






Original Research

# Mechanisms of Fertility Stress in Infertile Couples: A Pathway Analysis

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## Abstract

**Background:** Infertility has become a global public health and psychosocial challenge, bringing substantial psychological pressure to affected individuals and couples. To investigate the effects of fertility stress and social support in infertile patients and their spouses, and to examine the mediating role of irrational parenthood cognition. **Methods:** Using convenience sampling, 425 infertile couples were recruited from a reproductive center in Zhejiang Province from January 2023 to June 2024. Participants completed questionnaires including general demographic information, the Irrational Parenthood Cognition Scale, and the Fertility Problem Inventory (FPI) and the Social Support Rating Scale (SSRS). Data were analyzed using descriptive statistics, paired-samples *t*-tests, Harman's single-factor test, Pearson correlation analysis, and the Actor-Partner Interdependence Mediation Model (APIMeM). **Results:** In infertile couples, social support was negatively correlated with both irrational parenthood cognition and fertility stress ( $p < 0.01$ ), whereas irrational parenthood cognition was positively correlated with fertility stress ( $p < 0.01$ ). For actor effects, wives' social support influenced their own fertility stress through their own, but not their husbands', irrational parenthood cognition, whereas husbands' social support influenced their own fertility stress through both their own and their wives' irrational parenthood cognition. For partner effects, husbands' social support influenced wives' fertility stress through the wives, but not their own, irrational parenthood cognition, whereas wives' social support influenced husbands' fertility stress through both their own and their husbands' irrational parenthood cognition. **Conclusions:** Clinical interventions should address infertile patients and their spouses as an integrated unit, targeting both fertility cognition and social support to alleviate fertility stress.

**Keywords:** infertility; fertility stress; social support; irrational parenthood cognitions; Actor-Partner Interdependence Mediation Model (APIMeM)

## 1. Introduction

Infertility refers to the failure to conceive after one year of regular sexual intercourse without contraception [1]. Data from the World Health Organization shows [2] that the incidence of infertility has been increasing annually, reaching 10% to 20%, with one in every six couples experiencing fertility issues, making it the third major health concern after cancer and cardiovascular diseases [3]. Irrational fertility cognition refers to a cognitive bias in people's perception of reproduction, believing that one must have a child to achieve a happy life [4]. Influenced by traditional Chinese fertility concepts, many couples view having a child as the bond that sustains family and marital happiness, and parenting is considered one of life's important goals. As a special reproductive health defect, infertility affects over 80% of patients, who bear significant reproductive burdens and psychological stress [5]. A study has demonstrated [6] that support from a spouse is directly or indirectly related to stress experienced by oneself or the spouse. In family relationships, when women are more likely to feel support from their partners, they are more prone to conceive and engage in reproductive behavior [7], and family support plays a significant role in reproductive decision-making [8]. Research indicates that social support influences women's

fertility values, and there is a significant positive correlation between fertility cognition and social support among women [9]. Previous studies focusing solely on infertile women or men failed to fully understand the crucial role played by their spouses. For infertile couples, childbearing is a shared challenge, necessitating a comprehensive analysis of the couple as a whole. This study employs Kenny's Actor-Partner Interdependence Model Extended to Mediation (APIMeM) [10,11] to examine the relationship between social support, irrational fertility cognition, and fertility stress in infertile couples. In this model, an individual's dependent variable is influenced not only by their own independent variables (subject effect) but also by specific object variables within a defined scope (object effect). Independent variables affect outcome variables through both direct effects (direct effect) and mediated effects via intermediate variables (indirect effect). The study investigated whether fertility stress in infertile couples is simultaneously influenced by their own and their spouse's social support, and analyzed whether irrational fertility cognition serves as a mediating factor in this relationship. This study aimed to clarify the underlying mechanisms and provide theoretical foundations for clinical personalized interventions.



## 2. Materials and Methods

### 2.1 Participants

A convenience sampling method was employed to recruit 425 infertile couples from a reproductive medical center in Zhejiang Province between January 2023 and June 2024. Inclusion criteria: (i) meeting the diagnostic criteria for infertility as described by the World Health Organization [1]; (ii) infertility caused by female factors; (iii) all participants voluntarily participated and signed the informed consent form. Exclusion criteria: individuals with a history of mental illness or use of antipsychotic medications within the past three months; those unable to communicate effectively or comprehend written content; participants who declined cooperation after the researcher's explanation or withdrew during the study. The sample size was calculated based on the principle of 5–10 times the number of questionnaire items for analysis, yielding a required range of 415–830 participants. Accounting for a 20% potential attrition rate, the final target sample size was determined to be 498–996 participants. The study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Women's Hospital, School of Medicine, Zhejiang University (IRB-20220124-R). All participants provided informed consent prior to enrollment.

### 2.2 Measurements

The general information questionnaire was designed by the researcher according to the purpose of the survey, including age, residence, education level, occupation, annual family income, length of marriage, and marital history.

The Irrational Parenthood Cognition Questionnaire (IPCQ) was developed in the Netherlands and translated into Chinese [12]. It was created to test fertility awareness in women of reproductive age. The questionnaire contains 14 items, scored using a 5-point scale (1–5 points, from strongly disagree to strongly agree). The total score ranges from 14 to 70 points, with 42 points serving as the cutoff for irrational parenthood cognition. Higher scores indicate the belief that having a child would contribute to happiness. The Cronbach's alpha for the scale was 0.87.

Fertility stress was measured using the Fertility Problem Inventory (FPI) [13,14]. The inventory consists of 46 items categorized into subscales: social, sexual, and relationship concerns, rejection of child-free living, and the need for parenthood. The comprehensive FPI is frequently applied to assess infertility stress worldwide, and its total and subscale scores are reliable and valid. The total fertility pressure score and its sub-scales demonstrate high levels of reliability and validity, with Cronbach's alpha coefficients ranging from 0.77 to 0.93, making them widely used in international infertility research. Due to their strong specificity and comprehensiveness, they have been validated for clinical evaluation of infertility patients in China [15].

We used the Social Support Rating Scale (SSRS) [16] to assess the social support status of patients with infertili-

ty. It consists of 10 items that span objective and subjective assistance and social support utilization. The overall score comprises the sum of scores (64) from the 10 items, with higher scores indicating better social support. The Cronbach's alpha coefficients for all dimensions of social support ranged from 0.89 to 0.94, with an overall test-retest reliability of 0.92, and have been widely used in clinical practice [17].

Trained investigators explained the purpose and significance of the study to eligible infertile couples and obtained their informed consent. Participants then completed an electronic questionnaire via Questionnaire Star APP (Wenjuanxing, Changsha, Hunan, China), with on-site submission. Investigators provided standardized instructions for any queries during the process and verified submissions immediately. A total of 900 questionnaires were distributed, with 850 valid responses collected, yielding an effective response rate of 94.5%.

### 2.3 Statistical Analysis

Data analysis was performed using SPSS 26.0 statistical software (IBM Corp., Armonk, NY, USA). The data were analyzed using descriptive statistics, paired samples *t*-tests, Harman's single factor test, Pearson's correlation analysis, and the APIMeM model was employed using structural equation modeling to account for the non-independence of data from couples. The APIMeM model was constructed using Mplus 8.3 software (Los Angeles, CA, USA), with fertility pressure as the dependent variable, social support as the independent variable, and irrational parenthood cognition as the mediating variable. The APIMeM model was built using maximum likelihood estimation [18,19], with bootstrap mediation effect testing (repeated sampling 2000 times) at a significance level of  $\alpha = 0.05$ . Model fit was assessed using the Chi-square free degree ratio ( $\chi^2/df$ )  $< 3$ , root-mean-square error of approximation (RMSEA)  $< 0.08$ , comparative fit index (CFI)  $> 0.90$ , and Tucker-Lewis index (TLI)  $> 0.90$ .  $p < 0.05$  was considered statistically significant [20].

## 3. Results

### 3.1 Demographic Characteristics

General demographic data of 425 infertile couples: male age 22–50 years, female age 20–46 years. The demographic profiles of the 425 infertile couples, including age, residential area, ethnicity, marital history, duration of marriage, educational level, occupation, and annual household income, are presented in Table 1.

### 3.2 Common Method Bias Test

To assess potential common method bias, Harman's single-factor test was utilized. The results revealed 18 factors with eigenvalues  $> 1$  for wives and 15 for husbands. The first factor accounted for 25.48% and 31.86% of the total variance in wives and husbands, respectively,

**Table 1. General data for infertile couples [N = 425, n (%)].**

Variable	Groups	Wives	Husbands
Age (years)	≤30	145 (34.1)	88 (20.7)
	31–35	186 (43.8)	164 (38.6)
	36–40	82 (19.3)	103 (24.2)
	>40	12 (2.8)	70 (16.5)
Residence	Countryside	123 (28.9)	123 (28.9)
	City	270 (63.5)	270 (63.5)
	Urban and rural areas	32 (7.5)	32 (7.5)
Nationality	Han Chinese	414 (97.4)	411 (96.7)
	Minority	11 (2.6)	14 (3.3)
Marital Status	First Marriage	363 (85.4)	363 (85.4)
	Remarriage	62 (14.6)	62 (14.6)
Marriage duration (years)	1–2	100 (23.5)	100 (23.5)
	3–5	201 (47.3)	201 (47.3)
	6–10	90 (21.2)	90 (21.2)
	>10	34 (8.0)	34 (8.0)
Level of Education	Primary and less	65 (15.3)	57 (13.4)
	Junior	68 (16.0)	68 (16.0)
	Senior	110 (25.9)	87 (20.5)
	Tertiary	154 (36.2)	159 (37.4)
	College/university degree	28 (6.6)	54 (12.7)
Occupation	Worker	38 (8.9)	71 (16.7)
	Farmer	7 (1.6)	11 (2.6)
	Civil Servant	10 (2.4)	14 (3.3)
	Self-employed	39 (9.2)	57 (13.4)
	Teacher	37 (8.7)	15 (3.5)
	Professional/technical	52 (12.2)	118 (27.8)
	Freelance	84 (19.8)	56 (13.2)
	Others	158 (37.2)	83 (19.5)
Annual household income (RMB)	<50,000	56 (13.2)	56 (13.2)
	50,000–100,000	122 (28.7)	122 (28.7)
	100,001–300,000	149 (35.1)	149 (35.1)
	>300,000	98 (23.1)	98 (23.1)

Abbreviations: N, number of couples. 1 USD ≈ 7.3038 RMB (Accord by 18 December 2025).

**Table 2. Comparison of social support, irrational parenthood cognition, and fertility stress scores for infertile couples [N = 425].**

Variable	Wives	Husbands	<i>t</i>	<i>p</i>
SSRS	41.192 ± 8.204	43.795 ± 7.032	-7.537	<0.001
IPC	41.907 ± 8.755	38.586 ± 9.762	8.786	<0.001
FPI	146.414 ± 32.553	142.162 ± 34.626	3.306	0.001

Abbreviations: SSRS, Social Support Rating Scale; IPC, Irrational Parenthood Cognition; FPI, Fertility Problem Inventory.

both below the 40% threshold for critical common method bias [21]. These findings indicate no substantial common method bias in this study.

### 3.3 Comparison

The total social support scores for 425 wives were (41.192 ± 8.204), irrational parenthood cognition (41.907 ± 8.755), and fertility pressure (146.414 ± 32.553). For 425 husbands, the corresponding scores were 43.795 ± 7.032, 38.586 ± 9.762, and 142.162 ± 34.626. Statistically significant differences were observed in social support ( $p < 0.05$ ). Detailed data are presented in Table 2.

### 3.4 Correlation Analysis

The results demonstrated significant negative correlations between social support and both irrational parenthood cognitions and fertility stress among infertile couples. Conversely, irrational parenthood cognitions showed significant positive correlations with fertility stress. Detailed correlation coefficients are presented in Table 3.

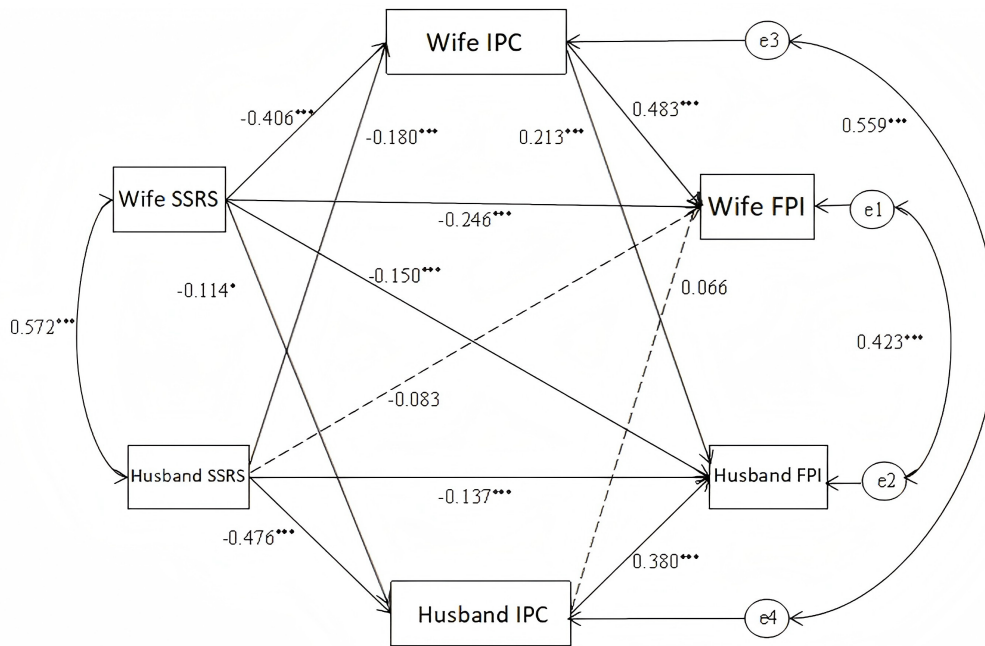


Fig. 1. Path analysis model in infertile couples. (e1–e4 are error terms, \* indicates  $p < 0.05$ , \*\*\* indicates  $p < 0.001$ ).

Table 3. Relevant analysis of social support, irrational parenthood cognition, and fertility stress in infertile couples [N = 425, r].

Variable	1	2	3	4	5	6
SSRS of wife	1					
SSRS of husband	0.572**	1				
IPC of wife	-0.509**	-0.413**	1			
IPC of husband	-0.387**	-0.541**	0.651**	1		
FPI of wife	-0.565**	-0.459**	0.685**	0.520**	1	
FPI of husband	-0.484**	-0.516**	0.593**	0.651**	0.690**	1

\*\* indicates  $p < 0.01$ .

### 3.5 APIMeM Analysis

An initial Actor-Partner Interdependence Mediation Model (APIMeM) was constructed with irrational parenthood cognitions as the mediating variable between social support and fertility stress. The model was tested using bootstrap resampling with 2000 iterations, with the final solution converging on a saturated model (Fig. 1). The results demonstrated that the model fit well with the binary data, with  $\chi^2/df = 1$ , RMSEA = 0.000, CFI = 1.000, and TLI = 1.000.

The effect size of the constrained simplified model is shown in Table 4. The social support of the individual significantly predicts the fertility pressure of the individual and the spouse (both the subject effect and the object effect are significant). Specifically, the wife's social support had a direct effect on her own fertility pressure ( $\beta = -0.246$ ,  $p < 0.001$ ) and a direct effect on her husband's fertility pressure ( $\beta = -0.150$ ,  $p < 0.01$ ). The husband's social support had a direct effect on his own fertility pressure ( $\beta = -0.137$ ,  $p < 0.01$ ) but a direct effect on his wife's fertility pressure ( $\beta = -0.083$ ,  $p > 0.05$ ), which was not statistically significant.

### 3.6 Contrastive Analysis

As shown in Table 4, the indirect effect of social support on fertility pressure through irrational fertility cognition is significant for both husband and wife. The wife's subjective indirect effect ( $\beta = -0.204$ ,  $p < 0.001$ ) accounted for 45.33% of the total effect, while the object's indirect effect ( $\beta = -0.118$ ,  $p < 0.001$ ) accounted for 58.71%. The husband's subjective indirect effect ( $\beta = -0.219$ ,  $p < 0.001$ ) accounted for 61.52% of the total effect, and the object's indirect effect ( $\beta = -0.130$ ,  $p < 0.001$ ) accounted for 46.43%. Further comparison shows that the subject effect is stronger than the object effect, and the direct effect is stronger than the indirect effect in the wife, while the subject effect is stronger than the object effect, and the indirect effect is stronger than the direct effect in the husband.

## 4. Discussion

This study employed the subject-object interdependence mediation model to investigate the underlying mechanisms linking social support, irrational fertility beliefs, and reproductive stress in infertile couples. The findings

**Table 4. Results of the Bootstrap-test for subject-object mediation effects [N = 425].**

Effect		$\beta$	SE	95% CI	Effect proportion (%)	$p$
Subject effect of wife	Total effect	-0.450	0.046	(-0.536, -0.363)		0.000
	Direct effect	-0.246	0.042	(-0.329, -0.164)	54.67%	0.000
	Total indirect effect	-0.204	0.030	(-0.264, -0.147)	45.33%	0.000
	Wife SSRS→Wife IPC→Wife FPI	-0.196	0.030	(-0.26, -0.140)	43.56%	0.000
	Wife SSRS→Husband IPC→Wife FPI	-0.008	0.007	(-0.023, 0.005)	1.78%	0.289
Object effect of wife	Total effect	-0.201	0.051	(-0.296, -0.102)		0.000
	Direct effect	-0.083	0.050	(-0.182, 0.012)	41.29%	0.097
	Total indirect effect	-0.118	0.033	(-0.185, -0.051)	58.71%	0.000
	Husband SSRS→Wife IPC→Wife FPI	-0.087	0.025	(-0.137, -0.042)	43.28%	0.001
	Husband SSRS→Husband IPC→Wife FPI	-0.031	0.026	(-0.082, 0.019)	15.42%	0.227
Subject effect of Husband	Total effect	-0.356	0.043	(-0.439, -0.267)		0.000
	Direct effect	-0.137	0.046	(-0.224, -0.042)	38.48%	0.003
	Total indirect effect	-0.219	0.029	(-0.278, -0.166)	61.52%	0.000
	Husband SSRS→Wife IPC→Husband FPI	-0.038	0.014	(-0.072, -0.015)	10.67%	0.007
	Husband SSRS→Husband IPC→Husband FPI	-0.181	0.026	(-0.234, -0.128)	50.84%	0.000
Object effect of Husband	Total effect	-0.280	0.049	(-0.379, -0.181)		0.000
	Direct effect	-0.150	0.046	(-0.242, -0.060)	53.57%	0.001
	Total indirect effect	-0.130	0.029	(-0.190, -0.073)	46.43%	0.000
	Wife SSRS→Wife IPC→Husband FPI	-0.087	0.020	(-0.131, -0.05)	31.07%	0.000
	Wife SSRS→Husband IPC→Husband FPI	-0.043	0.021	(-0.088, -0.005)	15.36%	0.041

demonstrated significant subject and object effects across these psychological variables, highlighting the importance of considering the bidirectional interaction between partners in psychological interventions for infertile couples.

#### 4.1 Gender Differences

The results revealed that the husband's social support level was significantly higher than that of the wife ( $p < 0.001$ ), while the level of irrational fertility cognition and fertility pressure was significantly lower than that of the wife ( $p \leq 0.001$ ). This finding aligns with previous studies [22,23], further confirming the universality of gender differences. Women are more susceptible to internalizing social stigma-induced stress, whereas men, as primary supporters in marital relationships, benefit from more visible and stable social support systems. Such support helps alleviate stress, potentially mitigating the development of irrational cognition to some extent. Li *et al.* [24] demonstrated that social support from partners significantly reduced anxiety levels, thereby validating the core tenet of the stress-buffering theory that 'social resources alleviate stress'. Lei *et al.* [25] found that family harmony and support from family members are essential components of women's fertility perspectives [25]. This support can actively help women reduce difficulties in childbirth and child-rearing, thereby serving as a positive influencing factor. In the current family relationships in China, although the proportion of the "spouse axis" is gradually increasing, the "parent-child axis" remains the core of the family. The continuation of the family line and the birth of children are still objective facts in many family relationships. Due to the emphasis

of social culture on the female reproductive role, women often bear more social expectations and psychological burden in the process of infertility diagnosis and treatment. It is easy for them to suffer from unequal treatment and bad social public opinion because of their inability to have children, which aggravates their inner pressure and cognitive distortion, and limits the buffering effect of social support. Therefore, before receiving assisted reproductive technology, the level of cognition and social support of the couple should be evaluated, and the irrational cognition of the couple should be improved, so as to realize the importance of family support and improve the utilization of social support, in order to increase the confidence of infertility treatment.

#### 4.2 Correlation

The correlation analysis demonstrated that social support was significantly negatively correlated with irrational fertility cognition and fertility pressure, while irrational fertility cognition was significantly positively correlated with fertility pressure. This study demonstrated that higher scores in irrational fertility cognition correlate with greater fertility pressure and lower utilization of social support, consistent with findings by Li *et al.* [26] and Li *et al.* [27]. It also validated the cognitive behavioral theory's perspective that irrational beliefs exacerbate psychological stress [28,29]. Fertility pressure refers to the various limiting factors faced by individuals or families when deciding to have children, which include physiological, psychological, material, and environmental factors. In addition to obvious pressure, such as economic pressure, there is an important hidden factor: the traditional fertility concept.

The traditional conception of fertility, shaped by centuries of socio-psychological and cultural sedimentation, has profoundly influenced reproductive behaviors. This cultural phenomenon is manifested in the pursuit of a large family size with the belief that more children mean greater blessings, the emphasis on male heirs for old-age support, the gender bias favoring sons over daughters, the value placed on continuing the family line, and the ideal of a large extended family where generations live under one roof. In the traditional cultural context of China, childbirth is considered necessary, so this invisible social pressure may increase the psychological burden of patients and may also damage the relationship between infertile patients and their family and friends [30]. For infertile couples, excessive reproductive pressure may lead to negative emotions such as inferiority, resulting in active or passive separation from family and social relationships, thereby damaging the quality of life. Therefore, we also need to pay attention to the number, size, and mutual relationships among family members.

Studies have shown that high levels of social support are crucial in preventing anxiety and depression, particularly after failed fertility treatments [31]. The rationality of these infertile patients' cognition of fertility is related to the degree of social support they get from family, friends, or society. The higher the degree of social support they get and the more effectively they can use the social support, the more rational their cognition of fertility. This suggests that social support, as an important psychological resource, may alleviate fertility pressure by reducing irrational fertility cognition. Strengthening the social support system may be an effective way to intervene in fertility pressure.

#### 4.3 Mediation and Binary Interaction

The APIMeM analysis further revealed the mediating role of irrational fertility cognition in the “social support-fertility pressure” pathway. Regarding the principal effect, the wife's social support primarily alleviates her reproductive stress by reducing her irrational beliefs about childbirth. This demonstrates that her cognitive regulation plays a central role in stress management. The social support received by individuals effectively modulates their irrational beliefs about reproduction, thereby mitigating reproductive stress. This finding aligns with the cognitive behavioral theory's assertion that “cognitive regulation is pivotal in stress formation” [28,29]. The husband's subjective effect also indirectly influences his fertility pressure through his own and his wife's irrational fertility cognition, which indicates that the husband's pressure experience is more easily influenced by the cognition mode of both husband and wife. In terms of object effect, the husband's social support can alleviate the wife's fertility pressure by reducing her irrational fertility cognition, while the wife's social support can indirectly affect the husband's stress level by regulating her own cognition, reflecting the bidirectional interaction of the psy-

chological process of the couple. The results of this study confirm the applicability of the “cognition-stress” theory model in the couple relationship, and suggest that the reconstruction of the cognitive pattern and the improvement of the emotional interaction process should be emphasized in the psychological intervention of infertile couples.

For most patients undergoing assisted reproductive therapy, the primary goal is to achieve pregnancy and have their own children, thereby enhancing marital happiness and quality of life [15]. Influenced by societal pressures and women's aspirations for parental roles, childbearing becomes a pivotal life mission. However, infertility deals a severe blow, causing immense psychological stress [22]. In conclusion, we should proactively provide patients with medical information and psychosocial support, helping them expand their sources of social support and enhance their utilization of such support. Through targeted psychological interventions and guidance—such as mindfulness therapy, group cognitive therapy, and rational-emotive behavior therapy—we can alleviate patients' fertility-related stress and guide them to replace irrational thought patterns and beliefs with rational ones.

#### 4.4 Clinical Implications and Intervention Recommendations

① Implement the integrated psychological intervention for couples: in clinical practice, we should break through the traditional individual-centered psychological service mode, and include both spouses in the intervention system, so as to build a more resilient family coping system by enhancing the emotional support and cognitive coordination between couples.

② Promote the application of cognitive restructuring in the field of reproductive health: adopt cognitive behavioral therapy to systematically identify and correct irrational reproductive concepts in couples, and establish a scientific and reasonable reproductive cognitive framework to effectively alleviate emotional distress and psychological stress caused by cognitive bias.

③ Build a diversified social support network: integrate medical institutions, community resources, and peer support groups, expand the social support dimension of infertile couples through group intervention, family system interview, and other forms, and improve their psychological capital and social resources needed to cope with the pressure of fertility.

④ Gender differentiated clinical psychological assessment and intervention: in the process of diagnosis and treatment, we should pay full attention to the influence of gender factors on the psychological adaptation process, especially paying attention to the vulnerability of female patients in irrational cognition and stress response, and make a gender sensitive stratified intervention program to achieve accurate psychological support.

#### 4.5 Limitations

There were some limitations in this study. Firstly, the cross-sectional design employed in the research cannot completely eliminate the possibility of selection bias. Secondly, our measure of household income was aggregate and did not capture the individual incomes of husbands and wives. As suggested by the reviewer, the proportional contribution to household income is a potential key factor in intra-household bargaining power, and future studies would benefit from collecting this disaggregated data. Thirdly, the single-center convenience sampling method used, combined with the fact that most participants were Han urban residents, may limit the generalizability of the findings to rural areas, ethnic minority groups, or couples with diverse cultural backgrounds. In the future, the scope of research will be further expanded to carry out multi-region and multi-center joint research.

### 5. Conclusions

This study demonstrated deep integration between stress-buffering theory and family systems theory. Social support exerts its influence through dual pathways: direct buffering of stress and indirect regulation of cognition, while spousal interaction patterns further illustrate the holistic nature of family systems. The research has certain limitations: the sample focuses on urban infertile couples in China, requiring cautious generalization of findings; the cross-sectional design makes it difficult to clarify causal temporal relationships between variables. Future studies should expand to cross-cultural populations and employ longitudinal tracking designs to explore the dynamic evolution of support-stress relationships.

#### Availability of Data and Materials

Data is available from the corresponding author on reasonable request.

#### Author Contributions

YL: conceptualization, writing-original draft, formal analysis, funding acquisition, data curation. DZ: investigation, methodology, formal analysis, data curation. WC: investigation, methodology, writing-review & editing. FZ: conceptualization, supervision, project administration, writing-review & editing. LX: conceptualization, project administration, supervision, writing-review & editing. All authors contributed to critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

#### Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki. This study

was reviewed and approved by the Ethics Committee of Women's Hospital, School of Medicine, Zhejiang University (Approval Number: IRB-20220124-R). A written consent was signed by the patients.

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#### Conflict of Interest

The authors declare no conflict of interest.

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