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ORIGINAL ARTICLE

Male Infertility

Psychological consequences of a diagnosis of infertility in men: a systematic analysis

Sarah N Biggs¹, Jane Halliday^{1,2}, Karin Hammarberg^{3,4}

Almost half of infertility cases involve male infertility. Understanding the consequence of a diagnosis of male infertility, as a sole or partial contributor to the couples' infertility, to the mental health of men is required to ensure clinical care meets their psychological needs. The aim of this systematic analysis was to synthesize the evidence regarding whether men diagnosed with male factor infertility experience greater psychological distress than (1) men described as fertile and (2) men in couples with other infertility diagnoses. Online databases were searched using a combination of Medical Subject Headings (MeSH) headings and keywords relating to male infertility and psychological distress. The search yielded 1016 unique publications, of which 23 were included: 8 case-control, 14 prospective cohort, and 1 data linkage studies. Seven aspects of psychological distress were identified: depression, anxiety, self-esteem, quality of life, fertility-related stress, general psychological stress or well-being, and psychiatric conditions. Case-control studies reported that men with male factor infertility have more symptoms of depression, anxiety and general psychological distress, worse quality of some aspects of life, and lower self-esteem than controls. When men with male factor infertility were compared to men in couples with other causes of infertility, there were few differences in the assessed aspects of psychological distress. Despite methodological limitations within the studies, this systematic analysis suggests that the experience of infertility, irrespective of its cause, negatively affects men's mental health and demonstrates the need for assisted reproduction technology (ART) providers to consider men undergoing assisted reproduction as individuals with their own unique support needs. *Asian Journal of Andrology* (2024) 26, 10–19; doi: 10.4103/aja202334; published online: 22 August 2023

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INTRODUCTION

Formalized patient-centered care processes are increasingly being implemented in assisted reproductive technology (ART) practice.^{1–3} Patient-centered care is defined as “care that is respectful of and responsive to the individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions”⁴

One of the biggest challenges for ART health professionals in providing patient-centered care is that, in most instances, the couple is the “patient”, one entity whose goal is to achieve a live birth, rather than two individuals with independent preferences, needs, and values. Moreover, the cause of infertility may lie solely with one or the other of the members of the couple, be attributed to both parties, or be unknown. Therefore, individuals within each of these subgroups may require specific support. Finally, for the most part, regardless of the diagnosis of infertility, it is the female who must undergo the invasive and uncomfortable treatment. As such, the focus of care is on the woman, with the man often left feeling that he is not involved as an equal partner.^{5,6}

Among couples seeking ART, however, both parties contribute emotionally and biologically to the shared goal of achieving parenthood. The desire and expectation to become a parent are similar for men and women.^{7,8} Although the contribution of male factor infertility to couple

childlessness is almost equal to that of female factors,⁹ most research on the psychological support needs during ART has focused on women.¹⁰

Dissatisfaction with care¹¹ and specifically the care given to the male partner^{6,12} are reported to be common reasons for ceasing ART treatment or changing clinics. Feelings of neglect, unimportance, or disassociation from the treatment process are also commonly expressed by men,¹³ potentially adding to the psychological distress that accompanies infertility and ART treatment. Therefore, when considering how patient-centered care can mitigate men's ART-related distress, the psychological impact on men of infertility diagnosis and treatment needs to be better understood. Some early empirical studies found that men with male factor infertility suffer greater distress than men in couples with other infertility diagnoses,^{14–16} suggesting that this group requires clinical focus.

The aim of this systematic analysis was to synthesize the evidence about the psychological consequences of a diagnosis of male factor infertility to guide the development of patient-centered ART care that meets the needs of infertile men.

MATERIALS AND METHODS

Data sources and searches

To answer the question of whether men diagnosed with male factor infertility experienced greater psychological distress than men

¹Reproductive Epidemiology, Murdoch Children's Research Institute, Melbourne 3052, Australia; ²Department of Paediatrics, University of Melbourne, Melbourne 3052, Australia; ³Public Health and Preventative Medicine, Monash University, Melbourne 3004, Australia; ⁴Victorian Assisted Reproductive Treatment Authority, Melbourne 3000, Australia.

Correspondence: Dr. K Hammarberg (karin.hammarberg@monash.edu)

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described as fertile (control group) or men in couples with other infertility diagnoses, a systematic analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁷ The search strategy was designed by a specialist information analyst. A search of online databases (OVID MEDLINE, Embase, PsycINFO and PubMed) was conducted in October 2022 to identify published studies relating to a combination of MeSH headings and keywords. These included “infertile*”, “sub-fertil*”, “male (or men)”, and “coping”, “quality of life”, “emotions”, “anger”, “anxiety”, “psychological distress”, “guilt”, “depression”, “masculinity”, or “social stigma”.

Study inclusion and exclusion criteria

Quantitative experimental studies were included if they were published in a peer-reviewed English language journal between January 2000 and October 2022, reported on psychological distress in males experiencing infertility and had a comparison group.

Studies were excluded if they included participants with a known medical condition causing infertility (*e.g.*, testicular cancer and Klinefelter syndrome), the results were not disaggregated; only descriptive data were reported, population norms were used as a comparison, or psychological distress was not an outcome measure.

Data extraction and quality assessment

Search results were exported into EndNote (EndNote 20, Clarivate, Philadelphia, PA, USA). Titles and abstracts were screened by the lead author (SNB). Full-text articles were reviewed independently by all three authors.

The data extracted from included studies were aim, study design, number of participants, inclusion criteria, recruitment setting, participant characteristics (*e.g.*, age), infertility diagnosis, data collection tools, outcome measure, timing of assessment, and main findings.

The quality of the studies was assessed independently by all authors using QualSyst developed by Kmet *et al.*¹⁸ This assessment tool provides a systematic, reproducible, and quantitative way of assessing the quality of quantitative studies. The QualSyst scores range between 0 and 1.0.

Any discrepancies in inclusion/exclusion or quality assessment were resolved through discussion.

RESULTS

Search results

The database search yielded 1016 records, from which 208 duplicates were removed (Figure 1). An additional 842 records were removed as they were not relevant or met the exclusion criteria after the title review. After the screening of abstracts, 51 full-text articles were reviewed. Of these, 28 were excluded for not meeting inclusion criteria or providing only descriptive data. Full-text copies of two articles^{19,20} were unavailable online, and a request for a copy from the corresponding author yielded no response. Two articles were added after handsearching manuscript reference lists. A total of 23 articles were included in the systematic analysis.

The study characteristics and main findings are described in Table 1 and 2.

Psychological distress

The included studies reported on seven different aspects of psychological distress: depression ($n = 9$),^{21–29} anxiety ($n = 7$),^{21,22,24–27,30} self-esteem ($n = 5$),^{21,24,31–33} quality of life or aspects of quality of life such as marital or sexual relationship ($n = 11$),^{22,24,27,32–39} fertility-related stress ($n = 4$),^{22,31,40,41} general psychological distress or well-being ($n = 7$),^{29–31,37,41–43} and psychiatric conditions ($n = 2$).^{21,43}

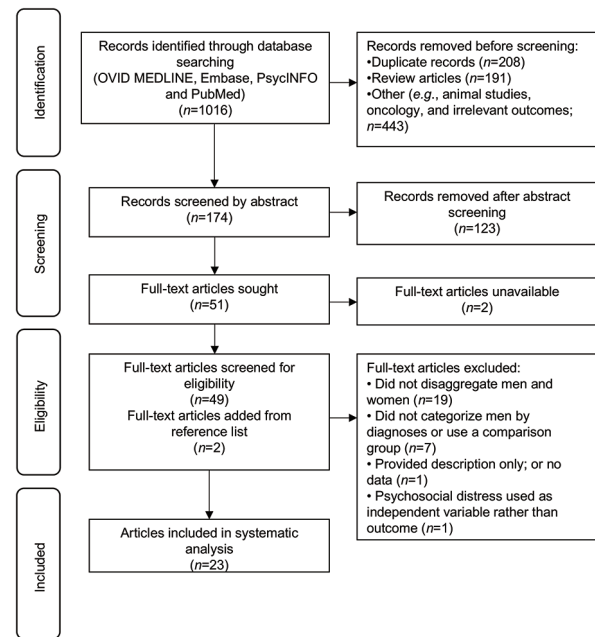


Figure 1: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram of literature search and study selection.

Study setting

The studies were conducted in 14 different countries: three in Iran,^{27,30,42} two each in Denmark,^{28,41} Italy,^{23,29} Poland,^{25,34,39,43} Tunisia,^{21,35} and China,^{26,33} and one each in Canada,²⁴ India,⁴⁰ Ireland,³¹ Japan,²² Pakistan,³² Sweden,³⁷ Turkey,³⁶ and the USA.³⁸ Some studies have multiple publications.

Study design and data sources

Data for the 23 publications originated from 21 studies. The publications by Drosdzol and Skrsypulec^{25,34} and by Worchol-Biedermann^{39,43} report on different outcomes from the same study. It appears that the publications of El Kissi *et al.*³⁵ and Amamou *et al.*²¹ are also based on the same study; however, as they are not cross-referenced and contain different methodological information, they have been reported here as separate studies. Eight publications were based on a case/control design (Table 1),^{21,24,25,30,32,34,35,42} ten employed a cross-sectional design,^{22,23,27,29,31,33,36–38,40} four were longitudinal,^{26,39,41,43} and one was based on a data linkage study²⁸ (Table 2). Except for the data linkage study, all used self-report questionnaires to obtain data. Most studies ($n = 15/23$) used validated assessment tools. Two studies used study-specific measures of emotional distress and two used both validated tools and study-specific measures.

Participants and recruitment

In all but three studies, participants were recruited from fertility clinics, either in public hospitals or private clinics. One study sourced participants from 10 fertility-related websites.³¹ Data for the linkage study were obtained from the Danish *in vitro* fertilization (IVF) register and Danish Psychiatric Central Research Register.²⁸ The description of the fertility status of the controls in case-control studies varied. In one study, men whose partner was currently pregnant²⁴ and in another male parents of children attending a vaccination clinic with no history of infertility³⁵ were presumed to be fertile. Controls from four other case-control studies were men whose fertility status was unknown as they were either attending a clinic for matters unrelated to infertility^{25,32,34}

Table 1: Study characteristics of case-control studies reporting psychological distress in infertile men compared to men describe as fertile

Author (year); location	Male participants (n)	Source of recruitment	Age and ID (year), mean±s.d.	Psychosocial assessment instrument	Outcome measures	Timing of psychosocial assessment	Main findings relevant to psychological distress in IMF infertility	QA score
Dhillon <i>et al.</i> (2000); ²⁴ Canada	Cases 1 (infertile men): 30 Cases 2 (unexplained infertility): 30 Controls: 30	Cases: hospital based academic fertility clinic Controls: physician in obstetric clinic. Partners of controls were currently pregnant	Cases 1: 36.4±1.3 ID: 1.6±0.3 Cases 2: 35.5±1.3 ID: 3±0.4 Controls: 34.2±1.4	1. IPAT Depression Scale ⁴⁹ 2. State-Trait Anxiety Inventory ⁶⁰ 3. State-Trait Anger Expression Inventory ⁶¹ 4. Index of Self Esteem ⁵² 5. Dyadic Adjustment Scale ⁵³ 6. Family Inventory of Life Events and Changes ⁵⁴ 7. Ways of Coping Inventory ⁵⁵	a. Depression b. Anxiety c. Anger d. Self-esteem e. Quality of the relationship f. Recent and past stresses influencing mood g. Personal coping strategies	During treatment	No significant differences on any measure between groups except Family Inventory of Life Events and change where stress was higher in the fertile group, whose partners were pregnant, compared to the infertile or unexplained groups	0.54
Drosdzol and Skrzypulec (2008) ³⁴ and (2009); ²⁵ Poland	Cases: 188 Controls: 190	Cases: patients in O and G clinics and infertility outpatient clinic under review for infertility diagnosis Controls: partners of patients in outpatient gynaecological clinics who attended for routine appointments	Cases: 31.4±4.7 ID: NR Controls: 32.8±6.5	1. SF-36 ^{45,56} 2. International Index of Erectile Function ⁵⁷ 3. Beck's Depression Inventory ⁵⁸ 4. Beck's Anxiety Inventory ⁵⁹	a. QoL b. Sexual functioning c. Depression d. Anxiety	At least 3 months following diagnosis	Cases and controls similar on QoL measure Cases scored significantly lower on sexual desire and intercourse satisfaction than controls Cases scored significantly higher on both depression and anxiety than controls Men with male infertility scored the highest and men in couples with female fertility scored the lowest on the depression scale compared to all other groups No differences by aetiology on the anxiety scale	2008: 0.95 2009: 0.91
Akhondi <i>et al.</i> (2013); ⁴² Iran	Cases: 80 Controls: 40	Cases: infertile men attending fertility clinic Controls: attended the same clinic as cases but with no infertility diagnosis	Cases: 37.5±7.3 ID: 7±1.1 Controls: 35±4.8	Author devised questionnaire of demographics and psychosocial development ⁴²	a. "Positive traits": trust, autonomy, initiative, industry, identity, intimacy, generativity, integrity b. "Negative traits": mistrust, shame and doubt, guilt, inferiority, confusion, isolation, stagnation, despair	NR	Controls showed significantly higher scores, indicating better psychosocial development, in the areas of trust, autonomy, identity, generativity and integrity Group differences on negative traits were NR	0.36
Amamou <i>et al.</i> (2013); ²¹ Tunisia	Cases: 100 Controls: 100	Cases: patients in the reproductive medicine unit of local hospital Controls: source NR	Cases: NR ID: 5.2±4.6 Controls: 37.6±5.7	1. The Symptom Checklist (SCL-90-R) ⁶⁰ 2. HAD-S ⁶¹ 3. RSES ⁶²	a. Psychotic symptoms b. Anxiety c. Depression d. Self-esteem	NR	Scores on psychotic symptoms, depression and anxiety measures significantly higher in cases than controls Self-esteem scores significantly lower in cases than controls	0.64
El Kissi <i>et al.</i> (2014); ³⁵ Tunisia	Cases: 100 Controls: 100	Cases: patients in the reproduction medicine unit of the local hospital Controls: parents of children attending first vaccination visit a local public health center.	Cases: 38.7±5.9 ID: NR Controls: 37.6±5.7	1. SF-36 ⁴⁵	a. Health related QoL	Cases: after diagnosis ⁶³ Controls: at child's vaccination visit	Cases had lower MCS scores than controls, indicating poorer mental well-being Cases had lower scores in the domains of vitality, social functioning and role-emotional than controls	0.72
Karimzadeh <i>et al.</i> (2017); ³⁰ Iran	Cases: 78 Controls: 50	Cases: infertile patients undergoing fertility treatment at local hospital and treatment center Controls: attended the same clinics as cases,	Cases: 31.7±3.4 ID: NR Controls: 33.4±6.0	1. SCL-90-R ⁶⁰ 2. Cattle Inventory ⁶⁴	a. Psychological distress b. Anxiety	NR	Cases had significantly higher scores on anxiety and paranoia than controls	0.86

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Table 1: Contd...

Author (year); Male location	Age and ID (year), mean±s.d.	Psychosocial assessment instrument	Outcome measures	Timing of psychosocial assessment	Main findings relevant to psychological distress in MF infertility	QA score
Jamil <i>et al.</i> (2020); ³² Pakistan	Cases: 45 Controls: 45	1. SEAR Questionnaire ⁶⁵	a. Sexual relationship b. Self-esteem c. Confidence d. Overall relationship	NR	Cases scored significantly lower than controls on all domains of the SEAR	0.91

IPAT: Institute of Personality and Ability Testing; s.d.: standard deviation; ID: infertility duration; NR: not reported; QA: quality assessment; O and G: obstetrics and gynecology; SF-36: Short Form Survey; QoL: quality of life; HAD-S: Hospital Anxiety and Depression Scale; RSES: Rosenberg Self-Esteem Scale; SCL-90-R: Symptom Checklist-90-revised; MCS: Mental Component Summary; SEAR: Self-Esteem and Relationship; MF: male factor

or were partners of women with an infertility diagnosis.^{30,32,42} Although these men were described as fertile, objective markers of fertility were not provided. One publication did not report the source of the control group, however having one child and no history of infertility was listed as an inclusion criterion.²¹

The number of participants ranged from 90 to 446. The total number of men categorized as infertile across all studies was 4057. The mean ± standard deviation (s.d.) age of participants, where reported, was 34.4 ± 5.0 years. Eleven studies reported the duration of infertility. Of these, nine reported the mean (pooled mean ± s.d.: 4.2±2.4 years),^{21,24,26,27,36,39,41–43} two reported the range (1–10 years²⁹ and 0–12 years⁴⁰), and one reported the median duration of infertility (3 years and 1 month²²). The percentage of men diagnosed with male factor infertility ranged from 6.3% to 52.7%. The pooled mean percentages for each infertility diagnostic category were: 29.2% (male factor), 32.2% (female factor), 15.1% (mixed factor), and 25.5% (unexplained). These figures do not add to 100% as some studies had additional categories^{22,29,31} or combined groups.³⁷

Study quality

Concordance in the assessment of study quality between the authors was high, with a mean difference in scores of 0.06 (range: 0–0.27). Overall, the included studies were of moderate-to-high quality as measured by QualSyst¹⁸ (Table 1 and 2). As none of the studies included an intervention, the three questions relating to this were removed. Of the remaining 11 questions, the mean score for all studies was 0.79 (range: 0.36–0.95). The criterion least addressed was controlling for confounders. Eleven of the 23 studies made no attempt to control for confounders, four made a partial attempt, and eight included confounders in their analyses.

Main findings

Eight case–control studies reported psychological distress in infertile men compared to men described as fertile (Table 1). Four assessed depression and/or anxiety,^{21,24,25,30} three examined quality of life,^{22,34,35} and three reported on general psychological distress^{21,30,42} and self-esteem,^{21,24,32} respectively.

Fifteen cohort studies reported differences in psychological distress between men with male factor infertility and men in couples with other infertility diagnoses (Table 2). Five examined the symptoms of depression and/or anxiety symptoms,^{22,23,26,27,29} eight reported on quality of life,^{22,27,33,36–39,44} five on general psychological distress,^{29,31,37,41,43} three on infertility-related stress,^{22,31,41} and one on self-esteem.³¹

Depression and anxiety

Compared to controls, men with diagnosed infertility were found to have significantly higher levels of depression and anxiety symptomology.^{21,25,30} The one study that did not show a difference was limited by a small sample size.²⁴ Having a male infertility diagnosis did not appear to increase the risk of depression or anxiety over and above the risk associated with other causes of infertility, with four^{22,23,27,29} of the five cohort studies reporting no difference between diagnostic groups. In the study that did find a difference,²⁶ 34% of men diagnosed with male infertility experienced depressive symptoms compared to 8.5%, 8.1%, and 15% of men with diagnoses of female factor, mixed factor, and unknown factors, respectively.

Quality of life (QoL)

Two case–control studies^{34,35} assessed the quality of life via the Short Form Survey (SF-36).⁴⁵ Lower scores in the vitality domain, indicative of poorer quality of life in this area, were reported by

Table 2: Study characteristics of cohort studies reporting psychological distress in men with male factor infertility compared to men in couples with other diagnoses

Author (year); location	Study design	Male participants (n)	Cause of infertility (%)	Age and ID (year), mean±s.d. or median (range)	Psychosocial assessment instrument	Outcome measures	Timing of assessment	Main findings relevant to psychological distress in MF infertility	QA score
Lee <i>et al.</i> (2001); ³³ Taiwan, China	Cross-sectional	138	MF: 38 FF: 31 MxP: 15 Unexplained: 15	Mean: 34.9 ID: NR	1. Chinese version of the Infertility Questionnaire ⁶⁶ 2. Marital Satisfaction Questionnaire ⁶⁷ 3. Sexual Satisfaction Questionnaire ⁶⁷	a. Self-esteem b. Blame/guilt c. Sexual impairment d. Marital satisfaction	NR	No differences on any domain between MF, FF, MxP or unexplained	0.64
Holter <i>et al.</i> (2007); ³⁷ Sweden	Cross-sectional	166	MF: 39 FF/MxP/unexplained combined: 61	MF: 35.0±6.4 Other: 33.6±4.9 ID: NR	1. Psychological General Well-being Index ⁶⁸ 2. Author devised questionnaire	a. Psychological well-being b. QoL, effects of infertility, relationship, support	2–4 weeks prior to treatment	MF reported less contact with friends and acquaintances than the other diagnoses groups combined	0.86
Peronace <i>et al.</i> (2007); ⁴¹ Denmark	Longitudinal	256	Self-reported MF: 29.3 FF: 30.9 MxP: 8.2 Unexplained: 31.6	34.0±5.0 ID: 4.3±2.4	1. Fertility Problem Stress Inventory ⁶⁹ 2. SF-36 ⁴⁵ 3. Stress Profile questionnaire ⁷⁰ 4. Ways of Coping Checklist ⁵⁵ 5. Four questions from the Danish Longitudinal Health Behaviour Study ⁷¹	a. Fertility problem related stress b. Mental health c. Physical health d. Coping e. Social environment f. Openness to infertility	T1: at first treatment T2: 12 months following T1	Mental health decreased between T1 and T2 but no difference between diagnostic groups or interaction Physical stress symptoms increased: no group difference or interaction Coping effort increased: no group difference or interaction Negative comments showed an interaction with the men in the unexplained group reporting more negative comments from social networks over time than female or MF	0.86
Dooley <i>et al.</i> (2014); ³¹ Ireland	Cross-sectional Study 1: participants recruited through 2 fertility clinics Study 2: participants completed an online survey in answer to an advertisement on 10 fertility related websites	Study 1: 111 Study 2: 55	Study 1 MF: 50 FF: 29.7 MxP: 22.5 remainder unreported Study 2 MF: 52.7 FF: 30.9 MxP: 16.3 remainder unreported	Study 1: 37.4±5.1 ID: NR Study 2: 35.2±5.7 ID: NR	1. GHQ-12 ⁷² 2. Fertility Problem Inventory ⁷³ 3. Dyadic Adjustment Scale ⁵³ 4. Male Role Attitudes Scale ⁷⁴ 5. RSES ⁶²	a. General mental well-being b. Fertility related stress c. Coping d. Attitudes towards masculinity e. Self-esteem	Study 1: after a fertility appointment Study 2: online	Study 1: MF reported less distress than FF Diagnosis type did not predict infertility distress Study 2: there were no significant difference in infertility distress between MF and FF Diagnosis type did not predict infertility distress	0.59
Patel <i>et al.</i> (2016); ⁴⁰ India	Cross-sectional	300	MF: 25.3 FF: 29.7 MxP: 30.3 Unexplained: 14.7	35 (24–54) ID: 1 (0–12)	1. Clinical interview using ICD-10 ⁵ 2. Psychological evaluation test for infertile couples ⁷⁶	a. Infertility specific related stress	After consultation with infertility specialist: referred for psychological evaluation	A diagnosis of MxP was 5 times more likely to elicit a high score of infertility distress than a diagnosis of FF An unexplained diagnosis was 4 times more likely to elicit a high score of infertility distress than FF	0.84
Valoriani <i>et al.</i> (2016); ²⁹ Italy	Cross-sectional	309	MF: 28.2 FF: 32 MxP: 11.7 Unexplained: 22.6 No examination: 5.5	37.2±5.0 ID: range 1–10	1. Edinburgh Postnatal Depression Scale ⁷⁷ 2. GHQ-12 ⁷²	a. Depression b. General psychological and physical well-being	After first consultation	No increased risk of depression based on diagnoses	0.93

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Table 2: Contd...

Author (year); location	Study design	Male participants (n)	Cause of infertility (%)	Age and ID (year), mean±s.d. or median (range)	Psychosocial assessment instrument	Outcome measures	Timing of assessment	Main findings relevant to psychological distress in MF infertility	QA score
Babore <i>et al.</i> (2017); ²³ Italy	Cross-sectional	170	Self-reported MF: 25.2 FF: 22.7 MxF 10.4 Unexpl-ained: 41.7	39.4±5.8 ID: NR	1. Zung Depression Scale ⁷⁸	a. Depression	Immediately after medical exam 69.4% were undergoing first treatment 30.6% had previous treatment(s)	MF had higher mean depression scores than other diagnoses, but this was not statistically significant	0.75
Goker <i>et al.</i> (2018); ³⁶ Turkey	Cross-sectional	127	MF: 6.3 FF: 29.1 MxF: 5.5 Unexplained: 59.1	31.4±5.9 ID: 3.8±3.3	1. Fertility QoL questionnaire ⁴⁴	a. QoL	NR	There were no differences on any QoL domain between MF, FF, MxF or unexplained	0.86
Liu <i>et al.</i> (2021); ²⁶ China	Longitudinal	247	MF: 19.0 FF: 47.8 MxF: 25.1 Unexplained: 8.1	31.72±4.9 ID: 3.1±1.9	1. Zung Self-Rating Anxiety Scale ⁷⁹ 2. Zung Self-rating Depression Scale ⁷⁸	a. Anxiety b. Depression	T1: day one of treatment T2: hCG administration T3: 4 days following transfer	Overall, proportionately more MF scored above the anxiety and depression cut-off compared to other diagnoses groups	0.89
Navid <i>et al.</i> (2017); ²⁷ Iran	Cross-sectional	248	MF: 39.5 FF: 30.6 MxF: 9.3 Unexplained: 20.6	33.3±5.7 ID: 4.8±3.5	1. HAD-S ⁶¹ 2. SWLS ⁸⁰	a. Anxiety b. Depression c. Life satisfaction	NR	No difference in mean anxiety or depression scores between MF, FF, MxF, or unexplained Men in the mixed infertility group had significantly lower scores on life satisfaction than the other three groups	0.89
Asazawa <i>et al.</i> (2019); ²² Japan	Cross-sectional	321	MF: 10.3 FF: 15.9 MxF: 2.1 Unexplained: 43.3% NYD: 18.4	37.9±5.2 ID: median 3 years and 1 month	1. Fertility QoL survey ⁴⁴ 2. Brief Scale of Social Support for Workers ⁸¹ 3. Jichi Medical School Social Support Scale ⁸² 4. Psychological distress – author devised questionnaire ⁸³	a. QoL b. Workplace support c. Spousal support d. Stress, anxiety, depressed mood	After treatment	MF scored significantly lower on FertiQoL than unexplained and FF MxF and NYD both scored significantly lower on FertiQoL than FF MF scored significantly higher on the distress scale than FF and NYD Unexplained and MxF scored significantly higher on the distress scale than FF MF was a significant predictor of QoL along with spousal support and prolonged duration of infertility	0.95
Smith <i>et al.</i> (2009); ³⁸ USA	Cross-sectional	357	Perceived infertility MF: 12 FF: 47 MxF: 16 Unexplained: 25	36.9±5.5 ID: NR	1. Author devised questionnaire ³⁸	a. Personal impact b. Social impact c. Sexual impact d. Marital impact	After treatment assessment	MF had higher sexual impact and personal impact score compared to FF after adjusting for confounders Unexplained infertility had higher social impact scores compared to FF, not significant after adjusting for confounders	0.93

Contd...

Table 2: Contd...

Author (year); location	Study design	Male participants (n)	Cause of infertility (%)	Age and ID (year), mean±s.d. or median (range)	Psychosocial assessment instrument	Outcome measures	Timing of assessment	Main findings relevant to psychological distress in MF infertility	QA score
Warchol-Biedermann (2019) ⁴³ and (2021); ³⁹ Poland	Longitudinal	255	MF: 29.8 FF: 31.4 Mx: 30.6 Unexplained: 8.2	30.2±4.3 ID: 1.2±0.3	1. GHQ-28 ⁷² 2. Fertility QoL Questionnaire ⁴⁴	a. Emotional distress b. Psychiatric morbidity c. Fertility related QoL	T1: before initial fertility evaluation T2: 2-3 months after diagnostic disclosure T3/4: before follow-up appointments	Prevalence of distress in MF 9.2% at T1, 59.2% at T2, 49.2% at T3 and 34.6% at T4 Prevalence of distress in FF 13.7% at T1, 21.5% at T2, 42.6% at T3, and 34.4% at T4 Prevalence of distress in Mx 11.5% at T1, 67.5% at T2, 50.7% at T3 and 16.3% at T4 Prevalence of distress in Unexplained 4.7% at T1, 9.5% at T2, 15.7% at T3 and 0% at T4 QoL reduces from T1 to T2 and then remains stable in MF and Mx QoL remains stable between T1 and T2 in FF but then decreases at T3 QoL does not change over time in unexplained At T1, FF reported the lowest QoL compared to all other groups. Mx had significantly poorer QoL compared to MF and unexplained At T2, MF, FF and Mx reported lower QoL than unexplained. Mx was also significantly lower than FF At T3, MF, FF and Mx scored significantly lower QoL than unexplained At T4, FF and Mx scored lower QoL than unexplained. There was no statistical difference between MF and unexplained Men with their first depression prior to ART were more likely to be diagnosed with MF than men with their first depression diagnosis after ART MF did not increase the risk of depression after ART treatment	2019: 0.73 2021: 0.68
Sejbaek <i>et al.</i> (2020); ²⁸ Denmark	Register-based study. Data linkage	446	MF: 33.7 FF: 42.2 Mx: 8.4 Unexplained: 15.7	36.4±6.7 ID: NR	1. Danish Psychiatric Central Research Register ⁸⁴	a. Unipolar depression	NA		0.82

s.d.: standard deviation; MF: male factor; FF: female factor; Mx: mixed factor (both parties have fertility concerns); ID: infertility duration; NR: not reported; QoL: quality of life; ART: assisted reproductive technology; QA: quality assessment; NYD: not yet determined; GHQ: General Health Questionnaire; SWLS: Satisfaction with Life Scale; SF-36: Short Form Survey; RSES: Rosenberg Self-Esteem Scale; HAD-S: Hospital Anxiety and Depression Scale; NA: Not available; ICD: International Classification of Diseases; hCG: human chorionic gonadotropin

infertile men than controls in both studies. Results for other domains were conflicting. Drozdol and Skrzypulec³⁴ found no differences in any of the other QoL domains, while El Kissi *et al.*³⁵ found infertile men scored lower (*i.e.*, poorer QoL) than controls on the domains of social functioning, role-emotional, and the overall summary domain of mental health.

Of the seven cohort studies examining QoL, four studies^{27,37–39} reported poorer QoL in at least one domain in men with male infertility compared to other infertility diagnoses. Asazawa *et al.*²² assessed QoL via the Fertility Quality of Life Scale⁴⁴ and found that men with male factor infertility reported poorer quality of life than men with other diagnoses, in particular those with female factor or unexplained infertility. Holter *et al.*³⁷ asked men to compare their ideal life to how their life was currently and found that men diagnosed with male factor infertility had a greater disconnect between ideal versus real life in the area of contact with friends and acquaintances than men in couples with other diagnoses. Navid *et al.*²⁷ found that men in couples with mixed factor infertility had reported poorer satisfaction with life than those in couples of other diagnoses. Smith *et al.*³⁸ found that the following areas of life were impacted by male factor infertility: sexual, personal, and social relationships. Warchol-Biedermann³⁹ reported that men with male factor infertility had better QoL than men in couples with female or mixed factor infertility before diagnosis; however, after diagnosis, there was no difference between these groups. Goker *et al.*³⁶ and Lee *et al.*³³ reported no differences between diagnostic groups.

General psychological distress and psychotic symptoms

Infertile men were reported to have greater paranoia,³⁰ psychotic symptoms,²¹ and reduced psychosocial development,^{21,42} when compared to men whose fertility status was unknown. Three of the five cohort studies reported no difference in psychological distress between diagnostic groups.^{29,37,41} In their clinical sample, Dooley *et al.*³¹ found that men with diagnosed infertility themselves reported less distress than men whose partners were infertile. No differences were found between diagnostic groups in their online sample. Warchol-Biedermann⁴³ reported that the proportion of men at risk of psychiatric morbidity following diagnosis increased by 50% in men with male factor and 56% in men in a couple with mixed factor, compared to an increase of 8% and 5% in men in couples diagnosed with female factor and unexplained infertility, respectively. Between-group comparisons were not statistically analyzed.

Self-esteem

Infertile men reported lower self-esteem score than men where fertility status was unknown in two^{21,32} of three case-control studies.^{21,24,32} As with depression and anxiety above, no difference was found in Dhillon *et al.*²⁴ potentially due to the small sample size. Of the cohort studies, Lee *et al.*³³ reported no difference in self-esteem scores between diagnostic groups. While self-esteem was measured in Dooley *et al.*,³¹ it was used as a predictor of distress, rather than an outcome variable. In that study, lower self-esteem was significantly related to higher infertility distress in both the clinical and online samples.

Infertility-related stress

Four of the cohort studies assessed infertility-related stress.^{22,31,40,41} Results varied depending on the assessment method used. Patel *et al.*⁴⁰ used clinical interviews and found significantly higher infertility-related stress in men with male factor infertility than in men in couples with other infertility diagnoses.⁴⁰ The two studies that used questionnaires to assess fertility-related stress did not find a difference.^{22,31} In their longitudinal study, Peronace *et al.*⁴¹ found that social and marital stress

increased over time in all diagnostic groups, with no difference between the groups or interaction between diagnosis and time.

DISCUSSION

The findings of this study suggest that a diagnosis of infertility, regardless of whether the cause of the infertility is male or female related, adversely affects the mental health of men. Compared to men who have been described as fertile, men with male factor infertility have more symptoms of depression, anxiety and general psychological distress, worse quality of life in some areas, and lower self-esteem. However, when men with male factor infertility were compared to men in couples with female factor, mixed factor, or unexplained infertility, there were more similarities than differences. This suggests that the experience of infertility, irrespective of its cause, negatively affects men's psychological well-being.

There are some limitations to this study. Due to the lack of consistent assessment tools used across the studies, we were unable to perform a meta-analysis. Between-study comparisons were difficult due to inconsistent definitions of the infertility status of cases (*e.g.*, medically assessed versus self-perception of infertility status) and the fertility status of controls (*e.g.*, men in currently pregnant couples versus male partners of women undergoing routine gynecological examinations). The use of generalized terms of psychological distress and varying recruitment sources also prevented direct comparisons. As such, caution must be taken when interpreting the findings of this study. While only reviewing articles in English can be considered a limitation, it must be noted that the majority of studies were conducted in countries where English was not the first language. In addition, many of the studies had been conducted in traditionally strong patriarchal societies (*e.g.*, Iran, Pakistan, and Turkey). Although there is a potential that men's cultural and religious backgrounds may create a belief bias around masculinity and infertility, the outcomes of the studies included in this study suggest that infertility distress is not culture-specific.

Although the methodological quality of the studies was rated as moderate to high, there are a number of study limitations to consider, including small sample sizes, the use of nonvalidated study-specific assessment tools, and lack of control of confounders, particularly the timing of the psychological assessments. The longitudinal studies included in this study^{26,39,41,43} clearly show that psychological distress reduces over the treatment journey, with the highest level of distress occurring just after the diagnosis and prior to starting treatment. Thus, any differences observed in case-control studies would likely differ in magnitude depending on when in the treatment journey the assessment took place.

In addition, these studies cannot be presumed to be addressing the full psychological profile of men experiencing infertility. Qualitative studies suggest that men might be more likely to express anger, frustration, guilt, disempowerment, or feelings of disconnection, rather than depression or anxiety.⁸ Although the terms "anger" and "guilt" were used as search terms for this study, few of the identified studies examined these concepts. In those that did, there was either no difference between the groups^{24,33} or the results were not presented.⁴² Interviews and discussions may be more likely to illicit an emotional response that more closely approximates how men are genuinely feeling.⁸ The contrary results in infertility-related stress between Patel *et al.*,⁴⁰ who conducted interviews, and three studies^{22,31,41} that employed questionnaires to gather data, lend some support to this. A more comprehensive review that includes qualitative studies is warranted to fully understand the breadth of emotions experienced by men undergoing ART and inform patient-centered care.

It may also be that men are reluctant to discuss their psychological distress as a way of protecting their partner. In qualitative studies, men report the need to “be strong”, with concern for their partner’s emotional and mental well-being taking precedence over their own feelings of despair and grief.^{8,13,46} Standardized assessment tools, such as those used in the studies of this systematic analysis, may not be sensitive enough to detect the nuances of psychological distress in men experiencing infertility. Interviews and discussions with medical staff may be more likely to reveal men’s true emotional responses to infertility, as is suggested by the different results when using clinical interview⁴⁰ versus self-reported questionnaires.^{22,31}

Despite the limitations, these findings emphasize the need for ART providers to consider men as individuals with their own unique support needs and implement patient-centered care that meets their needs, which may be different to women’s.⁴⁷ Aside from their partner, the most common place men seek support is from the clinic or medical staff.⁷ Yet, some studies are showing that men continue to feel disenfranchised in their encounters with ART clinic staff. A survey of 210 men undergoing fertility treatment in Denmark⁶ revealed that 63% of men reported that the medical staff communicated predominantly with their female partner, and only 10% agreed that the medical staff gave them the opportunity to discuss their experiences of infertility. Bringing them into the conversation regarding mental well-being during the ART process might validate and normalize their feelings as well as acknowledge they play an active role in the treatment process.⁴⁸

This analysis provides further evidence to the growing literature that calls for the systematic implementation of patient-centered care in ART settings. In particular, a model of care that caters for the unique needs of all men, irrespective of their personal infertility diagnosis, could potentially mitigate the psychological distress felt by these men.

AUTHOR CONTRIBUTIONS

SNB conceived the study, conducted the database searches and first screening of manuscripts, contributed in assessing the quality of the included manuscripts, extracted the data, and drafted the manuscript. JH provided the resources and supervision, contributed in the quality assessment of included manuscripts, and reviewed drafts of this manuscript. KH designed the methodology, contributed in the quality assessment of included manuscripts, and reviewed drafts of this manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declare no competing interests.

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