FACTORS ASSOCIATED WITH ANXIETY AND
DEPRESSION IN INFERTILE COUPLES:
A STUDY IN THAILAND

TONG YANG

**MASTER OF SCIENCE
IN MENTAL HEALTH**

**GRADUATE SCHOOL
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A THESIS SUBMITTED TO CHIANG MAI UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN MENTAL HEALTH

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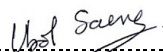

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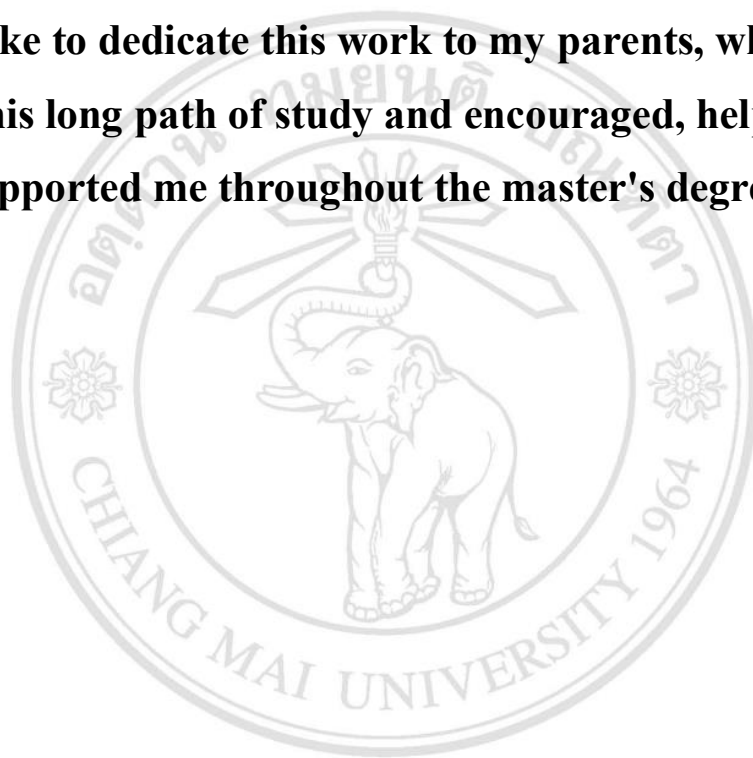
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9 February 2023

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To

I would like to dedicate this work to my parents, who started me on this long path of study and encouraged, helped, and supported me throughout the master's degree.

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ACKNOWLEDGEMENTS

Tong Yang

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| **หัวข้อวิทยานิพนธ์** | ปัจจัยที่สัมพันธ์กับภาวะวิตกกังวลและภาวะซึมเศร้าในคู่สมรสที่มี |
| | ภาวะมีบุตรยาก: การศึกษาในประเทศไทย |

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บทคัดย่อ

ความเป็นมา: ภาวะมีบุตรยากเกิดขึ้นประมาณร้อยละ 15 ทั่วโลก มีความสัมพันธ์ต่อความเครียด ความสัมพันธ์ในครอบครัวและกับสังคมภายนอกภาวะวิตกกังวลและภาวะซึมเศร้าพบได้บ่อยในคู่สมรสที่มีบุตรยาก

วัตถุประสงค์: การศึกษานี้ต้องการศึกษาความสัมพันธ์ระหว่างภาวะวิตกกังวลและภาวะซึมเศร้ากับความสัมพันธ์ในชีวิตสมรส บุคลิกภาพ และแนวคิดแบบเศรษฐกิจพอเพียง ในคู่สมรสที่มีบุตรยาก ปัจจัยต่าง ๆ เหล่านี้ยังไม่เคยมีการศึกษามาก่อน

วิธีการ: การวิจัยนี้เป็นการสำรวจภาคตัดขวางในคู่สมรส 150 คู่ที่มาเข้ารับการรักษาที่สถานพยาบาลสำหรับผู้มีบุตรยากในจังหวัดเชียงใหม่สองแห่งมีการเก็บข้อมูลด้านสังคมและประชากรศาสตร์ มีการใช้เครื่องมือ Outcome Inventory-21 (OI-21) ความพึงพอใจในชีวิตสมรส (ENRICH Marital Satisfaction Scale) แบบวัดเศรษฐกิจพอเพียง (Sufficiency Economy Scale (SES)) และบุคลิกลักษณะ 5 อย่าง ได้แก่ แบบก้าวร้าว (AG) แบบแสวงหาสัมผัส (SS) แบบแสดงออก (EX) แบบกิจกรรม (AC) และแบบนิวโรติซิสม (NE) ด้วย Zuckerman-Kuhlman-Aluja Personality Questionnaire (ZKA-PQ) มีการวิเคราะห์ข้อมูลด้วยสถิติแบบพรรณนาสำหรับข้อมูลสังคมและลักษณะประชากร ทดสอบ $\chi 2$ และ *t*-testในการหาความแตกต่างของภาวะวิตกกังวลและภาวะซึมเศร้าระหว่างกลุ่มต่าง ๆการวิเคราะห์สัมประสิทธิ์สหสัมพันธ์เพียร์สัน มีการวิเคราะห์การถดถอย

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แบบพหุคูณผลการทำนายของตัวแปรต่าง ๆ ต่อภาวะวิตกกังวลและภาวะซึมเศร้า และการวิเคราะห์โมเดลแบบ actor-partner interdependence model โดยโมเดลพหุระดับสำหรับการวิเคราะห์อิทธิพลของความเป็นคู่

ผลการศึกษา: อายุเฉลี่ยของผู้เข้าร่วมวิจัย 35.68 ± 5.4 ปี (20-62) เพศชาย 36.55±6.0 (20-62) เพศหญิง 34.81±4.6 (21-51) การไม่ประกอบอาชีพสัมพันธ์กับภาวะซึมเศร้า $F_{(4,293)} = 2.795$, p < .05. โดยรวม ร้อยละ 27.3 ของคู่สมรสรายงานอาการวิตกกังวลโดย OI-anxiety ร้อยละ 6.7 รายงานอาการซึมเศร้าโดย OI-depression และร้อยละ 6.3 มีทั้งอาการวิตกกังวลและอาการซึมเศร้า ค่าสหสัมพันธ์ระหว่างภาวะวิตกกังวลและคะแนนบุคลิกลักษณะแบบก้าวร้าว แบบนิวโรติซิสม แบบแสดงออก และแบบวัดเศรษฐกิจพอเพียง ได้แก่ .353 (p < .01), .625 (p < .01), .139 (p < .05) และ -.127 (p < .05) ตามลำดับในขณะที่ค่าสหสัมพันธ์ระหว่างภาวะซึมเศร้าและคะแนนบุคลิกลักษณะแบบก้าวร้าว แบบนิวโรติซิสม แบบแสดงออก และแบบวัดเศรษฐกิจพอเพียง ได้แก่ .317 (p < .01), .601 (p < .01), .133 (p < .05) และ -.157 (p < .01) ตามลำดับ ความคาดหวังในการมีลูกพบว่าไม่มีความสัมพันธ์ทางลบอย่างมีนัยสำคัญทางสถิติกับอาการวิตกกังวล แต่มีความสัมพันธ์ทางลบอย่างมีนัยสำคัญทางสถิติกับภาวะซึมเศร้า ($r = -.121$, p <.05). คะแนนความพอใจในความสัมพันธ์ระหว่างคู่สมรส (ENRICH) ไม่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับอาการวิตกกังวล แต่มีความสัมพันธ์ทางลบอย่างมีนัยสำคัญทางสถิติกับภาวะซึมเศร้า ($r = -.209$, p < .01) ผลการวิเคราะห์ด้วย APIM พบว่าผลโดยรวมในผู้กระทำ (actor) ระหว่าง บุคลิกลักษณะแบบก้าวร้าวและแบบแสดงออกมีนัยสำคัญทางสถิติต่อภาวะวิตกกังวล (p < .05) ผลโดยรวมระหว่างบุคลิกลักษณะแบบนิวโรติซิสมและ ENRICH และภาวะซึมเศร้ามีนัยสำคัญ (p < .05) ผลในผู้กระทำระหว่างภาวะวิตกกังวลและภาวะซึมเศร้ามีนัยสำคัญ (p < .001) ผลของคู่โดยรวมระหว่างความคาดหวังในการมีบุตรและภาวะซึมเศร้ามีนัยสำคัญ (p = .039)

สรุป ในคู่สมรสที่มีภาวะมีบุตรยาก พบว่าความวิตกกังวลมีความชุกไม่ต่างกับการศึกษาที่ผ่านมา ในขณะที่ความชุกของภาวะซึมเศร้าค่อนข้างน้อย ภาวะซึมเศร้าสัมพันธ์กับความคาดหวังในการมีบุตร และความพึงพอใจในชีวิตสมรส บุคลิกลักษณะแบบก้าวร้าว แบบแสดงออก และแบบนิวโรติซิสมเป็นปัจจัยทำนายภาวะวิตกกังวลและภาวะซึมเศร้า แนวคิดเศรษฐกิจพอเพียงมีความสัมพันธ์แบบผกผันกับภาวะวิตกกังวลและภาวะซึมเศร้า ปัจจัยต่าง ๆ เหล่านี้ส่วนใหญ่มีผลในตัวผู้นั้น ยกเว้นความคาดหวังในการมีบุตรของคู่มีผลต่อภาวะซึมเศร้า

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Thesis Title	Factors Associated with Anxiety and Depression in Infertile Couples: A study in Thailand
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ABSTRACT

Background: Infertility affects about 15% of couples worldwide, and is associated with stress, family and social relationships. Anxiety and depression are common in couples with infertility.

Objectives: The study investigated the prevalence of anxiety and depression and the relationships with marital satisfaction, personality, and sufficiency economy concept in infertile couples. These factors have never been explored.

Methods: This study comprised a cross-sectional survey of 150 couples seeking treatment at two fertility centers in Chiang Mai, Thailand. Sociodemographic information, Outcome Inventory-21 (OI-21), ENRICH Marital Satisfaction Scale, and Sufficiency Economy Scale (SES) were completed by both partners. Five personality traits, (aggression (AG), sensation seeking (SS), extraversion (EX), Activity (AC) and neuroticism (NE) measured by Zuckerman-Kuhlman-Aluja Personality Questionnaire, were completed. A description test was performed to analyze sociodemographic characteristics. The χ^2 and *t*-test were used to analyze the differences in anxiety and depression between groups, and a correlation between variables using Pearson's coefficient was applied. Multiple regression was used to analyze the predictive effects

of different variables on anxiety and depression. The dyads analysis was used to analyze the Actor – Partner Independence Model.

Results: The mean age of all participants was 35.68 ± 5.4 years old (20-62); males, 36.55 ± 6.0 (20-62); women, 34.81 ± 4.6 (21-51). Unemployment was associated with depression ($F_{(4, 293)} = 2.795$, $p < .05$). Overall, 27.3% of infertile couples reported anxiety on OI-anxiety, 6.7% reported depression on OI-depression, and 6.3% had both anxiety and depression. The correlational coefficients between OI-anxiety and AG, NE, EX, and sufficiency economy concept were $r's = .353$ ($p < .01$), .625 ($p < .01$), .139 ($p < .05$), and -.123 ($p < .05$), respectively. In comparison, the correlational coefficients between OI-depression and AG, NE, EX, and sufficiency economy were $r's = .317$ ($p < .01$), .601 ($p < .01$), .133 ($p < .05$), -.157 ($p < .01$), respectively. The expectation of having children was negatively correlated with depression ($r = -.121$, $p < .05$), while the ENRICH was negatively correlated with OI-depression ($r = -.209$, $p < .01$). APIM showed that the overall actor effect between AG and NE and OI-anxiety were significant ($p < .05$), as were the overall actor effects between NE and ENRICH and OI-depression ($p < .05$). The actor effect between OI-anxiety and OI-depression was significant ($p < .001$), as was the overall partner effect between the expectation of having children and OI-depression ($p = .039$).

Conclusions: The prevalence of anxiety among infertile couples is comparable to other studies, whereas the prevalence of depression is lower. Depression was associated with the expectation of having children and marital satisfaction. Aggression, extraversion and neuroticism were the predictors for anxiety and depression. Sufficiency economy concept was negatively associated with anxiety and depression. Most variables have only actor effects, only the expectation of having children exhibited a significant partner effect for depression.

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LIST OF ABBREVIATIONS

APIM	Actor–Partner Interdependence Model
IVF	In Vitro Fertilization
ART	Assisted Reproductive Technology
PIS	Participant Information Sheet
ICF	Informed Consent Form
OI-21	Outcome Inventory-21
ZKA-PQ	Zuckerman-Kuhlman-Aluja Personality Questionnaire
NE	Neuroticism
SS	Sensation Seeking
EX	Extraversion
AC	Activity
AG	Aggressiveness
ENRICH	Evaluation and Nurturing Relationship Issues, Communication and Happiness
SES	Sufficiency Economy Scale

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CHAPTER 1

INTRODUCTION

This chapter introduces the background, rationale and purpose of the study. In addition, the literature review, conceptual framework, hypothesis, scope of the studies and the benefit of the studies were included.

1.1 Background

Failure to conceive after 12 months or more of unprotected sexual intercourse is defined as infertility [1,2]. Infertility affects millions of people around the world, and is often blamed on women. Contrary to popular belief, infertility can be caused by male and female factors. Infertility affects individuals and their partners, family relationships, and even the development of society. A misunderstanding remains that when infertile couples seek professional infertility treatment, women are often the only ones involved. However, 50% of infertility is due to female factors. In addition, 20 to 30% are caused by a combination of male and female factors. Still, 30% of infertility is due to male factors. In other words, the problem of infertility should not be addressed only by the female partner but by the infertile couple [3-5]. About 85% of infertility cases can be identified, while the rest of the infertility cases remain unexplained. Tubal diseases, ovulation dysfunction and male factors account for the majority of infertility with a clear cause. Among women with ovulation disorders, polycystic ovary syndrome accounts for 70% [6]. The causes of female infertility include reproductive organ dysfunction, diseases other than reproductive organs and psychological factors. Male sperm quality, sperm concentration, vas deferens obstruction, and dyspareunia can cause infertility. Conversely, even if infertility is not caused by sexual dysfunction, infertility diagnosis can cause sexual dysfunction among infertile couples [7].

Infertility has been a common concern in developing and developed countries because the number of infertile couples has gradually increased. Infertility is not just a medical problem; it constitutes a social problem. Infertility can bring psychological stress to

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individuals and provoke family conflicts. The discrimination and stigmatization of infertility over a long time have significantly pressured many infertile couples. Especially in Asian cultures that encourage procreation, being childless is considered inappropriate [8]. The effects of infertility are multifaceted, including but not limited to psychological stress, family conflict, and social relationships [9]. Infertility can bring negative emotions to couples, even sadness and panic. Women also worry about being out of shape, and experiencing miscarriage [10]. Research shows that as infertility lasts longer, so does stress, in particular, among couples [11]. Since the 1990s, more and more studies have investigated anxiety/depression among infertile couples [12].

Infertility can be divided in primary infertility and secondary infertility. Primary infertility refers to the absence of childbirth from unprotected sexual intercourse. Secondary infertility is defined as having had one or more children but now having unprotected sexual intercourse without childbirth. Prevalence of secondary infertility was higher in developing countries [13].

1.2 Rationale

Infertility is linked to mental health. Anxiety and depression are the most common mental health outcomes for infertile couples. Additionally, women account for the majority of mental health problems [14,15]. Anxiety and depression among infertile women can be caused by different factors separately or combined. Mental health has been linked to infertility, as well as infertility treatment. In particular, anxiety and depression were associated with infertility. Couples seeking infertility treatment unsuccessfully [16], infertile couples with low income and polygamy [17] are more likely to experience anxiety and depression. Moreover, the level of anxiety and depression among infertile couples varies according to sex. Among infertile couples in Iran, the prevalence of anxiety among women was 2.54 times higher than among men [14]. Similar results were observed in Turkey. Among infertile couples treated with assisted reproductive technology in Turkey, women experienced a higher prevalence of anxiety and depression than men [18]. Generally speaking, reducing the chances of multiple pregnancies during infertility treatments is better, which are riskier for the mother. Couples having twins after infertility treatment have a higher risk of anxiety and depression than couples who have singletons [19]. Infertile

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couples strongly need to assess and treat anxiety and depression. These mental health outcomes can affect quality of life and can even be followed by more serious consequences such as substance abuse and suicide. It has been well documented that anxiety and depression among infertile couples can negatively affect their infertility treatment and even reduce follow-up compliance [16].

In addition to the information mentioned earlier, e.g., sex related, other factors may be involved in developing anxiety and depression. For example, the marital relationship should play a very crucial role in pursuing an advanced treatment. Infertility treatment is usually consensual between couples. The evaluation and consultation on the first visit for infertility treatment is a process both spouses must go through. Therefore, both infertile couples must consent to and cooperate with infertility treatment. A refusal of either partner to infertility treatment means the end of treatment; thus, the relationship quality could render mental health problems, mainly when infertility problems occur.

How a husband or wife copes with the problem also depends on an individual's personality. Personality traits are an essential part of mental health. Different characters reflect different attitudes toward life events and characteristics. Sensibility to anxiety and depression varies according to other personality traits [20]. Personality traits like neuroticism are significantly related to anxiety and depression across populations. This potent intrapersonal factor might influence an infertile couple.

In addition to a personality trait, individual's attitude to living on their own is crucial. Most Thais are influenced by the concept of sufficiency economy, developed by the late King Bhumibol. It constitutes a concept that encourages Thais to be self-sufficient by adopting a sensible way of life and making reasonable decisions [21]. A sufficiency economy encourages people to behave honestly, wisely, and kindly. The sufficiency economy advocates continuous progress on a good path to improve the quality of life. For example, couples with infertility problems might endeavor to solve their problems. To what extent the couple would proceed depends on how much effort they are willing to spend in terms of money and time. The decision based on their view of sufficiency economy might, theoretically, render less anxiety or depression.

Taken altogether, anxiety and depression should not be overlooked in managing infertility

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treatment. However, it remains clear about the prevalence of anxiety and depression among infertile couples in Thailand. Also, many unknown factors exist related to anxiety and depression among infertile couples. Therefore, the researchers would like to describe such phenomena and explore these yet unelucidated related factors.

1.3 Purposes of the study

The purposes of the study are listed below.

1.3.1 To investigate the prevalence of anxiety/depression among infertile couples

1.3.2 To investigate the relationship between demographics and associated factors and anxiety/depression among infertile couples

1.3.3 To investigate the relationship between personality traits and anxiety/ depression among infertile couples

1.3.4 To investigate the relationship between marital relationships and anxiety /depression among infertile couples

1.3.5 To investigate the relationship between sufficiency economy and anxiety /depression among infertile couples

1.3.6 To investigate the actor and partner effects of significant variables on anxiety/depression among infertile couples

1.4 Literature review

1.4.1 Infertility

Infertility is widely defined as the absence of pregnancy after 12 months or more of unprotected regular sex. In women over 35 years of age, 6 months or more of regular unprotected sex without pregnancy should be evaluated for infertility [22]. The WHO guidelines for Reproductive Health Indicators in 2006 states that the epidemiologic definition of infertility is a woman of childbearing age who has not become pregnant after two years of trying [23]. Between 2004 and 2012, the number of infertile people worldwide increased from 48.5 million to 186 million. The prevalence of infertility varies by region. This is related to income, environment, culture and other factors in the area. Sub-Saharan Africa, South Asia, East Asia and the Pacific, Central and Eastern Europe, and Central

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Asia are regions with higher rates of infertility. Although the number of infertile people has increased, the prevalence of infertility has not changed significantly in the past two decades. This is assumed to be due to the decline in fertility rates, which has slowed the growth rate of the world's total population. Primary infertility is defined as never becoming pregnant after unprotected sex. Secondary infertility is defined as having been pregnant once or more but is now unable to conceive again. A review of infertility prevalence around the world in more than 40 countries from 1990 to 2010 defined primary infertility as the absence of a live birth after unprotected sex. In addition, secondary pregnancy is defined as having had a live birth but is now unable to have a live birth after unprotected sex [13]. Infertility rates tend to be higher in areas with poor health care and resources. Reproductive tract infections can lead to secondary infertility. Without timely treatment and intervention, secondary infertility is more likely to occur. This is also reflected in the number of clinics with assisted reproductive technology in these areas. As of 2010, Ethiopia, Uganda, Cuba and Zimbabwe had only one In Vitro Fertilization (IVF) Clinic. However, more infertility treatments are available in developed countries than in developing ones, but the development of artificial Assisted Reproductive Technology (ART) is still far from sufficient [24]. The International Committee for Monitoring Assisted Reproductive Technologies (ICMART) published its 19th world report about the data of ART treatment in 2014. In the report in 2014, 76 countries submitted their ART treatment data and outcomes. In 2010, only 60 countries submitted data to the ICMART. This suggests that infertility treatment is being extended to more countries, meaning that more infertile couples have the opportunity to seek infertility treatment [25].

Worldwide, 186 million people experience infertility. In developed countries, the prevalence of infertility is about 14.3%. In developing countries, the prevalence of infertility is about 25%. In some poor areas, the prevalence of infertility is even higher, reaching 30% [26]. About 12.5% of women aged 15 to 49 seek treatment for infertility. Infertility affects nearly 9% of women in the US and causes physical and emotional stress [6]. In 2017, women aged 35 to 39 exhibited the highest prevalence of infertility, at more than 5.5%. Men aged 35 to 44 years had the highest prevalence of infertility, at about 4.5%. From 1990 to 2017, the global health burden of infertility continued to increase. The prevalence of infertility was higher among women than among men in 195 countries

and territories between 1990 and 2017. This may be because women's reproductive health issues receive more attention, while statistics on male infertility are less comprehensive. In addition, fallopian tubal causes are the most common cause of infertility. This explains why the prevalence of infertility is higher among women than among men [27]. A survey on the prevalence of infertility among married couples of childbearing ages in China showed that the prevalence of infertility among women was about 15.5%. About one in ten married women of childbearing age is primary infertile. The prevalence of secondary infertility is about 6% [28]. In 2008, about 10 million infertile couples resided in Thailand. The prevalence of infertility among couples of reproductive age in Thailand is between 10% and 15% [29].

The female factor of infertility falls into two broad categories. First, pelvic factors are the main causes of secondary infertility among women. Specific causes include a. tubal lesions, pelvic adhesions, pelvic inflammation and its sequelae, pelvic inflammation (neisseria gonorrhoeae, mycobacterium tuberculosis and chlamydia trachomatis infection) and tubal obstruction, adhesion, hydrosalpinx and impaired function caused by pelvic surgery adhesion etc. Next come uterine body lesions mainly refers to submucous myoma of the uterus, intermuscular myoma with a large volume affecting the morphology of the uterine cavity, adenomyosis, intrauterine adhesion and endometrial polyps etc. After that are cervical factors including cervical relaxation and cervical lesions etc. Followed by endometriosis, typical symptoms of pelvic pain and infertility. The exact relationship and mechanisms of infertility are not completely clear, possibly through the pelvic and uterine immune mechanism disorders caused by ovulation, fallopian tube function, fertilization, corpus luteum generated and endometrial receptivity of multiple changes in fertility impact. Then come congenital malformations including miller tube malformations, such as mediastinal uterus, congenital abnormal fallopian tubes, double horn uterus and double uterus. The second category comprised ovulatory obstacles. These include hypothalamic lesions such as hypogonadotropin anovulation followed by pituitary lesions such as hyperprolactinemia; ovarian lesions such as polycystic ovary syndrome, early onset ovarian dysfunction and congenital gonadal dysplasia followed by other endocrine diseases such as congenital adrenal hyperplasia and thyroid dysfunction [30]. Clinically, male infertility is divided in two categories: sexual dysfunction and normal sexual

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function. Male infertility with normal sexual function based on semen analysis results can be further divided in azoospermia, oligospermia, asthenospermia and normal sperm count infertility [5]. Infertility can be caused by physiological reasons such as reproductive organ dysfunction, and by lifestyle and economic status. Both men and women become less fertile as they age. The chance of pregnancy is twice as common under 25 as over 35. Environmental pollution may lead to increased prevalence of male reproductive diseases, such as testicular cancer and hypospadias, as well as affecting sperm concentration [31]. Psychological stress, interpersonal relationship, partner support and social pressure can affect sexual function and are associated with sexual dysfunction [32]. Overweight and obesity are associated with metabolic disorders affecting the endocrine system. The sperm quality of obese men was lower than that of men of normal weight. Men with diabetes had lower sperm concentration and motility. Environment and lifestyle can affect the quality and motility of male sperm, leading to a decline in male fertility [33]. Couples who having at least one child had a higher quality of life than couples who repeatedly failed fertility treatment or had not yet received fertility treatment [34].

The main treatment for male infertility is to improve sperm quality. Varicocele can be treated with surgery. In addition, evidence indicates anti-estrogen and gonadotropin therapy is effective for male infertility. Ovulation induction drugs are a routine choice for women with infertility caused by ovulation disorders. Notably, the specific ovulation induction drugs used vary depending on the cause of the ovulation disorder. In treating hypogonadism, gonadotropin and gonadotropin-releasing hormone are commonly used [35]. Clomiphene citrate and letrozole are commonly used to treat hypergonadism caused by polycystic ovary syndrome. These two drugs increase follicle growth through different pathways by increasing follicle stimulating hormone [36]. ART refers to the manipulation of gametes, embryos or genetic material to produce new life. The procedure involves removing an egg from a woman's body, cultivating it in a laboratory, adding technically processed sperm and developing it into an early-stage embryo after the egg is fertilized. However, the success rate of ART is not high. An ART cycle has a success rate of less than 30%, meaning that many couples undergoing infertility treatment have to take multiple ART cycles. The more ART cycles, the higher the success rate [37]. Male and female infertility can be treated using intra-uterine insemination (IUI). IUI refers to

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collecting semen, which is processed to remove seminal plasma and injected in the uterine cavity. Standardized management of IUI has contributed to an increase in IUI singleton pregnancy rates and a better prognosis [38]. For infertility caused by Aschermann syndrome, polycystic ovary syndrome, premature ovarian failure, endometriosis, and azoospermia, stem cell therapy is expected to solve infertility after ART failure [35]. For couples seeking infertility treatment, the number of times an infertile couple received infertility treatment was associated with prenatal anxiety and depression [39]. Women seeking treatment for infertility have higher levels of anxiety, especially when treatment fails or becomes prolonged [40].

    1.4.2 Anxiety

    Anxiety refers to the nervous, avoidant response to danger, and the active avoidance of danger. Anxiety is the brain's response to danger, and is not usually pathological. Nonetheless, when people overreact and outperform the brain, anxiety exceed controls [41]. Psychodynamic theory holds that anxiety stems from internal psychological conflicts, which are suppressed subconsciously in childhood or adolescence and activated in adulthood [42]. Clinically, some patients with anxiety disorders have experienced stressful life events. Particularly, threatening events are more likely to trigger anxiety. The evidence shows that insecure attachment, caregivers' ambivalence, overprotective parents, abuse and excessive separation from caregivers may be the causes of anxiety during childhood [43]. About 30% of adults are affected by an anxiety disorder at least once in their lives, and constitute one of the most common mental illnesses [44]. Anxiety is a feeling, which can be reflected by physical manifestations, such as bronchospasm, urgent urination, headache etc. As anxiety gained more attention, it began to be incorporated in medical diagnoses in the late 19th and early 20th centuries. In Diagnostic and Statistical Manual of Mental Disorders-III (DSM-III), anxiety disorders include phobias: agoraphobia, social phobia, and simple phobia; anxiety states: panic disorder, generalized anxiety disorder, and obsessive-compulsive disorder; and post-traumatic stress disorder. In the DSM-5, anxiety disorder and obsessive-compulsive disorder are divided in different categories [45]. Anxiety is influenced by genetic, neurobiological, and psychosocial factors [46]. In neurobiological aspects, both GABA, serotonin and

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norepinephrine are related to symptoms of anxiety [47].

Anxiety can be treated with medication and psychotherapy. In addition to physical and psychological factors affecting anxiety, lifestyle is also involved. A healthy lifestyle can reduce anxiety. In contrast, high consumption of sugary foods, prepared foods and processed meats, among other foods, increases anxiety. Sleep duration, depth and quality can also affect anxiety. Therefore, medication and psychotherapy can also help reduce anxiety. A healthy lifestyle is also very effective [48]. In January to May 2020, the prevalence of anxiety was 31.9% [49]. Meditation, relaxation and breathing comprised effective ways to deal with the sympathetic effects on emotional stability [50]. In 2020, the prevalence of anxiety was 25%, as measured using the Depression, Anxiety and Stress Scale (DASS), Generalized Anxiety Disorder scale (GAD), Beck Anxiety Inventory and so on [51]. The State-Trait Anxiety Inventory (STAI) is one of the most popular instruments to measure anxiety. This constitutes a self-rating scale. STAI can be used to measure the level of anxiety among adults and children. A higher score indicates a higher level of anxiety. Different scores of Beck Anxiety Inventory (BAI) interpret different levels of anxiety, which can be classified as normal (0-9), mild to moderate anxiety (10-18), moderate to severe anxiety (19-29), and severe anxiety (30-63). Hospital Anxiety and Depression Scale-Anxiety (HADS-A) can be used to measure generalized anxiety symptoms. A total score greater than 9 is helpful for the clinical diagnosis of anxiety [52]. For infertile couples, infertility treatments can lead to increased anxiety [53]. The cause of infertility is linked to a woman's level of anxiety. Infertile women experienced high levels of anxiety before and during infertility treatment [54]. Men, evaluated for infertility for the first time, exhibited low anxiety scores by using STAI and visual analog scales (VAS) [55].

1.4.3 Depression

Depression refers to persistent feelings of sadness or an inability to have happy feelings and an inability to function on a daily basis. Depression is a mood disorder caused by a variety of causes with significant and persistent depressive symptoms as the main clinical features [56]. Depression is one of the most common psychiatric problems. In the US, the prevalence of depression is about 5 to 10%. In any given year, about 6.7 % of adults report depression. About 16.6% of people experience depression once in their

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lifetime. Most people first experience depression in their late teens to mid-20s, and women are more likely than men to experience depression. One study showed that about 33.3% of women experience depression in their lifetime [57]. The etiology and pathogenesis of depression are very complex, including biological, psychological and social factors. Genetic factors are one of the important factors in the occurrence of depression. Factors associated with depression include sex, stressors and cognitive behavior. Cognitive vulnerability refers to the tendency of people to focus on negative information in the face of difficulties, leading to depression [58]. The core symptoms of Major Depressive Disorders are depressed mood and loss of interest according to DSM-5 [57]. When a first-degree relative has depression, the heritability is about 40%. Serotonin transporter, monoamine oxidase-A, brain-derived neurotrophic factor and neuroinflammatory markers are all associated with the onset of depression. Depression may involve abnormalities in more than one gene, and often interactions are observed between different genes [59]. Essentially, neurotransmitter function and homeostasis are out of balance among patients with depression. Norepinephrine, dopamine, 5 - hydroxytryptamine, acetylcholine, GABA, epinephrine and histamines are also closely related to the onset of depression. People with depression have abnormal hypothalamic – pituitary – adrenal (HPA) axis function, which is manifested by increased blood cortisol levels, changes in the circadian rhythm of stress-related hormones and no spontaneous inhibition of cortisol secretion at night. In addition, abnormal levels of corticotropin-releasing hormone (CRH) are noted in the cerebrospinal fluid. People with depression may have elevated CRH [60]. Related Magnetic Resonance Imaging (MRI) reports showed that the neurotransmitter concentration, response to negative/positive stimuli, white matter nerve fibers, gray matter volume and brain metabolism were abnormal in the neural circuitry of people with depression, reflecting different depressive symptoms [61]. The electroencephalogram (EEG) of patients with depression often shows abnormalities in the right hemisphere, mainly in the right frontal lobe [62].

Globally, depression causes more years of disability than any other illness. This phenomenon is largely because about 350 million people experience depression [63]. According to the bio-psycho-social model, depression is closely related to genetic factors, biological factors, various stressors, cultural environment, etc [64]. Depression was also a

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common outcome studied with anxiety, and most are depressive symptoms rather than depressive disorders [16]. Common treatments for depression include medication and psychotherapy. Behavioral cognitive therapy improves cognition, thinking and behavior. Monoamine inhibitors (MAOIs) prevent the destruction of neurotransmitters associated with mood, such as serotonin, adrenaline and norepinephrine. Selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are widely used drugs to treat depression, and produce fewer side effects. Combined of medication and psychotherapy is the recommended treatment for depression [65].

Patient Health Questionnaire-9 Item (PHQ-9) is one of the most common instruments used to measure the level of depression. PHQ-9 is based on the DSM-IV diagnostic criteria for major depression. The higher the score, the more the patient is depressed. Beck Depression Inventory-II (BDI-II) is a self-scoring scale classified as minimal, mild, moderate, and severe depression based on scores [66]. Comparing the depression scores of infertile women with those of patients with cancer, with heart diseases and with human immunodeficiency virus (HIV) showed that their psychological symptoms were similar [67]. Infertile women at infertility treatment clinics were assessed using the Mini-International Neuropsychiatric Interview (MINI), revealing that 17% had major depressive disorders. This was much higher than the prevalence of depression in the general population [68]. A study of 225 women, as measured by BDI, found that infertile women had higher depression scores than fertile women [69]. Infertile women who become pregnant after infertility treatment were more likely to experience depression if they miscarried. Psychological intervention for infertile women could effectively reduce their stress and improve the success rate of infertility treatment [70]. Among women treated for infertility, depression levels were higher among women who were not pregnant than women who were pregnant [71].

1.4.4 Personality

Many determinants are involved in mental health, including personality. Personality is the internal tendency of individual behavior, containing the stable psychological quality distinguishing one person from others. Personality reflects needs, motivations, interests, ideals, beliefs, and values with dynamic consistency and continuity. Generally speaking,

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the formation and development of personality are influenced by biological genetic factors, family environment and social and cultural factors. Social and cultural factors are the key factors affecting the formation and development of personality. A person's personality reflects their entire past life, and consists of a whole made up of many components. It has an internal unity of consistency that is regulated by self-consciousness. The interaction of social and genetic factors distinguishes each person's personality from that of others [72]. The researchers proposed the "Big Five" theory to promote research and communication among personality experts [73]. According to the Big Five personality traits model, the five basic dimensions of personality include extraversion, agreeableness, openness, conscientiousness and neuroticism. Extraversion refers to an individual's level of comfort with relationships and the capacity for pleasure. This dimension contrasts the conversable, optimistic and personally oriented individual with the prudent, calm and quiet person. People with higher extraversion appear energetic, optimistic, friendly and confident. They are social, active, talkative, gregarious, optimistic, fun-loving and affectionate. People with lower extraversion are calm, cautious, listless, aloof, bored, conciliatory and quiet. Agreeableness refers to an individual's tendency to obey others. On the one hand, good-natured, trusting, straightforward and soft-hearted are all included in this trait, and on the other hand, hostile, cynical, manipulative, vindictive and ruthless. Agreeableness represents whether earnest and accommodating are valued. People with higher agreeableness are understanding, trusting, altruistic, forthright, modest, and empathetic. Openness refers to an individual's interest and enthusiasm for novelty. Openness also refers to being imaginative, aesthetic, emotional, curious, creative and intelligent. This dimension compares individuals who are creative, curious, innovative, imaginative and unconventional with those who are practical, irrational and conventional. People with higher openness prefer abstract thinking and have broad interests. Conscientiousness measures an individual's credibility. Conscientiousness refers to the way in which we confront and deal with problems. It compares the reliable and diligent individual with those lazy and unreliable. People with higher conscientiousness are competent, fair, methodical, dutiful, accomplished, disciplined, cautious and restrained. Neuroticism refers to an individual's ability to withstand stress and negative emotions and emotional instability. Individuals with higher neuroticism tend to be anxious, hostile, depressed,

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self-conscious, impulsive and vulnerable. They are more emotional and uncomfortable with external stimuli than others. Not only that, they are more likely to be annoyed, stressed and depressed [74]. Neuroticism reflects negative emotions and emotional instability. Neuroticism tends to show lower inner strength [75]. Meanwhile, neuroticism is associated with depression [76] and anxiety [77]. Among infertile women, neuroticism correlates with their levels of depression [78]. However, research exploring the relationship between personality and anxiety and depression among infertile couples remains lacking, and this important gap needs to be addressed.

1.4.5 Substance use disorders

Substance use disorder is defined as the repeated use of substances that can affect a person's mood, behavior, state of consciousness and dependency, resulting in obvious adverse consequences, such as inability to complete important work and study and damage to physical and mental health. The causes of substance use cannot be explained by a single model but are generally believed to be closely related to biological, psychological and social factors. The interaction between these factors is related to substance use. Social factors include access to drugs, family environment, peer influence, cultural background and social environment. Studies have found that drug users have obvious personality problems, such as antisocial personality traits, poor emotional control, impulsivity, and lack of effective defense mechanisms. After drug dependence, a series of changes occur in neurotransmitters, receptors, and the second signal transduction system in the central nervous system. The reward system located in the limbic system is the structural basis of drug dependence, and the changes in monoamine transmitters is the direct consequence of psychoactive drugs. Different metabolic rates lead to different tolerance levels to psychoactive substances and different susceptibility to dependence. Common substances include opioids, marijuana, sedative-hypnotics, psychostimulants, ketamine, nicotine, and alcohol [79]. Alcohol is the most widely used psychoactive substance in the world. Alcohol is associated with anxiety disorders, including generalized anxiety disorder, social phobia and panic disorder [80].

Anxiety is associated with marijuana use. Limiting marijuana use can effectively reduce anxiety [81]. The link between substance abuse and anxiety will influence disease [82].

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Men who consistently use multiple substances have higher levels of depression [83]. Evidence reveals that substance abuse increases the risk of suicide among people with depression [84]. Early substance use has been associated with depression, including early use of alcohol, marijuana and other illegal drugs [85]. Studies on the relationship between substance use history, anxiety and depression among infertile couples are limited. If an association exists, it would be worth investigating whether a history of substance use has sex differences in anxiety and depression among infertile couples.

1.4.6.1 Family economic status

A strong correlation exists between health and income, and income affects the risk of developing the disease [86]. Moreover, social and economic downturns can lead to increased suicide rates. The government's financial support policy has been effective in reducing the suicide rate. In particular, it has helped reduce suicide rates among men. Declining birth rates and an aging society will affect economic growth and thus family income , affecting the quality of life. Income is also associated with physical health. Studies have found that income affects anxiety, depression and interpersonal relationships. Income had less effect on mental health among people with higher education levels and in urban areas than among people with lower education levels or in rural areas [87]. Further, income inequality is related to mental health. The higher the income inequality, the higher is the risk of depression [88]. Household incomes in Thailand have been rising since 2004. Still, research in Thailand has shown that people with higher incomes are less at risk of mental health problems [88]. People who lost less than 50% of their income during the COVID-19 situation in Thailand experienced a higher risk of anxiety [89]. Infertility evaluation and treatment can be costly for infertile couples. In particular, ART therapy usually requires three to six cycles, increasing the economic and psychological burden of infertile couples. Therefore, our research should include income as one of the mental health considerations for infertile couples.

1.4.6.2 Sufficiency economy concept

The sufficiency economy is a philosophical concept proposed by His Majesty King Bhumibol Adulyadej of Thailand in the last century based on Thai culture. Sufficiency economy advocates people to have a self-sufficient life, so as to obtain a higher economic

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level. Sufficiency economy is one strategy to guide people through wisdom and perseverance to live a better life in society. The philosophy of sufficiency economy can be applied to the economy, and all social aspects to promote the development of the whole society [90]. Sufficiency economy incorporates three pillars. The first pillar is moderation. Moderation is learning to produce and consume as much as you need, not too much or too little. Reasonableness is another pillar. Reasonableness refers to the reasons for making decisions and its likely consequences. The decision should be reasonable and feasible. Risk management means being prepared to deal with risks. There must be ways to adapt to various possibilities arising from a decision. The sufficiency economy suggests that people can enjoy life within their means. People should avoid achieving more than they can handle. As a result, life will be more stable. Some aspects may seem extravagant within one's ability, but they could also be worth securing as long as they bring happiness and benefits to oneself and society. Following the philosophy of sufficiency economy can bring goodness and produce wise qualities to people. The sufficiency economy encourages people to move forward in a good way, be honest and kind in their life, and persist in achieving self-sufficiency by acquiring more knowledge. Following the philosophy of sufficient economy incurs fewer social conflicts. When people fully understand the economic philosophy of sufficiency and apply it to their lives, it increases and life satisfaction [91]. The sufficiency economy is closely related to the Thai lifestyle. Surveys describing how well Thais understand the sufficiency economy are insufficient. Among infertile couples, the availability of sufficiency economy applications may affect their mental health.

1.4.7 Couples or intimate relationships

Marital (intimate) relationships and mental health affect each other. A good intimate relationship is good for mental health. Conversely, mental health problems can affect marital relationships. [92]. A good marriage has a positive impact not only on the individual, but also on the partner. Marital quality also affects social life [93]. Intimate partner violence refers to the physical, psychological and sexual abuse of women by male intimate partners. The prevalence of intimate partner violence is about 25%. Infertile women experience a higher prevalence of intimate partner violence. In low - and middle-income countries,

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about 47.2% of infertile women have experienced intimate partner violence, far higher than the WHO reported figure of 27% [94]. Patients with cancer, whose partners reported positive emotions, experienced a higher quality of life. Partners of patients with cancer reported that marital relationships change with the disease. The better the marital relationship, the better the outcome for patients with cancer [95]. Additionally, improved marital relationships during pregnancy were associated with lower depression [96]. Marital relationship and marital communication are associated with anxiety among pregnant women. Marital communication was negatively associated with depression among pregnant women, and poor marital relationships produced a negative impact on the mental health of pregnant women [97]. Infertile couples have lower marital satisfaction. The impact of infertility on marital relationships and quality of life varies according to how couples communicate and cope marital problems [98]. Involving marital relationship improvement in mental health interventions for infertile couples creates positive results for infertility treatment [99].

When analyzing a dyadic data set like marital relationship among couples, considering how partners interact with each other is important. The Actor–Partner Interdependence Model (APIM) is based on the interdependence theory; interdependence theory explains the problems and effects of interpersonal situations [100]. APIM can be used to analyze the interdependence between objects that interact with and depend on each other. APIM analysis results show the impacts of independent variables on their own dependent variables and on partner's dependent variables. The dyad variables are divided in three types. The between-dyads variables refer to variables that are the same for both individuals, while the within-dyads variables refer to variables that are different for two individuals but have the same total score. The mixed-dyads variables mean that the variables are both between-dyad and within-dyad variables [101]. The most commonly used dyad data analysis among interdependence of interpersonal relationships is the APIM [102]. Marital satisfaction has an impact on the mental health of both partners [103]. Among infertile couples, APIM analysis is suitable to explore the effect of marital relationship on partner's anxiety and depression.

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1.5 Gaps in knowledge

The studies have shown a link between anxiety among infertile women and infertility treatment failure. However, no studies have been conducted on infertile men, and a lack of research exists on the relationship between anxiety and depression among infertile couples and infertility treatment failure. Hitherto in this study, infertility will be defined by the clinician using the ICD-10 diagnostic criteria. To investigate the relationship between infertility treatment and anxiety and depression among infertile couples, both pretreatment and undergoing treatment (including at least one infertility treatment failure) will be involved. A paucity of evidence exists regarding the association between marital relationships and anxiety/depression among infertile couples, so raising awareness of the mental health of infertile couples is important. More importantly, this study is novel. No researchers have conducted such a study among both couples seeking infertility treatment and comprehensive research on the factors associated (such as economic patterns and personality) with anxiety and depression among infertile couples in Thailand or elsewhere before. Moreover, research is limited concerning the relationships among sufficiency economy, infertility treatments, other demographic factors (age, genetic history, the expectation of having children etc.) and anxiety/depression among infertile couples. More research is needed to explore the unknown factors associated with anxiety and depression among infertile couples in Thailand or Asia.

1.6 Conceptual framework

The conceptual framework shows the impact of variables on the mental health outcomes of infertile couples namely anxiety and depression. According to the literature review, socio-demographic factors and personal history (such as sex, income, education level, the expectation of having children, substance use, etc.), infertility treatment, personality traits, marital relationships, and sufficiency economy philosophy are associated with mental health. Therefore, whether these factors are related to anxiety and depression among infertile couples is the aim our study sought to determine. As for the variable of marital relationship, our study divided it in wife's and husband's marital relationship. The reason is that the study examined at whether the marital relationship of infertile couples has a partner effect on their partner's anxiety and depression (Figure 1).

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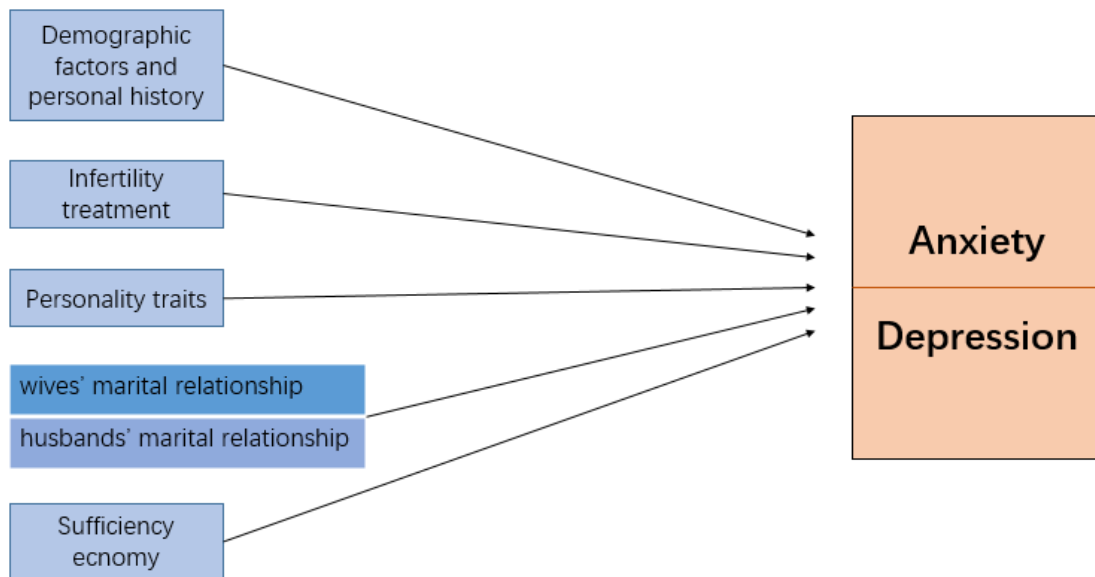
Figure 1. Conceptual framework

1.7 Hypotheses

The aim of the current study was to investigate the relationship between these independent variables, i.e., demographic factors and personal history, personality traits, marital relationships, sufficiency economy, and the dependent (outcome) variables of anxiety/depression among infertile couples.

Based on the reviews mentioned above, the researchers hypothesized that the following.

1.7.1 Demographic factors and personal history, e.g., sex, age, income and level of education, the expectation of having children, history of medication and substance use, infertility treatment, personality traits, marital satisfaction, and the concept of sufficiency economy are associated with anxiety and depression among infertile couples. More details can be found in Figure 1.

1.7.2 The interaction between spouses is linked to anxiety and depression in infertile couples. Specifically, three effects are shown in Figure 2. (1) For actor effect, participants' independent variables are correlated with their anxiety or depression. (2) Regarding partner effect, participants' independent variables are correlated with anxiety and depression in their spouses. (3) Concerning interaction effect, individuals' independent variables and their spouses' independent variables interact significantly. In other words,

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one partner's independent variables affect the other's anxiety and depression but only at certain levels.
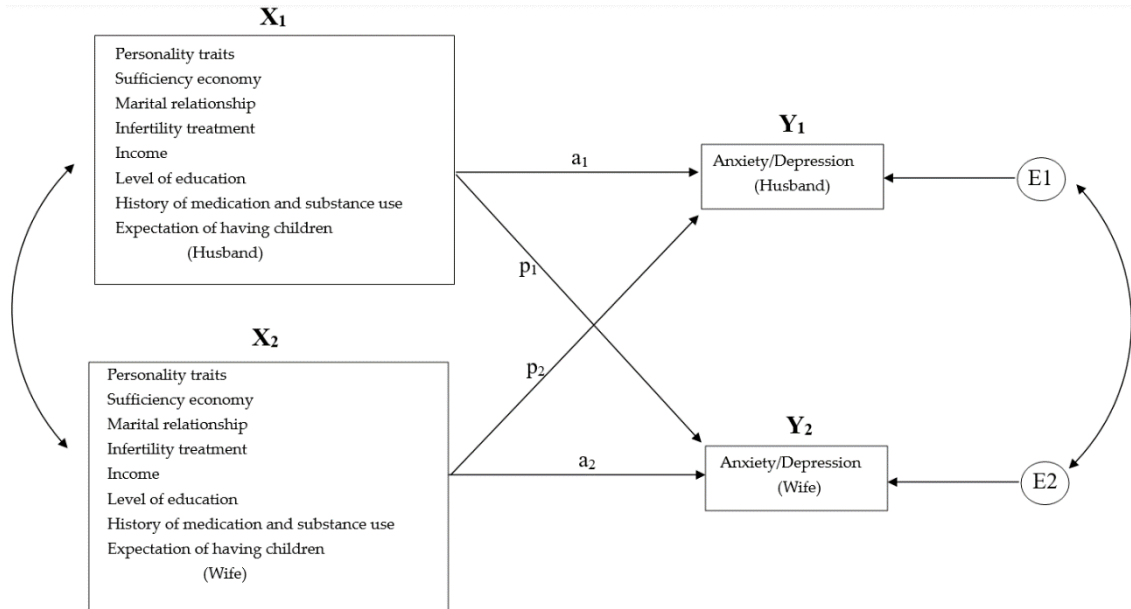
Figure 2. Actor–partner interdependence model (APIM) shows the actor, partner and interaction effects among infertile couples, e.g., X1: marital satisfaction; X2: wives' marital satisfaction; Y1: husbands' anxiety/depression; Y2: wives' anxiety/depression; and E1 & E2: corresponding error terms [104].

1.8 Scope of the study

A cross-sectional study was conducted. The population consisted of infertile different-gender couples attending the CMEx Fertility Center under the Faculty of Medicine, Chiang Mai University, and Chiang Mai IVF Polyclinic which is a private institute. A convenience sampling was carried out, and data were collected from July to August 2022 (Figure 3).
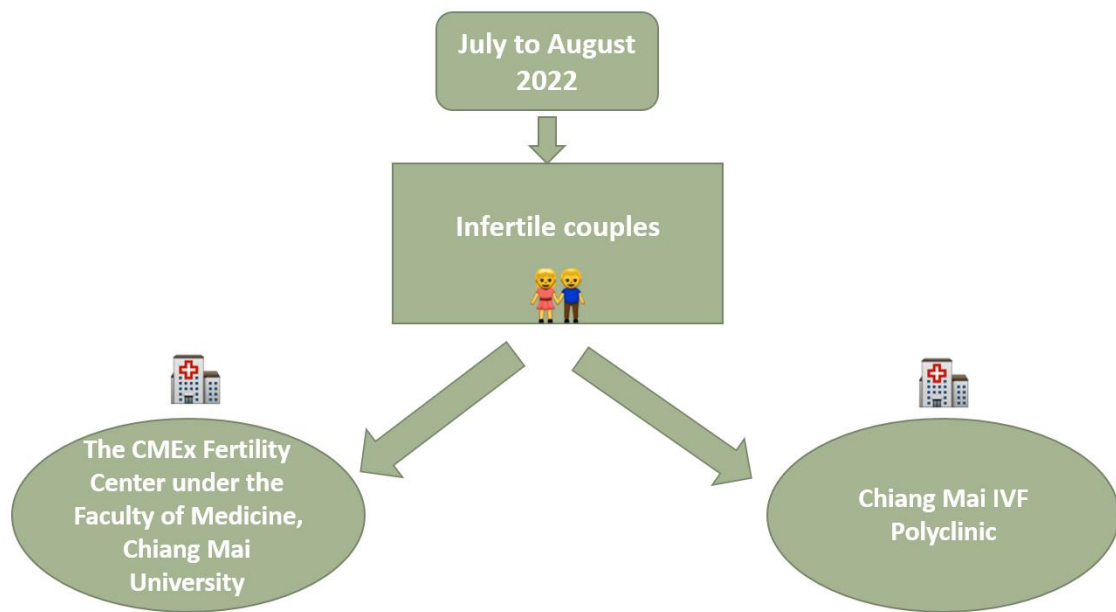
Figure 3. Scope of the study

CHAPTER 2

METHODS

This chapter explains the research methods. The research comprised a cross-sectional study to investigate the relationship among demographic factors and personal history, personality traits, marital satisfaction, the concept of sufficiency economy, and anxiety/depression among infertile couples.

2.1 Research design

This study employed a descriptive cross-sectional design. Data collection included both onsite and online methods. A one-time onsite or online questionnaire was used until the researchers obtained the expected sample size.

2.2 Population

The participants comprised infertile couples in Thailand. The participants were provided 1.52 USD as compensation for their time participating this research.

2.3 Sample size

2.3.1 Sample size calculation

Totally, 11 predictors were identified according to the conceptual framework. Researchers calculated the sample size based on the number of predictors. Sample size was calculated using GPower, while a priori analysis under F tests was used to estimate the sample size. The effect size f2 was equal to 0.15, the α err prob was equal to 0.05, while the power (1-β err prob) was equal to 0.80. Based on the number of predictors, the sample size totaled 123 couples (Figure 4). At the CMEx Fertility Center under the Faculty of Medicine, Chiang Mai University, about 5 to 10 couples made daily appointments. At Chiang Mai IVF Polyclinic, about 10 to 20 couples made daily appointments. To avoid the impact of invalid data, the researchers increased the sample size by about 20% based on patients flows. As a result, the final sample size was set at

150 couples.
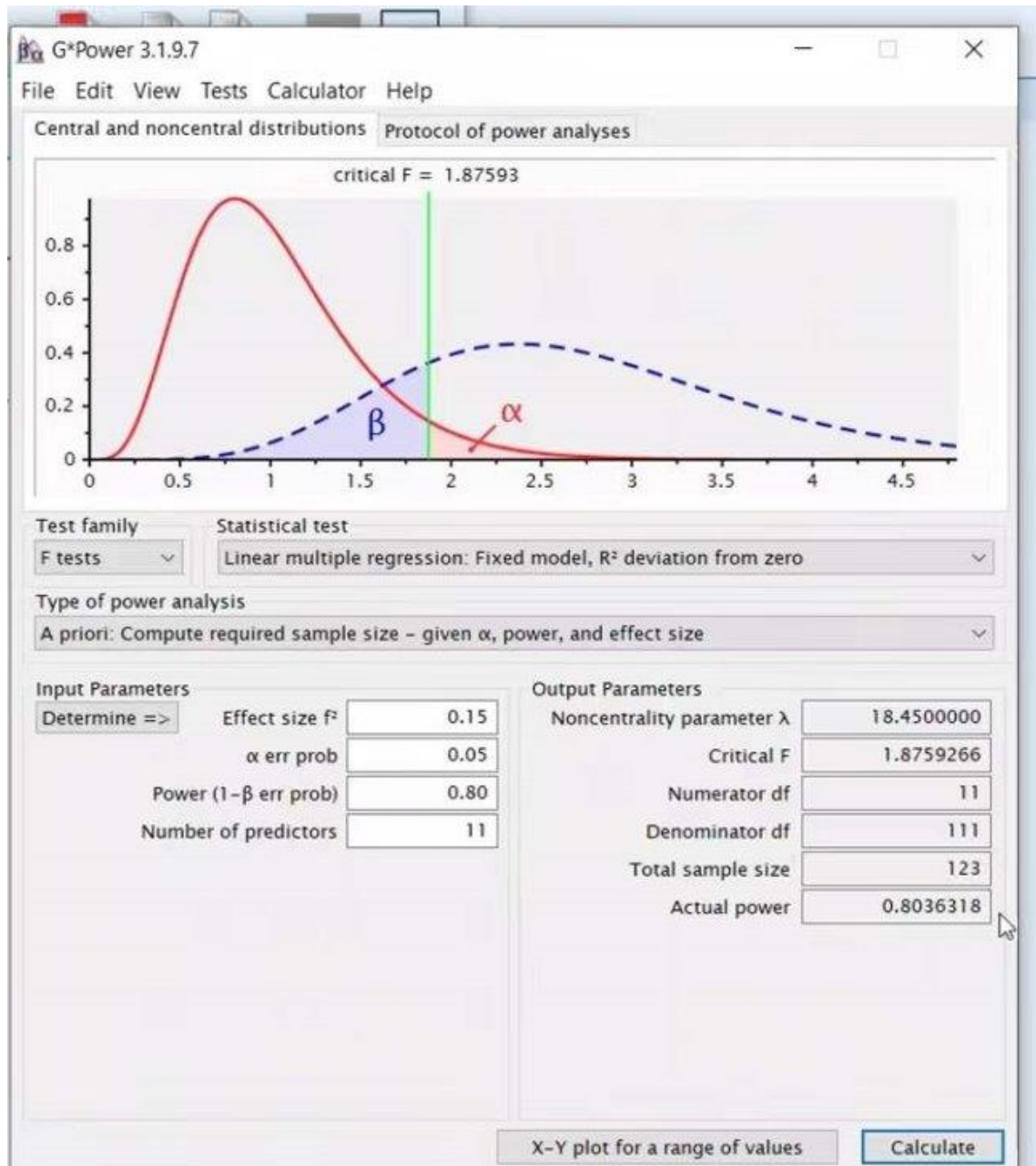
Figure 4. G*Power calculation

2.3.2 Sampling

The research team undertook a simple random sampling method, [105] went to the same center every other day and invited consecutive participants. The researcher and

research assistant visited the CMEx Fertility Center under the Faculty of Medicine, Chiang Mai University every Monday, Wednesday and Friday from 8:30 a.m. to 11 a.m. to request infertile couples to take part in the questionnaire. The researcher and research assistant visited the Chiang Mai IVF Polyclinic every Tuesday, Thursday, Saturday and Sunday from 2:30 p.m. to 5:30 p.m. to invite infertile couples to participate in the questionnaire. The researchers aimed to prevent selection bias using simple randomized data collection.

2.3.3 Inclusion criteria

1) At least one partner of a couple received a diagnosis of infertility according to ICD-10. Primary or secondary infertility were included in the diagnostic criteria. Participants sought counseling at the CMEx Fertility Center under the Faculty of Medicine, Chiang Mai University or Chiang Mai IVF Polyclinic

2) Able to read and write Thai or English

3) Attending two centers either in pretreatment or undergoing treatment

4) Both spouses agreed to participate in the study

2.2.4 Exclusion criteria

1) One spouse refused to participate.

2) Unstable vital signs or presenting emergency medical condition as stated by the attending physician.

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│ Ethics approval by Research Ethics Committee         │
│ of Faculty of Medicine, CMU                          │
└──────────────────────────────────────────────────────┘
┌──────────────────────────────────────────────────────┐
│ The research team asked permission to advertise by flyer and collect data at │
│ the CMEx Fertility Center, under the Faculty of Medicine, Chiang Mai University │
│ and the Chiang Mai IVF Polyclinic in 2022.           │
└──────────────────────────────────────────────────────┘
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Obtaining consent
Participants got PIS and ICF to consider participating in the research.
Participants was given 50 Baht per person as compensation.

The student PI was fluent in English along with a research assistant who was speaking Thai approached the candidates under a supervision by a co-advisor who serves a physician on duty of both centers.

COVID-19 sanity
There were both paper version and digital version for participants to answer the questionnaire.

Data storage
The data collection was code-linked (research code linked with their hospital number), the student separated the file for CRF from the identification list. Only the researcher could access the results of participant's questionnaire.

Time: July 4-Aug 31, 2022
CMEx: 61 couples (every Monday, Wednesday and Friday)
CM IVF: 89 couples (every Tuesday, Thursday, Saturday and Sunday)
(N=150 couples)

Invited: 192 couples
Refused: 42 couples

Data analysis

Figure 5. Flow diagram of the study

Figure 5 shows a total of 192 couples were invited, but 150 couples were finally recruited into this study.

2.4 Data collection

First, the study was approved by the Research Ethics Committee of Faculty of Medicine, Chiang Mai University. All measurements were available Thai and English. All tools had good internal consistency or Cronbach's alpha greater than 0.80. The student PIs who were fluent in English along with a research assistant (to the major advisor) who spoke Thai would approach the candidates under the supervision of a co-advisor who was fluent in English and Thai and served as a physician on duty at both centers. The student PI and the research assistant invited infertile couples receiving diagnosis of infertility and attending the CMEx Fertility Center under the Faculty of Medicine, Chiang Mai University and the Chiang Mai IVF Polyclinic to answer questionnaires. The language used in the invitation and consenting process was English and Thai upon the participants' preference. The approach was conducted upon the convenience of the participants and could be before or after the couples met with the doctors for treatment or counselling and under close advice and supervision by the field advisor.

The student and research assistant obtained permission by those centers to set up a private, confidential and safe area corner in the waiting area or a place where the centers allowed them to use for obtaining consent and explaining the research purpose as well as completing questionnaires if the participants preferred. The researchers explained our study to infertile couples and invited them to participate. In addition, infertile couples received the participant information sheet (PIS) and informed consent form (ICF) to learn more about the study and to consent to participate. Infertile couples could choose to fill out the questionnaire on paper or online. Most infertile couples filled out paper version questionnaires. Some participants came to the centers alone without a spouse. They answered the paper version of the questionnaire on site, and then researchers provided links to the online questionnaire for their absent spouse to fill out. Participants were provided a choice of Thai and English versions of the questionnaire. Most couples were Thai and chose the Thai version of the questionnaire. Some couples had one or both foreigners, so they chose the English version of the questionnaire. Participants could suspend or terminate participation at any time while answering the questionnaire, and were allowed to ask any questions related to the study. Participants were not asked to fill in personal information such as name, address and hospital number. The informed consent forms they signed were kept strictly confidential. Only the researchers had access to the questionnaires filled out by the participants. The data collection process lasted from July 4 to August 31, 2022. The research team invited 192 infertile couples at the CMEx Fertility Center under the Faculty of Medicine, Chiang Mai University and the Chiang Mai IVF Polyclinic. Altogether, 42 approached couples refused to participate in the study. The reasons included they were in a hurry to see a doctor, too many items were on the questionnaire for them to answer, their spouse didn't accompany with them, and they wanted to participate in the study with their spouse next time. The data collection process ended when a sufficient sample size was collected.

2.5 Measurements

Each spouse completed the questionnaire separately, and participants could choose either the English or Thai version. At the same time, according to the Coronavirus Disease (COVID-19) procedures, researchers also provide digital and paper versions for

participants to access. The measurements included the following.

2.5.1 Demographic data questionnaire: Altogether, 13 questions concerned socio-demographic factors. The basic information included age and sex. Occupations were divided in five options: freelance, government or state enterprise, self-employed, unemployed or others. Educational level consisted of six options including illiteracy, primary school, high school, vocational school, Bachelor's degree, and higher. Monthly income was divided in five categories: less than 760 USD, 760 to 1,520 USD, 1,520 to 2,280 USD, 2,280 to 3,040 USD and more than 3,040 USD. The duration of infertility was measured in months. The expectation of having children was based on a five-point scale: strongly expected, moderately expected, neither expected nor unexpected, moderately not expected and strongly not expected. Stage and nature of infertility treatment were also collected. The length of time spent attempting to conceive was measured in days. The number of infertility treatments was recorded in the questionnaire. Information regarding the use of tobacco, alcohol or other substances specified the amount used. The last item was whether a family history of infertility existed, and if so, the specific family relationship.

2.5.2 Outcome Inventory-21(OI-21): The OI-21 measures the level of anxiety, depression, somatization and interpersonal difficulty [106]. In the present study, only the scores of OI-anxiety and OI-depression were used in data analysis. The results of OI-somatization and OI-interpersonal difficulty were excluded. OI-21 incorporates a self-rating scale involving 21 items. OI-21 requires participants to describe their states and feelings over the past week and how often they experienced the following statements. Ratings range from 0 "never" to 4 "almost always." Items 3, 7, 9, 11, 15 and 20 are used to measure the level of anxiety, while items 2, 5, 14, 18 and 21 are used to measure the level of depression. Items 1, 6, 8, 12, 17 and 19 are used to measure somatization, and items 4, 10, 13 and 16 are used to measure interpersonal difficulty. The OI-21 surveyed 1,452 people with mental illness, their families, students, and residents. The results of the previous survey showed that the Cronbach's alpha of OI-21 was 0.92, and the Cronbach's alpha of interpersonal difficulty, anxiety, somatization and depression scales were 0.80, 0.82, 0.80 and 0.87, respectively. The scores of OI-21 range from 0 to 84. Higher score

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indicated the more symptoms were involved. The cut-off score for anxiety and depression was 7. The Cronbach's alpha of OI-21 among all participants, males, females were 0.920, 0.920, 0.921 in the current study.

2.5.3 Zuckerman-Kuhlman-Aluja Personality Questionnaire (ZKA-PQ): The Big Five model divided personality traits in five categories, including extraversion, agreeableness, conscientiousness, neuroticism, and openness [107]. The measurement was designed based on the Big Five model [108]. It constituted five domains, including neuroticism (NE), sensation seeking (SS), extraversion (EX), activity (AC) and aggressiveness (AG). The common version of ZKA-PQ contains 200 questions and 80 questions per facet. The short version we used totaled 40 questions. These items comprised descriptions of how participants thought and acted. It requires people to choose how much they agree with each statement. If people have not experienced certain states, they are requested to describe how they would behave in such a situation. The ZKA-PQ is a self-rating scale from 1 "strongly disagree" to 4 "strongly agree." The Cronbach's alpha of ZKA-PQ in each subscale were 0.829, 0.817, 0.750, 0.749 and 0.854 in the previous study. Scores for each facet range from 8 to 32. A higher score interprets a higher level of the corresponding personality traits. Items 11, 13, 21, 23, 24, 29, 31, 34, 35 and 36 required reverse scoring. The Cronbach's alpha of ZKA-PQ among all participants, males, females were 0.839, 0.816, 0.858 in the current study.

2.5.4 ENRICH (Evaluation and Nurturing Relationship Issues, Communication and Happiness) Marital Satisfaction Scale: This instrument was used to measure marital satisfaction and identify reasons for marital conflict [109]. The ENRICH scale constitutes a five-point scale that is self-rated. The scale ranges from 1 "strongly disagree" to 5 "strongly agree." with 15 items in total. Six items are scored in reverse: 2, 5, 8, 9, 12 and 14. The ENRICH scale mainly evaluates three aspects: individual factors include cultural background, values, the expectations for marriage, obligations undertaken in marriage, character and so on. Factors between marriages include the distribution of power and roles between couples, marital communication, problem-solving style and ability, and sex life. External factors include economic level, relationship with children and parents, and relationship with relatives and friends. The Thai ENRICH scale was translated with

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permission (Wongpakaran, unpublished data. 2022). The Cronbach's alpha was 0.86, and internal consistency coefficient was 0.74. The Cronbach's alpha of ENRICH Marital Relationship Scale among all participants, males, females were 0.836, 0.851, 0.821 in the current study.

2.5.5 Sufficiency Economy Scale (SES): This tool was used to measure sufficiency economy level [104,110]. SES contains nine items with a seven-point self-evaluation scale. Ratings range from 1 "strongly disagree" to 7 "strongly agree." The Cronbach's alpha was 0.75 in the previous survey. The SES score reflects whether the respondents adhere to the principles of moderation, prudence and virtue. In general, higher scores indicate a better understanding of sufficiency economy. SES was found a Cronbach's alpha of 0.70 in all participants in the current study.

The researchers pilot tested all the measurements to check the internal consistency of the measurements. The results from 20 questionnaires in Thai and 43 questionnaires in English showed that all the tools had a Cronbach's alpha greater than 0.7.

2.6 Data analysis

The data analysis of socio-demographic characteristics used descriptive analysis to calculate frequency, percentage, maximum, minimum, mean and standard deviation (SD). For descriptive analysis, the researchers divided the data into total participants, men, and women. Age was calculated with the mean, SD, maximum age and minimum age. The frequency and percentage of each category were calculated for occupation, income, the expectation of having children, and the number of infertility treatments. Smoking, alcohol use, other substance use, and infertile relatives were calculated for frequency and percentage. Anxiety, depression, personality traits, marital satisfaction, and sufficiency economy scores were also calculated as means and percentages by dividing in three groups, all participants, male participants and female participants. With a cut-off score of 7, the researchers calculated the prevalence of anxiety and depression using descriptive analysis among all participants, male participants and female participants.

The *t* test was used for sex differences in age, the expectation of having children and number of infertility treatments. Then, *t* test was applied to the scores of anxiety,

depression, personality traits, marital satisfaction and sufficiency economy for sex differences. Differences between smoking, alcohol use, other substance use and infertile relatives and anxiety/depression were calculated using the t test. The χ2 test was used for sex differences concerning occupation, income, education level, smoking, alcohol use, other substance abuse, infertile relatives and the prevalence of anxiety and depression. The df was performed. A p-value <.05 was considered statistically significant. The difference between socio-demographic characteristics and anxiety /depression was determined using the t test and ANOVA. The within group df and between group df were performed. The differences between occupation, education, income and anxiety/depression were calculated using ANOVA because these socio-demographic factors were categorical variables and had three or more categories. Similarly, a p-value less than 0.05 indicated a statistically significant difference.

Pearson's correlation coefficient was used to analyze the correlation between age, sex, the expectation of having children, number of infertility treatments, personality traits, marital satisfaction, sufficiency economy, and anxiety/depression. Point-biserial was used to analyze the correlation between smoking, alcohol use, other substance use, infertile relatives and anxiety/depression. The r coefficient represented the magnitude of the correlation. The r >0 represented a positive correlation, and r <0 represented a negative correlation. The closer the absolute value of r was to 1, the stronger the correlation was. A p-value <.05 indicated the correlation was statistically significant, while a p-value <.01 indicated the correlation was strongly significant.

Multiple regression was conducted to test the predictors of anxiety and depression among infertile couples. Factors significantly associated with anxiety and depression were employed for regression analysis. The $β$ >0 represented a positive predictor. The greater the $β$ value, the greater the positive influence of the factor on anxiety and depression among infertile couples. And $β$ <0 represented a negative predictor. The smaller the $β$ value, the greater the negative influence of the factor on anxiety and depression among infertile couples. A p-value <.05 indicated that this factor was a significant predictor of anxiety and depression, while a p-value <.01 indicated the predictor was strongly significant.

In the present research, David A. Kenny wrote the multilayer model was used to analyze the actor – partner interdependence model [111]. This modeling is described as detailed below.

Dyad data can be understood as matching data, and constitutes the most basic relationship in social relations, such as spouses, friends, father and son, mother and daughter, employment relationship and competition relationship. For the husband, the wife was the object. For the wife, the husband was the object. Regarding the subject effect, the influence of X1 on Y1 was expressed by the path coefficient a1; while the influence of X2 on Y2 was expressed by path coefficient a2. Concerning the object effect, the effect of X1 on Y2, was denoted by p1; while the influence of X2 on Y1 was represented by p2. For subject pattern, the subject effect was significant, but the object effect was not significant, and the dependent variable was mainly affected by subject effect, $p/a \approx 0$. Concerning object pattern, subject effect was not significant, the object effect was significant, and the dependent variable was mainly affected by object effect, $a \approx 0$, $p \neq 0$. Regarding the dyad pattern, the subject effect was significant, the object effect was significant, and the dependent variable was affected by the host-object effect, $p \neq 0$, $a \neq 0$, $p/a \approx 1$. For contrast pattern, the subject-object effect was significant, but the signs of the two were opposite, $p + a \approx 0$. Due to the two subject effects and object effects in the APIM model, we had to define two k's: $k1 = p1/a1$; $k2 = p2/a2$. The first step was to check whether the dyads variables were separable. The second step was to calculate the k value and its confidence interval, so as to judge the APIM pattern of couples. If the confidence interval contained 1, it meant that the subject-object effects were equal, but when the subject-object effects are both significant, it constitutes dyad pattern. When the confidence interval contains -1, and both subject and object effects are significant, it represents the contrast pattern. When the confidence interval contains 0 and the subject effect is significant, it constitutes the subject pattern, while the reverse represents the object pattern. The small effect size was indicated by the *r* value. When the *r* value was greater than 0.30 but less than 0.50, the effect size was medium. A large effect size was shown when the *r* value was greater than 0.50 [112]. The test of multiple categories, for example, ANOVA and chi – square test, was used to assess the Bonferroni correlation. APIM was used as well. Different patterns depended on different k parameters in APIM

analysis [111]. The k parameter was actor effect divided by partner effect. The four patterns were: (1) an actor-only pattern, when a k parameter was close to 0, and a ≠ 0, p = 0, 2) a partner-only pattern, when a k parameter was close to 0, and a = 0, p ≠ 0, 3) a couple-oriented pattern, when a k parameter was close to 1, and a = p and finally 4) a contrast pattern, when a k parameter was close to -1, and (a + p = 0) [113]. When the p – value was less than 0.05 and 95% confidence interval, the results were considered significant. Researchers used SPSS, Version 22 to analyze the data.

2.7 Ethics approval and confidentiality

The Research Ethics Committee of the Faculty of Medicine, Chiang Mai University, approved the study. The study code: PSY-2565-09017, certification number 208/2022 was effective 20 June 2022. The participants were provided relevant information on the PIS, and researchers explained the purpose to participants. When subjects agreed to participate in this research, they were requested to answer general information questions about themselves such as age, sex, etc. Questions investigated life experience as a couple, lifestyles, feelings and thoughts and problems of participants. Participants were informed that the questionnaire was divided in five small parts involving a total of 98 questions. The questions took approximately 15 to 20 mins to answer. There might have been low risk in participating in this research; however, if physical or mental discomfort arose from answering questions (questions about feelings, thoughts and problems were all very subjective; none of which were right or wrong), participants could take a break. Participants were allowed to skip answers to some questions that might make them feel inconvenient to answer and were allowed to exit the questionnaire at any time. Participants were provided 1.52 USD per person as compensation for their time volunteering for this research.

Participants' information and responses to questions in this study were confidential and protected. The ethics committee checked that the information was kept confidential. When the researchers obtained a sufficient sample size, the permission to fill in the questionnaire through the link was closed, and the offline invitation to participants was stopped. Only the researcher had access to download the data which were downloaded and saved every few days. The questionnaire information was stored for about one year.

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After that, all the accounts used to collect the data were permanently deleted. Personal information on the informed consent form, such as name, remained confidential. Participants' personal information and questionnaire data used for statistical analysis were kept separately. The researchers did not match participants' personal information with questionnaire data. Our data will be kept for five years after the last published article. After that, the researchers will erase all data. Identifiable information will not be published. Research findings will be published in academic journals and may be cited at conferences. According to international ethics standards for research of people and the Personal Data Protection Act, B.E. 2562, dissemination of research results in academic conferences or in academic journals requires that no personally identifiable information is submitted. If information is entered into a database by researchers, the data will be anonymous and not linked to participants.

CHAPTER 3

RESULTS

In this chapter, the results will show the prevalence of anxiety and depression among infertile couples. The relationship among demographic factors, personal history, personality traits, marital satisfaction, sufficiency economy and anxiety and depression among infertile couples will be clarified. The Actor-Partner effect is also shown.

The results will confirm our hypotheses.

a. Demographic factors, e.g., sex, age, income and level of education, are associated with anxiety/depression among infertile couples.

b. The expectation of having children positively correlates with anxiety /depression among infertile couples.

c. The number of infertility treatments positively correlates with anxiety /depression among infertile couples.

d. Substance use is positively correlated with anxiety/depression among infertile couples.

e. Having infertile relatives positively correlates with anxiety/depression among infertile couples.

f. Personality traits are factors associated with anxiety/depression among infertile couples.

g. Marital satisfaction is negatively correlated with anxiety/depression among infertile couples.

h. The concept of sufficiency economy is associated with anxiety/depression among infertile couples.

i. Participants' independent variables such as marital relationship and personality traits are correlated with anxiety and depression in their spouses

3.1 Sociodemographic characteristics and personal history of the participants

A total of 300 participants (150 couples) were included in the study. The sociodemographic characteristics of the participants is shown in Table 1. The age range was 20 to 62 years, with an average of 35.68 ± 5.40 years. The average age of male participants was 36.55 ± 5.98 years. The average age of female participants was 34.81 ± 4.61 years. Among all participants, the average age of males was higher than the average age of females. The difference was statistically significant, t (280) = 2.824, p <.01. More males than females smoked, and the difference was statistically significant, χ^2 (1) = 29.670, p <.001. More than one third of the participants were self-employed, or about 35.2%. Among them, 18.8% were males and 16.4% were females. About 14.1% of participants were freelancers. Males accounted for about 7.4% of the total. Females accounted for 6.7%, and about 30.9% of the participants worked for government or state enterprises. The percentages for both males and females were 15.4%, and approximately 1.7% of participants were unemployed, namely, 0.3% for males and 1.3% for females. About 18.1% of the participants were in other occupations; for males, 8.1% and for females, the proportion was about 10.1%.

More than one half of the participants had obtained a bachelor's degree, accounting for 58.7%; about 28.3% were males and 30.3% were females. Second, about 14.7% of the participants had higher education; both males and females accounted for 7.3%. About 13.7% of the participants had vocational school education, about 7.7% were males, while females accounted for 6.0%. Approximately 11.7% of the participants had obtained a high school degree; males accounted for 6.3% and females for 5.3%. The lowest percentage was at the educational level of primary school, with only 1.3% of participants; males accounted for 0.3% and females for 1.0%.

The majority of monthly income among participants was less than or equal to 760 USD; 21.3% were males and 24.7% were females. About 37.7% of the participants received their monthly income between 760 USD and 1,520 USD; males accounted for 18.3% and females 18.7%. Participants with a monthly income of 1,520 to 2,280 USD accounted for 7.3%; males accounted for 4.7% and females for 2.7%. Participants with a monthly income of 2,280 to 3,040 USD were the fewest, with a percentage of about 3.7%. Of these,

2.3% were males and 1.3% were females. About 6.0% of participants had a monthly income more than 3,040 USD, about 3.3% of males and 2.0% of females.

Most participants strongly agreed with the expectation of having children, at about 78.0%. Among them, about 39.7% were males and 38.3% were females. About 15.7% of participants had a moderate expectation of having children; about 6.0% were males and 9.7% were females. About 5.0% of participants chose neither agree nor disagree with the expectation of having children. Of those, about 4.3% were males and 0.7% were females. Only one female participant (0.3%) was moderately disagreed with the expectation of having children. Three female participants (1.0%) strongly disagreed with the expectation of having children.

About 16% of the participants were not receiving treatment for infertility. Males accounted for 8.7% and females for 7.3%. The largest group, 46.0% of participants had received one infertility treatment. Among them, 24.0% were males and 22.0% were females. About 23.3% of the participants had received two treatments for infertility. Approximately 10.3% were males and 13.0% were females. The number of participants who had received three infertility treatments was 8.3%. Males accounted for 4.3% and females for 4.0%. About 3% of the participants had received four treatments for infertility. For males, it was 1.3% and for females, 1.7%. The proportion of participants who had received five infertility treatments was 1.3%. Both males and females accounted for 0.7%. About 1.7% of the participants had received six infertility treatments. Males accounted for 0.7% of the total and females for 1.0%. Only one female participant (0.3%) had received seven infertility treatments.

More than 90% of the participants did not smoke. Males accounted for 41% and females for 50%. About 9.0% of the participants smoked, and all were males. More than half of the participants did not drink alcohol. Approximately 16.0% were males and 37% were females. About 47% of the participants drank alcohol. Males accounted for 34.0% and females for 13.0%. The percentage of participants without substance abuse was 53.0%. Among them, 16.0% were males and 37.0% were females. About 47% of the participants had substance abuse, including marijuana, cocaine or other drugs. Males accounted for 34.0% and females for 13.0%. Among participants who used alcohol and substance abuse,

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males were more likely than females. The difference was statistically significant, $\chi^2(1) =$ 53.111, p $<$ .001.

Most of the participants did not have infertile relatives, the proportion was about 86.3%. Among them, 44.3% were males and 42.0% were females. About 13.7% of the participants had infertile relatives. Males accounted for 5.7% and females for 8.0%.

The prevalence of anxiety was about 27.3% in all participants. The prevalence of anxiety in female participants (15.0%) was higher than in male participants (12.3%). The prevalence of depression in all participants was about 6.7%. The prevalence of depression in male participants was the same as in female participants (3.3%). The prevalence of anxiety and depression was 6.7%, no significant difference between males and females.

No significant sex differences were found in other sociodemographic characteristics. More details can be found in Table 1.

Table 1. Sociodemographic characteristics of the participants

Variables		N(%) Mean±SD	N(%) Mean±SD	N(%), Mean±SD	Test difference, (*df*), p
		Male (N = 150)	Female (N = 150)	Total (N = 300)	
Age		36.55±5.98 (20-62)	34.81±4.61 (21-51)	35.68±5.40 (20-62)	*t* (280) = 2.824, p <.01
Occupation	Freelance	22(7.4%)	20(6.7%)	42 (14.1%)	$\chi^2(4) = 3.029$, p = .553
	Government or state enterprise	46(15.4%)	46(15.4%)	92 (30.9%)	
	Self-employed	56(18.8%)	49(16.4%)	105 (35.2%)	
	Unemployed	1(0.3%)	4(1.3%)	5 (1.7%)	
	Other	24(8.1%)	30(10.1%)	54 (18.1%)	
Education	Illiterate	0	0	0	$\chi^2(4) = 2.071$, p = .723
	Primary school	1(0.3%)	3(1.0%)	4 (1.3%)	
	High school	19(6.3%)	16(5.3%)	35 (11.7%)	
	Vocational school	23(7.7%)	18(6.0%)	41 (13.7%)	
	Bachelor's degree	85(28.3%)	91(30.3%)	176 (58.7%)	
	Higher	22(7.3%)	22(7.3%)	44 (14.7%)	

Table 1 (Continue)

Variables		N(%) Mean±SD	N(%) Mean±SD	N(%), Mean±SD	Test difference, (*df*), p
		Male (N = 150)	Female (N = 150)	Total (N = 300)	
Monthly Income	0-25,000	64(21.3%)	74(24.7%)	138 (46.0%)	$\chi^2(4) = 3.410$, p = .492
	25,001-50,000	55(18.3%)	56(18.7%)	111(37.0%)	
	50,001-75,000	14(4.7%)	8(2.7%)	22 (7.3%)	
	75,001-100,000	7(2.3%)	4(1.3%)	11 (3.7%)	
	100,001 or higher	10(3.3%)	8(2.7%)	18 (6.0%)	
Expect to have children	Strongly disagree	0	3(1.0%)	3 (1.0%)	$t(298) = 0.342$, p = .732
	Moderately disagree	0	1(0.3%)	1 (0.3%)	
	Neither agree nor disagree	13(4.3%)	2(0.7%)	15 (5.0%)	
	Moderately agree	18(6.0%)	29(9.7%)	47 (15.7%)	
	Strongly agree	119(39.7%)	115(38.3%)	234 (78.0%)	
Infertility treatment times	1	72(24.0%)	66(22.0%)	138 (46.0%)	$t(298) = -1.126$, p = .261
	2	31(10.3%)	39(13.0%)	70 (23.3%)	
	3	13(4.3%)	12(4.0%)	25 (8.3%)	
	4	4(1.3%)	5(1.7%)	9 (3.0%)	
	5	2(0.7%)	2(0.7%)	4 (1.3%)	
	6	2(0.7%)	3(1.0%)	5 (1.7%)	
	7	0	1(0.3%)	1 (0.3%)	
Smoke	No	123(41.0%)	150(50%)	273 (91.0%)	$\chi^2(1) = 29.670$, p (Fisher's) $<.001$
	Yes	27(9.0%)	0	27 (9.0%)	
Alcohol	No	48(16.0%)	111(37.0%)	159 (53.0%)	$\chi^2(1) = 53.11$, p $<.001$
	Yes	102(34.0%)	39(13.0%)	141 (47.0%)	
Other substance use	No	48(16.0%)	111(37.0%)	159 (53.0%)	$\chi^2(1) = 53.111$, p $<.001$
	Yes	102(34.0%)	39(13.0%)	141 (47.0%)	
Infertile relatives	No	133(44.3%)	126(42.0%)	259 (86.3%)	$\chi^2(1) = 1.384$, p = .313
	Yes	17(5.7%)	24(8.0%)	41 (13.7%)	
Prevalence of anxiety		37(12.3%)	45(15.0%)	82 (27.3%)	$\chi^2(1) = 29.670$, p (Fisher's) = .365
Prevalence of depression		10(3.3%)	10(3.3%)	20 (6.7%)	$\chi^2(1) = 29.670$, p (Fisher's) = 1.000
Prevalence of both anxiety and depression		10 (6.7%)	9 (6.0%)	19 (6.3%)	$\chi^2(1) = 0.056$, p = .813, p (Fisher's) = 1.000

SD = Standard Deviation, *df* = degree of freedom

3.2 Descriptive statistics and Test difference

Among the 150 couples (total 300 participants), the mean anxiety score was 4.28 (SD = 3.79). Male participants' mean anxiety score was 3.86 (SD = 3.656), and among female participants, the score was 4.69 (SD = 3.877). The mean score of depression among all participants was 1.80 (SD = 2.60). The mean score of depression among male participants was 1.67 (SD = 2.451), and among female participants was 1.93 (SD = 2.735). The mean score of aggression among all participants was 15.01 (SD = 4.51). The mean score of aggression among male participants was 15.07 (SD = 4.370), and among female participants was 14.95 (SD = 4.659). All participants' mean sensation seeking score was 25.14 (SD = 3.98). The mean sensation-seeking score among male participants was 24.86 (SD = 3.698), and among female participants was 25.41 (SD = 4.241). The mean score of activity among all participants was 20.39 (SD = 3.60). The mean score of activity among male participants was 20.50 (SD = 3.417), and among female participants was 20.27 (SD = 3.75). The mean scores ± SD of extraversion among all male and female participants were 20.38 ± 2.690, 21.67 ± 2.298, 21.09 ± 3.011. Females had a higher mean score of neuroticism (NE) than men (15.87 ± 4.890, 14.61 ± 4.356, *t* (298) = -2.356, p < 0.05). The difference was statistically significant. The mean score ± SD of ENRICH marital satisfaction among all participants, males and females were 53.33 ± 9.81, 52.85 ± 9.781, 53.81 ± 9.858, respectively. The mean score ± SD of sufficiency economy in all participants, males, and females were 35.82 ± 7.70, 35.53 ± 6.280, 36.12 ± 8.912, respectively. The remaining results showed no significant differences regarding sex (Table 2).

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Table 2. Test difference and descriptive statistics

Variables	N(%), Mean±SD			Test difference, (*df*), p
	Male (N = 150)	Female (N = 150)	Total (N = 300)	
Anxiety	3.86±3.656	4.69±3.877	4.28±3.79	*t* (298) = -1.915, p = .056
Depression	1.67±2.451	1.93±2.735	1.80±2.60	*t* (298) = -0.845, p = .399
AG	15.07±4.370	14.95±4.659	15.01±4.51	*t* (298) = 0.230, p = .818
SS	24.86±3.698	25.41±4.241	25.14±3.98	t (298) = -1.204, p = .229
AC	20.50±3.417	20.27±3.775	20.39±3.60	*t* (298) = 0.545, p = .586
EX	21.67±2.298	21.09±3.011	21.38±2.690	*t* (298) = 1.875, p = .062
NE	14.61±4.356	15.87±4.890	15.24±4.67	*t* (298) = -2.356, p <.05
ENRICH	52.85±9.781	53.81±9.858	53.33±9.82	*t* (298) = -0.847 p = .398
SES	35.53±6.280	36.12±8.912	35.82±7.70	*t* (268) = -0.667, p = .506

(AG = aggression, SS = sensation seeking, AC = activity, EX = extraversion, NE = neuroticism, from ZKA – PQ. ENRICH=ENRICH scale, SES = Sufficiency Economy Scale, *df* = degree of freedom, SD = Standard Deviation)

Hypothesis #1. demographic factors, e.g., sex, age, income and level of education, are associated with anxiety/depression among infertile couples.

3.3 Test differences between sociodemographic factors and anxiety/depression

The results of the test of the differences between sociodemographic factors and anxiety/depression showed that participants with different occupations had different depression scores measured by OI-21. The difference was statistically significant, *F* (4) = 2.795, p <.05 (Table 3). Sociodemographic factors and anxiety/depression were not statistically significant among male participants (Table 4). Among female participants, the difference between occupation and depression scores was statistically significant, *F* (4) = 4.223, p <.01 (Table 5).

Table 3. Test differences between sociodemographic factors and anxiety/depression in all participants (N = 300)

Variables		Test differences (*df*), p
Occupation	Anxiety	F (4, 293) = 1.184, p = .318
	Depression	F (4, 293) = 2.795, p $<$ .05
Education	Anxiety	F (4, 295) = 0.077, p = .989
	Depression	F (4, 295) = 0.387, p = .818
Monthly Income	Anxiety	F (4, 295) = .314, p = .868
	Depression	F (4, 295) = 0.362, p = .836
Smoke	Anxiety	t (298) = .717, p = .474
	Depression	t (298) = -.109, p = .914
Alcohol	Anxiety	t (298) = -.305, p = .761
	Depression	t (298) = -.811, p = .418
Other substance use	Anxiety	t (298) = -.305, p = .761
	Depression	t (298) = -.811, p = .418
Infertile relatives	Anxiety	t (298) = -1.229 p = .220
	Depression	t (298) = -.401, p = .689

t = t-statistic, *F* = F-statistic, *df* = degree of freedom

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Table 4. Test differences between sociodemographic factors and anxiety/depression in male participants (N = 150)

Variables		Test differences (*df*), p
Occupation	Anxiety	F (4, 144) = 0.720, p = .580
	Depression	F (4, 144) = 0.595, p = .667
Education	Anxiety	F (4, 145) = 0.389, p = .816
	Depression	F (4, 145) = 0.796, p = .530
Monthly Income	Anxiety	F (4, 145) = 0.571, p = .684
	Depression	F (4, 145) = 0.387, p = .818
Smoke	Anxiety	t (148) = 0.129, p = .898
	Depression	t (148) = -0.417, p = .677
Alcohol	Anxiety	t (148) = 0.130, p = .897
	Depression	t (148) = 0.405, p = .686
Other substance use	Anxiety	t (148) = 0.130, p = .897
	Depression	t (152) = 0.405, p = .686
Infertile relatives	Anxiety	t (148) = 0.114, p = .910
	Depression	t (148) = 0.152, p = .880

t = t-statistic, *F* = F-statistic, *df* = degree of freedom

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Table 5. Test differences between sociodemographic factors and anxiety/depression in female participants (N = 150)

Variables		Test differences (*df*), p
Occupation	Anxiety	*F* (4, 144) = 2.383, p = .054
	Depression	*F* (4, 144) = 4.223, p < .01
Education	Anxiety	*F* (4, 145) = 0.315, p = .867
	Depression	*F* (4, 145) = 0.914, p = .457
Monthly Income	Anxiety	*F* (4, 145) = 1.603, p = .177
	Depression	*F* (4, 145) = 1.149, p = .336
Alcohol	Anxiety	*t* (148) = -1.886, p = .061
	Depression	*t* (152) = -1.872, p = .067
Other substance use	Anxiety	*t* (148) = -1.886, p = .061
	Depression	*t* (152) = -1.872, p = .067
Infertile relatives	Anxiety	*t* (148) = -1.521, p = .130
	Depression	*t* (148) = -0.549, p = .584

t = t-statistic, *F* = F-statistic, *df* = degree of freedom

3.4 Pearson's Correlation between variables and anxiety/depression

Hypothesis #2. the expectation of having children is positively correlated with anxiety/depression among infertile couples

Pearson's correlation showed that the expectation of having children was negatively correlated with depression among all participants ($r = -.121$, p <.05). More details can be found in Table 6. At the same time, the expectation of having children was negatively correlated with depression among female participants ($r = -.228$, p <.001). More details can be found in Table 8.

Hypothesis # number of infertility treatments is positively correlated with anxiety/depression among infertile couples

It appeared that infertility treatments were not significantly correlated to anxiety and depression ($r = .044, -.019$, p >.05, respectively). More details can be found in Table 6, Table 7 and Table 8.

Hypothesis # substance use is positively correlated with anxiety/depression among infertile couples

Alcohol use and other substance use positively correlated with depression among female participants ($r = .178$, p <.05 and $r = .178$, p <.05), respectively). More details can be found in Table 8.

Hypothesis # personality traits are factors associated with anxiety/depression among infertile couples

Pearson's correlation showed that aggression ($r = .353$, p <.01), extraversion ($r = .139$, p <.05) and neuroticism ($r = .625$, p <.01) positively correlated with anxiety among all participants (Table 6). Sufficiency economy negatively correlated with anxiety. Aggression ($r = .331$, p <.01) and neuroticism ($r = .616$, p <.01) positively correlated with anxiety in male participants (Table 7). Aggression ($r = .380$, p <.01), extraversion ($r = .208$, p <.05) and neuroticism ($r = .622$, p <.01) positively correlated with anxiety in female participants (Table 8). Aggression ($r = .317$, p <.01), extraversion ($r = .133$, p <.05) and neuroticism ($r = .601$, p <.01) positively correlated with depression in all participants (Table 6). Aggression ($r = .294$, p <.01) and neuroticism ($r = .546$, p <.05) positively

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correlated with depression among male participants (Table 7). Similarly, aggression (r = .339, p <.05), extraversion (r = .201, p <.05) and neuroticism (r = .644, p <.05) positively correlated with depression among female participants (Table 8).

Hypothesis # marital satisfaction is negatively correlated with anxiety/depression among infertile couples

ENRICH marital satisfaction negatively correlated with depression among all participants (r = -.209, p < .01)). More details can be found in Table 6. Also, a negative correlation was noted between marital satisfaction and depression among male (r = -.225, p <.01) and female participants (r = -.201, p <.05). More details can be found in Table 7 and Table 8.

Hypothesis # the concept of sufficiency economy is associated with anxiety/depression among infertile couples

Sufficiency economy was negatively correlated with anxiety (r = -.123, p<.05) and depression (r = -.157, p <.01) among all participants (Table 6)). Sufficiency economy was negatively correlated with anxiety among male participants (r = -.197, p <.05). In addition, sufficiency economy negatively correlated with depression among male participants (r = -.214, p <.01). More details can be found in Table 7. Sufficiency economy was not significantly correlated with anxiety and depression among female participants (Table 8).

At the same time, the researchers found a correlation between the two outcomes. A significant positive correlation was observed between anxiety and depression among all participants (r = .775, p <.05), among male participants (r = .763, p <.05), and among female participants (r = .786, p <.05). More details can be found in Table 6, Table 7 and Table 8.

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Table 6. Correlations between variables and outcomes in all participants (N = 300)

	age	gender	expect	smoke	alcohol	drugs	relatives	times	AG	SS	AC	EX	NE	ENRICH	SES	anxiety	depression
age	1																
gender	-.161**	1															
expect	-.024	-.020	1														
smoke	.122*	-.314**	.091	1													
alcohol	.081	-.421**	-.008	.264**	1												
drugs	.081	-.421**	-.008	.264**	1.000**	1											
relatives	-.031	.068	-.035	-.023	.034	.034	1										
times	.254**	.065	.104	-.011	-.101	-.101	-.071	1									
AG	-.125*	-.013	-.069	.100	.104	.104	.032	-.039	1								
SS	.080	.070	.204**	-.031	.020	.020	-.009	.030	-.026	1							
AC	.019	-.032	.085	-.005	.072	.072	.009	.086	.225**	.499**	1						
EX	.078	-.108	.015	.085	.107	.107	.030	.095	.217**	.407**	.535**	1					
NE	-.132*	.135*	-.084	-.091	-.079	-.079	.002	.063	.444**	-.041	.279**	.232**	1				
ENRICH	.041	.049	.058	-.100	-.026	-.026	-.038	-.024	-.125*	.248**	.004	.005	-.246**	1			
SES	-.091	.039	.088	.001	.082	.082	-.005	.142*	.267**	.126*	.209**	.151**	.080	-.095	1		
anxiety	.030	.110	-.098	-.042	.018	.018	.071	.044	.353**	-.032	.088	.139*	.625**	-.110	-.123*	1	
depression	-.037	.049	-.121*	.006	.047	.047	.023	-.019	.317**	-.066	.099	.133*	.601**	-.209**	-.157**	.775**	1

*p <.05, **p <.01, AG = aggression, SS = sensation seeking, AC = activity, EX = extraversion, NE = neuroticism, from ZKA - PQ. ENRICH = ENRICH scale,

SES = Sufficiency Economy Scale

Table 7. Correlations between variables and outcomes in male participants (N = 150)

	age	expect	smoke	alcohol	drugs	relatives	times	AG	SS	AC	EX	NE	ENRICH	SES	anxiety	depression
age	1															
expect	-.025	1														
smoke	.096	.138	1													
alcohol	.018	-.048	.210**	1												
drugs	.018	-.048	.210**	1.000**	1											
relatives	-.040	.000	-.003	-.070	-.070	1										
times	.299**	.073	.015	-.031	-.031	-.089	1									
AG	-.093	-.060	.148	.050	.050	-.034	.072	1								
SS	.024	.202*	-.015	-.049	-.049	-.055	.049	-.061	1							
AC	-.051	.000	-.023	-.025	-.025	-.071	.092	.251**	.503**	1						
EX	.016	.012	.090	.064	.064	-.004	.030	.161*	.322**	.444**	1					
NE	-.049	.057	-.078	-.097	-.097	-.070	.156	.452**	-.054	.184*	.184*	1				
ENRICH	.044	-.136	-.126	.048	.048	-.027	-.116	-.110	.230**	-.001	-.001	-.277**	1			
SES	.061	.029	-.046	.011	.011	.068	-.284**	-.352**	.149	-.078	-.078	-.260**	.194*	1		
anxiety	.009	-.033	-.011	-.011	-.011	-.009	.054	.331**	-.124	.024	.024	.616**	-.106	-.197*	1	
depression	-.023	.020	.034	-.033	-.033	-.012	.033	.294**	-.085	.055	.055	.546**	-.225**	-.214**	.763**	1

*p <.05, **p <.01, AG = aggression, SS = sensation seeking, AC = activity, EX = extraversion, NE = neuroticism, from ZKA - PQ. ENRICH = ENRICH scale, SES = Sufficiency Economy Scale

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Table 8. Correlations between variables and outcomes in female participants (N = 150)

	age	expect	alcohol	drugs	relatives	times	AG	SS	AC	EX	NE	ENRICH	SES	anxiety	depression
age	1														
expect	-.032	1													
alcohol	.011	.010	1												
drugs	.011	.010	1.000**	1											
relatives	.002	-.058	.197*	.197*	1										
times	.242**	.130	-.131	-.131	-.065	1									
AG	-.176*	-.076	.167*	.167*	.087	-.132	1								
SS	.175*	.209*	.151	.151	.018	.007	.004	1							
AC	.092	.150	.151	.151	.075	.085	.203*	.503**	1						
EX	.112	.014	.073	.073	.065	.154	.259**	.483**	.601**	1					
NE	-.189*	-.187*	.043	.043	.041	-.027	.449**	-.048	.368**	.351**	1				
ENRICH	.058	.225**	-.063	-.063	-.054	.051	-.139	.259**	.011	.010	-.237**	1			
SES	.120	-.067	-.179*	-.179*	-.108	-.015	-.420**	.069	-.154	-.116	-.229**	.302**	1		
anxiety	.097	-.147	.153	.153	.124	.022	.380**	.028	.150	.208*	.622**	-.127	-.029	1	
depression	-.038	-.228**	.178*	.178*	.045	-.066	.339**	-.058	.137	.201*	.644**	-.201*	-.080	.786**	1

*p <.05, **p <.01, AG = aggression, SS = sensation seeking, AC = activity, EX = extraversion, NE = neuroticism, from ZKA - PQ. ENRICH = ENRICH scale, SES = Sufficiency Economy Scale

3.5 The multiple regression predicting anxiety and depression symptom

Multiple regression results showed predictors of anxiety and depression in infertile couples. Aggression (β = .116, p = .031) and neuroticism (β = .593, p <.001) were significant predictors of anxiety among all participants. Neuroticism (β = .608, p <.001) and sufficiency economy (β = .174, p = .013) were significant predictors of anxiety among male participants. Neuroticism was the only predictor of anxiety among female participants (β = .576, p <.001). In addition, neuroticism (β = .160, p = .001), marital satisfaction (β = -.093, p = .015) and anxiety (β = .661, p <.001) were significant predictors of depression among all participants. Marital satisfaction (β = -.122, p = .030) and anxiety (β = .709, p <.001) were significant predictors of depression among male participants. Neuroticism (β = .233, p = .001) and anxiety (β = .628, p <.001) were significant predictors of depression among female participants (Table 9).

Table 9. Multiple regression predicting anxiety and depression symptom

Variables	Anxiety				Depression			
	B	Standard error	β	p	B	Standard error	β	p
Whole sample (N = 300)								
Aggression	.098	.045	.116	.031	-.005	.025	-.008	.849
Extraversion	-.024	.066	-.017	.717	.005	.036	.005	.897
Neuroticism	.482	.042	.593	.000	.089	.028	.160	.001
Sufficiency economy	.048	.039	.060	.221	-.008	.022	-.014	.720
Expectation					-.150	.138	-.039	.279
Marital satisfaction					-.025	.010	-.093	.015
Anxiety					.453	.032	.661	.000
Male (N = 150)								
Aggression	.098	.063	.117	.122	.006	.035	.011	.863
Extraversion	.007	.103	.005	.942	-.015	.057	-.014	.789
Neuroticism	.510	.061	.608	.000	.035	.042	.063	.403
Sufficiency economy	.149	.059	.174	.013	-.018	.034	-.031	.595
Expectation					.101	.212	.025	.635
Marital satisfaction					-.031	.014	-.122	.030
Anxiety					.475	.046	.709	.000

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Table 9 (Continue)

Variables	anxiety				depression			
	B	Standard error	β	P	B	Standard error	β	P
Female (N = 150)								
Aggression	.096	.065	.116	.140	-.016	.035	-.027	.649
Extraversion	-.031	.089	-.024	.727	-.007	.048	-.008	.887
Neuroticism	.457	.060	.576	.000	.131	.039	.233	.001
Sufficiency economy	-.020	.054	-.027	.707	-.015	.030	-.027	.631
Expectation					-.326	.195	-.087	.096
Marital satisfaction					-.012	.015	-.042	.436
Anxiety					.443	.045	.628	.000

aggression, extraversion and neuroticism refer to ZKA personality traits

3.6 The effect of variables on anxiety/depression of the partner on APIM

Hypothesis # individuals' independent variables predicted anxiety and depression in themselves (actor effect) and their spouses (partner effect)

This study focused on the effects of the expectation of having children, AG, NE, ENRICH, SES and anxiety on depression. Both the effect of one's own expectations, AG, NE, ENRICH, SES and anxiety (actor) and the effect of partner's expectations, AG, NE, ENRICH, SES and anxiety (partner) on depression were studied. The researchers estimated the separate actor and partner effects for husbands and wives, and the dyad members being distinguishable by their sex. For the APIM analysis, 148 dyads (296 individuals) were included. Missing data were noted on at least one variable from four participants. Therefore, the researchers excluded them.

For husbands, the standard deviation of the residuals was 1.583 and for wives was 1.598. The R squared of the full model for husbands was .586 and for wives was .662. The null hypothesis showed that these R squared values were zero, yielding a χ^2 with *df* = 24, equaling 316.458 (p < .001). As this test was statistically significant, the result indicated that the R squared values were statistically greater than zero. The partial correlation for depression controlling for actor and partner variables equaled -.066 without significance (p = .433). Hence, the residuals of husbands and wives were hardly correlated. The intercept for husbands was 1.409 and did not statistically significantly differ from zero (p = .456) while the intercept for wives was 1.058 without significance (p = .579). The

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difference between the two, main effect test of sex, was without significance (p = .899). The overall intercept was 1.234 and did not differ from zero (p = .342). The analyses used generalized least squares analysis with correlated errors and restricted maximum likelihood estimation. The Z tests and the tests of correlations were coefficients tests using t-tests of correlation coefficients. Actor and partner effects sizes were partial correlations and d when the predictor was dichotomous. Betas were given twice. One beta used the overall standard deviation across all individuals (o). The other beta was used as the standard deviation for husbands and wives separately (s). The beta (o) value should be tested if betas are to be compared among the members. For all analyses, alpha was set at .050.

The expectation of having children

Regarding the expectation of having children, the combined partner effect for both husbands and wives equaled -0.323 and was significant (p = .039). The standardized effect equaled -0.083 (r = -.126), which was considered a small effect size. The ratio of the partner effect to the actor effect was overall k, equaling 22.905. The Monte Carlo Method was used for a 95% confidence interval for k, i.e., the parametric bootstrap, was from -33.859 to 31.254. The 95% confidence interval for k was wide. Therefore, it could not be concluded which model was the most likely (Figure 6).
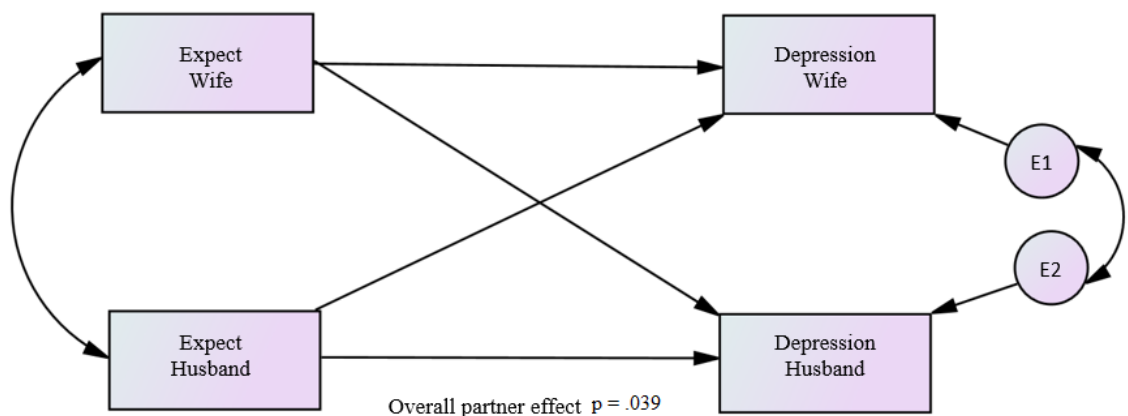

Figure 6. Overall effects between the expectation of having children and depression among couples

Aggression personality trait

Regarding aggression personality trait, the combined actor effect across both husbands and wives equaled 0.085, which was statistically significant (p = .048). The standardized effect equaled 0.101 (*r* = .116), which was considered a small effect size (Figure 7).
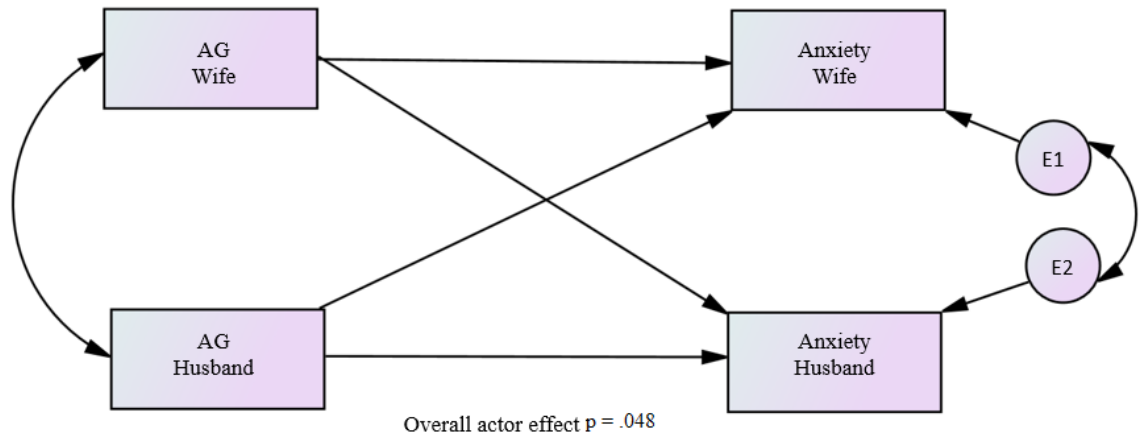

Figure 7. Overall effects between aggression and anxiety among couples

Neuroticism personality trait

Regarding neuroticism, the actor effect for husbands equaled 0.491 and was statistically significant (p <.05). The standardized effect equaled 0.605 (*r* = .547), and was considered a large effect size. The actor effect for wives equaled 0.455 and was statistically significant (p <.05). The standardized effect equaled 0.560 (*r* = .550), and was considered a large effect size (Figure 8). The combined actor effect between neuroticism and depression across both husbands and wives equaled 0.473 and was statistically significant (p <.01). The standardized effect equaled 0.585 (*r* = .547), and was considered a large effect size (Figure 9).
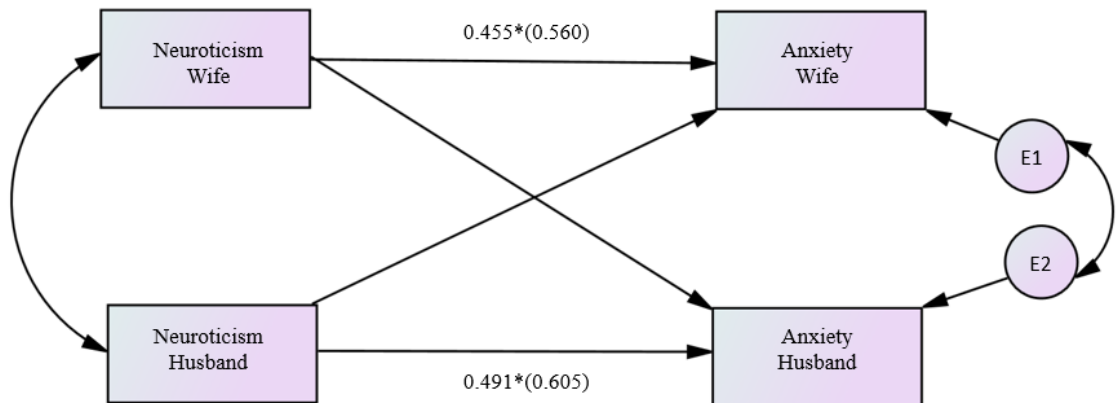
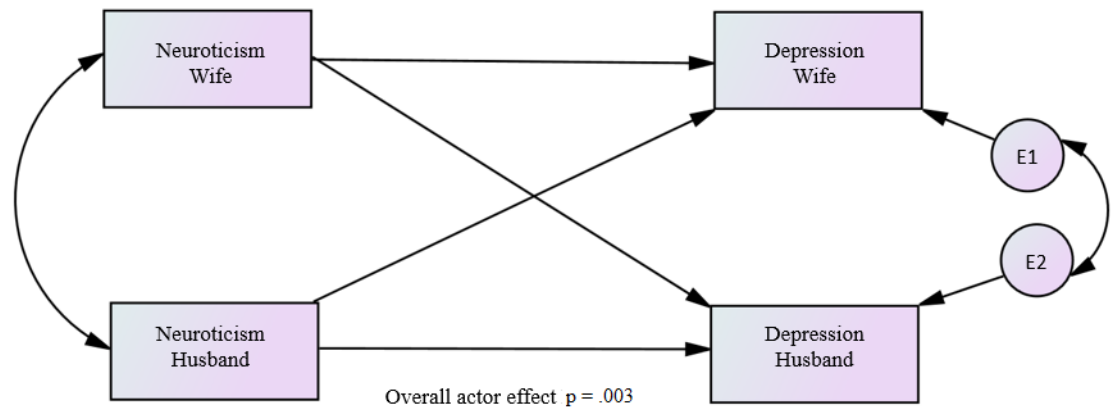*Figure 8. Actor effect between neuroticism and anxiety among couples*

Figure 9. Overall effects between neuroticism and depression among couples

ENRICH marital satisfaction

Regarding marital satisfaction, the combined actor effects across both husbands and wives equaled -0.022 and was statistically significant (p = .039). The standardized effect equaled -0.084 (*r* = -.126), and was considered a small effect size (Figure 10).
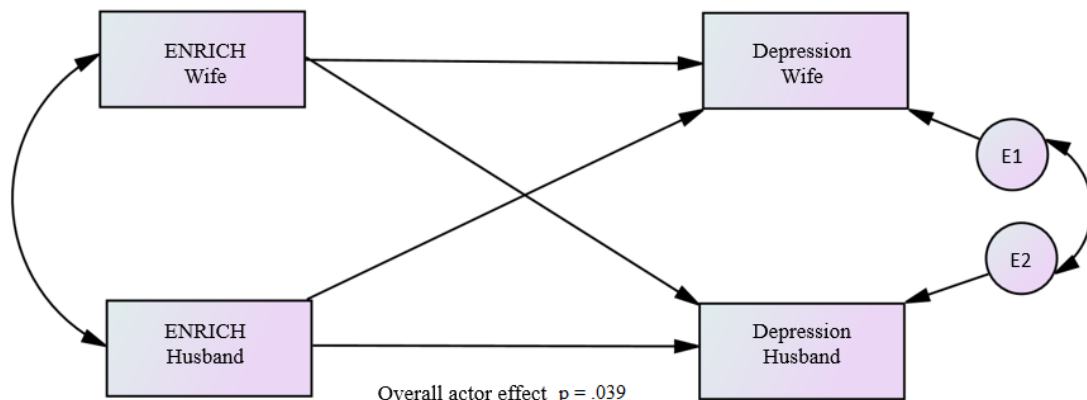
Figure 10. Ooverall effects between marital satisfaction and depression among couples

Regarding the interactive effect between anxiety and depression, the actor effect for husbands equaled 0.487 and was statistically significant (p <.05). The standardized effect equaled 0.708 (r = .644), and was considered a large effect size. The actor effect for wives equaled 0.407 and was statistically significant (p <.05). The standardized effect equaled 0.590 (r = .589), and was considered a large effect size. The test that the two actor effects were statistically significantly different was without significance, Z = -1.180 (p = .239). The combined actor effect across both husbands and wives equaled 0.447 and was statistically significant (p <.001). The standardized effect equaled 0.652 (r = .618), and was considered a large effect size (Figure 11).
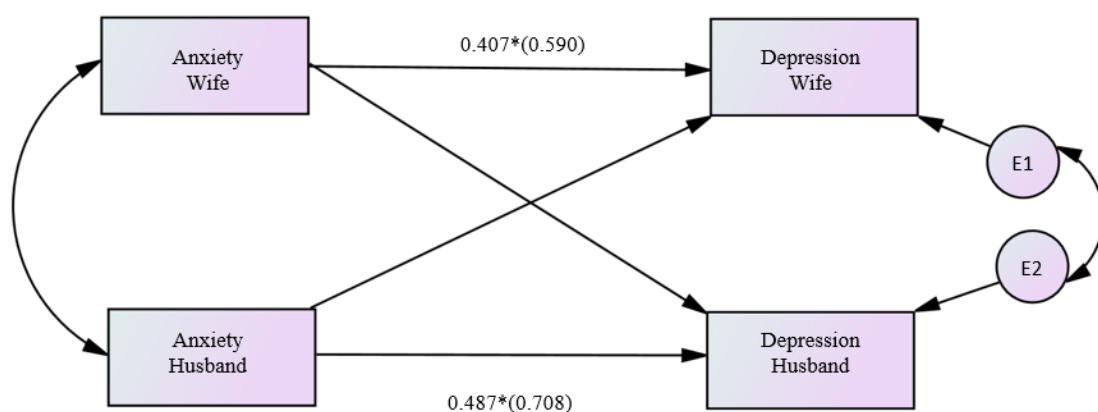

Figure 11. Actor effect between anxiety and depression among couples

Summary of APIM results

Infertile couples' expectations of having children affected their partner's depression levels. Aggression could affect an individual's anxiety among infertile couples. Neuroticism was associated with an individual's anxiety and depression among infertile couples. Marital satisfaction among infertile couples affected their own levels of depression. Results of the correlation analysis showed that the sufficiency economy concept was associated with anxiety and depression among infertile couples. Still, the results of SES in APIM were not statistically significant.

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CHAPTER 4

DISCUSSION AND CONCLUSION

This chapter consists of a discussion on the results of the studies, strengths, limitation, conclusions and suggestions. It constitutes a descriptive cross-sectional study on the relationship among personality traits, marital relationships, sufficiency economy, demographic factors, and anxiety/depression among infertile couples.

4.1 Discussion

4.1.1 Prevalence and factors associated with anxiety and depression among infertile couples

1) Prevalence

The researchers had no prior hypotheses for the prevalence of anxiety and depression. Consistent with a related study in India where 58% of participants reported depression among female participants using HDRS, 24% reported anxiety on HAM-A, and 24% had both depression and anxiety on HDRS and HAM-A [114], whereas the present study found 27.3% for anxiety, 6.7% for depression and 6.7% for combined anxiety and depression. The different prevalences especially depression rate could be because the measurements used are differed. The study of Dadhwal and colleagues used clinician-rated HDRS, whereas self-reported measurement of Outcome inventory-21 was used in the present study. The study supported the discrepancy between clinician-rated and self-reported measurement on depression in that the results from clinician-rated measurement tended to be higher than that from the self-reported questionnaire [115]. On the contrary, some researchers found no difference between both methods [116]. Most researchers agreed that discrepancy or agreement is related to other factors that need to be accounted for, e.g., education and personality.

2) Socio-demographic factors

A related study showed that females among couples undergoing infertility

treatment exhibited significantly higher stress, anxiety and depression scores than men [117]. The researchers hypothesized that demographic factors, e.g., sex, age, income, and level of education were associated with anxiety and/depression among infertile couples. The mean age of our participants was higher among men (36.55) than women (34.81), as detailed in Table 1. In the current research, occupation was shown to be associated with depression among all participants, $F(4) = 2.795$, p $<$ .05. The unemployed group reported the highest score on depression than other groups. However, such findings are supported by much research [118].

3) The expectation of having children

The researchers hypothesized that the expectation of having children correlated with anxiety or depression among infertile couples. One study found that not having children constitutes a risk factor for anxiety among women [119]. The expectations of having children vary from country to country. About 79% of Chinese couples want to have their first child. Approximately 14.7% of Chinese couples want a second child [120]. About 75% of Australian women desire a child [121]. Approximately 55.4% of Thai women expect to have children [122]. However, no such study reported the expectation of having a child was related to anxiety or depression. What the researchers hypothesize is more harmful – the expectation will be associated with anxiety/ depression, but because it's a single question, it might not give us the same interpretation between participants and researchers. The researchers assume from the results that this item is addressed positively rather than negatively. It's more like hope (which is positive), and the persons who score high should be in good spirits because they are clinging to hope. That's why the results are a negative correlation. One more thing is about the stage, most are at the early phase. This's why the expectation is associated with hope rather than hopeless.

4) Number of infertility treatments

Failure of infertility treatment and prolonged treatment were associated with emotional distress [123]. Infertility among women was associated with increased stress. The researchers expected that the number of infertility treatment would positively correlate with anxiety and depression among infertile couples; however, the result was not statistically significant. This suggested that despite the fact that the frequency of infertility

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treatment was related to stress, it did not necessary imply that the infertile couples would experience anxiety or depression. There might have been other intervening factors such as personality or coping strategy to deal with the stress.

5) Substance use

Excessive drinking, smoking and drug abuse can affect fertility [124]. Pregnant women with a history of infertility who binge drink increase their risk of mental illness more than those who do not [125]. The researchers hypothesized substance use positively correlated with anxiety and depression among infertile couples. The results showed a positive correlation between alcohol use and other substance use and depression among wives. This could be because substance use can lead to mental problems as endorsed by other research [125].

6) Having infertile relatives

The researchers hypothesized that having infertile couples positively correlated with anxiety and depression among infertile couples. The results were not statistically significant, possibly because participants in our research were unsure whether their relatives were infertile, and infertile couples had fewer infertile relatives.

7) Personality traits

The researchers hypothesized personality traits were factors associated with anxiety and depression among infertile couples. As a result, sensation seeking personality trait was a significant predictor of substance use [126]. Neuroticism has been inversely associated with mental health among Canadians during COVID-19 [127]. Our research showed females (15.87 ± 4.890) had higher level of neuroticism personality traits than males (14.61 ± 4.356), p <.05. A correlation was found between aggression, the level of anxiety and alcohol use [128]. Aggression, extraversion and neuroticism appeared to be associated with anxiety and depression among infertile couples.

Aggression personality involves irritability and exhibits uncontrollable impulses and driving forces. They are often outwardly aggressive, reckless and blind in character. Impulsivity can be motivated consciously or unconsciously. Actions are capricious and can be planned or unplanned. Intense feelings involve tension before

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action and feelings of pleasure, satisfaction or relief afterwards, with no real remorse, self-remorse, or guilt. Psychological development is unsound and immature, often leading to psychological imbalance [129]. Extraversion personality refers to a personality type in which a person's mental energy, interests, and attention are generally directed outward toward others or external stimuli, and whose behavior is characterized by being guided primarily by external considerations rather than their own thoughts and feelings [130]. That is, high neuroticism traits correspond to lower emotional stability, and low neuroticism traits correspond to higher emotional stability. Compared with low neurotics, high neuroticism is more likely to recall negative events in the past, to absorb negative information in the present, and to anticipate the future in a negative direction [131].

8) Marital satisfaction

The researchers hypothesized marital satisfaction negatively correlated with anxiety and depression among infertile couples. The results showed marital satisfaction negatively correlated with depression among infertile couples. Consistent with the study of Maroufizadeh and colleagues, both men and females' marital satisfaction exerted an actor effect on their own depression. Men's marital satisfaction exerted a significant partner effect on their wives' depression symptoms. They also found that the wives' marital satisfaction was unrelated to their husbands' depressive symptoms [132].

9) Concept of sufficiency economy

The researchers hypothesized that sufficiency economy was associated with decreased anxiety and depression among infertile couples. In our research, the correlation between sufficiency economy and anxiety/depression was statistically significant among men but not among women. Sufficiency economy promotes individual's moderation, prudence, and virtues. Low levels of this notion may lead to mental health risks. Despite the fact that the sufficiency economy concept has never been examined before, another related research implied support for this concept. One study demonstrated an inverse association between a more salient approach by Buddhists who frequently practice their faith and depressive symptoms [133]. Moderation, one of the characteristics of sufficiency economy, is related to the Noble Eightfold Path in Buddhism, constituting right view, right resolve, right speech, right action, right livelihood, right effort, right mindfulness,

and right concentration. These elements of the Eightfold Path can be taken as guiding principles in holistic care, including mitigating mental health problems [134]

10) The actor – partner effect between infertile couples

Among infertile couples, women's anxiety and depression positively correlated with men's anxiety and depression, and with their own depression and anxiety [119]. Family and spousal support comprised protective factors for anxiety and depression among infertile women [114]. The researchers hypothesized that participants' independent variables correlated with anxiety and depression among their spouses. According to the APIM results, aggression and neuroticism affected an individual's anxiety among infertile couples. Infertile couples' expectations of having children were associated with their partner's depression. Neuroticism, marital satisfaction and anxiety among infertile couples correlated with their depression individually.

4.1.2. Clinical implication and future research

The current study will advocate the application of psychological evaluation in infertility treatment centers from the first visit by infertile couples and suggest clinicians to make infertility treatment plans based on mental health evaluation. In addition, early intervention of anxiety and depression among infertile couples can be conducted using psychological evaluation to reduce the influence of mental health problems especially anxiety and depression on the outcome of infertility treatment.

Researchers recommend that health departments include infertility treatment in universal health insurance. It can reduce the financial burden of infertile couples. Reproductive departments should be set up in to provide infertility diagnosis and treatment services. To organize and carry out reproductive health education and related medicine and treatment technology training and promote the advantages of infertility treatment programs. To strengthen the construction of professional personnel, encourage excellent doctors to practice in multiple places, and bring treatment technology and services to more infertile couples in need.

Further research on longitudinal study is encouraged to strengthen the causal relationship between the interested predictors and outcomes. Positive aspects such as the

sufficiency economy concept and marital relationships should be further investigated. Intervention studies of promoting and providing such concepts in these populations are warranted.

4.1.3 Strengths and limitations

This study provided evidence about factors associated with anxiety and depression among infertile couples. Our study constitutes the first to explore the prevalence of anxiety and depression among infertile couples in Thailand, the relationship between the sufficiency economy and mental health as well as to use the ENRICH Marital Satisfaction scale in infertile couples in Thailand. The present study also included personality traits to predict anxiety and depression.

The limitation encountered the present study was that couples not seeking infertility treatment were excluded from this study. Researchers only invited infertile couples to participate in our study at the IVF Centers in Chiang Mai. The findings may not be representative of Thais. Generalizing the results to people with different geographic, environmental, and cultural dimensions should be performed cautiously. The present study lacked data on infertile couples not seeking treatment. In addition, the questionnaire was a self-rating instrument. Social desirability bias could not be avoided. In addition, participants might have a recall bias or a different understanding of the questions. Researchers did not specify what stage of treatment infertile couples seeking were in and what medicines were used for infertility treatment. The current study was conducted during the COVID-19 pandemic and did not compare differences in prevalence before and after the pandemic. The present study didn't provide evidence on whether the pandemic had an impact on anxiety and depression among infertile couples. The measurements on marital relationships did not include information on extramarital affairs. Measurements on polygamy and religion were also missing from our study. Last, the cross-sectional nature of the research limited causal relationships of the outcome. The causality between associated factors and anxiety/depression should be clarified in longitudinal study. The prevalence of anxiety and depression among infertile couples in Thailand can be compared with the prevalence of anxiety and depression in infertile couples in other countries such as China in future studies.

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4.2 Conclusions

The prevalence of depression was relatively low among infertile couples in Chiang Mai. Regarding sociodemographics, only occupation was related to depression among infertile couples. The expectation of having children and marital satisfaction were associated with depression among infertile couples. Personality traits of neuroticism, aggression and extraversion appeared to be associated with anxiety and depression among infertile couples. Almost all predictors demonstrated an actor effect on the outcome. Only the expectation of having children showed a partner effect on individual's depression.

Integrating mental health evaluations and interventions in infertility treatment would be a support measure that health systems should consider, increasing birth rates and slowing the development of aging societies. Infertile couples seek treatment simultaneously, but also should actively adjust their mental health to cooperate with the treatment. Improving the mental health of infertile couples requires the understanding of individuals, families and society so that infertility is no longer stigmatized. Infertility treatment requires the participation of the couples, so timely detection of the spouse's mental health problems and providing family support can make the treatment more efficient.

Sufficiency economy, which was first examined among infertile couples, could be further investigated especially regarding how they can be applied in the intervention to reduce or prevent depression. Longitudinal studies are also encouraged to ensure the tendency of causal inference.

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APPENDIX

1. EC approval certificate

ใบรับรองจริยธรรมการวิจัยในมนุษย์

ชื่อคณะกรรมการจริยธรรมการวิจัย :	คณะกรรมการจริยธรรมการวิจัย ชุดที่ 5 คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

ที่อยู่ : 110 ถนนอินทวโรรส ตำบลศรีภูมิ อำเภอเมือง จังหวัดเชียงใหม่ 50200

ชื่อหัวหน้าโครงการวิจัย : ศ.พญ. ณหทัย วงศ์ปการันย์

สังกัด : ภาควิชาจิตเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

ชื่อโครงการวิจัย : ปัจจัยที่สัมพันธ์กับภาวะวิตกกังวลและภาวะซึมเศร้าในคู่สมรสที่มีภาวะมีบุตรยาก: การศึกษาในประเทศไทย

Study Code (ถ้ามี) : PSY-2565-09017 **Research ID:** 9017

ผู้ให้ทุนวิจัย : -

เอกสารที่รับรอง	ฉบับที่รับรอง
โครงการวิจัย	ฉบับที่ 2.0 วันที่ 2 มิถุนายน 2565
ส่วนแก้ไขเพิ่มเติม	-
เอกสารให้ข้อมูลและหนังสือแสดงความยินยอม	
-เอกสารให้ข้อมูลและหนังสือแสดงความยินยอม (ฉบับภาษาไทย)	ฉบับที่ 2.0 วันที่ 2 มิถุนายน 2565
-เอกสารให้ข้อมูลและหนังสือแสดงความยินยอม (ฉบับภาษาอังกฤษ)	ฉบับที่ 1.0 วันที่ 14 พฤษภาคม 2565
เอกสารเชื้อเชิญ	
-โปสเตอร์ (ฉบับภาษาไทย)	ฉบับที่ 2.0 วันที่ 2 มิถุนายน 2565
-โปสเตอร์ (ฉบับภาษาอังกฤษ)	ฉบับที่ 2.0 วันที่ 2 มิถุนายน 2565
แบบบันทึกข้อมูล	
-แบบบันทึกข้อมูล	ฉบับที่ 1.0 วันที่ 14 พฤษภาคม 2565
-แบบสอบถาม	ฉบับที่ 1.0 วันที่ 14 พฤษภาคม 2565
-แบบบันทึกข้อมูล (ฉบับภาษาไทย)	ฉบับที่ 2.0 วันที่ 2 มิถุนายน 2565
-แบบบันทึกข้อมูล (ฉบับภาษาอังกฤษ)	ฉบับที่ 2.0 วันที่ 2 มิถุนายน 2565
บัตรประจำตัวและเอกสารอื่นที่ใช้กับผู้เข้าร่วมการวิจัย	-
เอกสารประกอบการพิจารณา เอกสารคู่มือผู้วิจัย - อัตตประวัติหัวหน้าโครงการวิจัย	

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- ศ.พญ. ณหทัย วงศ์ปการันย์   ฉบับ วันที่ 9 พฤษภาคม 2565
อัตตประวัติผู้วิจัยร่วม
-ศ.นพ.ทินกร วงศ์ปการันย์   ฉบับ วันที่ 9 พฤษภาคม 2565
-ผศ.พญ.อุบล แสงอนันต์   ฉบับ วันที่ 4 พฤษภาคม 2565
-ผศ.ดร.จารึก สิงหปรีชา   ฉบับ วันที่ 6 พฤษภาคม 2565
-ผศ.เรวดี เจนร่วมจิต   ฉบับ วันที่ 5 พฤษภาคม 2565
-Prof.Carmelle Peisah, M.D.   ฉบับ วันที่ 5 พฤษภาคม 2565
-Ms.Tong Yang   ฉบับ วันที่ 4 พฤษภาคม 2565
เอกสารประกันการชดเชย -

การวิจัยได้รับความเห็นชอบโดยวิธีเร่งด่วน (Expedited review)

ความเห็นชอบ มีผลตั้งแต่ วันที่ ..20. เดือน มิถุนายน พ.ศ. 2565 ถึงวันที่ ...19..เดือน มิถุนายน พ.ศ. 2566

คณะกรรมการจริยธรรมการวิจัย คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ จัดตั้งและ
ดำเนินการตามแนวทางการปฏิบัติการวิจัยทางคลินิกที่ดี (ICH GCP) และแนวทาง
จริยธรรมสากล กฎหมายและข้อบังคับที่เกี่ยวข้อง

ลงชื่อ : ....,
(ศาสตราจารย์เกียรติคุณ นายแพทย์ปัญจะ กุลพงษ์)
ประธานคณะกรรมการจริยธรรมการวิจัย

การปฏิบัติหลังจากรับรอง
- ผู้วิจัยควรขอความเห็นชอบต่ออายุใบรับรองภายใน 1 เดือน ก่อนใบรับรองหมดอายุหากจะ
ดำเนินการวิจัยต่อ
- หากจะแก้ไขเปลี่ยนแปลงใด ๆ ในโครงการวิจัย เอกสารข้อมูลและขอความยินยอม ต้องขอความ
เห็นชอบจากคณะกรรมการจริยธรรมการวิจัยก่อน เว้นแต่ (ก) เป็นเรื่องจำเป็นเพื่อสวัสดิภาพของ
ผู้เข้าร่วมการวิจัย (ข) เป็นเรื่องเล็กน้อยเกี่ยวกับทางโลจิสติกส์หรือการบริหารโครงการวิจัย เช่น
เปลี่ยนหมายเลขโทรศัพท์ เปลี่ยนกำกับดูแลการวิจัย
- หากมีข้อมูลใหม่หรือเหตุการณ์ใด ๆ ที่อาจมีผลต่อความปลอดภัยของผู้เข้าร่วมการวิจัยหรือการ
ดำเนินการของการศึกษาวิจัย ให้รายงานต่อคณะกรรมการจริยธรรมการวิจัยโดยรีบด่วน
- การเบี่ยงเบนไปจากโครงการวิจัย ต้องแจ้งคณะกรรมการจริยธรรมการวิจัยทุกครั้ง
- หากพบเหตุการณ์ไม่พึงประสงค์ที่ร้ายแรงต้องรายงานให้คณะกรรมการจริยธรรมการวิจัยโดยเร็ว
ตามประกาศคณะ

No.208/2022

Certificate of Ethical Approval

Name of Ethics Committee:	Research Ethics Committee Panel **5**
	Faculty of Medicine, Chiang Mai University
Address of Ethics Committee: 110 Intavaroros Rd., Amphoe Mueang, Chiang Mai, Thailand 50200	

Principal Investigator: Prof.Nahathai Wongpakaran, M.D.

Department of Psychiatry, Faculty of Medicine, Chiang Mai University.

Protocol title: Factors Associated with Anxiety and Depression in Infertile Couples: A study in Thailand

STUDY CODE: PSY-2565-09017   Research ID: 9017

Sponsor: -

Documents approved	Document reference
Research protocol	Version 2.0 date 2 June 2022
Protocol amendment	-
Participant information sheet/ Informed consent form	
- Participant information sheet/ Informed consent form (Thai Version)	Version 2.0 date 2 June 2022
- Participant information sheet/ Informed consent form (English Version)	Version 1.0 date 14 May 2022
Recruitment material -Poster (Thai Version) -Poster (English Version)	Version 2.0 date 2 June 2022 Version 2.0 date 2 June 2022
Case report form	
- Case report form	Version 1.0 date 14 May 2022
- Questionnaire	Version 1.0 date 14 May 2022
- Case report form (Thai Version)	Version 2.0 date 2 June 2022
- Case report form (English Version)	Version 2.0 date 2 June 2022
Patient's card and other documents given to research participants	-
Supplementary documents reviewed	

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No.208/2022

Investigator's brochure -	
Principal Investigator Curriculum vitae	
- Prof.Nahathai Wongpakaran, M.D.	Version date 9 May 2022
Co-Investigator Curriculum vitae	
- Prof. Tinakon Wongpakaran, M.D.	Version date 9 May 2022
- Assist.Prof.Ubol Saeng-Anan, M.D.	Version date 4 May 2022
- Assist.Prof.Charuk Singhapreecha, Ph.D.	Version date 6 May 2022
- Assist.Prof.Rewadee Jenraumjit	Version date 5 May 2022
- Prof.Carmelle Peisah, M.D.	Version date 5 May 2022
- Ms.Tong Yang	Version date 4 May 2022
Certificate of Insurance -	

The research has been approved by expedited review

Date of Approval: ......10.... June 2022   Expiration Date: ......19.......... June 2023

The Research Ethics Committee, Faculty of Medicine, Chiang Mai University is organized and operates according to Guideline for Good Clinical Practice (ICH GCP) and relevant international ethical guidelines, the applicable laws and regulations.

Signature : ....P. Kulapongs........

(Emeritus Professor Panja Kulapongs, M.D.)
Chairman of REC, Faculty of Medicine, CMU

POSTAPPROVAL REQUIREMENT:

- Investigator should make a request to renew approval within one month prior to the expiration date if the research is to be continued.
- In case there are any changes in the research protocol or informed consent form, the investigator must obtain REC approval prior to implementation unless (a) these changes are necessary for the safely of subjects, (b) minor changes such as logistical or administrative aspects of the trial (e.g., change of monitor(s), telephone number(s)).
- Any event or new information that adversely affects the safety of the subject or conduct of the trial must be reported to the REC promptly.
- Any protocol deviation/violation/noncompliance must be reported to the REC.
- Any serious adverse event must be reported to the REC promptly as stated in the Faculty of Medicine Notice.

2. CITI training

This is to certify that:

Tong Yang

Has completed the following CITI Program course:

Biomedical Research - Basic/Refresher
(Curriculum Group)
Biomedical Research
(Course Learner Group)
1 - Basic Course
(Stage)

Under requirements set by:

Chiang Mai University - Central Research Center

Completion Date 24-Aug-2021
Expiration Date 23-Aug-2024
Record ID 44408846

Not valid for renewal of certification through CME.

Verify at www.citiprogram.org/verify/?w3abf0e20-1f2a-40a0-a5e4-4118eb685315-44408846

CURRICULUM VITAE

Author's name	Ms.Tong Yang
Place of Birth	Kunming, Yunnan, China
Education	2015 – 2020 Bachelor's Degree in Clinical Medicine, Kunming Medical University, China
	2021 – Present Master of Science in Mental Health, Graduate School, Chiang Mai University, Thailand
Scholarship	2021 - 2023 Teaching Assistant/Research Assistant Scholarship, Chiang Mai University
Publications	1) **Yang T,** Wongpakaran N, Wongpakaran T, Saeng-Anan U, Singhapreecha C, Jenraumjit R, Peisah C. Factors associated with anxiety and depression in infertile couples-study protocol. Healthcare (Basel). 2022 Jul 21;10(7):1352. doi: 10.3390/healthcare10071352.
	2) Taranop V, Ruangrajitpakorn Y, Praputpittaya P, Lippanon K, Tharnpipat R, Wongpakaran N, Wongpakaran T, Srisaikaew P, Mahakkanukrauh P, Varnado P, **Yang T**, Peisah C. Development of the story telling examination for early mild cognitive impairment (pre-mild cognitive impairment) screening. Dement Geriatr Cogn Disord. 2022 Nov 18:1-9. doi: 10.1159/000527086.
	3) Wongpakaran T, **Yang T**, Varnado P, Siriai Y, Mirnics Z, Kövi Z, Wongpakaran N. The development and validation of a new resilience inventory based on inner strength. Sci Rep. 2023 Feb 13;13(1):2506. doi: 10.1038/s41598-023-29848-7.

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