JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

COMPARATIVE STUDY OF EFFICACY OF TRANSDERMAL PATCH WITH ORAL BIRTH CONTROL PILL FOR CONTRACEPTION

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Abstract : The use of various birth control methods or devices is known as contraception, commonly referred to as anticonception or fertility control. Family planning is equally important for preventing unintended pregnancies through correct use and accessibility to various birth control methods as needed. Certain sections of society oppose birth control access because they believe it to be immoral, unreligious, or politically unwise. This is a review based study which includes comparison of efficacy of transdermal patch with oral birth control pill for contraception through various search engines like Google scholar and PubMed. Various research papers were studied in which different individuals including randomized users, adolescents and women older than 35 years of age were included. It will provide a better understanding about the contraception and comparison will give a clear view of the easiest route of administration along with minimal side effects of contraceptives.

Index Terms - Contraception, Pregnancy, Anticonception, Birth control, Efficacy

I. INTRODUCTION

1.1 Definition

Birth control, also known as contraception, anticonception, and fertility control, is the use of methods or devices to prevent unwanted pregnancy. Birth control has been used since ancient times, but effective and safe methods of birth control only became available in the 20th century. Planning, making available, and using birth control is called family planning. Some cultures limit or discourage access to birth control because they consider it to be morally, religiously, or politically undesirable. [16]

1.2 Methods of Contraception

Barrier techniques, hormonal birth control, intrauterine devices (IUDs), sterilization, and behavioral techniques are examples of birth control approaches.

Hormonal: There are several different types of hormonal contraception, including oral pills, skin implants, injections, patches, IUDs, and a vaginal ring. They are currently solely available for women but for men they have been and are being clinically investigated.[21] Oral birth control pills are of two types: progestogen-only tablets, also known as minipills and combined oral contraceptives, which include both an estrogen and a progestin.[2] If either is consumed while pregnant, it neither raises the chances of miscarriage nor results in birth defects or abnormalities. Both the varieties of birth control pill prevents fertilization primarily by inhibiting ovulation and cervical mucus thickening. Additionally, they might alter the uterus lining, which would decrease implantation. The user's adherence to take the tablets consistently determines the efficacy of tablets.[19]

Blood clots in the veins and the arteries are slightly more likely when using combined hormonal contraceptives. The average rise in venous clots per 10,000 women years is from 2.8 to 9.8, which is still less than the rate linked with pregnancy.[5] They are not advised for women over 35 years of age who continue to smoke.[25] Because of the elevated risk, they are included in decision-making methods for predicting the risk of blood clots such as the PERC rule and DASH score.[28]

The impact on sexual drive varies by either increasing or decreasing in some cases or having no effect in most.[24] The risk of breast cancer is unaffected by combined oral contraceptives, however they do lower the risk of ovarian and endometrial cancer.[6,17] They frequently reduce painful period cramps and bleeding. The vaginal ring's lower estrogen levels might reduce the likelihood of side effects like headaches, nausea, and breast tenderness which are linked to higher dose estrogen products.[17]

Women with a history of blood clots in their veins may continue to take progestin-only pills, injections, and intrauterine devices with no increased risk of blood clots. Non-hormonal birth control or a progestin-only technique other than the injectable kind should be used in people with a history of arterial blood clots.[5] Breastfeeding mothers can use progestin-only tablets to improve menstrual symptoms as it will not affect the milk production. With progestin-only methods, irregular bleeding could occur and some individuals might not get periods even.[6] The progestins desogestrel and drospirenone reduce the androgenic adverse effects but raise the risk of blood clots, making them second-line treatments. Injectable progestin has a 0.2% perfect use first-year failure rate and 6% normal use first failure rate.[29]

Sterilization : For women, tubal ligation and for men, vasectomy are available surgical methods of sterilization. The risk of ovarian cancer is reduced by tubal ligation. Vasectomy is twenty times less likely to result in short-term difficulties than tubal ligation.[1] Scrotal swelling and soreness are possible after a vasectomy, although these side effects often go away within a week or two.[18]

Behavioral : In order to prevent the entry of sperm into the female reproductive system, either completely or while an egg may be present, behavioral approaches controls the timing or manner of sexual activity.[15] The first-year failure rate may be around 3.4% when used flawlessly, but it may reach 85% when used incorrectly.[20]

Emergency : Emergency contraceptive methods are drugs or devices that are used after unprotected sexual intercourse with the intention of preventing pregnancy which are often incorrectly referred to as "morning-after pills". These are usually given to rape victims as they typically prevent ovulation or fertilization.[14]

Figure 1.1 Contraception Methods

1.3 World Contraception Day

World Contraception Day marked on September 26, aims to improve sexual and reproductive health education and awareness with the goal of creating a society in which every pregnancy is desired. The European Society of Contraception and Reproductive Health, the German Foundation for World Population, the International Federation of Pediatric and Adolescent Gynecology, the International Planned Parenthood Federation, the Marie Stopes International, Population Services International, and the Office of Population Affairs are amongst the international NGOs and governments which supports this.

1.4 Contraceptive Patch

A contraceptive patch, sometimes referred to as "the patch," is a transdermal patch which is placed on the skin that delivers synthetic estrogen and progestogen hormones to prevent conception. With perfect use, they have been demonstrated to be as effective as the combined oral contraceptive pill, and the patch may even be more effective.[13]

The usage of Xulane and Twirla is authorized in the US. Evra is approved in Canada for use and is marketed by Janssen Inc. It has also been approved for use in the UK and Europe and is marketed by Janssen-Cilag. The patches come in boxes of three and may only be purchased with a prescription.

Medical Uses: Many of the advantages of the patch are similar to those of birth control pills because of how similarly they function. For instance, the patch can lighten and regularize a woman's period. Additionally, it could lessen PMS symptoms, cramping, and acne. The patch is also linked to enhanced protection against ovarian cysts, pelvic inflammatory disease, endometrial cancer, and anemia from iron shortage. The patch is an easy-to-use birth control method that needs weekly maintenance. The moment a woman quits using the patch, her chance of getting pregnant swiftly returns.

EVRA/ ORTHO EVRA:

Safety: The risk of venous thromboembolism (VTE) is marginally elevated with the patch compared to women not using hormonal contraceptives, as with any estrogen- containing contraceptive. There was a concern that the patch's overall higher exposure to estrogen (60% larger AUC) compared to COCs would result in a higher risk of thromboembolism events than in women taking pills.[16]

Method: On the beginning day of the menstrual cycle (day 1) or the first Sunday after that day, whichever is desired, the patch is first placed on the upper outer arm, buttocks, abdomen, or thigh. From that point on, patch change day will be referred to as the application day. On patch change day seven days later, the user applies a new patch to one of the suitable location on the body. On the next patch change day, same procedure is repeated. The patch is not replaced; it is instead removed on the next patch change day. The user waits seven days without applying a patch before doing so on the next patch change day. Extended use regimens, which involve using patches for a number of weeks before a week without them, have been researched.[22]

Applying the patch requires clean, dry, and unbroken skin. This indicates that the patch shouldn't be applied to skin that is red, irritated, or cut. Additionally, stay away from applying lotions, powder, or makeup in the vicinity of the patch or where it will be applied.

Backup contraception: The patch can take action in time to prevent ovulation if the person decides to start changing it on day one of their menstrual cycle. After an abortion or miscarriage in the first trimester, the contraceptive patch can be applied right away if the user wants to start using it. There is no need for backup contraception since this can be viewed as equivalent to the day one start described above. For the first week of patch wear, a backup method of contraception, such as spermicide or condoms, must be used if a user decides to start with their patch change day as the first Sunday after day 1. The user should apply the patch right away and then use a backup type of barrier protection for a week if they are more than two days late in applying the patch during the first week or more than two days late in applying the patch during the second and third weeks.

Mechanism of Action: Ortho Evra/Evra, like all combined hormonal contraceptives, functions primarily by halting ovulation. Sperm penetration inhibition caused by changes in the cervical mucus is a secondary mode of action. Although there is no scientific proof that the use of hormonal contraceptives truly prevents implantation, they do have effects on the endometrium that theoretically may impair implantation.[30]

Pharmacology and pharmacodynamics: The 20 cm^2 adhesive Ortho Evra contraceptive patch releases 35 g EE and 150 g norelgestromin (NGMN) daily. NGMN is a progestin found in the OCs Ortho-Cyclen® and Ortho Tri-Cyclen® that is an active metabolite of norgestimate. Three patch sizes—10, 15 and 20 cm^2—were examined while this product was being developed in a trial involving 610 participants. The 20 cm^2 patch was proven to suppress ovulation and control cycles similarly to Ortho-Cyclen (6.2% 20 cm^2 patch, 7.2% Ortho-Cyclen); as a result, the 20 cm patch is the only size available.[9]

Efficacy: An initial open-label 73-center trial from 2001 found that transdermal delivery had an overall failure rate of 0.7% and a method failure rate of 0.4% after 13 cycles. The number of pregnancies per 100 woman-years, or the Pearl index (PI), was 0.71 for overall failure and 0.59 for technique failure. Similar results were found in a later investigation that combined information from three studies including 3,319 women. Overall failure rates were 0.8%, while method failure failure rates were 0.6%, resulting in PIs of 0.88 and 0.7, respectively.[26]

Tolerability: Side effects of patch are identical to COCs. Complaints and causes for stopping treatment are mild-to-moderate in severity which includes application site responses, nausea, emotional lability, headaches, and breast soreness.[23,27]

Patient satisfaction: The patch had the lowest continuation rate (49.1%) compared to other forms of contraception (55.1% for COCs to 87.5% for LNG-IUD), according to study of continuation and satisfaction among women aged 14 to 45 in the Contraceptive CHOICE Project. Only 35.1% of women who used the patch were extremely satisfied with the treatment, while 55.7% were not.[10]

1.5 Combined Oral Contraceptive Pill

Birth control that is taken orally by women is called the combined oral contraceptive pill (COCP), also known as the birth control pill or simply "the pill." Progestin, a synthetic version of the hormone progestogen/progesterone, and estrogen (often ethinyl estradiol and 17 estradiol) are two crucial hormones present in the tablet. When used properly, it changes the menstrual cycle to stop ovulation and avoid pregnancy. A highly well-liked method of birth control, COCPs received their first approval for contraceptive usage in the US in 1960.

Although there is a large selection and a variety of doses available, all of them contain a progestogen and an estrogen. Blocking ovulation is the main way to prevent pregnancy. Changes in the endometrium and cervical mucus are additional significant variables that inhibit conception.[11]

Estrogens and progestogens are among the modifiable risk factors for breast cancer (BC), and this has been demonstrated, for instance, in the post-menopausal population receiving hormone replacement therapy (HRT). For COCs, a comparable proposal has been made ever since their introduction. Estrogen and progesterone both have a proliferative effect on the breast, most likely as a result of stimulating stem cells. By way of a gene-damaging method, inherent estrogens (estradiol and estrone) are indicated mutagens over carcinogens, however the mediating pathway of progestin is more difficult.[3,4,12]

Overall risk of cancer : There haven't been any studies up to this point that demonstrate an increase in overall cancer risk or mortality from cancer in general among COC users. When assessing the overall proportion of hazards and benefits connected to a COC exposure, cohort studies are notably helpful. Three large cohort studies, including the Oxford Family Planning Association research, the Nurse's Health Study, and the Royal College of General Practitioners (RCGP) study, assessed the absolute risk of cancer mortality in COC users; none of these studies found significant differences between ever-users and never-users.[8,29]

Contraceptive use: Combined oral contraceptives are a class of oral medications that were initially intended to be taken each day at the same time in order to prevent conception. Although there are many different formulations and manufacturers, the typical pack is made to be taken throughout a cycle of 28 days. Users take a daily pill containing two hormones, estrogen and progestogen, for the first 21 days of the cycle. Users take daily placebo (biologically inactive) pills for the final seven days of the cycle, which are regarded as hormone-free days. Although there are no hormones present during these days, users are nonetheless safeguarded against pregnancy.

Users are advised not to take any pills during the final seven days of the cycle because some COCP packs only contain 21 pills. Other COCP formulations come in 91 tablet form (Seasonale), with 84 days of active hormones and 7 days of placebo. To decrease the intensity of placebo effects, COCP formulations, such as Yaz 28 and Loestrin 24 Fe, can comprise 24 days of active hormone pills followed by 4 days of placebo pills. Cyclic COCPs are these COCPs with active hormones and a placebo/hormone-free period. Users begin a new pack and cycle of cyclical COCP treatment once a pack is finished.

The majority of monophasic COCPs can be taken constantly, allowing patients to skip placebo days and take hormone-active pills continually from a COCP pack. To prevent or mitigate withdrawal bleeding is among the most popular motives for users to engage in this behavior. Most female users of cyclic COCPs experience regularly scheduled withdrawal bleeding, which is vaginal bleeding that closely resembles user's menstrual cycles with the exception of lighter menstrual flow than was the case previous to the start of COCP usage. As a result, a recent study found that over a 90-day standard reference period, 90% of the 1003 women receiving COCPs reported regularly scheduled withdrawal bleeding. It frequently happens during the days when the patient is not taking the hormone-free placebo. Therefore, avoiding placebo days can reduce additional placebo effects such as withdrawal bleeding.

Effectiveness: A woman taking COCPs has an estimated 0.3% chance of becoming pregnant if she follows all instructions, which means that 3 out of every 1000 of them will do so within a year. However, consumers frequently use COCPs inadvertently, forget to take their pills, or experience undesirable side effects. When COCPs are used as recommended, the estimated probability of becoming pregnant is at 9%, which means that 9 out of every 100 women will do so within a year. The usual use failure rate is based on a weighted average of estimates from the 1995 and 2002 U.S. National Surveys of Family Growth (NSFG), corrected for underreporting of abortions, whereas the perfect use failure rate is based on an analysis of pregnancy rates in clinical trials.

The fact that ordinary use effectiveness is lower than perfect use effectiveness is due to a number of reasons including:

- Errors made by individuals who are giving guidance on how to apply the method.
- Errors made by the user.
- Knowing disregard for instructions on the part of the user.

Non-contraceptive use : In addition to treating PCOS, endometriosis, adenomyosis, acne, hirsutism, amenorrhea, menstrual cramps, migraines, menorrhagia (excessive menstrual bleeding), menstruation-related or fibroid-related anemia, and dysmenorrhea (painful menstruation), the hormones in the pill have also been used to treat other medical conditions. Despite widespread use for the disorders described above—aside from acne—no oral contraceptives have received FDA approval for these.

PCOS: Polycystic ovarian syndrome (PCOS) has a complex etiology that is poorly understood. Luteinizing hormone (LH) and androgen levels are frequently greater in women with PCOS than normal, which affects the ovaries ability to function normally. The ovary produces a number of tiny follicles, but none of them can mature into the dominant follicle that causes ovulation. LH, follicle-stimulating hormone, estrogen, and progesterone become unbalanced as a result. Unopposed estrogen can cause endometrial hyperplasia, or an enlargement of uterine tissue, in the absence of ovulation. Compared to healthy endometrial tissue, this endometrial overgrowth is more likely to develop into cancer. Thus, despite conflicting findings, the majority of gynecological organizations concur that women with PCOS are more likely to develop endometrial cancer as a result of the unopposed estrogen.

Women with PCOS who do not want to become pregnant are frequently advised to use hormonal contraception to block the effects of unopposed estrogen in order to lower their chance of developing endometrial cancer. COCPs and progestin-only techniques are both advised. A woman with PCOS has a lower risk of developing endometrial cancer because of COCP's progestin component, which guards against endometrial hyperplasia. Since COCPs can assist cure these symptoms, they are recommended to progestin-only treatments in women who also have uncontrolled acne, hirsutism symptoms, and androgenic alopecia.

Acne and hirsutism: COCPs are occasionally given to treat androgenization-related symptoms like acne and hirsutism. The COCP's estrogen component seems to reduce the ovaries ability to produce androgen. Additionally, estrogen increases the production of sex hormone binding globulin, which lowers the levels of free testosterone.

In the end, the reduction in free androgens causes a reduction in sebum production, a key factor in the emergence of acne. If the patient has moderate acne, needs contraception, and is at least 14 or 15 years old, four different oral contraceptives have been approved by FDA to treat it. Ortho Tri-Cyclen, Estrostep, Beyaz, and YAZ are a few of these.

In contrast to how women generally grow, hirsutism is the development of coarse, black hair. Higher levels or the action of androgens also mediate this hair development on the face, chest, and belly. Decreased amounts of freely circulating androgens therefore aid in the treatment of these symptoms by COCPs.

Endometriosis: Along with NSAIDs, GnRH agonists, and aromatase inhibitors, COCPs are regarded as a first-line medical treatment for endometriosis-related pelvic pain. COCPs inhibit the proliferation of endometrial tissue outside the uterus. This reduces the inflammatory effects of it. COCPs and the other medical procedures mentioned above only alleviate the symptoms of extra-uterine tissue development. The only effective treatment is surgery. Continuous COCP use is more successful at reducing the recurrence of pain than cyclic use, according to studies looking at rates of pelvic pain recurrence after surgery.

Mechanism of Action: By reducing the water content and raising the viscosity of the cervical mucus, all progestogen-containing contraceptives also impede sperm passage past the cervix into the upper genital tract (uterus and fallopian tubes).

Although the estrogen and progesterone in COCPs have other effects on the reproductive system, it has not been established that these effects increase the effectiveness of the contraceptives:

• Delaying ova transit and tubal motility, which might prevent fertilization.
• Endometrial atrophy and changes to the metalloproteinase content, which might hypothetically prevent implantation or impair sperm viability and motility.
• Endometrial edema, which could make implantation difficult.

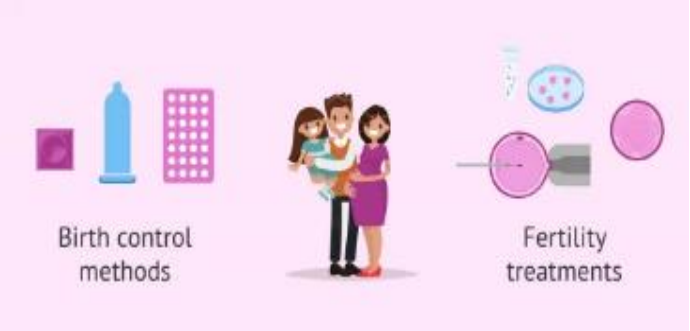

Figure 1.2 Family Planning

II. MATERIAL AND METHODS

This is a review based study which includes comparison of efficacy of transdermal patch with oral birth control pill for contraception through various search engines like Google scholar and PubMed. Various research papers were studied in which different individuals including randomized users, adolescents and women older than 35 years of age were included. This study promotes the use of contraception to eliminate the rising population and sexually transmitted diseases risk in and around the world. It will provide a better understanding about the contraception and comparison will give a clear view of the easiest route of administration along with minimal side effects of contraceptives.

III. RESULT

Various research papers were studied in which different individuals including randomized users, adolescents and women older than 35 years of age were included.

- For Randomized users: 1417 healthy adult women with reproductive potential were selected and it was found that the patch had lower Pearl Indexes than the oral pill. The mean percentage of cycles when participants had complete compliance was 88.2% with the patch and 77.7 with the oral pill.

- For Adolescents: 40 teens selected the patch and other 40 selected tablets. Users of the patch and pills claimed that their premenstrual depression had lessened and that their periods had become lighter and more predictable. Only the pill group, however, reported improvement in premenstrual rage. Both groups reported equal levels of method satisfaction, with the exception that patch users were more likely to say that their contraceptive method improved daily activities as usual.

- For Women older than 35 years of age: One hundred and sixteen women over the age of 35 were randomly assigned to receive either an oral contraceptive or a transdermal contraceptive patch. There were no statistically significant differences in cycle length between the two groups. With a statistically significant difference, the transdermal contraceptive group's mean duration was longer than the COC group's. Comparatively more patients in the COC group than the transdermal contraceptive group had spotting. Both groups did not experience amenorrhea or pregnancy.

IV. CONCLUSION

According to the study including various research papers , it concludes that in terms of contraceptive efficacy and cycle control, the contraceptive patch is comparable to a combined oral contraceptive. The weekly contraceptive patch has higher compliance than the oral contraceptive (OC). Despite the pills apparent advantages over the patch, it remains difficult for teens to utilize contraception effectively and consistently. The transdermal contraceptive patch has shown contraceptive effectiveness. It also offers Thai women over 35 years old good cycle control comparable to COC. However, when compared to oral contraceptives containing ethinyl estradiol (EE) 30 g and levonorgestrel 150 g, a higher prevalence of minor side effects, such as breast tenderness and nausea, were shown.

V. REFERENCES

1. Adams CE, Wald M , Risks and complications of vasectomy, The Urologic Clinics of North America, August 2009, 36 (3): 331–6

2. Ammer C, Oral contraceptive, The encyclopedia of women's health (6th ed.), New York, 2009, 312–15

3. Audet Marie-Claude, Moreau Michele, Koltun D William, Waldbaum S Arthur, Shangold Gary, Fisher C Alan, Creasy W George, Evaluation of Contraceptive Efficacy and cycle control of Transdermal contraceptive patch vs an Oral contraceptive, May 2001, 285-18

4. Black AY, Fleming NA, Rome ES, Pregnancy in adolescents: Adolescent Medicine, April 2012, 123–38

5. Brito MB, Nobre F, Vieira CS, Hormonal contraception and cardiovascular system, April 2011, **96** (4)

6. Burke AE, The state of hormonal contraception today: benefits and risks of hormonal contraceptives: progestin-only contraceptives, American Journal of Obstetrics and Gynecology, October 2011, **205** (4 Suppl): S14-7.

7. Burrows LJ, Basha M, Goldstein AT, The effects of hormonal contraceptives on female sexuality: a review, The Journal of Sexual Medicine, September 2012, **9** (9): 2213–23.

8. Canning D, Schultz TP, The economic consequences of reproductive health and family planning, July 2012,165–71

9. Carr B, Gates MF, Mitchell A, Shah R, Giving women the power to plan their families, July 2012, 80–2

10. Christin-Maitre S, History of oral contraceptive drugs and their use worldwide: Best Practice & Research, Clinical Endocrinology & Metabolism, February 2013, 3–12

11. Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, U.S. Medical Eligibility Criteria for Contraceptive Use, July 2016, 1– 103

12. DiCenso A, Guyatt G, Willan A, Griffith L, Interventions to reduce unintended pregnancies among adolescents: systematic review of randomised controlled trials, June 2002

13. Duffy K, Lynch DA, Santinelli J, Santelli J, Government support for abstinence-only-until-marriage education, Clinical Pharmacology and Therapeutics, December 2008, 746–8

14. Gizzo S, Fanelli T, Di Gangi S, Saccardi C, Patrelli TS, Zambon A, Nowadays which emergency contraception? Comparison between past and present: latest news in terms of clinical efficacy, side effects and contraindications, Gynecological Endocrinology, October 2012, **28** (10): 758–63.

15. Grimes DA, Gallo MF, Grigorieva V, Nanda K, Schulz KF , Fertility awareness-based methods for contraception, The Cochrane Database of Systematic Reviews, October 2004

16. Hanson SJ, Burke AE , Fertility control: contraception, sterilization, and abortion, The Johns Hopkins manual of gynecology and obstetrics (4th ed.), Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2010, 382–395

17. Havrilesky LJ, Moorman PG, Lowery WJ, Gierisch JM, Coeytaux RR, Urrutia RP, Oral contraceptive pills as primary prevention for ovarian cancer: a systematic review and meta-analysis, Obstetrics and Gynecology, July 2013, **122** (1): 139–47

18. Hillard PA, The 5-minute obstetrics and gynecology consult, Hagerstwon, MD: Lippincott Williams & Wilkins, 2008, 265

19. Hoffman BL, 5 Second-Tier Contraceptive Methods—Very Effective, Williams gynecology (2nd ed.), 2011

20. Lawrence R, Breast feeding : a guide for the medical professional (7th ed.). Philadelphia: Saunders, 2010, 673

21. Mackenzie J, The male pill? Bring it on, The Guardian, December 6, 2013

22. Nanda K, Burke A, Contraceptive patch and vaginal contraceptive ring, 2011

23. Sech LA, Mishell DR, Oral steroid contraception, November 2015, 743–748

24. Shulman LP, The state of hormonal contraception today: benefits and risks of hormonal contraceptives: combined estrogen and progestin contraceptives, American Journal of Obstetrics and Gynecology, October 2011, **205** (4 Suppl): S9-13

25. Stegeman BH, de Bastos M, Rosendaal FR, van Hylckama Vlieg A, Helmerhorst FM, Stijnen T, Dekkers OM, Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis, September 2013

26. Taliaferro LA, Sieving R, Brady SS, Bearinger LH, We have the evidence to enhance adolescent sexual and reproductive health--do we have the will, Adolescent Medicine, December 2011, 521–43

27. Teal S, Edelman A, Contraception Selection, Effectiveness, and Adverse Effects: A Review, December 2021, 326 (24)

28. Tosetto A, Iorio A, Marcucci M, Baglin T, Cushman M, Eichinger S, Predicting disease recurrence in patients with previous unprovoked venous thromboembolism: a proposed prediction score (DASH), Journal of Thrombosis and Hemostasis, June 2012, **10** (6): 1019–25

29. Trussell J, Contraceptive efficacy, In Hatcher RA, Trussell J, Nelson AL, Cates Jr W, Kowal D, Policar MS (eds.), Contraceptive technology (20th revised ed.), New York: Ardent Media, 2011, 779–863

30. Van Braeckel D, Temmerman M, Roelens K, Degomme O, Slowing population growth for wellbeing and development, July 2012, 84–5