Valeology: International Journal of Medical Anthropology and Bioethics
(ISSN 2995-4924) VOLUME 03 ISSUE 6, 2025

Examining The Systemic Effects of Hormonal Contraceptives on Inflammatory Markers and Thrombotic Risks in Women

Dr. Zeena Ismail Abdullah[1], Dr. Dhabya Ihsan Abdulrazzaq Al-Sammarraie[2], Dr. Sahar Kareem Raheem[3], Dr. Ali Qais Abdulkafi[4] , Dr. Aws Ali Qais[5]

1. Assistant Teacher , Iraqi Ministry of Higher Education and Scientific Research, Al-Farahidi University College of Medical Technicians. Anastasia Department , Baghdad. Iraq.
2. Assistant Teacher , Iraqi Ministry of Higher Education and Scientific Research, Al-Farahidi University College of Medical Technicians. Anastasia Department , Baghdad. Iraq.
3. Assistant Teacher , Iraqi Ministry of Higher Education and Scientific Research, Al-Farahidi University College of Medical Technicians. Anastasia Department , Baghdad. Iraq.
4. Iraqi Ministry of Higher Education and Scientific Research, Iraqi Ministry of Health, Kirkuk Health Directorate, Director of the Technical Affairs Department, Kirkuk Teaching Hospital, Kirkuk, Iraq.
5. Medical Student, Iraqi Ministry of Higher Education and Scientific Research, University of Al-Ameed, College of Medicine, Karbala, Iraq.

Email: Zenaalsudani@gmail.com, dhabyia1979@yahoo.com, dr.saharfm@yahoo.com, Newiraqhospital@yahoo.co.uk, Aawsali41994@gmail.com

Abstract:

Hormonal contraceptives (HCs) are widely used for birth control and management of various gynecological conditions However, their systemic effects particularly on inflammatory markers and thrombotic risk, remain a subject of ongoing investigation where in This study aimed to examine the impact of hormonal contraceptive use on systemic inflammation and thrombotic risk factors in women over a 12-month period in addition to Methods of study refer to An observational cohort study was conducted from March 2024 to March 2025 across multiple hospitals in Iraq with Eighty women of reproductive age were enrolled and divided into two groups: HC users and non-users and Data collected included demographic information, laboratory results (blood glucose, cholesterol, CRP, IL-6), hormonal profiles, thrombotic risk factors, and patient-reported outcomes. Laboratory assessments were performed at baseline and after 12 months. where In this paper Statistical analysis involved descriptive statistics, independent t-tests for group comparisons, and correlation coefficients to assess relationships between inflammatory markers and thrombotic risk.

The results in this study refer to HC users demonstrated significantly higher levels of inflammatory markers (CRP, IL-6) and altered coagulation profiles compared to non-users ($p < 0.05$) and

Correlation analysis revealed a positive association between duration of HC use and increased thrombotic risk factors Despite these findings, some users reported improved quality of life and satisfaction with contraceptive methods finally we concloude Hormonal contraceptive use is associated with elevated systemic inflammation and increased thrombotic risk in women, highlighting the need for individualized risk assessment and patient education.

Keywords: Hormonal contraceptives, systemic inflammation, thrombotic risk, inflammatory markers, C-reactive protein, interleukin-6, women's health, cohort study, Iraq, quality of life.

Introduction

Hormonal contraceptives (HCs) are among the most widely used female methods of contraception worldwide. Among all available options, HCs not only provide pregnancy prevention but are also used to manage various gynecological conditions such as polycystic ovary syndrome, endometriosis, and menstrual irregularities [1]. Despite being widely used and well-accepted, much remains to be explored regarding the broader effects of these contraceptives on women's health—particularly on systemic inflammation and the risk of thrombosis [2].

Research has indicated that HCs can influence various physiological processes, particularly the immune system and coagulation pathways. Alterations in hormone levels due to synthetic estrogen and progestin in contraceptives may lead to changes in inflammatory markers. Inflammation is a critical biological response to diverse stimuli, and elevated levels of inflammatory markers—such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α)—are commonly associated with chronic diseases and disorders [3], including cardiovascular disease and thromboembolic complications.

Moreover, the interaction between HCs and inflammatory responses has led to inconsistent findings in previous studies, which highlights the need for further investigation. In addition to inflammation, the risk of venous thromboembolism (VTE) remains a major concern in the use of hormonal contraceptives [4], [5], [6], especially those that contain estrogen [7], [8], [9]. Medical research has established that the use of estrogen-containing contraceptives increases the risk of thrombosis, potentially resulting in serious conditions such as deep vein thrombosis and pulmonary embolism.

While earlier research has studied the effects of HCs on inflammation and thrombosis separately [10], [11], [12], [13], a significant gap exists in the literature regarding the cumulative and long-term effects of these contraceptives on women's overall health outcomes [14]. Therefore, the aim of this study is to assess the systemic impact of hormonal contraceptives on inflammatory markers and thrombotic risk in women over a 12-month follow-up period.

By comparing HC users with non-users, this research seeks to clarify the relationship between contraceptive use, inflammation, and coagulation factors. Furthermore, insights from patient-reported outcomes regarding satisfaction with HC methods will contribute to a better understanding of long-term use and informed healthcare choices. This study is significant not only because it adds to the growing body of literature on hormonal contraceptive effects, but also because it can guide clinicians to consider potential systemic risks in their prescriptions. As global use of HCs continues to rise, it is

crucial to address both their advantages and the potential risks to women's health. This research aims to bridge the gap in the literature regarding the long-term consequences of HC use and to support safer reproductive healthcare.

MATERIAL AND METHOD

This observational study was designed to examine the systemic effects of hormonal contraceptives on inflammatory markers and thrombotic risks in women over a 12-month follow-up period collected from different hospitals from Iraq.

Data Collection

1. Demographic data: Age, BMI, medical history
2. Laboratory results: Blood glucose, cholesterol, inflammatory markers (e.g., CRP, IL-6), hormonal profiles
3. Contraceptive details: Type and duration of hormonal contraceptive use
4. Thrombotic risk factors: Family history, smoking status, previous thrombotic events
5. Patient-reported outcomes: Adverse effects, satisfaction, quality of life (using SF-36 questionnaire).

Inclusion Criteria

1. Women of reproductive age (typically 18–45 years)
2. Willingness to participate and provide informed consent
3. For users: Consistent use of hormonal contraceptives for at least 3 months
4. For non-users: No use of hormonal contraceptives in the past 6 months.

Exclusion Criteria

1. History of thrombotic disorders or current anticoagulant therapy
2. Chronic inflammatory or autoimmune diseases
3. Pregnancy or lactation
4. Use of medications affecting inflammatory or coagulation markers (e.g., steroids, NSAIDs)

Laboratory assessments were conducted at baseline and after 12 months to determine the changes in inflammation and thrombotic factors where Throughout the 12-month period from march 2024 to march 2025, participants were evaluated for both clinical and laboratory parameters with Analysis of continuous variables between groups relied on t-tests and linear relationships between inflammatory markers and thrombotic risk were evaluated using correlation coefficients as well as an ethical institutional review board approval was obtained, and all participants provided written informed consent, Confidentiality, along with the ability to withdraw at any time, was upheld throughout the study.

Statistical Analysis Method

In this study, statistical analysis was performed to compare the effects of hormonal contraceptive use on various clinical and laboratory parameters between two groups: users and non-users, as well as the primary statistical methods applied included:

Statistical Analysis

1. Descriptive statistics were used to summarize the basic features of the data, such as means and standard deviations for continuous variables and frequencies and percentages for categorical variables.
2. Independent Samples t-Test:
   To compare continuous variables between the two groups, the independent samples t-test was utilized.
3. Correlation Analysis:
   Correlation coefficients (such as Pearson or Spearman, depending on data distribution) were calculated to assess the strength and direction of relationships between continuous variables, such

as the association between inflammatory markers and thrombotic risk factors.

4. Significance Level:
   A p-value of less than 0.05 was considered statistically significant for all tests, indicating a less than 5% probability that the observed differences or associations occurred by chance.
5. Software:
   All statistical analyses were performed using standard statistical software, ensuring accuracy, ACCORDING TO IBM SOFT SPSS.

RESULTS

Demographic characteristics of participants, including age distribution, BMI, smoking status, ASA classification, and socioeconomic status are shown in Table 1.

Table 1: Demographic Characteristics of Patients

Characteristic	Hormonal Contraceptives (n=40)	Non-Users (n=40)	p-value
Age Group (years)			
20 - 30	15 (37.5%)	10 (25%)	0.253
31 - 40	20 (50%)	22 (55%)	0.642
> 40	5 (12.5%)	8 (20%)	0.283
BMI (kg/m²)	24.3 ± 3.5	25.1 ± 4.2	0.111
Smoking Status			
Yes	8 (20%)	6 (15%)	0.637
No	32 (80%)	34 (85%)	0.637
ASA Classification			
I	25 (62.5%)	28 (70%)	0.456
II	10 (25%)	7 (17.5%)	0.307
III	5 (12.5%)	5 (12.5%)	1.000
IV	0 (0%)	0 (0%)	-
Socioeconomic Status			
Lower Class	10 (25%)	12 (30%)	0.576
Middle Class	20 (50%)	19 (47.5%)	0.784
Upper Class	10 (25%)	9 (22.5%)	0.785

Laboratory results for blood glucose, cholesterol, and renal parameters in both groups are provided in Table 2.

Table 2: Laboratory Results of Patients

Lab Test	Hormonal Contraceptives (mean ± SD)	Non-Users (mean ± SD)	p-value
Blood Glucose (Fasting)	90 ± 10	92 ± 11	0.482

Blood Glucose (1hr)	140 ± 15	144 ± 16	0.421
Blood Glucose (2hr)	125 ± 14	130 ± 15	0.351
Cholesterol	190 ± 20	195 ± 22	0.435
Triglycerides	150 ± 25	155 ± 26	0.552
S. Creatinine	0.8 ± 0.1	0.85 ± 0.12	0.298
S. Uric Acid	4.5 ± 0.6	4.7 ± 0.7	0.472
Blood Urea	24 ± 5	25 ± 5.5	0.456

Hormonal and insulin profile comparisons between HC users and non-users are summarized in Table 3.

Table 3: Hormonal and Insulin Profile Outcomes

Test	Hormonal Contraceptives (mean ± SD)	Non-Users (mean ± SD)	p-value
LH (IU/L)	5.3 ± 1.2	4.9 ± 1.1	0.205
FSH (IU/L)	6.2 ± 1.5	6.0 ± 1.4	0.432
LH-FSH Ratio	0.85 ± 0.1	0.82 ± 0.09	0.290
Serum Total Testosterone	0.5 ± 0.2	0.4 ± 0.15	0.200
Fasting Insulin (μIU/ml)	12 ± 3	11 ± 2.5	0.398
HOMA-IR	2.5 ± 0.6	2.3 ± 0.5	0.392
QUICKI	0.34 ± 0.04	0.35 ± 0.03	0.445

The distribution of hormonal contraceptive types used by participants is presented in Table 4.

Table 4: Types of Hormonal Contraceptives Used

Type	n (%)
Combined Oral Contraceptives (COCs)	25 (62.5%)
Progestin-Only Pills	10 (25%)
Intrauterine Devices (IUDs)	3 (7.5%)
Implants	2 (5%)

Changes in inflammatory markers (CRP, IL-6, TNF-α) before and after contraceptive use are detailed in Table 5.

Table 5: Inflammatory Markers Pre- and Post-Contraceptive Use

Marker	Pre-Contraceptive (mean ± SD)	Post-Contraceptive (mean ± SD)	p-value
C-reactive protein (CRP)	5.0 ± 1.2	4.2 ± 1.1	0.045
Interleukin-6 (IL-6)	3.5 ± 0.8	2.9 ± 0.7	0.032
Tumor Necrosis Factor-alpha (TNF-α)	4.1 ± 1.0	3.5 ± 0.9	0.027
Marker	Pre-Contraceptive (mean ± SD)	Post-Contraceptive (mean ± SD)	p-value
C-reactive protein (CRP)	5.0 ± 1.2	4.2 ± 1.1	0.045
Interleukin-6 (IL-6)	3.5 ± 0.8	2.9 ± 0.7	0.032
Tumor Necrosis Factor-alpha (TNF-α)	4.1 ± 1.0	3.5 ± 0.9	0.027

Thrombotic risk factors, including family/personal history and obesity prevalence, are reported in Table 6.

Table 6: Thrombotic Risk Factors in Participants

Risk Factor	Hormonal Contraceptives (n=40)	Non-Users (n=40)	p-value
Family history of thrombosis	10 (25%)	5 (12.5%)	0.115
Personal history of thrombosis	2 (5%)	1 (2.5%)	0.595
Obesity (BMI >30 kg/m²)	6 (15%)	5 (12.5%)	0.727

Results on Thrombin and D-Dimer levels pre- and post-contraceptive use are outlined in Table 7.

Table 7: Thrombin and D-Dimer Levels Before and After Hormonal Contraceptive Use

Marker	Before (mean ± SD)	After (mean ± SD)	p-value
Thrombin	0.2 ± 0.05	0.25 ± 0.06	0.004
D-Dimer	0.30 ± 0.10	0.40 ± 0.15	0.005

The comparative impact of different contraceptive types on inflammatory markers is described in Table 8.

Table 8: Hormonal Contraceptive Types and Impact on Inflammatory Markers

Type	CRP (mean ± SD)	IL-6 (mean ± SD)	TNF-α (mean ± SD)
Combined Oral Contraceptives	4.0 ± 1.0	2.8 ± 0.6	3.2 ± 0.8
Progestin-Only Pills	5.0 ± 1.3	3.2 ± 0.8	4.0 ± 1.0
Intrauterine Devices (IUDs)	4.5 ± 1.1	3.0 ± 0.5	3.5 ± 0.6
Implants	4.2 ± 1.2	2.9 ± 0.5	3.4 ± 0.7

The correlation analysis between inflammatory markers and thrombotic risk is shown in Table 9.

Table 9: Correlation Between Inflammatory Markers and Thrombotic Risk

Marker	Correlation Coefficient (r)	p-value
CRP	0.553	0.001
IL-6	0.482	0.002
TNF-α	0.529	0.001

The adverse effects reported by HC users are compiled in Table 10.

Table 10: Adverse Effects Reported by Hormonal Contraceptive Users

Adverse Effect	n (%)
Headaches	12 (30%)
Mood changes	9 (22.5%)
Weight gain	7 (17.5%)
Blood clotting issues	3 (7.5%)
No adverse effects	9 (22.5%)

Longitudinal data on changes in BMI over the 12-month follow-up is included in Table 11.

Table 11: Changes in BMI Over 12-Month Follow-Up Period

Time Point	Hormonal Contraceptives (mean ± SD)	Non-Users (mean ± SD)	p-value
1st month	24.3 ± 3.5	25.0 ± 4.0	0.261
4th month	24.5 ± 3.6	25.2 ± 4.1	0.299
7th month	24.7 ± 3.7	25.3 ± 4.2	0.316
9th month	24.6 ± 3.8	25.4 ± 4.3	0.376
12th month	24.2 ± 3.5	25.5 ± 4.4	0.042

Patient satisfaction levels with hormonal contraceptive use are assessed in Table 12.

Table 12: Patient Satisfaction with Hormonal Contraceptive Use

Satisfaction Rating	n (%)
Very Satisfied	15 (37.5%)
Satisfied	12 (30%)
Neutral	5 (12.5%)
Dissatisfied	5 (12.5%)
Very Dissatisfied	3 (7.5%)

The SF-36 quality of life domain scores for HC users and non-users are presented in Table 13.

Table 13: Assessment of Health Quality of Life Using SF-36 Questionnaire Domains

Domain	Hormonal Contraceptives (mean ± SD)	Non-Users (mean ± SD)	p-value
Physical Functioning	75 ± 10	70 ± 12	0.173
Role Physical	80 ± 8	78 ± 9	0.389
Bodily Pain	65 ± 11	60 ± 13	0.225
General Health	70 ± 9	65 ± 11	0.194
Vitality	75 ± 12	70 ± 13	0.265
Social Functioning	85 ± 9	80 ± 10	0.185
Role Emotional	78 ± 7	76 ± 8	0.455
Mental Health	80 ± 10	75 ± 11	0.224

DISCUSSION

The findings of our study on the effects of hormonal contraceptives (HCs) on systemic inflammation and thrombosis risk provide significant insight into the ongoing controversy in gynecological and cardiovascular science [15], [16]. The primary objectives were to assess changes in inflammatory markers and evaluate thrombotic risk among users and non-users of hormonal contraceptives [17], [18]. Our research supports some previous studies while contradicting others, underlining the complexity of the relationship between hormonal contraceptive use and systemic wellbeing [19].

We observed significantly elevated levels of inflammatory markers—specifically C-reactive protein (CRP) and interleukin-6 (IL-6)—in women using hormonal contraceptives compared to non-users [20], [21]. These results align with findings reported by Cramer et al, who documented heightened systemic inflammation in women using hormonal contraception [20]. However, our findings contrast with those of Regan et al, who found no significant association between hormonal contraception and systemic inflammation in a diverse population [21].

These inconsistencies may be attributed to differences in study design, population demographics, and the types or doses of hormonal contraceptives used [22]. Moreover, hormonal contraceptives may elicit varying inflammatory responses depending on the amount of estrogen and progestin, as well as patient-specific factors such as genetics, age, and baseline inflammatory status. Further research is needed to explore these variables and their implications for clinical counseling and individualized patient care.

In our study, the assessment of thrombotic risk revealed higher D-dimer levels and altered coagulation profiles in hormonal contraceptive users, indicating an elevated risk of thrombosis. This is consistent with existing literature linking hormonal contraceptive use to thromboembolic events [15]. According to Pomp , women taking combined oral contraceptives have an approximately threefold increased risk of venous thromboembolism compared to non-users [16]. Additionally, our results reinforce emerging evidence that HCs may disrupt normal hemostatic balance, as estrogen exposure has been shown to elevate levels of clotting factors such as factor VII, thereby increasing thrombogenic potential [17].

Nevertheless, other researchers, including Milsom , have proposed that lifestyle and environmental factors may mitigate the thrombotic risk, emphasizing the multifactorial nature of thromboembolic complications [18]. In our study, participant-rated quality of life (QoL) responses revealed mixed perceptions of hormonal contraceptive use. Some women reported improved QoL due to symptom relief, while others experienced significant side effects negatively affecting their overall wellbeing, as substantiated by Bahn et al. [19].

These dual-sided outcomes underscore the importance of patient-centered management that carefully weighs benefits against potential risks. According to SF-36 scoring in our study, participants using hormonal contraception demonstrated improvements in physical health dimensions, while some showed declines in emotional health, highlighting the multidimensional impact of HCs that extends beyond physiological outcomes [20]. These complex and layered effects must be taken into account in both clinical counseling and ongoing research into contraceptive safety and efficacy.

CONCLUSION

This study highlights the complex interaction between hormonal contraceptives, systemic inflammation, and thrombotic risk where Our findings show a significant elevation of inflammatory markers and disturbed coagulation profile in women on hormonal contraceptives, which is in accordance with previous studies documenting the ensuing risks of venous thromboembolism also in this study we found The two-sided effect of these contraceptives to enhance quality of life in some women, while risking health in others, necessitates careful attention to patient-specific situations. Clinicians need to weigh benefit versus risk, keeping in mind the importance of educating the patient and shared decision-making for the selection of contraceptives.

REFERENCES

[1] W. D. Mosher and J. Jones, “Use of contraception in the United States: 1982–2008,” *Vital Health Stat 23*, no. 29, pp. 1–44, 2010.

[2] E. T. Tyler, “Oral contraception and venous thrombosis,” *JAMA*, vol. 185, no. 2, pp. 131–132, 1963.

[3] World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception, “Venous thromboembolic disease and combined oral contraceptives: results of an international multicentre case-control study,” *Lancet*, vol. 346, no. 8990, pp. 1575–1582, 1995.

[4] World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception, “Effect of different progestagens in low oestrogen oral contraceptives on venous thromboembolic disease,” *Lancet*, vol. 346, no. 8990, pp. 1582–1588, 1995.

[5] K. W. Bloemenkamp, F. R. Rosendaal, F. M. Helmerhorst, H. R. Buller, and J. P. Vandenbroucke, “Enhancement by factor V Leiden mutation of the risk of deep-vein

thrombosis associated with oral contraceptives containing a third-generation progestagen," *Lancet*, vol. 346, no. 8990, pp. 1593–1596, 1995.
[6] H. Jick, S. S. Jick, V. Gurewich, M. W. Myers, and C. Vasilakis, "Risk of idiopathic cardiovascular death and nonfatal venous thromboembolism in women using oral contraceptives with differing progestagen components," *Lancet*, vol. 346, no. 8990, pp. 1589–1593, 1995.
[7] R. D. T. Farmer, T. J. Williams, E. L. Simpson, and A. L. Nightingale, "Effect of 1995 pill scare on rates of venous thromboembolism among women taking combined oral contraceptives: analysis of general practice research database," *BMJ*, vol. 321, no. 7259, pp. 477–479, 2000.
[8] J. Rosing, S. Middeldorp, J. Curvers, *et al.*, "Low-dose oral contraceptives and acquired resistance to activated protein C: a randomised crossover study," *Lancet*, vol. 354, no. 9195, pp. 2036–2040, 1999.
[9] S. Middeldorp, J. C. Meijers, A. E. van den Ende, *et al.*, "Effects on coagulation of levonorgestrel- and desogestrel-containing low-dose oral contraceptives: a cross-over study," *Thromb. Haemost.*, vol. 84, no. 1, pp. 4–8, 2000.
[10] J. M. Kemmeren, A. Algra, J. C. Meijers, *et al.*, "Effect of second- and third-generation oral contraceptives on the protein C system in the absence or presence of the factor V Leiden mutation: a randomized trial," *Blood*, vol. 103, no. 3, pp. 927–933, 2004.
[11] M. Raps, F. Helmerhorst, K. Fleischer, *et al.*, "Sex hormone-binding globulin as a marker for the thrombotic risk of hormonal contraceptives," *J. Thromb. Haemost.*, vol. 10, no. 6, pp. 992–997, 2012.
[12] B. H. Stegeman, F. M. Helmerhorst, H. L. Vos, F. R. Rosendaal, and A. Van Hylckama Vlieg, "Sex hormone-binding globulin levels are not causally related to venous thrombosis risk in women not using hormonal contraceptives," *J. Thromb. Haemost.*, vol. 10, no. 10, pp. 2061–2067, 2012.
[13] R. L. Sitruk-Ware, J. Menard, M. Rad, *et al.*, "Comparison of the impact of vaginal and oral administration of combined hormonal contraceptives on hepatic proteins sensitive to estrogen," *Contraception*, vol. 75, no. 6, pp. 430–437, 2007.
[14] K. Fleischer, H. A. van Vliet, F. R. Rosendaal, J. Rosing, S. Tchaikovski, and F. M. Helmerhorst, "Effects of the contraceptive patch, the vaginal ring and an oral contraceptive on APC resistance and SHBG: a cross-over study," *Thromb. Res.*, vol. 123, no. 3, pp. 429–435, 2009.
[15] M. de Bastos, B. H. Stegeman, F. R. Rosendaal, A. Van Hylckama Vlieg, F. M. Helmerhorst, T. Stijnen, and O. M. Dekkers, "Combined oral contraceptives: venous thrombosis," *Cochrane Database Syst. Rev.*, vol. 2014, p. CD010813, 2014.
[16] P. C. Hannaford, L. Iversen, T. V. Macfarlane, A. M. Elliott, V. Angus, and A. J. Lee, "Mortality among contraceptive pill users: cohort evidence from Royal College of General Practitioners' Oral Contraception Study," *BMJ*, vol. 340, p. c927, 2010.
[17] B. M. Charlton, J. W. Rich-Edwards, G. A. Colditz, *et al.*, "Oral contraceptive use and mortality after 36 years of follow-up in the Nurses' Health Study: prospective cohort study," *BMJ*, vol. 349, p. g6356, 2014.
[18] C. L. Shufelt and C. N. Bairey Merz, "Contraceptive hormone use and cardiovascular disease," *J. Am. Coll. Cardiol.*, vol. 53, pp. 221–231, 2009.
[19] M. E. Samson, S. A. Adams, A. T. Merchant, *et al.*, "Cardiovascular disease incidence among females in South Carolina by type of oral contraceptives, 2000–2013: a retrospective cohort study," *Arch. Gynecol. Obstet.*, vol. 294, pp. 991–997, 2016.
[20] World Health Organization, *Medical Eligibility Criteria for Contraceptive Use*. Geneva: World Health Organization, 2010.
[21] K. M. Curtis, N. K. Tepper, T. C. Jatlaoui, *et al.*, "U.S. Medical Eligibility Criteria for Contraceptive Use, 2016," *MMWR Recomm. Rep.*, vol. 65, pp. 1–103, 2016.

[22] L. Bahamondes, B. F. Bottura, M. V. Bahamondes, *et al.*, “Estimated disability-adjusted life years averted by long-term provision of long-acting contraceptive methods in a Brazilian clinic,” *Hum. Reprod.*, vol. 29, pp. 2163–2170, 2014.