**



735
736

737 **Note.** Sample size varies according to domain or total score.

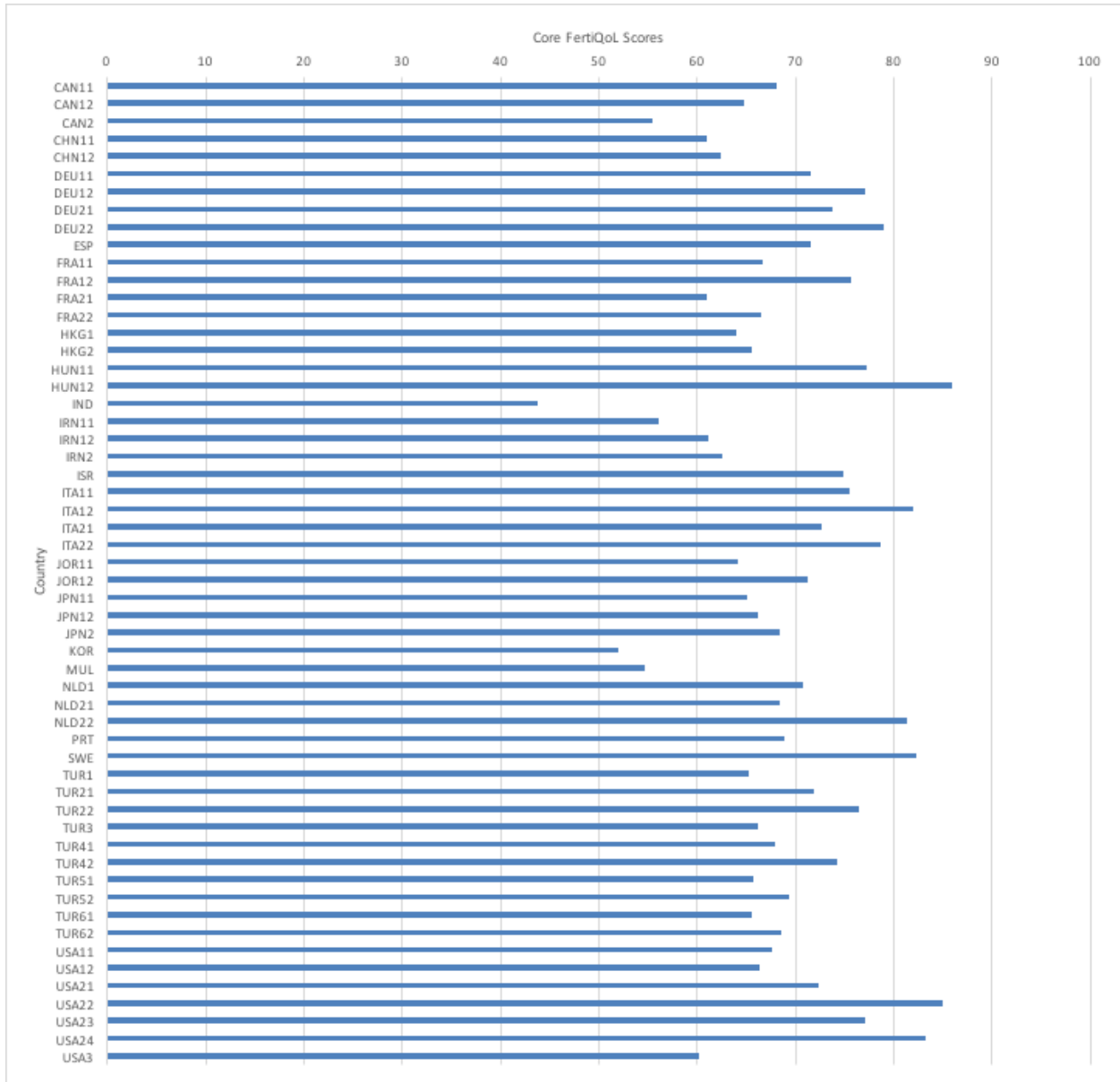
738 N=31 only independent samples included; mean scores from all studies ranged from 42.1 – 91.7, medians
739 for each subscale ranged from 59.80 - 75.42.

740 The scores shown in the graph are the medians of the distribution of mean subscale scores for the selected
741 studies (from Supplementary Table 13)

742

743

744 **Figure 3: Mean Core FertiQoL scores by country from selected studies**



745

746 **Note.** Three-letter country abbreviations used. First number after abbreviation is used when multiple
 747 studies for a country (studies numbered alphabetically) and second number is used when multiple
 748 independent groups within a study.

749 N=31 only independent samples included.

750 CAN=Canada, CNH=China, DEU=Germany, ESP=Spain, FRA=France, HKG=Hong Kong,
 751 HUN=Hungary, IND=India, IRN=Iran, ISR=Israel, ITA=Italy, JOR=Jordan, JPN=Japan, KOR=Korea,
 752 MUL=Multiple countries combined, NLD=Netherlands, PRT=Portugal, SWE=Sweden, TUR=Turkey,
 753 USA=United States.

754

755 See Supplementary Table 13 for list of mean Core scores by country.

756