

The Intersections Between Contraception & Menstrual Health: **An Annotated Bibliography**

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A compilation of journal articles, reports, and briefs on the intersection of menstrual health and
contraception.

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DOCUMENT OVERVIEW

While the areas of contraception and menstruation are closely related, the linkages between the two often remain unappreciated. To help address that gap, this annotated bibliography serves as a collection of relevant literature related to the intersection of contraception and menstrual health.

This version (2021) builds on an original document which collected articles and reports using a snowball method, starting with key documents and utilizing reference lists to identify additional resources. The updated version incorporates additional literature primarily focused on contraceptive-induced menstrual changes (CIMCs), the treatment of menstrual disorders and CIMCs, and prevalence of menstrual disorders. There is specific attention given to the literature on prevalence of menstrual disorders in low-income countries. The development of this resource did not involve a systematic review; rather, additional sources were incorporated through literature reviews and via communication with experts in the field.

The bibliography begins with **background** information, with resources included to offer context on the intersection of menstrual health and contraception. It then transitions to a broad overview of the **sociological context**, primarily of menstrual health. This is followed by **biological context**, which includes an overview of the biological mechanisms of the menstrual cycle, followed by a review menstrual disorders and their treatment. The next section includes the **literature on CIMCs**, highlighting frequency, acceptability and user preferences, with a final section on evidence related to **programmatically interventions** for menstrual health and counseling including on CIMCs.

Key themes within these broad categories have been identified and resources are categorized by these themes. Articles are first organized within sections by sub-theme and then by author last name. Articles that fit into multiple themes have been cross-referenced in corresponding sections accordingly.

SITUATING IN MENSTRUAL HEALTH & FAMILY PLANNING

Overview

1. Folger, S. G., Jamieson, D. J., Godfrey, E. M., Zapata, L. B., & Curtis, K. M. (2013). Evidence-based guidance on selected practice recommendations for contraceptive use: Identification of research gaps. *Contraception*, 87(5), 517-523. <https://doi.org/10.1016/j.contraception.2012.08.003>

Introduction: The Centers for Disease Control and Prevention (CDC) is developing the US Selected Practice Recommendations (US SPR) for Contraceptive Use, an adaptation of the World Health Organization's (WHO's) evidence-based SPR guidance addressing contraceptive management issues that, while common, may also be complex or controversial. The recommendations in the US SPR will be based on the best available existing scientific evidence and expert guidance on such issues. The evidence was reviewed at an expert meeting held by the CDC in October 2011. In addition to informing development of recommendations for the US SPR, the meeting also served to identify research gaps for which additional evidence is needed to address or further clarify some common questions on contraceptive management and use. These research gaps are listed in Table 1, categorized by general area of interest. In this paper, we discuss three of the research gaps for purposes of illustration: (a) What are the most effective approaches to improve patient and provider understanding of and adherence to instructions for actions to take following dosing errors with oral contraceptive pills (OCPs) (missed pills), the transdermal contraceptive patch and the contraceptive ring? (b) What are the most effective and feasible approaches for prevention and management of bleeding irregularities among women using hormonal or intrauterine contraception? (c) What are the long-term effectiveness and safety of, and patient satisfaction with, hysteroscopic sterilization? For each of these questions, we discuss the significance of the issue, the type of evidence that is needed and the methodological challenges for conducting the needed research.

2. Geertz, A., Iyer, L., Kasen, P., Mazzola, F., & Peterson, K. (2016). *An Opportunity to Address Menstrual Health and Gender Equity*. Retrieved from FSG website: <https://www.fsg.org/publications/opportunity-address-menstrual-health-and-gender-equity#download-area>.

Summary: This overview report includes a description of the evidence base on menstrual health challenges and outcomes, the response to these challenges, and opportunities for future programs and innovation. The report addresses the response from multiple sectors including sexual and reproductive health; water, sanitation and hygiene; and education. Within the sexual and reproductive health sector, there is an increasing focus on using puberty as an entry point for reproductive health education. Comprehensive programs that address puberty education and menstrual hygiene are mentioned as "bright spots" in the field. In the conclusion, the authors describe four cross-cutting opportunities to ameliorate menstrual health challenges. These opportunities include: using menstruation as an entry point for other services, encouraging collaboration across menstrual health actors, tackling social norms surrounding puberty, and catalyzing market development.

3. Harlow, S. D., & Campbell, O. M. (2000). Menstrual dysfunction: a missed opportunity for improving reproductive health in developing countries. *Reproductive Health Matters*, 8(15), 142–147. <http://www.ncbi.nlm.nih.gov/pubmed/11424262>

Abstract: The field of population has undergone a paradigm shift to a broader focus on reproductive health, which recognises women's self-perceived health needs. Investigations in various countries reveal that menstruation is a primary concern of women. Yet sparse attention has been paid to understanding or ameliorating women's menstrual complaints. We propose including the management of menstrual complaints as part of reproductive health programming. Next steps should include further quantitative and qualitative research to understand the prevalence, determinants and consequences of menstrual dysfunction; developing appropriate protocols and low-cost interventions for diagnosis and treatment of menstrual morbidity and training of health care workers in resource-scarce settings; and developing educational interventions to facilitate women's understanding of normal menstrual function and variability as well as of the types, causes and appropriate treatments for menstrual dysfunction.

4. Heise, L., Greene, M. E., Opper, N., Stavropoulou, M., Harper, C., Nascimento, M., Zewdie, D., Darmstadt, G. L., Greene, M. E., Hawkes, S., Henry, S., Heymann, J., Klugman, J., Levine, R., Raj, A., & Rao Gupta, G. (2019). Gender inequality and restrictive gender norms: framing the challenges to health. *The Lancet*, 393(10189), 2440-2454. [https://doi.org/10.1016/S0140-6736\(19\)30652-X](https://doi.org/10.1016/S0140-6736(19)30652-X)

Abstract: Gender is not accurately captured by the traditional male and female dichotomy of sex. Instead, it is a complex social system that structures the life experience of all human beings. This paper, the first in a Series of five papers, investigates the relationships between gender inequality, restrictive gender norms, and health and wellbeing. Building upon past work, we offer a consolidated conceptual framework that shows how individuals born biologically male or female develop into gendered beings, and how sexism and patriarchy intersect with other forms of discrimination, such as racism, classism, and homophobia, to structure pathways to poor health. We discuss the ample evidence showing the far-reaching consequences of these pathways, including how gender inequality and restrictive gender norms impact health through differential exposures, health-related behaviours and access to care, as well as how gender-biased health research and health-care systems reinforce and reproduce gender inequalities, with serious implications for health. The cumulative consequences of structured disadvantage, mediated through discriminatory laws, policies, and institutions, as well as diet, stress, substance use, and environmental toxins, have triggered important discussions about the role of social injustice in the creation and maintenance of health inequities, especially along racial and socioeconomic lines. This Series paper raises the parallel question of whether discrimination based on gender likewise becomes embodied, with negative consequences for health. For decades, advocates have worked to eliminate gender discrimination in global health, with only modest success. A new plan and new political commitment are needed if these global health aspirations and the wider Sustainable Development Goals of the UN are to be achieved.

5. Hennegan, J., Tsui, A. O., & Sommer, M. (2019). Missed Opportunities: Menstruation

Matters for Family Planning. *Perspectives on Sexual and Reproductive Health*, 45, 55–59. <https://doi.org/10.1363/45e7919>

Abstract: Increased global attention is being paid to the importance of adolescent and adult women's experiences of menstruation in low- and middle-income countries, and the challenges these experiences present to health, education and gender equality.^{1–5} Although much of the focus has been on menarche as a window of opportunity for early engagement in young women's sexual and reproductive health,⁶ minimal attention has been paid to the natural linkages between menstrual health and hygiene and females' management of reproduction over their life course.

6. Keith, B. (2016). *Girls' and women's right to menstrual health: Evidence and opportunities. Outlook on reproductive health*. Retrieved from PATH website: https://path.azureedge.net/media/documents/RH_outlook_mh_022016.pdf

Summary: This commentary argues that menstrual health is a sexual and reproductive health and rights issue, emphasizes the importance of focusing on menstrual health, and provides examples of how menstrual health can be improved. Challenges related to menstrual health include cultural taboos and lack of access to information, products, and an adequate health environment. In defining menstrual health as part of sexual and reproductive health, the author addresses the potential links to infection and high-risk sexual behavior such as transactional sex for sanitary products. The impact of menstrual hygiene management on education and gender-based violence is also discussed and the author advocates for a cross-sectoral response.

7. Lin, K., & Barnhart, K. (2007). *The clinical rationale for menses-free contraception. J Womens Health (Larchmt)*, 16(8), 1171-1180. <https://doi.org/10.1089/jwh.2007.0332>

Abstract: The impact of monthly menstruation may range from a minor inconvenience for some women to a major health concern for those who suffer from menstrual disorders and health conditions that are aggravated during their menstrual cycle. Oral contraceptives (OCs) have been used safely in continuous regimens for the treatment of menstrual disorders in some women and for others who choose to extend their 28-day menstrual cycle to accommodate major life events. There is no physiological requirement for the monthly hormone withdrawal bleed that is experienced by women taking cyclic OCs or for a menstrual period in women who do not desire to (or cannot) become pregnant. Thus, the use of continuous or extended-cycle OC regimens that eliminate the menstrual cycle represents a viable and attractive option for many women. The availability of more choices for menstrual suppression, such as continuous use of OCs, will improve the quality of life for many women who suffer from menstrual-related disorders and provide greater convenience for women with busy and active lifestyles.

8. Mmari, K., & Sabherwal, S. (2013). *A review of risk and protective factors for adolescent sexual and reproductive health in developing countries: An update. Journal of Adolescent Health*, 53(5), 562-572. <https://doi.org/10.1016/j.jadohealth.2013.07.018>

Abstract: To conduct a literature review of studies that examined risk and protective factors related to adolescent sexual and reproductive health in developing countries. A literature

search was conducted using multiple databases, including PubMed, PsycINFO, Scopus, JSTOR, and the Interagency Youth Working Group. Review criteria included publications that: were conducted in a low- or middle-income country; had a sample size of at least 100 young people aged 10–24 years, and used multivariate analysis. All studies that were identified were also conducted between 1990 and 2010, a 20-year time frame. The literature search and initial review yielded a total of 244 studies that met the criteria and analyzed risk and protective factors related to the following outcomes: sexual initiation, number of sexual partners, condom use, contraceptive use, pregnancy and early childbearing, human immunodeficiency virus, sexually transmitted infections, and sexual coercion. Most studies that were conducted on adolescent sexual and reproductive health in developing countries were largely focused in Sub-Saharan African contexts, and primarily examined factors related to sexual initiation and condom use. Most factors that examined an adolescent sexual and reproductive health outcome were also focused on the individual level, although an increasing number of studies within the past 10 years have focused on family-level factors. Few studies examined factors at the community or neighborhood level, which, to date, has largely been ignored in developing country contexts. The review not only summarizes what is currently known in terms of risk and protective factors that relate to adolescent sexual and reproductive health in developing countries, but also highlights the gaps. Implications for future research are discussed.

- 9. Phillips-Howard, P. A., Hennegan, J., Weiss, H. A., Hytti, L., & Sommer, M. (2018). Inclusion of menstrual health in sexual and reproductive health and rights. *The Lancet Child & Adolescent Health*, 2(8), e18. [https://doi.org/10.1016/s2352-4642\(18\)30204-9](https://doi.org/10.1016/s2352-4642(18)30204-9)**

Summary: This was written as a reply to the Guttmacher-*Lancet* Commission on sexual and reproductive health and rights. The authors write that the commission included menstruation as a part of reproductive health but did not consider its impact on sexual and reproductive health risks and did not adequately address menstrual health and hygiene. They emphasize that the inclusion of menstrual health within sexual and reproductive health is vital to satisfying menstrual needs on a global scale.

- 10. Singh, S. (2018). Inclusion of menstrual health in sexual and reproductive health and rights – Authors' reply. *The Lancet Child & Adolescent Health*, 2(8), e19. [https://doi.org/10.1016/S2352-4642\(18\)30219-0](https://doi.org/10.1016/S2352-4642(18)30219-0)**

Summary: This correspondence is in reply to the response to the Guttmacher-*Lancet* Commission on sexual and reproductive health and rights. The author writes that the commission's agenda is aligned with improving the rights of women and girls to effectively manage their menstruation and that they hope to move the sexual and reproductive health field forward. The commission did not originally offer a comprehensive definition of the components of sexual education but in the reply wrote that curricula should include information on menstrual health.

- 11. Sommer, M., Caruso, B. A., Sahin, M., Calderon, T., Cavill, S., Mahon, T., & Phillips-Howard, P. A. (2016). A Time for Global Action: Addressing Girls' Menstrual Hygiene Management Needs in Schools. *PLoS Med*, 13(2), e1001962.**

<https://doi.org/10.1371/journal.pmed.1001962>

Summary: This article details the landscape of evidence on menstrual hygiene management within schools and the present gaps in research and provides five priorities to guide action. The priorities are: expanding the evidence base on effective interventions; creating global guidelines for MHM in schools; improving MHM advocacy work; having national governments oversee MHM provision in schools; and integrating inclusive MHM into the education sector. The authors mention that progress in improving MHM in schools has mostly been through the WASH sector and that there needs to be further engagement from the education and sexual and reproductive health sectors. Specifically, they encourage the sexual and reproductive health sector to include puberty and menstrual care in their work and emphasize a cross-sectoral response. The five priorities identified to guide action focus on increasing girls' knowledge about menstruation and improving their ability to manage menses at school; these priorities were developed at "MHM in Ten", a conference organized by Columbia University and the United Nations Children's Fund (UNICEF).

12. Sommer, M., Hirsch, J. S., Nathanson, C., & Parker, R. G. (2015). Comfortably, Safely, and Without Shame: Defining Menstrual Hygiene Management as a Public Health Issue. *Am J Public Health, 105*(7), 1302-1311.

<https://dx.doi.org/10.2105%2FAJPH.2014.302525>

Abstract: In recent years, the menstrual hygiene management challenges facing schoolgirls in low-income-country contexts have gained global attention. We applied Gusfield's sociological analysis of the culture of public problems to better understand how this relatively newly recognized public health challenge rose to the level of global public health awareness and action. We similarly applied the conceptualization by Dorfman et al. of the role of public health messaging in changing corporate practice to explore the conceptual frames and the news frames that are being used to shape the perceptions of menstrual hygiene management as an issue of social justice within the context of public health. Important lessons were revealed for getting other public health problems onto the global-, national-, and local-level agendas.

13. Sommer, M., & Sahin, M. (2013). Overcoming the Taboo: Advancing the global agenda for menstrual hygiene management for schoolgirls. *Am J Public Health, 103*(9), 1556–1559. <https://dx.doi.org/10.2105%2FAJPH.2013.301374>

Summary: This article describes findings on the experience of schoolgirls with menstrual hygiene management and the difficulties that girls face in managing their menses. There are many gaps in knowledge pertaining to menstruation and inadequate menstrual management can affect girls' participation in school. The authors call for further research into the topic, particularly quantitative studies, in order to develop an effective multi-sectoral response.

14. Sommer, M., Sutherland, C., & Chandra-Mouli, V. (2015). Putting menarche and girls into the global population health agenda. *Reprod Health, 12*, 24.

<https://doi.org/10.1186/s12978-015-0009-8>

Abstract: Menarche, the onset of menstruation is a fundamental part of a girl's transition from childhood to adolescence. Studies show that girls in many countries experience menarche with

insufficient information and support. Girls from around the world report feeling ashamed and afraid. The potential health effects of such experiences include a weakening of girls' sense of self-confidence and competence, which in turn may comprise girls' abilities to assert themselves in different situations, including in relation to their sexuality and sexual and reproductive health. There is an important need for the public health community to assure that girls receive the education and support they need about menstruation, so they are able to feel more confident about their bodies, and navigate preventable health problems – now and in the future. For too long, the global health community has overlooked the window of opportunity presented by menarche. Family planning programs have generally focused their efforts on married couples and HIV programs have focused safer sex promotion on older adolescent girls and boys. Starting the conversation at menarche with girls in early adolescence would fully use this window of opportunity. It would engage young adolescent girls and be a natural first step for later, more comprehensive conversations about sexuality, reproduction and reproductive health. There are a number of initiatives beginning to tackle the provision of puberty information to girls and boys, but the global health community is overdue to set a global standard for the provision of such guidance.

15. Starrs, A. (2015). A Lancet Commission on sexual and reproductive health and rights: going beyond the Sustainable Development Goals. *The Lancet*, 386(9999), 1111-1112. [https://doi.org/10.1016/S0140-6736\(15\)00250-0](https://doi.org/10.1016/S0140-6736(15)00250-0)

Summary: In this article, the author discusses how sexual and reproductive health and rights are addressed within the sustainable development goals. She writes that the sustainable development goals are missing certain elements of sexual and reproductive health and rights and that there is a lack of progress on developing a holistic agenda to advance the field. As a result, the Guttmacher Institute and *The Lancet* have partnered to create the commission on sexual and reproductive health and rights. The commission's goal is to establish a world-wide agenda for sexual and reproductive health and rights and encourage the implementation of policies and programs that further this goal. The commission will provide evidence-based recommendations to move the field forward and was intended to begin work in 2016.

16. Starrs, A. M., Ezeh, A. C., Barker, G., Basu, A., Bertrand, J. T., Blum, R., et al. (2018). Accelerate progress—sexual and reproductive health and rights for all: report of the Guttmacher– Lancet Commission. *The Lancet*, 391(10140), 2642-2692. [https://doi.org/10.1016/S0140-6736\(18\)30293-9](https://doi.org/10.1016/S0140-6736(18)30293-9)

Summary: This *Lancet* report details the literature on the sexual and reproductive health and rights agenda and where it is lacking. The authors present a broad definition of sexual and reproductive health and rights and identify the services and information that should be consistently available. In addition to contraceptive access, maternal care, and HIV, the components that they argue should be addressed within sexual and reproductive health and rights are: “care for STIs other than HIV; comprehensive sexuality education; safe abortion care; prevention, detection, and counselling for gender-based violence; prevention, detection, and treatment of infertility and cervical cancer; and counselling and care for sexual health and wellbeing” (p.2643). They also argue that a multi-sectoral response to sexual and reproductive health and rights is essential to advancing the agenda.

17. Weber, A. M., Cislighi, B., Meausoone, V., Abdalla, S., Mejía-Guevara, I., Loftus, P., Hallgren, E., Seff, I., Stark, L., Victora, C. G., Buffarini, R., Barros, A. J. D., Domingue, B. W., Bhushan, D., Gupta, R., Nagata, J. M., Shakya, H. B., Richter, L. M., Norris, S. A., ... Rao Gupta, G. (2019). Gender norms and health: insights from global survey data. *The Lancet*, 393(10189), 2455-2468. [https://doi.org/10.1016/S0140-6736\(19\)30765-2](https://doi.org/10.1016/S0140-6736(19)30765-2)

Abstract: Despite global commitments to achieving gender equality and improving health and wellbeing for all, quantitative data and methods to precisely estimate the effect of gender norms on health inequities are underdeveloped. Nonetheless, existing global, national, and subnational data provide some key opportunities for testing associations between gender norms and health. Using innovative approaches to analysing proxies for gender norms, we generated evidence that gender norms impact the health of women and men across life stages, health sectors, and world regions. Six case studies showed that: (1) gender norms are complex and can intersect with other social factors to impact health over the life course; (2) early gender-normative influences by parents and peers can have multiple and differing health consequences for girls and boys; (3) non-conformity with, and transgression of, gender norms can be harmful to health, particularly when they trigger negative sanctions; and (4) the impact of gender norms on health can be context-specific, demanding care when designing effective gender-transformative health policies and programmes. Limitations of survey-based data are described that resulted in missed opportunities for investigating certain populations and domains. Recommendations for optimising and advancing research on the health impacts of gender norms are made.

18. Wilson, L., Rademacher, KH., Rosenbaum, J., Callahan, R., Nanda, G., Fry, S., Mackenzie, AC. (2021). Seeking synergies: understanding the evidence that links menstrual health and sexual and reproductive health and rights. *Sex Reprod Health Matters*, 29(1), <https://doi.org/10.1080/26410397.2021.1882791>

Abstract: Global efforts to improve menstrual health and sexual and reproductive health and rights (SRHR) are fundamentally intertwined and share similar goals for improving health and well-being and increasing gender equality. Historically, however, the two fields have operated independently and missed opportunities to build upon their biological and sociocultural linkages. Biological touchpoints connecting the two fields include genital tract infections, menstrual disorders, contraception, and menopause. From a sociocultural perspective, intersections occur in relation to the experience of puberty and menarche, gender norms and equity, education, gender-based violence, and transactional sex. We describe evidence linking menstrual health and SRHR and offer recommendations for integration that could strengthen the impact of both fields.

SOCIOLOGICAL CONTEXT

Experience with Puberty and Menarche

1. Aniebue, U. U., Aniebue, P. N., & Nwankwo, T. O. (2009). The impact of pre- menarcheal training on menstrual practices and hygiene of Nigerian school girls. *The Pan African Medical Journal*, 2, 9.

Abstract: BACKGROUND: The menstrual practices of adolescents derive largely from health issues associated with their adjustment to reproductive life. The objective of the study was to assess the effect of pre-menarcheal training on the menstrual and hygiene practices of Nigerian school girls.

METHODS: A cross-sectional questionnaire-based survey of randomly selected post-menarcheal school girls using a pre-tested, semi-structured questionnaire was done.

RESULTS: The mean age of the school girls was 14.9 ± 1.7 years. Pre-menarcheal training was given to 273 (55.2%) of them. Mothers (74.7%) were the more common source of information. Inappropriate experience of menarche, adverse effect of menstruation on schooling and social life and the use of unhygienic menstrual absorbents were common in girls who had no pre-menarcheal training than those who did.

CONCLUSION: Lack of timely information results in inappropriate menstrual experiences and poor menstrual hygiene practices. Ways to promote menstrual education and hygiene practices are suggested.

2. Bhavik Rana; Arpit Prajapati; Sonaliya, K. N. . V. S. M. P. A. S. (2010). An assessment of menstrual hygiene practices amongst adolescent females at Kheda district of Gujarat state, India. *Healthline*, 6(1), 23-29. http://iapsmgc.org/index_pdf/169.pdf

Abstract: BACKGROUND: In the developing country like India, females are facing many menstruation related health problems, which are significant causes of morbidity, hampering daily life. Improper menstrual hygiene practices predispose the females towards many communicable diseases. The knowledge, attitudes and practices regarding menstrual hygiene, which establish at adolescent age, are usually followed by them throughout life and also passed on to the next generation.

OBJECTIVES: 1. To detect the menstrual health problems 2. To assess menstrual hygiene practices 3. To assess the restrictions in daily activities considered appropriate by the adolescents.

METHOD: Current cross sectional study was conducted at Kheda district of Gujarat State, India. The sampling was done using multi stage sampling technique. The sample included 400 adolescent girls of 14 to 17 years of age. Considering the dropout rate, 30% sample was constituted by non school going subjects and 70 % by school going subjects.

RESULTS: 76(19%) participants had irregularity in menstruation. 103 (25.8%) participants had problem in doing daily activities whereas 112 (28%) participants had problem in doing specific activities like playing, exercise etc. 244 (61%) participants have used cloth while 156 (39%) used sanitary pad during last menstruation.

CONCLUSION As revealed by the study, the adolescent girls are facing various menstrual health problems like abdominal pain, menorrhagea, polymenorrhoea etc. They are unaware of proper disposal techniques of sanitary pad or other material used as absorbent.

3. Chandra-Mouli, V., & Patel, S. V. (2017). Mapping the knowledge and understanding of menarche, menstrual hygiene and menstrual health among adolescent girls in low- and middle-income countries. *Reprod Health*, 14(1), 30. <https://doi.org/10.1186/s12978-017-0293-6>

Abstract: BACKGROUND: Menstruation is a natural physiological process that requires proper

management. Unlike other normal bodily processes, menstruation is linked with religious and cultural meanings that can affect the perceptions of young girls as well as the ways in which the adults in the communities around them respond to their needs.

OBJECTIVES: This review aims to answer the following questions: (1) how knowledgeable are adolescent girls in low- and middle-income countries about menstruation and how prepared are they for reaching menarche, (2) who are their sources of information regarding menstruation, (3) how well do the adults around them respond to their information needs, (4) what negative health and social effects do adolescents experience as a result of menstruation, and (5) how do adolescents respond when they experience these negative effects and what practices do they develop as a result?

METHODS: Using a structured search strategy, articles that investigate young girls' preparedness for menarche, knowledge of menstruation and practices surrounding menstrual hygiene in LMIC were identified. A total of 81 studies published in peer-reviewed journals between the years 2000 and 2015 that describe the experiences of adolescent girls from 25 different countries were included.

RESULTS: Adolescent girls in LMIC are often uninformed and unprepared for menarche. Information is primarily obtained from mothers and other female family members who are not necessarily well equipped to fill gaps in girls' knowledge. Exclusion and shame lead to misconceptions and unhygienic practices during menstruation. Rather than seek medical consultation, girls tend to miss school, self-medicate and refrain from social interaction. Also problematic is that relatives and teachers are often not prepared to respond to the needs of girls.

CONCLUSION: LMIC must recognize that lack of preparation, knowledge and poor practices surrounding menstruation are key impediments not only to girls' education, but also to self-confidence and personal development. In addition to investment in private latrines with clean water for girls in both schools and communities, countries must consider how to improve the provision of knowledge and understanding and how to better respond to the needs of adolescent girls.

4. Marván, M. L., & Molina-Abolnik, M. (2012). Mexican Adolescents' Experience of Menarche and Attitudes Toward Menstruation: Role of Communication Between Mothers and Daughters. *Journal of Pediatric and Adolescent Gynecology*, 25(6), 358–363. <https://doi.org/10.1016/j.jpag.2012.05.003>

Abstract: **OBJECTIVES:** First, to explore the kind of information that Mexican mothers give their daughters about menstruation before their menarche, and to study the impact of this communication on how prepared the daughters felt when they experienced their menarche. Second, to investigate the influence of the menarcheal experience on attitudes toward menstruation.

DESIGN: Cross-sectional survey.

SETTINGS: Sample of adolescents attending 3 different public schools.

PARTICIPANTS: 405 Mexican postmenarcheal adolescents, aged 12-15 years.

Intervention: Participants answered a questionnaire that had 3 parts: (a) General data, (b) topics related to menses that participants had discussed with their mothers prior to menarche, and (c) menarcheal experience. They also answered a questionnaire about menstrual attitudes.

RESULTS: Although most of the participants knew what they should do when they experienced their menarche, only 39% stated they had felt prepared to start menstruating. Regarding menstrual attitudes, adolescents scored highest on Negative Feelings and Secrecy rather than on Positive Feelings. Participants who had previously discussed the emotional aspects of menses with their mothers were more likely to claim they had felt prepared to start menstruating when they got their first period (OR = 3.45). The fact that adolescents felt prepared to start menstruating predicted positive attitudes toward menstruation ($\beta = .19$)

CONCLUSIONS: Discussing the emotional aspects of menses prior to menarche is crucial to being prepared for menarche, and to holding positive attitudes toward menstruation. Information on biological knowledge and practical aspects of menses needs to be supplemented with emotional issues.

5. Patton, G. C., & Viner, R. (2007). Pubertal transitions in health. *The Lancet*, 369(9567), 1130-1139. [https://doi.org/10.1016/S0140-6736\(07\)60366-3](https://doi.org/10.1016/S0140-6736(07)60366-3)

Summary: Puberty is accompanied by physical, psychological, and emotional changes adapted to ensure reproductive and parenting success. Human puberty stands out in the animal world for its association with brain maturation and physical growth. Its effects on health and wellbeing are profound and paradoxical. On the one hand, physical maturation propels an individual into adolescence with peaks in strength, speed, and fitness. Clinicians have viewed puberty as a point of maturing out of childhood-onset conditions. However, puberty's relevance for health has shifted with a modern rise in psychosocial disorders of young people. It marks a transition in risks for depression and other mental disorders, psychosomatic syndromes, substance misuse, and antisocial behaviors. Recent secular trends in these psychosocial disorders coincide with a growing mismatch between biological and social maturation, and the emergence of more dominant youth cultures.

6. Schoep, M. E., Adang, E. M. M., Maas, J. W. M., De Bie, B., Aarts, J. W. M., & Nieboer, T. E. (2019). Productivity loss due to menstruation-related symptoms: A nationwide cross-sectional survey among 32 748 women. *BMJ Open*, 9(6), e026186. <https://doi.org/10.1136/bmjopen-2018-026186>

Abstract: OBJECTIVE: To evaluate age-dependent productivity loss caused by menstruation-related symptoms, measured in absenteeism (time away from work or school) and presenteeism (productivity loss while present at work or school).

METHODS DESIGN/SETTING: internet-based, cross-sectional survey conducted in the Netherlands from July to October 2017.

PARTICIPANTS: 32 748 women aged 15–45 years, recruited through social media.

OUTCOME MEASURES: self-reported lost productivity in days, divided into absenteeism and presenteeism; impact of menstrual symptoms; reasons women give when calling in sick; and women's preferences regarding the implications of menstruation-related symptoms for schools and workplaces.

RESULTS: A total of 13.8% (n=4514) of all women reported absenteeism during their menstrual periods with 3.4% (n=1108) reporting absenteeism every or almost every menstrual cycle. The mean absenteeism related to a woman's period was 1.3 days per year. A total of 80.7% (n=26 438) of the respondents reported presenteeism and decreased productivity a mean of 23.2

days per year. An average productivity loss of 33% resulted in a mean of 8.9 days of total lost productivity per year due to presenteeism. Women under 21 years were more likely to report absenteeism due to menstruation-related symptoms (OR 3.3, 95% CI 3.1 to 3.6). When women called in sick due to their periods, only 20.1% (n=908) told their employer or school that their absence was due to menstrual complaints. Notably, 67.7% (n=22 154) of the participants wished they had greater flexibility in their tasks and working hours at work or school during their periods.

CONCLUSIONS: Menstruation-related symptoms cause a great deal of lost productivity, and presenteeism is a bigger contributor to this than absenteeism. There is an urgent need for more focus on the impact of these symptoms, especially in women aged under 21 years, for discussions of treatment options with women of all ages and, ideally, more flexibility for women who work or go to school.

7. Sommer, M. (2011). An overlooked priority: Puberty in sub-Saharan Africa. *American Journal of Public Health, 101(6), 979-981.* <https://doi.org/10.2105/AJPH.2010.300092>

Abstract: Early adolescence remains an overlooked window of opportunity for public health intervention with girls and boys in sub-Saharan Africa. Minimal health data exist on pubescent girls and boys. Considerable morbidity and mortality related to HIV, sexually transmitted infections, and pregnancy emerge soon after puberty, suggesting the importance of targeting early adolescents. The fundamental goal of primary prevention would be better served if girls and boys between the ages of 10 and 14 years were targeted for effective and contextually relevant interventions. Such interventions should address healthy transitions to young adulthood to effectively advance the public health agenda with postpubescent (aged 15 to 24 years) young women and men. The global health community is overdue to build the empirical database for intervention with this age group.

Relevant Articles Cross-Referenced from Other Sections

In Access and Needs

Jewitt, S., & Ryley, H. (2014). It's a girl thing: Menstruation, school attendance, spatial mobility and wider gender inequalities in Kenya. *Geoforum, 56*, 137-147.

McMahon, S. A., Winch, P. J., Caruso, B. A., Obure, A. F., Ogutu, E. A., Ochari, I. A., & Rheingans, R. D. (2011). 'The girl with her period is the one to hang her head' Reflections on menstrual management among schoolgirls in rural Kenya. *BMC International Health and Human Rights, 11(1)*, 7.

Nanda, G., Lupee, J., & Tharaldson, J. (2016). *Menstrual Hygiene Management among Schoolgirls in Eastern Province of Zambia Qualitative Research Final Report.*

Retrieved from: http://menstrualhygieneday.org/wp-content/uploads/2016/12/USAID_MHM-among-Schoolgirls-in-Eastern-Province-of-Zambia-FINAL508.pdf

Oruko, K., Nyothach, E., Zielinski-Gutierrez, E., Mason, L., Alexander, K., Vulule, J., et al. (2015).

'He is the one who is providing you with everything so whatever he says is what you do': A Qualitative Study on Factors Affecting Secondary Schoolgirls' Dropout in Rural Western Kenya. *PLoS One*, 10(12), e0144321.

In Programmatic Interventions

Fakhri, M., Hamzehgardeshi, Z., Hajikhani Golchin, N. A., & Komili, A. (2012). Promoting menstrual health among Persian adolescent girls from low socioeconomic backgrounds: a quasi-experimental study. *BMC Public Health*, 12(1), 193.

Sommer, M. (2011). An Early Window of Opportunity for Promoting Girls' Health: Policy Implications of the Girl's Puberty Book Project in Tanzania. *International Electronic Journal of Health Education*, 14, 77–92.

Access and Needs

- 1. Hennegan, J., Shannon, A. K., Schwab, K. J., & investigators, P. M. A. (2018). Wealthy, urban, educated. Who is represented in population surveys of women's menstrual hygiene management? *Reprod Health Matters*, 26(52), 81-91. <https://doi.org/10.1080/09688080.2018.1484220>**

Abstract: Inadequate menstrual hygiene presents a barrier to women's dignity and health. Recent attention to this marginalized challenge has resulted in the first national assessments of menstrual practices. Intuitively, surveys require women to have had a recent menses to be eligible. This study seeks to determine if there are demographic differences between women who are eligible and ineligible to answer questions about their menstrual hygiene during these assessments. Secondary analyses were undertaken on nationally or state representative data collected by the Performance Monitoring and Accountability 2020 survey program across eight countries (Burkina Faso, Ethiopia, Ghana, India, Kenya, Niger, Nigeria, and Uganda). Female respondents were included in the study and compared on whether they had a menstrual period within the past three months and thus were eligible to answer questions regarding menstrual practices. On average, 29% of surveyed women across samples were ineligible to be asked menstrual hygiene questions. Higher levels of education, wealth, and urban residence were associated with higher odds of eligibility. Young and unmarried women were also more likely to be eligible. Demographic differences between eligible and ineligible women were consistent across all countries. Wealthy, urban, and educated women are more likely to be eligible to answer survey questions about menstrual hygiene. While population surveys may be representative of menstruating women, proportions of menstrual hygiene practices reported underrepresent the experiences of more vulnerable groups. These groups are likely to have greater struggles with menstrual hygiene when they are menstruating.

- 2. Menstrual Hygiene Management. (2018). *Performance Monitoring and Accountability 2020*. Bill & Melinda Gates Institute for Population and Reproductive Health at the Johns Hopkins Bloomberg School of Public Health. Retrieved from PMA 2020 website: <https://www.pma2020.org/mhm-briefs>**

Summary: The Performance Monitoring and Accountability 2020 (PMA2020) project at the Bill

& Melinda Gates Institute for Population and Reproductive Health at the Johns Hopkins Bloomberg School of Public Health collects household data to monitor health and development indicators. In some of their surveys, menstrual hygiene management is included as a topic with multiple indicators. In the description of menstrual hygiene management (MHM), the report's authors write that not adequately addressing MHM needs leads to consequences for women's reproductive health. As of July 2018, there are 12 country, state, or province-specific briefs that provide data on MHM on the PMA 2020 webpage. The indicators summarized on each brief include types of menstrual materials used, disposal of menstrual materials, and percentages of women who report that they have everything they need to manage their menstruation. Full datasets are available for analysis from the PMA2020 project.

3. Phillips-Howard, P. A., Otieno, G., Burmen, B., Otieno, F., Odongo, F., Odour, C., et al. (2015). Menstrual Needs and Associations with Sexual and Reproductive Risks in Rural Kenyan Females: A Cross-Sectional Behavioral Survey Linked with HIV Prevalence. *J Womens Health (Larchmt)*, 24(10), 801-811. <https://doi.org/10.1089/jwh.2014.5031>

Abstract: BACKGROUND: Females in low and middle-income countries (LMICs) have difficulty coping with menstrual needs, but few studies have examined the social or health implications of these needs.

METHODS: Responses from 3418 menstruating females aged 13–29 years were extracted from an HIV and behavioral risks cross-sectional survey conducted in rural western Kenya. We examined sanitary products used, provision of products from sexual partners or from transactional sex, and demographic and sexual exposures.

RESULTS: Overall, 75% of females reported using commercial pads and 25% used traditional materials such as cloth or items like paper or tissue, with 10% of girls <15 years old depending on makeshift items. Two-thirds of females with no education relied on traditional items. Having attended secondary school increased the odds of using commercial pads among married (adjusted odds ratios [AOR] 4.8, 95% confidence interval [CI] 3.25–7.12) and single females (AOR 2.17, 95% CI 1.04–4.55). Married females had lower odds of pad use if they reported early (<12 years of age) compared with later (≥18 years) sexual debut (64% vs. 78%, AOR 0.45, 95% CI 0.21–0.97). Two-thirds of pad users received them from sexual partners. Receipt was lower among married females if partners were violent (AOR 0.67, 95% CI 0.53–0.85). Receipt among single females was higher if they had two or more sexual partners in the past year (AOR 2.11, 95% CI 1.04–4.29). Prevalence of engaging in sex for money to buy pads was low (1.3%); however, 10% of 15-year-olds reported this, with girls ≤15 having significantly higher odds compared with females over 15 (AOR 2.84, 95% CI 0.89–9.11). The odds of having transactional sex for pads was higher among females having two or more partners in the past 12 months (AOR 4.86, 95% CI 2.06–11.43).

CONCLUSIONS: Menstrual needs of impoverished females in rural LMICs settings likely leads to increased physical and sexual harms. Studies are required to strengthen knowledge and to evaluate interventions to reduce these harms.

4. Sebastian, A., Hoffmann, V., & Adelman, S. (2013). Menstrual management in low-income countries: needs and trends. *Waterlines*, 32(2), 135-153.

DOI: [10.3362/1756-3488.2013.015](https://doi.org/10.3362/1756-3488.2013.015)

Abstract: Access to appropriate facilities for menstrual hygiene and management (MHM) is recognized as a neglected need within the sanitation sector globally. However, little is known about the magnitude or trajectory of this need. Further, the particular services and facilities required to meet MHM needs depend on the practices and products employed by women and girls. We use nationally representative data from 58 low and lower-middle income countries to estimate that 800 million women in such countries menstruate regularly. Positive correlations between menstruation and nutritional status, as well as menstruation and household wealth, imply a growing need for menstrual management solutions as poverty declines, but both effects are dwarfed by the impact of declining fertility rates. Data on imports of disposable menstrual products reveal exponential growth in their use in low and especially lower-middle income countries. This trend is likely to continue as incomes grow and markets develop, making ever greater the need for provision of appropriate disposal facilities.

5. Sommer, M., Chandraratna, S., Cavill, S., Mahon, T., & Phillips-Howard, P. (2016). **Managing menstruation in the workplace: an overlooked issue in low- and middle-income countries.** *Int J Equity Health*, 15(1), 86. <https://dx.doi.org/10.1186%2Fs12939-016-0379-8>

Abstract: The potential menstrual hygiene management barriers faced by adolescent girls and women in workplace environments in low- and middle-income countries has been under addressed in research, programming and policy. Despite global efforts to reduce poverty among women in such contexts, there has been insufficient attention to the water and sanitation related barriers, specifically in relation to managing monthly menstruation, that may hinder girls' and women's contributions to the workplace, and their health and wellbeing. There is an urgent need to document the specific social and environmental barriers they may be facing in relation to menstrual management, to conduct a costing of the implications of inadequate supportive workplace environments for menstrual hygiene management, and to understand the implications for girls' and women's health and wellbeing. This will provide essential evidence for guiding national policy makers, the private sector, donors and activists focused on advancing girls' and women's rights.

6. Sommer, M., Ackatia-Armah, N., Connolly, S., & Smiles, D. (2015). **A comparison of the menstruation and education experiences of girls in Tanzania, Ghana, Cambodia and Ethiopia.** *Compare: A Journal of Comparative and International Education*, 45(4), 589-609. <https://doi.org/10.1080/03057925.2013.871399>

Abstract: The barriers to menstrual hygiene management faced by adolescent schoolgirls in low-income countries are gaining interest at practice and policy levels. The challenges include inadequate water, sanitation and disposal facilities for the management of menses with privacy and dignity, and insufficient guidance to help girls feel confident in attending school during menses. The studies described here aimed to examine how menarche impacts the lives of schoolgirls in three low-income countries (Ghana, Cambodia and Ethiopia). The focus included girls' school participation; their relationship with parents, teachers and peers; their evolving sanitation and hygiene needs; their understanding of cultural issues and taboos around menses; and what education, if any, they received prior to and during puberty. This comparative analysis was aimed at identifying similarities between the three countries that

would enable the adaptation to each context of a training book on menstruation issues for girls, which was developed from a previous study conducted in Tanzania. In all three countries, participatory activities were utilised with girls and results were analysed using grounded theory. Findings included: similarities regarding the importance of culture in perpetuating negative attitudes towards menstruation, limited provision of health information and insufficient facilities within schools. Differences were revealed regarding menstrual myths, parent–child dynamics, sources of guidance and student–teacher relations. There is a critical knowledge gap around menstruation and girls’ education in these contexts that must be addressed to ensure that girls experience a positive menarche and can manage menstrual hygiene.

In Emergency Contexts

- 7. Budhathoki, S. S., Bhattachan, M., Castro-Sanchez, E., Sagtani, R. A., Rayamajhi, R. B., Rai, P., & Sharma, G. (2018). Menstrual hygiene management among women and adolescent girls in the aftermath of the earthquake in Nepal. *BMC Womens Health*, 18(1), 33. <https://doi.org/10.1186/s12905-018-0527-y>**

Abstract: BACKGROUND: Menstrual hygiene management is an essential aspect of hygiene for women and adolescent girls between menarche and menopause. Despite being an important issue concerning women and girls in the menstruating age group menstrual hygiene management is often overlooked in post-disaster responses. Further, there is limited evidence of menstrual hygiene management in humanitarian settings. This study aims to describe the experiences and perceptions of women and adolescent girls on menstrual hygiene management in post-earthquake Nepal.

METHODS: A mixed methods study was carried out among the earthquake affected women and adolescent girls in three villages of Sindhupalchowk district of Nepal. Data was (sic) collected using a semi-structured questionnaire that captured experiences and perceptions of respondents on menstrual hygiene management in the aftermath of the Nepal earthquake. Quantitative data were triangulated with in-depth interview regarding respondent’s personal experiences of menstrual hygiene management.

RESULTS: Menstrual hygiene was rated as the sixth highest overall need and perceived as an immediate need by 18.8% of the respondents. There were 42.8% women & girls who menstruated within first week of the earthquake. Reusable sanitary cloth were (sic) used by about 66.7% of the respondents before the earthquake and remained a popular method (76.1%) post-earthquake. None of the respondents reported receiving menstrual adsorbents as relief materials in the first month following the earthquake. Disposable pads (77.8%) were preferred by respondents as they were perceived to be clean and convenient to use. Most respondents (73.5%) felt that reusable sanitary pads were a sustainable choice. Women who were in the age group of 15-34 years (OR=3.14; CI=(1.07-9.20), did not go to school (OR=9.68; CI=2.16-43.33), married (OR=2.99; CI=1.22-7.31) and previously used reusable sanitary cloth (OR=5.82; CI=2.33-14.55) were more likely to use the reusable sanitary cloth.

CONCLUSIONS: In the immediate aftermath of the earthquake, women and girls completely depended on the use of locally available resources as adsorbents during menstruation. Immediate relief activities by humanitarian agencies, lacked menstrual hygiene management activities. Understanding the previous practice and using local resources, the reusable sanitary

cloth is a way to address the menstrual hygiene needs in the post-disaster situations in Nepal.

- 8. VanLeeuwen, C., & Torondel, B. (2018). Improving menstrual hygiene management in emergency contexts: literature review of current perspectives. *Int J Womens Health*, 10, 169-186. <https://doi.org/10.2147/IJWH.S135587>**

Abstract: Management of menstruation in contexts of humanitarian emergencies can be challenging. A lack of empirical research about effective interventions which improve menstrual hygiene management (MHM) among female populations in humanitarian emergencies and a lack of clarity about which sectors within a humanitarian response should deliver MHM interventions can both be attributable to the lack of clear guidance on design and delivery of culturally appropriate MHM intervention in settings of humanitarian emergencies. The objective of this review was to collate, summarize, and appraise existing peer-reviewed and gray literature that describes the current scenario of MHM in emergency contexts in order to describe the breadth and depth of current policies, guidelines, empirical research, and humanitarian aid activities addressing populations' menstrual needs. A structured-search strategy was conducted for peer-reviewed and gray literature to identify studies, published reports, guidelines, and policy papers related to menstrual response in emergency humanitarian contexts. Of the 51 articles included in the review, 16 were peer-reviewed papers and 35 were gray literature. Most of the literature agreed that hardware interventions should focus on the supply of adequate material (not only absorbent material but also other supportive material) and adequate sanitation facilities, with access to water and private space for washing, changing, drying, and disposing menstrual materials. Software interventions should focus on education in the usage of materials to manage menstruation hygienically and education about the female body's biological processes. There was clear agreement that the needs of the target population should be assessed before designing any intervention. Although there is insight about which factors should be included in an effective menstrual hygiene intervention, there is insufficient empirical evidence to establish which interventions are most effective in humanitarian emergencies and which sectors should be responsible for the coordination and implementation of such. Increased monitoring and evaluation studies of interventions should be completed and publicly shared, in order to feed evidence-based guidelines in the humanitarian sector.

In Schools

- 9. Benshaul-Tolonen, A., Zulaika, G., Nyothach, E., Oduor, C., Mason, L., Obor, D., Alexander, K. T., Laserson, K. F., & Phillips-Howard, P. A. (2019). *Pupil Absenteeism, Measurement, and Menstruation: Evidence from Western Kenya*. Columbia CDEP-CGEG. Retrieved from Columbia Menstrual Health and Gender Justice Working Group Site. https://periodsatcolumbia.files.wordpress.com/2019/03/cdep_absenteeism-2.pdf**

Abstract: Due to data limitations it is unclear if biological processes such as periods hinder girls in developing countries from participating in school to a greater extent than boys. We collect 32,000 unannounced random spot-checks for 6,000 primary school students

in Kenya to assess if girls miss more school than boys. Absenteeism is common among both boys and girls, with pubescent girls missing more schooldays because of school transfers, but less if transfer students are excluded. Boys miss more days because of illness compared to girls. Cohen's kappa coefficient reveals non-random inconsistencies across the spot-check data and school registers, which would lead to bias if school register data were used in impact evaluations. To illustrate this point, we replicate the results from a three-arm pilot cluster randomized control study that provided sanitary products to schoolgirls to reduce absenteeism using the school records instead of the spot-checks for the same calendar dates. As shown, the school register data would lead to erroneous conclusions regarding the treatment effects.

10. Boosey, R., Prestwich, G., & Deave, T. (2014). Menstrual hygiene management amongst schoolgirls in the Rukungiri district of Uganda and the impact on their education: a cross-sectional study. *Pan Afr Med J*, 19, 253. <https://doi.org/10.11604/pamj.2014.19.253.5313>

Abstract: INTRODUCTION: an increasing number of studies have found that girls in low-income settings miss or struggle at school during menstruation if they are unable to manage their menstrual hygiene effectively. This study explores the menstrual hygiene practices and knowledge of girls at rural government primary schools in the Rukungiri district in Uganda and assesses the extent to which poor menstrual hygiene management (MHM) affects their education.

METHODS: a self-administered questionnaire was completed by schoolgirls in six government-run primary schools in the Rukungiri district. Focus groups were held with girls from each school and semi-structured interviews were conducted with headteachers and female teachers from the participating schools. A toilet assessment was also conducted in each school.

RESULTS: one hundred and forty schoolgirls completed the questionnaire. The girls reported a lack of access to adequate resources, facilities and accurate information to manage their menstrual hygiene effectively at school. They reported that, as a result, during menstruation they often struggle at school or miss school. Eighty-six girls (61.7%) reported missing school each month for menstrual-related reasons (mean 1.64, range 0-10, SD. 1.84).

CONCLUSION: it is common for girls who attend government-run primary schools in the Rukungiri district to miss school or struggle in lessons during menstruation because they do not have access to the resources, facilities, or information they need to manage for effective MHM. This is likely to have detrimental effects on their education and future prospects. A large-scale study is needed to explore the extent of this issue.

11. Caruso, B. A., Fehr, A., Inden, K., Sahin, M., Ellis, A., Andes, K. L., & Freeman, M. C. (2013). *WASH in Schools Empowers Girls' Education in Freetown, Sierra Leone: An Assessment of Menstrual Hygiene Management in Schools*. UNICEF. Retrieved from: http://www.ungei.org/files/WASH_Sierra_Leone.pdf

Summary: This study aimed to identify the challenges that accompany menstruation for schoolgirls in Freetown, Sierra Leone. The participants mentioned how dealing with menses had consequences such as missing school. The most prevalent challenge in management of menstruation was menstrual pain. Other identified challenges included shame about

menstruation, leaks or odors, little knowledge of menstruation, lack of preparation, and inadequate management of menstrual flow. Reported potential risks for education and health included unintended pregnancy as a result of not understanding the fertility cycle and hindered education due to menstruation. Of those who participated in in-depth interviews, the average age of menarche was 12.8 years old.

- 12. Grant, M. J., Lloyd, C. B., & Mensch, B. S. (2013). Menstruation and school absenteeism: Evidence from rural Malawi. *Comparative Education Review*, 18(9), 230– 284. <https://doi.org/10.1086/669121>**

Abstract: The provision of toilets and menstrual supplies appears to be a promising strategy to promote adolescent girls' school attendance and performance in less developed countries. In this article, we use the first round of the Malawi Schooling and Adolescent Survey (MSAS) to examine the individual- and school-level factors associated with menstruation-related school absenteeism. Although one-third of female students reported missing at least 1 day of school during their previous menstrual period, our data suggest that menstruation accounts only for a small proportion of all female absenteeism and does not create a gender gap in absenteeism. We find no evidence for school-level variance in menstruation-related absenteeism, suggesting that absenteeism due to menstruation is not sensitive to school environments. Rather, coresidence with a grandmother and spending time on schoolwork at home are associated with lower odds of absence during the last menstrual period.

- 13. Jewitt, S., & Ryley, H. (2014). It's a girl thing: Menstruation, school attendance, spatial mobility and wider gender inequalities in Kenya. *Geoforum*, 56, 137-147. <https://doi.org/10.1016/j.geoforum.2014.07.006>**

Abstract: Recent attention has been drawn to possible linkages between poor sanitation in sub-Saharan African schools and low attendance rates amongst post-pubescent girls. In particular, questions have been raised about the influence of menstruation and access to sanitary products on schoolgirl absenteeism but research on this topic is scarce. Moreover, the few detailed empirical studies that have been conducted in sub-Saharan Africa on this topic have produced contradictory results. These uncertainties coupled with theories of how concepts of pollution and taboo are used to construct or police spatial boundaries (and maintain power relations within society) provide an interesting context for examining everyday geographies of menstruation. Kisumu, Kenya provides the context for the study which utilizes a feminist political ecology framework to investigate cultural and spatial limitations associated with menstruation and puberty. Drawing on schoolgirls' lived experiences, we illustrate how emotional geographies of puberty and menstruation are productive of and help to reproduce gender inequalities in mobility and access to social capital resources (especially education). At the same time, we show how poverty coupled with low levels of sexual and reproductive health and rights education can exacerbate gendered bodily inequalities as girls face an increased risk of sexual exploitation when they reach puberty.

- 14. Long, J., Caruso, B.A., Lopez, D., Vancraeynest, K., Sahin, M., Andes, K.L., Freeman, M. (2013). *WASH in Schools Empowers Girls' Education in Rural Cochabamba, Bolivia: An assessment of menstrual hygiene management in schools*. UNICEF. Retrieved from: _**

https://www.unicef.org/wash/schools/files/Bolivia_MHM_Booklet_DM_15_Nov_sing le_0940_Bolivia.pdf

Summary: This study aimed to assess the challenges surrounding menstrual hygiene management among schoolgirls in Cochabamba, Bolivia. The researchers identified five factors that underlie menstrual-related challenges: societal, environmental, interpersonal, personal, and biological. One of the research findings was that at the personal level, many girls lack adequate information on menstruation and how to manage their menses, which can negatively affect their health. In order to improve schoolgirls' experience with menstruation, the researchers advocate for cross-sectoral responses. One of their key recommendations involved equipping girls with the knowledge and skillset to manage menstruation effectively; this included educating girls on menstruation before they get their first period and for students to receive teachings on both reproductive health and water, sanitation, and hygiene training.

15. Mason, L., Nyothach, E., Alexander, K., Odhiambo, F. O., Eleveld, A., Vulule, J, et al. (2013). 'We keep it secret so no one should know'--a qualitative study to explore young schoolgirls attitudes and experiences with menstruation in rural western Kenya. *PLoS One*, 8(11), e79132. <https://doi.org/10.1371/journal.pone.0079132>

Abstract: BACKGROUND: Keeping girls in school offers them protection against early marriage, teen pregnancy, and sexual harms, and enhances social and economic equity. Studies report menstruation exacerbates school-drop out and poor attendance, although evidence is sparse. This study qualitatively examines the menstrual experiences of young adolescent schoolgirls. METHODS AND FINDINGS: The study was conducted in Siaya County in rural western Kenya. A sample of 120 girls aged 14–16 years took part in 11 focus group discussions, which were analyzed thematically. The data gathered were supplemented by information from six FGDs with parents and community members. Emergent themes were: lack of preparation for menarche; maturation and sexual vulnerability; menstruation as an illness; secrecy, fear and shame of leaking; coping with inadequate alternatives; paying for pads with sex; and problems with menstrual hygiene. Girls were unprepared and demonstrated poor reproductive knowledge, but devised practical methods to cope with menstrual difficulties, often alone. Parental and school support of menstrual needs is limited, and information sparse or inaccurate. Girls' physical changes prompt boys and adults to target and brand girls as ripe for sexual activity including coercion and marriage. Girls admitted 'others' rather than themselves were absent from school during menstruation, due to physical symptoms or inadequate sanitary protection. They described difficulties engaging in class, due to fear of smelling and leakage, and subsequent teasing. Sanitary pads were valued but resource and time constraints result in prolonged use causing chafing. Improvised alternatives, including rags and grass, were prone to leak, caused soreness, and were perceived as harmful. Girls reported 'other girls' but not themselves participated in transactional sex to buy pads, and received pads from boyfriends.

CONCLUSIONS: In the absence of parental and school support, girls cope, sometimes alone, with menarche in practical and sometimes hazardous ways. Emotional and physical support mechanisms need to be included within a package of measures to enable adolescent girls to reach their potential.

16. McMahon, S. A., Winch, P. J., Caruso, B. A., Obure, A. F., Ogotu, E. A., Ochari, I. A., & Rheingans, R. D. (2011). 'The girl with her period is the one to hang her head' Reflections on menstrual management among schoolgirls in rural Kenya. *BMC International Health and Human Rights*, 11(1), 7. <https://doi.org/10.1186/1472-698x-11-7>

Abstract: BACKGROUND: The onset of menstruation is a landmark event in the life of a young woman. Yet the complications and challenges that can accompany such an event have been understudied, specifically in resource-poor settings. As interventions aim to improve female attendance in schools, it is important to explore how menstruation is perceived and navigated by girls in the school setting. This research conveys rural Kenyan schoolgirls' perceptions and practices related to menstruation.

METHODS: Data were collected at six rural schools in the Nyanza Province of Western Kenya. Using focus group discussions, in-depth interviews, and field notes from observations, researchers collected information from 48 primary schoolgirls and nine teachers. Systematic analysis began with a reading of transcripts and debriefing notes, followed by manual coding of the narratives.

RESULTS: Focus group discussions became opportunities for girls to share thoughts on menstruation, instruct one another on management practices and advise one another on coping mechanisms. Girls expressed fear, shame, distraction and confusion as feelings associated with menstruation. These feelings are largely linked to a sense of embarrassment, concerns about being stigmatized by fellow students and, as teachers explained, a perception that the onset of menstruation signals the advent of a girl's sexual status. Among the many methods for managing their periods, girls most frequently said they folded, bunched up or sewed cloth, including cloth from shirts or dresses, scraps of old cloth, or strips of an old blanket. Cloth was reported to frequently leak and cause chafing, which made school attendance difficult particularly as the day progressed. Attitudes and practices of girls toward menstruation have been arranged into personal, environmental and behavioral factors.

CONCLUSION: Further research on menstrual management options that are practical, sustainable and culturally acceptable must be conducted to inform future programs and policies that aim to empower young girls as they transition into womanhood. Stakeholders working within this and similar contexts must consider systematic mechanisms to explain to young girls what menstruation is and how to manage it. Providing sanitary supplies or guiding girls on how to create supplies serve as critical components for future interventions

17. Nanda, G., Lupee, J., & Tharaldson, J. (2016). *Menstrual Hygiene Management among Schoolgirls in Eastern Province of Zambia Qualitative Research Final Report*. Retrieved from: http://menstrualhygieneday.org/wp-content/uploads/2016/12/USAID_MHM-among-Schoolgirls-in-Eastern-Province-of-Zambia-FINAL508.pdf

Summary: This report is on qualitative research, conducted under the Schools Promoting Learning Achievement through Sanitation and Hygiene (SPLASH) project, to understand menstrual-related challenges for schoolgirls in Zambia. Through focus group discussions and key informant interviews, the researchers identified prevalent issues in relation to menstrual hygiene management. Issues were identified and organized through a socio-ecological model of change at the individual, interpersonal, community, and environmental level. Individual level

challenges included menstrual pain, fear at menarche, lack of access to products and knowledge on how to manage menses. Harassment and exclusion were discussed at the interpersonal level and beliefs surrounding menstruation at the community level; lack of access to adequate and private WASH facilities at school were among barriers at the environmental level. The authors conclude by encouraging the progression of menstrual hygiene management programs that address barriers at all levels, which their results show is necessary.

- 18. Oduor, C., Alexander, K. T., Oruko, K., Nyothach, E., Mason, L., Odhiambo, F. O., Vulule, J., Laserson, K. F., & Phillips-Howard, P. A. (2015). Schoolgirls' experiences of changing and disposal of menstrual hygiene items and inferences for WASH in schools. *Waterlines*, 34(4), 397–411. <https://doi.org/10.3362/1756-3488.2015.037>**

Abstract: Menstrual hygiene management (MHM) challenges during changing and disposal of menstrual items are important in low-income countries (LICs) where schools lack sufficient water and sanitation. Changing in poorly maintained latrines may expose girls to excrement and infection. We examine the frequency of dropping menstrual items and disposal of waste by schoolgirls in a menstrual solutions feasibility study in western Kenya. Drops when changing were reported in 17 per cent (20 per cent <16 years; 16.5 per cent 16 years plus; $p=0.04$) of girls' reports overall. Differences by socio-economic status were not evident. Fifty-four per cent of girls dropped at least once. A quarter of girls using pads and cups reported drops in the first few months, reducing to 10 per cent over time, compared with ~30 per cent among traditional item users. One in four accidental drops occurred at school during the study. When dropped at school, most girls swapped the dropped item for a new one, but 24 per cent brushed/washed the item and reused it. While no clinical events occurred during this study, data suggest dropping within latrines could place girls at potential risk of exposure to infection. Disposal of items, or emptying cups, was mostly into the latrine. We conclude that accidental dropping of menstrual items while changing is common, including at school. Prevention will be helped by improving poorly constructed sanitation facilities, shelving, privacy, and staggering/increasing break time for girls to change. Provision of special garbage bins to prevent clogging and overflow of latrines is recommended.

- 19. Oruko, K., Nyothach, E., Zielinski-Gutierrez, E., Mason, L., Alexander, K., Vulule, J., et al. (2015). 'He is the one who is providing you with everything so whatever he says is what you do': A Qualitative Study on Factors Affecting Secondary Schoolgirls' Dropout in Rural Western Kenya. *PLoS One*, 10(12), e0144321. <https://doi.org/10.1371/journal.pone.0144321>**

Abstract: Education is an effective way to improve girls' self-worth, health, and productivity; however there remains a gender gap between girls' and boys' completion of school. The literature around factors influencing girls' decision to stay in school is limited. Seven focus group discussions took place among 79 girls in forms 2 to 4 at secondary schools in rural western Kenya, to examine their views on why girls absent themselves or dropout from school. Data were analyzed thematically. Lack of resources, sexual relationships with boyfriends, and menstrual care problems were reported to lead directly to dropout or school absence. These were tied to girls increased vulnerability to pregnancy, poor performance in school, and punishments, which further increase school absence and risk of dropout. Poverty, unmet

essential needs, coercive sexual relationships, and an inequitable school environment collude to counter girls' resolve to complete their schooling. Lack of resources drive girls to have sex with boyfriends or men who provide them with essentials their family cannot afford, such as sanitary pads and transport to school. While these improve quality of their school life, this dynamic increases their exposure to sexual risk, pregnancy, punishment, and dropout. Evaluation of interventions to ameliorate these challenges is warranted, including provision of pocket money to address their needs.

20. *School Menstrual Hygiene Management in Malawi: More than Toilets | Toolkits.* (n.d.).

Retrieved November 24, 2020, from

<https://toolkits.knowledgesuccess.org/toolkits/very-young-adolescent-sexual-and-reproductive-health-clearinghouse/school-menstrual-hygiene>

Summary: This study answers a call from WaterAid (2009) for 'evidence from the field' that provides data on menstrual hygiene management (MHM) for school age girls in Malawi. Participatory group workshops, together with a questionnaire, semi-structured interviews, a literature review and observations are here presented to WaterAid with a view to determining one or several recommendations for improved MHM in Malawian schools.

21. Su, J. J., & Lindell, D. (2016). Promoting the menstrual health of adolescent girls in China. *Nursing & Health Sciences*, 18(4), 481–487.

<https://doi.org/10.1111/nhs.12295>

Abstract: In China, nurses have limited presence in schools, thus, adolescent girls often lack accurate information about menstrual health, which may lead to incorrect and unhealthy menstrual-related behavior. This study investigated the effects of a culturally and developmentally tailored nursing intervention on the menstrual health of adolescent girls in China. Following institutional review board approval, adolescent girls aged 12–15 were recruited from two schools. A quasi-experimental, pretest-posttest design examined the effects of five interactive education sessions on menstrual health. The final sample included 116 adolescent girls. Significant improvement was observed in the intervention group regarding menstrual knowledge, confidence in performing menstrual healthcare behavior, and dysmenorrhea related self-care behavior. A nurse-managed education program improved adolescent girls' menstrual knowledge, promoted a more positive attitude, encouraged confidence, and improved pain relief practice. We recommend that professional nurses globally advocate for school nursing and routine menstrual health education for adolescent girls.

22. Tamiru, S., Mamo, K., Acidria, P., Mushi, R., Ali, C. S., & Ndebele, L. (2015). Towards a sustainable solution for school menstrual hygiene management: cases of Ethiopia, Uganda, South-Sudan, Tanzania, and Zimbabwe. *Waterlines*, 34(1), 92-102. DOI: 10.3362/1756-3488.2015.009

Abstract: African schoolgirls face considerable challenges as a result of menstruation and its management. Menstruation is seen as secret and regarded as taboo. As a result, girls are not receiving adequate support from home, schools, or the community. They are left to address the challenge on their own, which consequently affects their school performance. Development

interventions that deal only with the supply of materials cannot resolve the problem in a sustainable manner. We need to have a comprehensive approach that can improve: knowledge, attitude, and practice of girls, parents, and the community; sanitary materials supply; the policy environment; and the physical infrastructure. The issue of menstrual hygiene management is gaining recognition as part of the development agenda for improving girls' school participation. But there is little research and few practical case studies have been conducted to inform policy and practice. SNV Netherlands Development Organization is addressing menstrual hygiene under its WASH in School program in Asia, Africa, and Latin America. This article highlights baseline survey findings of the current menstrual hygiene management practices in the project areas of Ethiopia, South Sudan, Uganda, Tanzania, and Zimbabwe and recommends the approach piloted.

Empowerment

- 23. Prata, N., Fraser, A., Huchko, M. J., Gipson, J. D., Withers, M., Lewis, S., et al. (2017). Women's Empowerment and Family Planning: A Review of the Literature. *Journal of Biosocial Science*, 49(6), 713–743. <https://doi.org/10.1017/s0021932016000663>**

Summary: This paper reviews the literature examining the relationship between women's empowerment and contraceptive use, unmet need for contraception and related family planning topics in developing countries. Searches were conducted using PubMed, Popline and Web of Science search engines in May 2013 to examine literature published between January 1990 and December 2012. Among the 46 articles included in the review, the majority were conducted in South Asia (n=24). Household decision-making (n=21) and mobility (n=17) were the most commonly examined domains of women's empowerment. Findings show that the relationship between empowerment and family planning is complex, with mixed positive and null associations. Consistently positive associations between empowerment and family planning outcomes were found for most family planning outcomes but those investigations represented fewer than two-fifths of the analyses. Current use of contraception was the most commonly studied family planning outcome, examined in more than half the analyses, but reviewed articles showed inconsistent findings. This review provides the first critical synthesis of the literature and assesses existing evidence between women's empowerment and family planning use.

- 24. Schooler, D., Ward, L. M., Merriwether, A., & Caruthers, A. S. (2005). Cycles of shame: Menstrual shame, body shame, and sexual decision-making. *Journal of Sex Research*, 42(4), 324–334. <https://doi.org/10.1080/00224490509552288>**

Summary: Although numerous factors have been implicated in women's sexual decision-making, less attention has been focused on how their feelings about their bodies and reproductive functions affect these processes. Recent findings link menstrual shame to lower levels of sexual activity and higher levels of sexual risk; however, the mechanisms behind these relations remain unexplored. Accordingly, this study investigates the contributions of menstrual shame and global body shame to sexual decision-making among 199 undergraduate women. Using structural equation modeling, we evaluated a mediated model, whereby menstrual shame is indirectly associated with sexual decision-making via body shame. As expected, women who reported feeling more comfort about menstruation also reported more body

comfort and, in turn, more sexual assertiveness, more sexual experience, and less sexual risk.

25. Sommer, M., Ferron, S., Cavill, S., & House, S. (2014). Violence, gender and WASH: spurring action on a complex, under-documented and sensitive topic. *Environment and Urbanization*, 27(1), 105-116. <https://doi.org/10.1177%2F0956247814564528>

Abstract: The global community of water, sanitation and hygiene (WASH) researchers, practitioners and policy makers has to date inadequately addressed the challenge of vulnerability to violence in relation to access to water and sanitation in development and humanitarian emergency contexts. Reasons may include the lack of valid and reliable documentation of girls', boys', women's, and men's experiences of violence while accessing water and/or sanitation facilities; the sensitivity of the topic, with secrecy around individuals' experiences of violence and their sanitation needs further hindering the collection of reliable data; the complexity of understanding the gendered dimensions of vulnerability to violence, with girls and women at least anecdotally reported to be more likely to experience violence in relation to WASH; and the likelihood that many WASH practitioners lack training in gender and violence, affecting their ability to deliver adequate programming and evaluation. In an effort to encourage increased action and learning on the intersection of gender, violence and WASH, a review of the existing evidence and practice was conducted. Findings indicate the need for more systematic, reliable, and ethically conducted monitoring and learning on this topic to build a more solid evidence base, while also refining key principles for improved policy and programming.

26. Westeneng, J., & D'Exelle, B. (2017). Reproductive Health and Bodily Integrity in Tanzania. *Studies in Family Planning*, 48(4), 323–341.

Abstract: Several policy initiatives support the empowerment of women to improve their reproductive health. Little is known, however, about the inverse effect that reproductive health might have on women's empowerment. Women are pressured to conform to their reproductive role, and an inability to do so might affect their empowerment, including control over their own body. Using a panel dataset of 504 married women in Northern Tanzania, we find that women who experienced a pregnancy loss show more tolerant views of partner violence and that child mortality lowers their perceived control over the sexual relationship with their spouse. The number of living children did not affect bodily integrity. These results confirm that women's bodily integrity is partly dependent on the ability to fulfill their reproductive role. They strengthen the case for policies and programs that improve women's reproductive health and underline the importance of counselling after pregnancy or child loss.

Relevant Articles Cross-Referenced from Other Sections

In Urogenital Tract Infections

Sumpter, C., & Torondel, B. (2013). A Systematic Review of the Health and Social Effects of Menstrual Hygiene Management. *PLoS One*, 8(4), e62004.

In Experience with Puberty and Menarche

Aniebue, U. U., Aniebue, P. N., & Nwankwo, T. O. (2009). The impact of pre-menarcheal training

on menstrual practices and hygiene of Nigerian school girls. *The Pan African Medical Journal*, 2, 9.

Chandra-Mouli, V., & Patel, S. V. (2017). Mapping the knowledge and understanding of menarche, menstrual hygiene and menstrual health among adolescent girls in low- and middle- income countries. *Reprod Health*, 14(1), 30.

In Programmatic Interventions

Montgomery, P., Hennegan, J., Dolan, C., Wu, M., Steinfield, L., & Scott, L. (2016). Menstruation and the Cycle of Poverty: A Cluster Quasi-Randomised Control Trial of Sanitary Pad and Puberty Education Provision in Uganda. *PLoS One*, 11(12), e0166122.

Montgomery, P., Ryus, C. R., Dolan, C. S., Dopson, S., & Scott, L. M. (2012). Sanitary Pad Interventions for Girls' Education in Ghana: A Pilot Study. *PLoS One*, 7(10), e48274.

Oster, E., & Thornton, R. (2009). *Menstruation and education in Nepal*. NBER Working Paper Series. Retrieved from: www.nber.org/papers/w14853.

BIOLOGICAL CONTEXT

Biological Mechanisms of the Menstrual Cycle

1. Critchley, H. O. D., Brenner, R. M., Henderson, T. A., Williams, K., Nayak, N. R., Slayden, O. D., Millar, M. R., & Saunders, P. T. K. (2001). Estrogen Receptor β , But Not Estrogen Receptor α , Is Present in the Vascular Endothelium of the Human and Nonhuman Primate Endometrium 1. *The Journal of Clinical Endocrinology & Metabolism*, 86(3), 1370–1378. <https://doi.org/10.1210/jcem.86.3.7317>

Abstract: Estrogen action is dependent upon the presence of specific ligand-activated receptors in target tissues. The aim of the present experiments was to compare the spatial and temporal pattern of expression of estrogen receptor β (ER β) with that of ER α in full thickness endometrial samples (from the superficial to the basal zone) obtained from both women and rhesus macaques. Immunohistochemical localization with specific antibodies revealed that ER α and ER β were both expressed in nuclei of the glands and stroma. Consistent with previous studies, expression of ER α declined in the glands and stroma of the functionalis during the secretory phase. The luminal epithelium also displayed positive immunoreactivity for ER β . Expression of ER β declined in glandular cell nuclei, but not stroma, within the functionalis during the late secretory phase. Levels of expression of ER α and ER β in all cellular compartments remained unchanged in the basalis. Both receptor subtypes were detected on Western blots using proteins extracted from uterine samples obtained throughout the menstrual cycle. There was a striking contrast between the pattern of expression of ER α and ER β in the vascular endothelium and the perivascular cells surrounding endometrial blood vessels; only ER β was present in the endothelial cell population, although both forms of ER were expressed in perivascular cells. We conclude that estrogen action(s) within the vascular endothelium in the endometrium may be mediated via direct binding to the ER β isoform and that these cells could therefore be a target for agonists or antagonists that selectively target the β form of the ER.

2. Critchley, H. O. D., Henderson, T. A., Kelly, R. W., Scobie, G. S., Evans, L. R., Groome, N. P., & Saunders, P. T. K. (2002). Wild-type estrogen receptor (ER β 1) and the splice variant (ER β cx/ β 2) are both expressed within the human endometrium throughout the normal menstrual cycle. *Journal of Clinical Endocrinology and Metabolism*, 87(11), 5265–5273. <https://doi.org/10.1210/jc.2002-020502>

Abstract: Estrogen action is mediated via two subtypes of the estrogen receptor (ER), usually referred to as ER α and ER β . We have previously compared the spatial and temporal expressions of ER α and ER β proteins in human endometrium and reported that endothelial cells exclusively express ER β . In the present study we have extended our investigations to compare the pattern of expression of wild-type (ER β 1) and a newly identified ER β variant isoform (ER β cx/ β 2) that lacks the ability to bind steroids. mRNAs encoding both ER β 1 and ER β cx/ β 2 receptors were identified in human endometrial extracts by RT-PCR. Quantitative TaqMan R-TPCR demonstrated that levels of total mRNAs were increased significantly premenstrually as circulating progesterone levels declined. ER β 1 and ER β cx/ β 2 proteins were

identified within multiple cell types within the endometrium using isotype-specific monoclonal antibodies; immunoexpression of ER β cx/ β 2 appeared less intense than that of ER β 1 in endometrial glandular epithelium and endothelial cells. Immunoexpression of ER β 1 appeared unchanged throughout the menstrual cycle. In contrast, levels of ER β cx/ β 2-specific immunoreactivity were specifically reduced in gland cells within the functional layer, but not in those of the basal layer, in the midsecretory phase. It is possible that coexpression of ER β cx/ β 2 in cells containing ER β 1 and/or ER α may modulate the effects of estrogens on the endometrium.

3. Funk, C. D. (2001). Prostaglandins and leukotrienes: Advances in eicosanoid biology. *Science*, 294(5548), 1871-1875. <https://doi.org/10.1126/science.294.5548.1871>

Abstract: Prostaglandins and leukotrienes are potent eicosanoid lipid mediators derived from phospholipase-released arachidonic acid that are involved in numerous homeostatic biological functions and inflammation. They are generated by cyclooxygenase isozymes and 5-lipoxygenase, respectively, and their biosynthesis and actions are blocked by clinically relevant nonsteroidal anti-inflammatory drugs, the newer generation coxibs (selective inhibitors of cyclooxygenase-2), and leukotriene modifiers. The prime mode of prostaglandin and leukotriene action is through specific G protein-coupled receptors, many of which have been cloned recently, thus enabling specific receptor agonist and antagonist development. Important insights into the mechanisms of inflammatory responses, pain, and fever have been gleaned from our current understanding of eicosanoid biology.

4. Galant, C., Berlière, M., Dubois, D., Verougstraete, J. C., Charles, A., Lemoine, P., Kokorine, I., Eeckhout, Y., Courtoy, P. J., & Marbaix, E. (2004). Focal expression and final activity of matrix metalloproteinases may explain irregular dysfunctional endometrial bleeding. *American Journal of Pathology*, 165(1), 83–94. [https://doi.org/10.1016/S0002-9440\(10\)63277-4](https://doi.org/10.1016/S0002-9440(10)63277-4)

Abstract: Irregular dysfunctional bleeding of the endometrium (ie, metrorrhagia without organic lesion) is common in women, whether treated or not with ovarian hormones. Several matrix metalloproteinases (MMPs) become normally expressed and/or activated at menstruation and cause extracellular matrix breakdown. We therefore explored whether episodes of irregular dysfunctional bleeding could be associated with untimely MMP activity. By histology, foci of stromal breakdown were exclusively found in the endometrium of metrorrhagic women at bleeding. In these foci, 1) expression of estrogen receptor- α and progesterone receptor was altered; 2) collagenase-1 (MMP-1), stromelysin-1 (MMP-3), and gelatinase B (MMP-9) became detected in stromal cells, together with MMP-9 in neutrophils; and 3) gelatinase A (MMP-2) was more expressed and immunolocalized at the membrane of stromal cells. By biochemistry, endometrial lysates from nonbleeding metrorrhagic patients contained more latent and active MMP-2 and -9 than age-matched controls; at bleeding, collagenase activity, MMP-9, and active MMP-2 were strikingly increased whereas tissue inhibitor of metalloproteinases-1 (TIMP-1) was considerably decreased. As a functional assay, in situ gelatin zymography revealed large areas of gelatinolytic activity only in endometrium of bleeding patients. Altogether, these results strongly suggest that inappropriate focal expression and activation of several MMPs, combined with decreased inhibition, trigger

irregular dysfunctional endometrial bleeding.

- 5. Jacobsen, B. M., & Horwitz, K. B. (2012). Progesterone receptors, their isoforms and progesterone regulated transcription. *Molecular and Cellular Endocrinology*, 357(1-2), 18-29. <https://doi.org/10.1016/j.mce.2011.09.016>**

Abstract: This review discusses mechanisms by which progesterone receptors (PR) regulate transcription. We examine available data in different species and tissues regarding: (1) regulation of PR levels; and (2) expression profiling of progestin-regulated genes by total PRs, or their PRA and PRB isoforms. (3) We address current views about the composition of progesterone response elements, and postulate that PR monomers acting through “half-site” elements are common, entailing cooperativity with neighboring DNA-bound transcription factors. (4) We summarize transcription data for multiple progestin-regulated promoters as directed by total PR, or PRA vs. PRB. We conclude that current models and methods used to study PR function are problematical, and recommend that future work employ cells and receptors appropriate to the species, focusing on analyses of the effects of endogenous receptors targeting endogenous genes in native chromatin.

- 6. Krikun, G., Schatz, F., Taylor, R., Critchley, H. O. D., Rogers, P. A. W., Huang, J., & Lockwood, C. J. (2005). Endometrial endothelial cell steroid receptor expression and steroid effects on gene expression. *Journal of Clinical Endocrinology and Metabolism*, 90(3), 1812–1818. <https://doi.org/10.1210/jc.2004-1814>**

Abstract: Controversy exists regarding the expression of specific steroid receptor proteins and mRNA in human microvascular endometrial endothelial cells (HEECs). Thus, we studied steroid receptor expression in early passaged HEEC cultures and freshly isolated HEECs. Analysis of estrogen receptor (ER) and progesterone receptor (PR) mRNA levels was carried out with real-time quantitative RT-PCR, and the repertoire of genes activated by their respective steroid ligands was assessed by mRNA microarray analyses of 18,400 genes and expressed sequence tags. We observed that cultured and freshly isolated HEECs each express ER- β mRNA but not ER- α . In addition, PR mRNA was also detectable in both HEEC sources. Microarray analysis demonstrated that treatment of HEEC cultures with either estradiol or medroxyprogesterone acetate produced differential effects on a wide variety of genes, and cluster analysis demonstrated that many of the genes are involved in intracellular signaling and enzymatic pathways. Thus, quantitative RT-PCR and microarray analyses demonstrate that HEECs express ER- β and PR mRNA and that gene expression by HEECs is differentially regulated by treatment with estrogen or progestin.

- 7. Mertens, H. J. M. M., Heineman, M. J., Theunissen, P. H. M. H., De Jong, F. H., & Evers, J. L. H. (2001). Androgen, estrogen and progesterone receptor expression in the human uterus during the menstrual cycle. *European Journal of Obstetrics and Gynecology and Reproductive Biology*, 98(1), 58–65. [https://doi.org/10.1016/S0301-2115\(00\)00554-6](https://doi.org/10.1016/S0301-2115(00)00554-6)**

Abstract: Cyclic changes in steroid receptor expression in endometrial cells are considered a reflection of its differential functions. Besides estrogen and progestogens, androgens have also been suggested to affect the biological function of the female reproductive tract. We

investigated the distribution and intensity of immuno-cytochemical estrogen receptor (ER), progesterone receptor (PR) and androgen receptor (AR) staining in the various cell types of human endometrium and myometrium during the different menstrual cycle phases in 30 paraffin-embedded sections. AR expression in endometrial stromal cells decreased gradually from early proliferative till mid secretory phase. In the late secretory phase, AR expression in all cell types distinguished. Staining of epithelial cells was moderate. The disappearance of AR expression before cyclic separation of endometrial tissue may be causally related or just an epiphenomenon. Due to local competition for 5 α -reduction of testosterone and the excess of progesterone in the secretory phase, the level of dihydrotestosterone (DHT) will be diminished. Hypothetically, if AR synthesis in endometrium would be DHT-dependent, it would explain the lack of AR expression in the late secretory phase.

8. Mesiano, S. (2007). Myometrial progesterone responsiveness. *Seminars in Reproductive Medicine*, 25(1), 5-13. <https://doi.org/10.1055/s-2006-956771>

Abstract: Progesterone actions in human pregnancy are controlled by the extent of myometrial progesterone responsiveness. Current progress in unraveling the biochemistry for myometrial progesterone responsiveness at the genomic and nongenomic levels have lead to novel hypotheses regarding the role of these pathways in the hormonal control of human pregnancy and parturition. For the genomic pathway, progesterone interacts with the type-B nuclear progesterone receptor (nPR-B), which decreases expression of contraction-associated genes. For the nongenomic pathway, progesterone interacts with membrane-associated PRs (mPRs) to modulate directly intracellular Ca²⁺ and cyclic adenosine monophosphate (cAMP) levels. During most of human pregnancy the genomic and nongenomic pathway cooperate to maintain myometrial relaxation. However, at parturition the relaxing actions of progesterone are nullified by changes in myometrial progesterone responsiveness. This occurs by (1) increased expression of the nPR variants (e.g., PR-A and/or PR-C) and changes in nPR coregulator levels that together repress the transcriptional activity of PR-B; and (2) increased expression of specific mPRs, especially mPR β , which augments contractility by decreasing intracellular cAMP. Functional progesterone withdrawal may be induced by locally produced prostaglandins that alter myometrial nPR expression. This may be an important physiological link between the control of parturition and the immune/inflammatory process.

9. Milne, S. A., Perchick, G. B., Boddy, S. C., & Jabbour, H. N. (2001). Expression, localization, and signaling of PGE₂ and EP₂/EP₄ receptors in human nonpregnant endometrium across the menstrual cycle. *Journal of Clinical Endocrinology and Metabolism*, 86(9), 4453–4459. <https://doi.org/10.1210/jcem.86.9.7856>

Abstract: This study was designed to elucidate the sites of synthesis and action of PGE₂ in the nonpregnant human uterus across the menstrual cycle. The sites of expression of PGE synthase and synthesis of PGE₂ were investigated by immunohistochemistry using full thickness uterine biopsies. Expression of PGE synthase and synthesis of PGE₂ were localized to glandular epithelial and endothelial cells in both basalis and functionalis regions of the human endometrium. By contrast, stromal staining was predominantly localized in the functionalis layer. Some cyclical variation in expression of PGE synthase and PGE₂ synthesis was observed, with reduced expression/synthesis detected in the stromal compartment of the functionalis

during the late secretory phase of the menstrual cycle. Subsequently, we assessed the site of action of PGE₂ by investigating the expression of two PGE₂ receptor isoforms, namely EP₂ and EP₄. Cyclical variation in endometrial EP₂ and EP₄ receptor mRNA expression was quantified by TaqMan quantitative RT-PCR using RNA isolated from endometrial tissue collected across the menstrual cycle. No differences in EP₂ receptor mRNA expression were detected; however, EP₄ receptor mRNA expression was significantly higher in late proliferative stage ($P < 0.05$) than in early, mid, and late secretory stage endometrium. Expression patterns of EP₂ and EP₄ receptors were localized by nonradioactive in situ hybridization using fluorescein isothiocyanate end-labeled oligonucleotide probes. Expression of both receptors was observed in endometrial glandular epithelial and vascular cells, with no notable spatial or temporal variation. Finally, signaling of EP₂/EP₄ receptors was assessed by investigating cAMP generation in vitro after stimulation with PGE₂. Endometrial cAMP generation in response to PGE₂ was significantly greater in proliferative tissue compared with early and midsecretory stage tissue (3.77 ± 0.85 vs. 1.96 ± 0.28 and 1.38 ± 0.23 , respectively; $P < 0.05$). In conclusion, this study demonstrates glandular and vascular coexpression of PGE synthase, PGE₂, EP₂, and EP₄ receptors and suggests an autocrine/paracrine role for PGE₂ in epithelial/endothelial cell function in the human endometrium.

- 10. Mueller, M. D., Vigne, J. L., Minchenko, A., Lebovic, D. I., Leitman, D. C., & Taylor, R. N. (2000). Regulation of vascular endothelial growth factor (VEGF) gene transcription by estrogen receptors α and β . *Proceedings of the National Academy of Sciences of the United States of America*, 97(20), 10972–10977.
<https://doi.org/10.1073/pnas.200377097>**

Abstract: Vascular endothelial growth factor (VEGF) mediates angiogenic activity in a variety of estrogen target tissues. To determine whether estrogen has a direct transcriptional effect on VEGF gene expression, we developed a model system by transiently transfecting human VEGF promoter-luciferase reporter constructs into primary human endometrial cells and into Ishikawa cells, derived from a well-differentiated human endometrial adenocarcinoma. In primary endometrial epithelial cells, treatment with 17 β -estradiol (E₂) resulted in a 3.8-fold increase in luciferase activity, whereas a 3.2-fold induction was demonstrated for stromal cells. Our Ishikawa cells had less than 100 functional estrogen receptors (ER)/cell and were therefore cotransfected with expression vectors encoding either the α - or the β -form of the human ER. In cells cotransfected with ER α , E₂ induced 3.2-fold induction in VEGF-promoter luciferase activity. A 2.3-fold increase was observed in cells cotransfected with ER β . Through specific deletions, the E₂ response was restricted to a single 385-bp PvuII-SstI fragment in the 5' flanking DNA. Cotransfection of this upstream region with a DNA binding domain ER mutant, or site-directed mutagenesis of a variant ERE within this fragment, resulted in the loss of the E₂ response. Electromobility shift assays demonstrated that this same ERE sequence specifically binds estradiol-ER complexes. These studies demonstrate that E₂-regulated VEGF gene transcription requires a variant ERE located 1.5 kb upstream from the transcriptional start site. Site-directed mutagenesis of this ERE abrogated E₂-induced VEGF gene expression.

- 11. Nagase, H., Visse, R., & Murphy, G. (2006). Structure and function of matrix metalloproteinases and TIMPs. *Cardiovascular Research*, 69(3), 562-573.**

<https://doi.org/10.1016/j.cardiores.2005.12.002>

Abstract: Matrix metalloproteinases (MMPs), also called matrixins, function in the extracellular environment of cells and degrade both matrix and non-matrix proteins. They play central roles in morphogenesis, wound healing, tissue repair and remodelling in response to injury, e.g. after myocardial infarction, and in progression of diseases such as atheroma, arthritis, cancer and chronic tissue ulcers. They are multi-domain proteins and their activities are regulated by tissue inhibitors of metalloproteinases (TIMPs). This review introduces the members of the MMP family and discusses their domain structure and function, proenzyme activation, the mechanism of inhibition by TIMPs and their significance in physiology and pathology.

12. Raffetto, J. D., & Khalil, R. A. (2008). Matrix metalloproteinases and their inhibitors in vascular remodeling and vascular disease. *Biochemical Pharmacology*, 75(2), 346–359. <https://doi.org/10.1016/j.bcp.2007.07.004>

Abstract: Matrix metalloproteinases (MMPs) are a family of proteolytic enzymes that degrade various components of the extracellular matrix (ECM). Members of the MMP family include collagenases, gelatinases, stromelysins, matrilysins and membrane-type MMPs. ProMMPs are cleaved into active forms that promote degradation of ECM proteins. Also, recent evidence suggests direct or indirect effects of MMPs on ion channels in the endothelium and vascular smooth muscle, and on other mechanisms of vascular relaxation/contraction. Endogenous tissue inhibitors of metalloproteinases (TIMPs) reduce excessive proteolytic ECM degradation by MMPs. The balance between MMPs and TIMPs plays a major role in vascular remodeling, angiogenesis, and the uterine and systemic vasodilation during normal pregnancy. An imbalance in the MMPs/TIMPs activity ratio may underlie the pathogenesis of vascular diseases such as abdominal aortic aneurysm, varicose veins, hypertension and preeclampsia. Downregulation of MMPs using genetic manipulations of endogenous TIMPs, or synthetic pharmacological inhibitors such as BB-94 (Batimastat) and doxycycline, and Ro-28-2653, a more specific inhibitor of gelatinases and membrane type 1-MMP, could be beneficial in reducing the MMP-mediated vascular dysfunction and the progressive vessel wall damage associated with vascular disease.

13. Tamura, K., Sakurai, T., & Kogo, H. (2006). Relationship between prostaglandin E2 and vascular endothelial growth factor (VEGF) in angiogenesis in human vascular endothelial cells. *Vascular Pharmacology*, 44(6), 411–416. <https://doi.org/10.1016/j.vph.2006.02.009>

Abstract: To address the role of prostaglandin E2 (PGE2) in tube formation of endothelial cells and the relationships between the action of PGE2 and vascular endothelial growth factor (VEGF), cultured human umbilical vein endothelial cells (HUVECs) were used to evaluate tube formation on Matrigel and the expression of angiogenesis-related genes. PGE2 treatment stimulated the tube-like formation of HUVECs. Whereas VEGF-induced tube formation was significantly suppressed by ETYA, an inhibitor of arachidonic acid metabolism, or SU5614, an inhibitor of VEGF-receptor tyrosine kinase, the stimulatory effect of PGE2 was observed in the presence of ETYA or SU5614. Thus, PGE2 counteracted both ETYA- and SU5614-induced blockage of angiogenesis in the presence of VEGF. VEGF induced cyclooxygenase (COX) -2 mRNA expression in HUVECs and increased the PGE2 concentration in the medium. PGE2

treatment enhanced the expression of VEGF mRNA. These findings suggest that PGE2 directly stimulates angiogenesis, apart from VEGF signaling, and further induces VEGF expression in HUVECs. In addition, the effect of VEGF on angiogenesis may be mediated, in part, by PGE2 secretion.

14. Wenger, R. H. (2002). Cellular adaptation to hypoxia: O₂-sensing protein hydroxylases, hypoxia-inducible transcription factors, and O₂-regulated gene expression . *The FASEB Journal*, 16(10), 1151–1162. <https://doi.org/10.1096/fj.01-0944rev>

Abstract: Although it was known for a long time that oxygen deprivation leads to the transcriptional induction of the gene encoding erythropoietin, the molecular mechanisms behind this process remained enigmatic. The cloning of the hypoxia-inducible factors (HIFs), the finding that HIF-1 regulates the expression of many more genes apart from erythropoietin, and the elucidation of the oxygen-dependent mechanisms degrading the HIF a subunits recently led to the spectacular discovery of the molecular principles of oxygen sensing. This review aims to summarize our current knowledge of oxygen-regulated gene expression.— Wenger, R. H. Cellular adaptation to hypoxia: O₂-sensing protein hydroxylases, hypoxia-inducible transcription factors, and O₂-regulated gene expression. *FASEB J.* 16, 1151–1162 (2002)

Menstrual Disorders

General

1. Adebimpe, W., Farinloye, E., & Adeleke, N. (2016). Menstrual pattern and disorders and impact on quality of life among university students in South-Western Nigeria. *Journal of Basic and Clinical Reproductive Sciences*, 5(1), 27. <https://doi.org/10.4103/2278-960X.175741>

Abstract: BACKGROUND: Menarche is one of the signals of a woman's transition from childhood to adulthood. Abnormal menstrual pattern could cause morbidities that may disrupt daily activities. AIM: To assess the pattern of menstrual disorders and impact on the quality of life among university students in South-Western Nigeria. SUBJECTS AND METHODS: This descriptive, cross-sectional study was carried out among 494 university students in South-Western Nigeria, selected using multistage sampling method. Research instruments were semi-structured, self-administered, and pretested questionnaires. Data were analyzed using the SPSS software, version 17.0 (Chicago, IL, USA). RESULTS: Mean age at menarche was 13.6 (1.1) years. About 89.1% (440/494) were aware or foretold of the coming of menarche. Major sources of information include parents, relatives, friends, and health care workers. About 82.8% (409/494) had regular monthly menstrual flow pattern, 21.9% (108/494) had menorrhagia, 16.0% (79/494) had oligomenorrhoea, 9.1% (45/494) had polymenorrhoea, while 65.8% (325/494) had occasional associated dysmenorrhoea. About 10.7% (53/494) had treated dysmenorrhoea in a health facility in the last 1 year. Menstruation usually puts tension on 46.2% (228/494) of respondents, disrupted work at school in 38.9% (192/494), and at home among 42.9% (212/494) of them, while it had prevented going to school for at least 1 day in the last 6 months among 15.6% (77/494) of respondents. Girls with irregular menstrual pattern were 1.4,

1.8, and 1.6 times more likely to have experienced pressure or lenition on them, had school work, and home work disrupted, respectively. Girls who were precounseled about menarche were twice less likely to have had disruptions of school activities compared to those who were not precounseled (odds ratio = 0.5, 05% confidence interval: 1.96–3.01, P = 0.01).

CONCLUSION: This study demonstrated that menstrual disorders constitute a challenge to a significant percentage of adolescents. This also underscores the need for guided sexuality and menstrual related information targeted at youths.

**2. Amaza, D. S., Sambo, N., Zirahei, J. V., Dalori, M. B., Japhet, H., Toyin, H. (2011).
Menstrual pattern among female medical students in University of Maiduguri,
Nigeria. *British Journal of Medicine & Medical Research*, 2(3), 327-337.
<https://imsear.searo.who.int/handle/123456789/162732>**

Abstract: AIMS: To determine menstrual pattern and disorder associated with it among female medical students.

STUDY DESIGN: Cross-sectional study.

PLACE AND DURATION OF STUDY: College of Medical Sciences, University of Maiduguri, Borno State, Nigeria between February – September 2010.

METHODOLOGY: Self descriptive cross-sectional study was carried out among 169 Medical students (MBBS II-V) between the ages 19-46 years. Respondents were selected from each class using stratified random sampling method. Stratification was done according to their class. Questionnaires were designed and administered to the respondents to complete. Three researchers and two research assistances were on site to assist. Students were briefed on the objective of the study and duly completed questionnaires were collected and analyzed. Subjects who had primary amenorrhea and/or history of abdominal or pelvic surgery were not eligible for the study. The questionnaire included data such as; age of menarche, menstrual pattern, severity of pain (dysmenorrheal), marital status, effects of exercise, socioeconomic status, Body mass Index (BMI) and Diet. The method of observation involved personal interaction and questioning of respondent to find out if they had anything peculiar about their cycle. The number of days of menstrual flow on menarche and number of pads use per day were in the questionnaire.

RESULTS: It was observed that 148(87.6%) respondents had regular length of menstrual cycle, particularly in the age groups 20-22 and 23-26 years which recorded 39 and 43 respondents respectively. Irregular menstrual cycle was found in 21(12.4%) respondents, which showed its peak at the age group of 17-19(33.3%) years, between age groups. It was also observed that 118(69.8%) respondents had painful menstrual flow, out of which 71(60.2%) had mild pain, 30(29.7%) had moderate pain while 17(14.4%) had severe pain. Result of length of menstrual cycle between single and married respondents showed that, 20(71.4%) of single respondents had short menstrual length compared to 8(28.6%) married respondents of corresponding short menstrual length. It was revealed that in 148(87.6) respondents that had regular menstrual cycle type, 106(71.6%) menstrual flow was average, while in 31(21.0%), it was scanty and heavy in 11(7.4%) respondents. 10(47.6%) respondent had average irregular menstrual cycle, while 9(42.9%) and 2(9.5%) respondents had scanty and heavy irregular menstrual cycles The result showed no significant variation in frequency of menstrual

cycle ($p=0.5$). 99(58.6%) of respondents did no physical exercise; while 70(41.4%) did at least 30 minutes exercise ($p=0.38$). 101(59.8%) respondents belong to high upper, 51(30.2%) in upper-middle and 17(10.0%) belonged to lower socioeconomic status ($p=0.14$). 135(80.0%) respondents had daily fast food habits, out of which 95(80.5%) had positive history of pain and 34(20.0%) had no daily fast food ($P=0.80$). 30(17.8) respondents were underweight, 120(71.0%) had average weight and 19(11.2%) respondents were overweight ($p=0.20$).

CONCLUSION: Study has established mean age at menarche, menstrual pattern and menstrual disorder (pain) in relation to BMI, exercise and socioeconomic factor among female Medical Students of University of Maiduguri, Nigeria. The prevalence of dysmenorrhea was very high among the female medical students. Although further research is needed, as relationship between Menstrual cycle, obesity, diet and exercise are conflicting with other studies.

3. Amu, E. O., Bamidele, J. O. (2014). Prevalence of menstrual disorders among adolescent girls in Osogbo, South Western Nigeria, *Int J Adolesc Med Health*, 26(1), 101-106. <https://doi.org/10.1515/ijamh-2013-0500>

BACKGROUND: Menstrual disorders are common sources of morbidity among adolescent girls and often cause anxiety for these girls and their families.

OBJECTIVE: This paper aims to determine the patterns of menstruation as well as the prevalence of menstrual disorders and their consequences among adolescent girls in Osogbo, South Western Nigeria.

SUBJECTS: Adolescent school girls aged 10-19 years comprised the sample.

METHODS: The study employed a descriptive cross-sectional design. A pre-tested, self administered, semi-structured questionnaire was used to elicit information from 402 adolescents selected from private secondary schools in the Osogbo Local Government Area (LGA) of Osun State, using a multistage sampling technique. Data were analyzed using SPSS version 15.

RESULTS: A total of 391 (97.8%) respondents had heard about menstruation before, with the three most important sources of information being their mothers (81.8%), teachers (7.4%), and peer groups (6.1%). The mean age at menarche was 12.5 ± 1.0 years. Menstrual bleeding lasted between 2-7 days in 81.1% and cycle length lasted for 21-35 days in 81.6% of the respondents. The three most important menstrual disorders they experienced were dysmenorrhea (77.8%), menorrhagia (57.4%) and metrorrhagia (18.6%), among others. Menstrual disorders, especially dysmenorrhea, interfered with the daily activities of the respondents.

CONCLUSION: The prevalence of menstrual disorders among adolescents in the Osogbo LGA is high. Measures should be undertaken to educate the adolescents and their mothers about menstrual disorders and to mitigate their effects on the social and academic lives of these adolescents.

4. Baidya, S., Debnath, M., Das, R. (2014). A study of reproductive health problems among rural adolescent girls of Mohanpur block of West Tripura district. *Al Ameen J Med Sci*, 7(1), 78-82.

<http://ajms.alameenmedical.org/ArticlePDFs/AJMS%20V.7.N1.2014%20p%2078->

82.pdf

Abstract: OBJECTIVES: (1) To study the various reproductive health problems among rural adolescent girls in study area. (2) To ascertain the knowledge of reproductive health and health care-seeking behavior among rural adolescent girls.

BACKGROUND: Adolescence is characterized by menarche among girls which is often associated with several reproductive problems. It is necessary to assess the enormity of the problem to take appropriate interventions.

MATERIALS AND METHOD: This cross-sectional study was conducted in July and August, 2011 in a randomly selected sub-center area, under Mohanpur CHC. The sample size was calculated and 200 adolescent girls in the age group 10-19 years were selected by simple random sampling for the study.

RESULTS: The study showed that the prevalence of dysmenorrhea was 59.50 percent. 14.50 percent of the respondents had menstrual irregularity, 5.50 percent had menorrhagia, while Pre-Menstrual Syndrome was perceived by 8.50 percent of the respondents. Higher age of attainment of menarche had significant trend of pain during menstruation. 37.00 percent of the respondent adolescent girls used household remedy for reproductive health problems.

CONCLUSIONS: The study indicates that the problem is enormous and there is need for appropriate intervention to utilize and upgrade the services for the benefit of the adolescent girls.

**5. Barcelos, R. S.; Zanini, R. de V.; Santos, I. da S. dos. (2013). Menstrual disorders among women 15 to 54 years of age in Pelotas, Rio Grande do Sul State, Brazil: a population-based study, *Can. Saúde Pública*, 29(11), 2333-2346.
<http://dx.doi.org/10.1590/0102-311x00002813>**

Abstract: A cross-sectional population-based study was conducted in Pelotas, Rio Grande do Sul State, Brazil, to assess the prevalence of menstrual disorders and their distribution according to parity and demographic, social, and behavioral characteristics among 1,078 women aged 15-54 years. Menstrual disorders included heavy menstrual bleeding, inter-menstrual bleeding, short cycle, long cycle, and prolonged menses. Prevalence rates and 95% confidence intervals were calculated. Overall prevalence of menstrual disorders was 46.4% (43.3-49.4). The most prevalent disorder was heavy menstrual bleeding (23.2%; 20.5-25.8), followed by short cycle (19.2%; 16.6-21.8), long cycle (14.8%; 12.7-16.9), inter-menstrual bleeding (11.1%; 9.1-13.2), and prolonged menses (7.9%; 6.3-9.4). Menstrual disorders are frequent in the population and are associated with age 35 years or older, low schooling, high parity, tubal ligation, and smoking.

**6. Fawole, A. O., Babarinsa, I. A., Fawole, O. I., Obisesan, K. A., & Ojengbede, O. A. (2009). Menstrual characteristics of secondary school girls in Ibadan, Nigeria. *West African Journal of Medicine*, 28(2), 92–96.
<http://www.ncbi.nlm.nih.gov/pubmed/19761170>**

Abstract: BACKGROUND: Disturbances of menstrual function are the commonest complaints among adolescents. Disorders of menstruation may have implications for future reproductive health.

OBJECTIVE: To assess menstrual patterns among school girls in Ibadan, south-western Nigeria.

METHODS: This was cross-sectional descriptive study in which 1,213 apparently healthy school girls were selected by multistage sampling technique in fifteen secondary schools from the five local governments within the metropolis. Information about details of menstrual experience was obtained with a self-administered questionnaire.

RESULTS: The girls were aged between 9 and 23 years. Majority of respondents 768 (633%) experienced normal cycle length, 391 (32.2%) had short cycles; and 55 (4.5%) had cycle length greater than 35 days. Prevalence of normal cycles increased with increasing age; abnormalities of cycle length tended to decrease with increasing age ($p < 0.01$). The majority, 1,152 (95%), had normal menstrual loss. The majority 882 (72.7%) experienced dysmenorrhoea; severe dysmenorrhoea was reported by 154 (12.7%). Cycle length was not associated with presence of dysmenorrhoea ($p > 0.05$); 695 (57.3%) had symptoms of pre-menstrual syndrome.

CONCLUSION: Prevalence of menstrual abnormalities among adolescent schoolgirls is high. More attention should be paid to identify and treat these menstrual morbidities.

7. Harlow, S. D., & Campbell, O. M. R. (2004). Epidemiology of menstrual disorders in developing countries: A systematic review. In *BJOG: An International Journal of Obstetrics and Gynaecology*, 111(1), 6-16. <https://doi.org/10.1111/j.1471-0528.2004.00012.x>

Summary: This article reviews the literature on the prevalence of menstrual morbidity in developing countries and suggests a strategy for improving the quality of services provided to women with menstrual complaints. Findings suggest that approximately 4–8% of women report having menstrual periods longer than 7–8 days when interviewed. Similarly, the self-reported prevalence of excessive, profuse or heavy bleeding was 4 – 9% in most studies, although in the WHO multi-country study, the three-month, self-reported prevalence of excessive bleeding was higher, ranging from 8% to 27%. Among women of reproductive age, the prevalence of amenorrhea ranged from approximately 5% to 13% with the highest prevalence reported in a study of medical residents. The prevalence of oligomenorrhea or cycles longer than 35 days ranged from 8% to 22%. Between 25% and 58% of women participating in a WHO multi-country study reported having menstrual pain in the past three months. In other studies, 15-70% of adult women report dysmenorrhea. Severe pain or pain that kept a woman from work or her daily activities ranged from 3% to 18%. In summary, menstrual morbidities constitute an important unmet area of reproductive health services for women in developing countries and more attention should be given to inclusion of diagnosis and treatment of menstrual complaints within reproductive health care programs.

8. Jaikhani, S. M. K.; Naik, J. D.; Thakur, M. S.; Langre, S. D.; Pandey, V. O. (2019). Patterns & problems of menstruation amongst the adolescent girls residing in the urban slum. *Journal of applied Medical Sciences*, 2(2A), 529-534.

<http://saspublisher.com/wp-content/uploads/2014/03/SJAMS-22A529-534.pdf>

Abstract: Menstruation is a normal physiological phenomenon for females indicating her capability for procreation and abnormalities of menstruation are a major gynaecological problem in adolescence. However, variability in menstrual cycle characteristics and menstrual disorders are common. The objectives of the study were to find out the age of menarche among the Adolescent girls of the urban slum, to study different menstrual patterns and

practices among them & to find out the prevalence and types of menstrual disorders in Adolescent girls. A Cross sectional study was undertaken in an urban slum area of GMC, Miraj for period of 3 months. All unmarried adolescent girls from 10–19 years of age, who had attained menarche were included. Information was gathered on menarcheal age, menstrual patterns, practices & problems using a pretested semi-structured questionnaire. A total of 268 girls were interviewed. Mother was the source of information regarding menstruation in 45.5% of girls. Mean age of menarche was 13.43 + 1.01 years. 21.3% adolescents had abnormal cycle length, 24.2% had irregular menstrual cycle, 67.2% experienced dysmenorrhoea & 51.5% had premenstrual syndrome. Significant association was found between cycle length, duration of menstruation & amount of flow. Out of 199 girls who had ever experienced menstrual problem, 31% had any consultation & of them only 45.2% consulted doctors. There is an urgent need for strong health educational activities among the adolescent girls, their parents and teachers for effective management of menstrual problems & improvement of their health seeking behavior as regards menstrual abnormalities.

9. Nooh, A. M., Abdul-Hady, A., & El-Attar, N. (2016). Nature and Prevalence of Menstrual Disorders among Teenage Female Students at Zagazig University, Zagazig, Egypt. *Journal of Pediatric and Adolescent Gynecology*, 29(2), 137–142. <https://doi.org/10.1016/j.jpag.2015.08.008>

Abstract: Study Objective: To determine the nature and prevalence of menstrual disorders among teenage girls.

Design: An observational descriptive cross-sectional study.

Setting: Zagazig University Students' Hospital, Zagazig, Egypt.

Participants: A representative sample of female students who attended the university pre-enrollment medical examination.

Interventions: Self-administered questionnaire covering items on the adolescents' demographic data and menstruation characteristics.

Main Outcome Measures: Information about menarche, body mass index, physical exercise, cycle length and regularity, duration of menses, menstrual blood loss, dysmenorrhea, and premenstrual syndrome.

Results: A total of 285 questionnaires were analyzed. Mean age at menarche was 12.3 ± 1.5 years. Oligomenorrhea was reported by 18 participants (6.3%) and 5 others (1.8%) mentioned having polymenorrhea. Hypomenorrhea was noted in 25 students (8.8%), and hypermenorrhea was reported by 12 (4.2%). Irregular periods were mentioned by 24 students (8.4%).

Dysmenorrhea was reported in 188 students (66.0%). Of these, 81 (28.4%) graded their pain as mild, 69 (24.2%) as moderate, and 38 (13.3%) as severe. Premenstrual syndrome was mentioned by 160 girls (56.1%). Consulting somebody regarding their menstrual problems was reported by 36 students (12.6%).

Conclusion: Our results are not greatly different from those in other parts of the world. Data on nature and prevalence of menstrual disorders and their effect on young women's health status, quality of life, and social integration suggest that management of these disorders should be given more attention within the available reproductive health care programs. Further research into prevalence of and risk factors for menstrual disorders and their morbidity is warranted and anxiously awaited.

Anemia

- 10. Bellizzi, S., & Ali, M. M. (2018). Effect of oral contraception on anemia in 12 low- and middle-income countries. *Contraception*, 97(3), 236-242.**
<https://doi.org/10.1016/j.contraception.2017.11.001>

Abstract: CONTEXT: In low- and middle-income countries, anemia is a major public health issue in women of reproductive age for a series of factors including iron deficiency.

OBJECTIVE: To estimate prevalence of anemia and to assess the association of low level of hemoglobin versus duration of use of oral contraceptives (OC).

METHODS: Demographic and Health Surveys of 12 countries, conducted between 2005 and 2012, were analyzed. The status of anemia was separately evaluated for nonpregnant women using OC for at least 6 months, 1 year and 2 years, and for women using no method of contraception and/or using nonhormonal contraception.

RESULTS: The total study population comprised 201,720 women, with 40% diagnosed with anemia; around 1 out of 25 women was using oral contraception. The current and continuous use of oral contraception was of benefit against anemia, with the risk for anemia decreasing from odds ratio (OR) 0.68 [95% confidence interval (CI) 0.64–0.73] for use of at least 6 months to OR 0.56 (95% CI 0.52–0.61) for use of at least 1 year and to OR 0.50 (95% CI 0.46–0.54) for use of at least 2 years.

CONCLUSIONS: Findings reinforce evidence of the noncontraceptive benefit of long-term use of OC and provide valuable information for policy makers, family planning staff and clinicians working in low- and middle-income countries in efforts to control anemia.

- 11. Lowe, R. F., & Prata, N. (2013). Hemoglobin and serum ferritin levels in women using copper-releasing or levonorgestrel-releasing intrauterine devices: a systematic review. *Contraception*, 87(4), 486- 496.**
<https://doi.org/10.1016/j.contraception.2012.09.025>

Abstract: BACKGROUND: The use of intrauterine devices as a contraceptive method has been steadily growing in developing countries. Anemia in reproductive-age women is a growing concern in those settings.

STUDY DESIGN: A systematic review of studies with measured hemoglobin and serum ferritin at baseline and after 1 year of use of copper intrauterine devices (IUDs) or a levonorgestrel-releasing intrauterine system (LNG IUS) was performed.

RESULTS: Fourteen studies involving copper IUDs in nonanemic women and 4 studies in anemic women and 6 involving the LNG IUS met the criteria for the systematic review. Meta-analyses for hemoglobin changes showed significant decreases for users of copper IUDs and an increase for the LNG IUS, but with limited data. In general, ferritin levels followed the same pattern.

CONCLUSION: Decreases in hemoglobin mean values in copper IUD users were not sufficient to induce anemia in previously nonanemic women. Women who are borderline anemic would likely benefit from using the LNG IUS.

Dysmenorrhea

- 12. Armour, M., Parry, K., Al-Dabbas, M. A., Curry, C., Holmes, K., MacMillan, F., ... & Smith, C. A. (2019). Self-care strategies and sources of knowledge on menstruation in 12,526 young women with dysmenorrhea: A systematic review and meta-analysis. *PloS one*, 14(7), e0220103. <https://doi.org/10.1371/journal.pone.0220103>**

Introduction: Dysmenorrhea (period pain) is common and affects around three quarters of all young women under the age of 25. The majority of young women, for a variety of reasons, think of period pain as 'normal' and something to be managed or endured. This normalisation of pain often is reinforced by family and friends and results in young women using self-care strategies to manage their pain rather than seeking medical advice. This systematic review and meta-analysis examined observational studies reporting on the prevalence of different types of self-care, both pharmaceutical and non-pharmaceutical, self-rated effectiveness of self-care and the sources of information on menstruation in young women under 25
Methods: A search of Medline, PsychINFO, EMBASE and CINAHL in English was carried out from 1980 to December 2018. Studies that reported on menstrual self-care strategies in young women were included.
Results: Nine hundred and forty-seven articles were screened. Twenty-four studies including 12,526 young women were eligible and included in the meta-analysis. Fifteen studies were from low, lower-middle or upper-middle-income countries (LMIC) and nine studies were from high income countries (HIC). Self-care was used by over half of all young women (55%, 95%CI 34.1–74.3) with both pharmaceutical (48%, 95%CI 40.0–57.0) and non-pharmaceutical (51.8%, 95%CI 31.3–71.7) options used. Paracetamol was the most common analgesic used (28.7%, 95%CI 19.6–39.9) but did not always provide sufficient pain relief in almost half of those using it. Contraceptive use was significantly higher ($P<0.001$) in HIC (22%) compared to LMIC (1%). Only 11% (95%CI 8.4–15.2) of young women reported seeing a medical doctor for their period pain.
Conclusions: Self-care usage, both pharmaceutical and non-pharmaceutical, was common, but young women were not necessarily choosing the most effective options for pain management. High-quality information on self-care for period pain is urgently needed.

- 13. Armour, M., Parry, K., Manohar, N., Holmes, K., Ferfolja, T., Curry, C., ... & Smith, C. A. (2019). The prevalence and academic impact of dysmenorrhea in 21,573 young women: a systematic review and meta-analysis. *Journal of Women's Health*, 28(8), 1161-1171. <https://doi.org/10.1089/jwh.2018.7615>**

Introduction: Dysmenorrhea (period pain) and associated symptoms are very common in young women <25 years. This time corresponds with a significant stage in adolescents and young women's academic lives at both school and in higher education. Dysmenorrhea may cause absenteeism from class or result in reduced classroom concentration and performance. Owing to cultural and economic differences, any impact may vary by country. This systematic review and meta-analysis examines the prevalence of dysmenorrhea in young women and explores any impact it has on their academic performance and other school-related activities.
Materials and Methods: A search in Medline, PsychINFO, EMBASE, and Cumulative Index to Nursing and Allied Health Literature was carried out in June 2018.

Results: Thirty-eight studies including 21,573 young women were eligible and included in the meta-analysis. Twenty-three studies were from low-, lower middle-, or upper middle-income

countries, and 15 studies were from high-income countries. The prevalence of dysmenorrhea was high 71.1% (N = 37, n = 20,813, 95% confidence interval [CI] 66.6–75.2) irrespective of the economic status of the country. Rates of dysmenorrhea were similar between students at school (N = 24, 72.5%, 95% CI 67.5–77.0) and at university (N = 7, 74.9%, 95% CI 62.9–84.0). Academic impact was significant, with 20.1% reporting absence from school or university due to dysmenorrhea (N = 19, n = 11,226, 95% CI 14.9–26.7) and 40.9% reporting classroom performance or concentration being negatively affected (N = 10, n = 5126, 95% CI 28.3–54.9). Conclusions: The prevalence of dysmenorrhea was high, irrespective of country, with dysmenorrhea having a significant negative impact on academic performance both at school and during higher education.

14. Armour, M., Smith, C.A., Steel, L.A., Macmillan, F. (2012). The effectiveness of self-care and lifestyle interventions in primary dysmenorrhea: A systematic review and meta-analysis. *BMC Complement Alternative Medicine*, 19(22). doi: [10.1186/s12906-019-2433-8](https://doi.org/10.1186/s12906-019-2433-8)

Abstract: BACKGROUND: Menstrual pain is very common amongst young women. Despite the significant impact that menstrual pain has on academic attendance and performance, social activities and quality of life, most young women do not seek medical treatment but prefer to use self-care; commonly OTC analgesic medications and rest. Many women do not get significant pain relief from these methods, therefore other low cost, easy to learn self-care methods may be a valuable approach to management. This review and meta-analysis examines the evidence for participant lead self-care techniques.

METHODS: A search of Medline, PsychINFO, Google Scholar and CINAHL was carried out in September 2017.

RESULTS: Twenty-three trials including 2302 women were eligible and included in the meta-analysis. Studies examined self-delivered acupuncture, exercise and heat as interventions. Risk of bias was unclear for many domains. All interventions showed a reduction in menstrual pain symptoms; exercise (g = 2.16, 95% CI 0.97 to 3.35) showed the largest effect size, with heat (g = 0.73, 95% CI 0.06 to 1.40) and acupuncture (g = 0.56, 95% CI 0.10 to 1.03) showing more moderate effect sizes. Exercise (g = 0.48, 95% CI 0.12 to 0.83) and heat (g = 0.48, 95% CI 0.10 to 0.87), were more effective than analgesics in reducing pain intensity, whereas acupuncture was significantly less effective (g = - 0.76, 95% CI -1.37 to - 0.15).

CONCLUSION: Exercise showed large effects, while acupuncture and heat showed moderate effects in reducing menstrual pain compared to no treatment. Both exercise and heat are potential alternatives to analgesic medication. However, difficulties in controlling for non-specific effects, along with potential for bias, may influence study findings.

15. Aziato, L., Dedey, F., & Clegg-Lamprey, J. N. A. (2014). The experience of dysmenorrhoea among Ghanaian senior high and university students: pain characteristics and effects. *Reproductive health*, 11(1), 58. <https://doi.org/10.1186/1742-4755-11-58>

Abstract: BACKGROUND: Dysmenorrhoea is a common problem of women at the reproductive age and may have negative effect on the education of females at various stages on the educational ladder.

CONTEXT AND PURPOSE: This study sought to gain an in-depth understanding of the

experience of dysmenorrhoea and its effect on female students in a secondary and a tertiary institution in Accra, Ghana.

METHODS: The study employed a descriptive phenomenology design and was conducted at a University and a Senior High School (SHS) in Accra. Purposive and snowball sampling techniques were used to recruit participants and data was saturated with 16 participants. Concurrent analysis was done by applying the processes of content analysis and the NVivo software was used to manage the data.

RESULTS: It was realized that dysmenorrhoea is associated with symptoms such as diarrhoea, headache and vomiting. Pain may start one week to the day of menstruation and the severity differed across the days of menstruation. The effect of dysmenorrhoea included activity intolerance, altered emotion and interaction, altered sleep pattern, absenteeism and inattentiveness, wishes and regrets, and misconceptions.

CONCLUSIONS: It was concluded that severe dysmenorrhoea has a debilitating effect on female students and is associated with misconceptions that could result in drastic action with fatal consequences. Thus, there is the need to enhance education on dysmenorrhoea, and an aggressive step should be taken to effectively manage dysmenorrhoea.

16. Iacovides, S., Avidon, I., & Baker, F. C. (2015). What we know about primary dysmenorrhea today: a critical review. *Hum Reprod Update*, 21(6), 762-778. <https://doi.org/10.1093/humupd/dmv039>

Abstract: BACKGROUND: Primary dysmenorrhea, or painful menstruation in the absence of pelvic pathology, is a common, and often debilitating, gynecological condition that affects between 45 and 95% of menstruating women. Despite the high prevalence, dysmenorrhea is often poorly treated, and even disregarded, by health professionals, pain researchers, and the women themselves, who may accept it as a normal part of the menstrual cycle. This review reports on current knowledge, particularly with regards to the impact and consequences of recurrent menstrual pain on pain sensitivity, mood, quality of life and sleep in women with primary dysmenorrhea.

METHODS: Comprehensive literature searches on primary dysmenorrhea were performed using the electronic databases PubMed, Google Scholar and the Cochrane Library. Full-text manuscripts published between the years 1944 and 2015 were reviewed for relevancy and reference lists were cross-checked for additional relevant studies. In combination with the word 'dysmenorrhea' one or more of the following search terms were used to obtain articles published in peer-reviewed journals only: pain, risk factors, etiology, experimental pain, clinical pain, adenomyosis, chronic pain, women, menstrual cycle, hyperalgesia, pain threshold, pain tolerance, pain sensitivity, pain reactivity, pain perception, central sensitization, quality of life, sleep, treatment, non-steroidal anti-inflammatory drugs.

RESULTS: Women with dysmenorrhea, compared with women without dysmenorrhea, have greater sensitivity to experimental pain both within and outside areas of referred menstrual pain. Importantly, the enhanced pain sensitivity is evident even in phases of the menstrual cycle when women are not experiencing menstrual pain, illustrating that long-term differences in pain perception extend outside of the painful menstruation phase. This enhanced pain sensitivity may increase susceptibility to other chronic pain conditions in later life; dysmenorrhea is a risk factor for fibromyalgia. Further, dysmenorrheic pain has an immediate

negative impact on quality of life, for up to a few days every month. Women with primary dysmenorrhea have a significantly reduced quality of life, poorer mood and poorer sleep quality during menstruation compared with their pain-free follicular phase, and compared with the menstruation phase of pain-free control women. The prescribed first-line therapy for menstrual pain remains non-steroidal anti-inflammatory drugs, which are effective in relieving daytime and night-time pain.

CONCLUSION: Further study is needed to determine whether effectively blocking dysmenorrheic pain ameliorates risk for the development of chronic pain disorders and to explore whether it is possible to prevent the development—and not just treat—severe dysmenorrheic pain in adolescent girls. In conclusion, we demonstrate the extensive multifactorial impact of dysmenorrhea and we encourage and direct researchers to necessary future studies.

17. Ju, H., Jones, M., & Mishra, G. (2014). The prevalence and risk factors of dysmenorrhea. *Epidemiol Rev*, 36, 104-113. <https://doi.org/10.1093/epirev/mxt009>

Abstract: Dysmenorrhea is a common menstrual complaint with a major impact on women's quality of life, work productivity, and health-care utilization. A comprehensive review was performed on longitudinal or case-control or cross-sectional studies with large community-based samples to accurately determine the prevalence and/or incidence and risk factors of dysmenorrhea. Fifteen primary studies, published between 2002 and 2011, met the inclusion criteria. The prevalence of dysmenorrhea varies between 16% and 91% in women of reproductive age, with severe pain in 2%–29% of the women studied. Women's age, parity, and use of oral contraceptives were inversely associated with dysmenorrhea, and high stress increased the risk of dysmenorrhea. The effect sizes were generally modest to moderate, with odds ratios varying between 1 and 4. Family history of dysmenorrhea strongly increased its risk, with odds ratios between 3.8 and 20.7. Inconclusive evidence was found for modifiable factors such as cigarette smoking, diet, obesity, depression, and abuse. Dysmenorrhea is a significant symptom for a large proportion of women of reproductive age; however, severe pain limiting daily activities is less common. This review confirms that dysmenorrhea improves with increased age, parity, and use of oral contraceptives and is positively associated with stress and family history of dysmenorrhea.

18. Patel, V., Tanksale, V., Sahasrabhojane, M., Gupte, S., & Nevrekar, P. (2006). The burden and determinants of dysmenorrhoea: a population-based survey of 2262 women in Goa, India. *BJOG: An International Journal of Obstetrics & Gynaecology*, 113(4), 453-463. <https://doi.org/10.1111/j.1471-0528.2006.00874.x>

OBJECTIVE: To describe the prevalence and determinants of dysmenorrhoea, the most common menstrual complaint, in a community in India.

DESIGN: Cross-sectional survey.

SETTING: Catchment area of primary health centre in Goa, India.

POPULATION: Three thousand women aged 18–45 years randomly selected. A total of 2494 women consented to participate (83.1%).

METHODS: Eligible participants were asked standardised questions regarding menstrual

complaints over the past 12 months, and socio-demographic, psychosocial and reproductive risk factors. Vaginal or urine specimens were collected for the diagnosis of reproductive tract infections.

MAIN OUTCOME MEASURES: Dysmenorrhoea of moderate to severe intensity.

RESULTS: A total of 2262 women were eligible. More than half reported dysmenorrhoea; moderate to severe dysmenorrhoea was reported by 755 participants (33.4%, 95% CI 31.4–35.4). There was a linear association between severity of pain and impact (medication and taking rest) and the onset of pain (premenstrual onset associated with more severe pain). On multivariate analyses, the risk of moderate–severe dysmenorrhoea was associated with the experience of violence (OR 2.23, 95% CI 1.5–3.4); other somatic complaints (OR 3.67, 95% CI 2.7–4.9 for highest somatoform symptom score category compared with the lowest); gynaecological complaints (non-menstrual lower abdominal pain: OR 1.78, 95% CI 1.3–2.3; dysuria: OR 1.98, 1.4–2.7); menorrhagia (OR 1.92, 95% CI 1.4–2.6); and illiteracy (OR 1.32, 95% CI 1.0–1.7). Having had a pregnancy (OR 0.53, 95% CI 0.4–0.7), older age of menarche (OR 0.70, 95% CI 0.5–0.9, for age >14 compared with <13 years) and older age (OR 0.43, 0.3–0.6 for age 40–50, compared with 18–24 years) were protective.

CONCLUSIONS: The burden of dysmenorrhoea is greater than any other gynaecological complaint, and is associated with significant impact. Social disadvantage, co-morbidity with other somatic syndromes and reproductive factors are determinants of this complaint.

Endometriosis

- 19. Annan, J. J., Larsen-Reindorf, R. E., Frimpong, G. A., & Owusu-Afriyie, O. (2019). Endometriosis: An “Unexplored,” “Neglected” or “Forgotten” Condition in Africa? *Open Journal of Obstetrics and Gynecology*, 9(1), 29-41. <https://doi.org/10.4236/ojog.2019.91004>**

Abstract: Endometriosis is a condition that is commonly encountered in gynaecological practice. Endometriosis has varied, non-specific clinical presentations and its diagnosis sometimes poses a challenge to the clinician. We have encountered various women with clinical presentation highly suggestive of endometriosis. Further diagnosis using imaging and biopsy confirmed endometriosis. This paper presents our experience of endometriosis in our care of African women and a review of the literature on endometriosis. We want to highlight the various clinical presentations of endometriosis, appraise the various methods for diagnosis, discuss the treatment modalities available and evaluate the impact of this condition on women. We want to emphasize the fact that African women also suffer from this condition, and impress upon clinicians, the necessity for closer look for the condition, stimulate discussion and research into endometriosis in Africa as it seems this condition is “neglected or forgotten” in Africa.

- 20. Brown, J., & Farquhar, C. (2014). Endometriosis: an overview of Cochrane Reviews. *Cochrane Database Syst Rev*, (3), CD009590. <https://doi.org/10.1002/14651858.CD009590.pub2>**

Abstract (redacted for length and relevance): BACKGROUND: This overview reports on interventions for pain relief and for subfertility in pre-menopausal women with clinically diagnosed endometriosis.

OBJECTIVES: The objective of this overview was to summarize the evidence from Cochrane systematic reviews on treatment options for women with pain or subfertility associated with endometriosis.

METHODS: Published Cochrane systematic reviews reporting pain or fertility outcomes in women with clinically diagnosed endometriosis were eligible for inclusion in the overview. We also identified Cochrane reviews in preparation (protocols and titles) for future inclusion. The reviews, protocols and titles were identified by searching the Cochrane Database of Systematic Reviews and Archie (the Cochrane information management system) in March 2014. Pain-related outcomes of the overview were pain relief, clinical improvement or resolution and pain recurrence. Fertility-related outcomes were live birth, clinical pregnancy, ongoing pregnancy, miscarriage and adverse events. Selection of systematic reviews, data extraction and quality assessment were undertaken in duplicate. Review quality was assessed using the AMSTAR tool. The quality of the evidence for each outcome was assessed using GRADE methods. Review findings were summarized in the text and the data for each outcome were reported in 'Additional tables'.

MAIN RESULTS: Seventeen systematic reviews published in The Cochrane Library were included. All the reviews were high quality. The quality of the evidence for specific comparisons ranged from very low to moderate. Limitations in the evidence included risk of bias in the primary studies, inconsistency between the studies, and imprecision in effect estimates. [...]

AUTHORS' CONCLUSIONS: For women with pain and endometriosis, suppression of menstrual cycles with gonadotrophin-releasing hormone (GnRH) analogues, the levonorgestrel-releasing intrauterine system (LNG-IUD) and danazol were beneficial interventions. Laparoscopic treatment of endometriosis and excision of endometriomata were also associated with improvements in pain. The evidence on NSAIDs was inconclusive. There was no evidence of benefit with post-surgical medical treatment. In women with endometriosis undergoing assisted reproduction, three months of treatment with GnRH agonist improved pregnancy rates. Excisional surgery improved spontaneous pregnancy rates in the nine to 12 months after surgery compared to ablative surgery. Laparoscopic surgery improved live birth and pregnancy rates compared to diagnostic laparoscopy alone. There was no evidence that medical treatment improved clinical pregnancy rates. Evidence on harms was scanty, but GnRH analogues, danazol and depot progestagens were associated with higher rates than other interventions.

21. Cheewadhanaraks, S., Choksuchat, C., Dhanaworavibul, K., & Liabsuetrakul, T. (2012).

Postoperative depot medroxyprogesterone acetate versus continuous oral contraceptive pills in the treatment of endometriosis-associated pain: a randomized comparative trial. *Gynecol Obstet Invest*, 74(2), 151-156.

<https://doi.org/10.1159/000337713>

Abstract: BACKGROUND/AIM: To evaluate the efficacy and tolerability of postoperative depot medroxyprogesterone acetate (DMPA) versus postoperative continuous oral contraceptive (OC) pills in the treatment of endometriosis-associated pain.

METHODS: After a conservative surgery, 84 patients with symptomatic endometriosis were randomized to receive either intramuscular DMPA (150 mg) every 12 weeks for 24 weeks or continuous OC pills (ethinyl estradiol 0.03 mg and gestodene 0.075 mg) daily for 24 weeks. At weeks 12 and 24 of the treatment phase, patients rated their satisfaction with treatment and

reported pain improvement and adverse effects.

RESULTS: There was no significant difference in the percentages of patients who reported satisfaction between the DMPA group and the OC group at weeks 12 and 24 (92.9 vs. 90.5%, and 92.9 vs. 88.1%, respectively). The rates of withdrawal because of persistent pain or side effects in the two groups were similar. Pain scores improved significantly in both groups, but dysmenorrhea scores on a visual analog scale at week 24 were significantly higher in the OC group than in the DMPA group ($p = 0.039$).

CONCLUSION: Both postoperative DMPA and postoperative OC pills for 24 weeks were found to be effective and acceptable options for treating endometriosis-associated pain.

22. Culley, L., Law, C., Hudson, N., Denny, E., Mitchell, H., Baumgarten, M., & Raine-Fenning, N. (2013). The social and psychological impact of endometriosis on women's lives: A critical narrative review. *Human Reproduction Update*, 19(6), 625–639.

<https://doi.org/10.1093/humupd/dmt027>

Abstract: BACKGROUND: Endometriosis is a chronic condition affecting between 2 and 17% of women of reproductive age. Common symptoms are chronic pelvic pain, fatigue, congestive dysmenorrhoea, heavy menstrual bleeding and deep dyspareunia. Studies have demonstrated the considerable negative impact of this condition on women's quality of life (QoL), especially in the domains of pain and psychosocial functioning. The impact of endometriosis is likely to be exacerbated by the absence of an obvious cause and the likelihood of chronic, recurring symptoms. The aims of this paper are to review the current body of knowledge on the social and psychological impact of endometriosis on women's lives; to provide insights into women's experience of endometriosis; to provide a critical commentary on the current state of knowledge and to make recommendations for future psycho-social research.

METHODS: The review draws on a method of critical narrative synthesis to discuss a heterogeneous range of both quantitative and qualitative studies from several disciplines. This included a systematic search, a structured process for selecting and collecting data and a systematic thematic analysis of results.

RESULTS: A total of 42 papers were included in the review; 23 used quantitative methods, 16 used qualitative methods and 3 were mixed methods studies. The majority of papers came from just four countries: UK (10), Australia (8), Brazil (6) and the USA (5). Key categories of impact identified in the thematic analysis were diagnostic delay and uncertainty; 'QoL' and everyday activities; intimate relationships; planning for and having children; education and work; mental health and emotional wellbeing and medical management and self-management.

CONCLUSIONS: Endometriosis has a significant social and psychological impact on the lives of women across several domains. Many studies have methodological limitations and there are significant gaps in the literature especially in relation to a consideration of the impact on partners and children. We recommend additional prospective and longitudinal research utilizing mixed methods approaches and endometriosis-specific instruments to explore the impact of endometriosis in more diverse populations and settings. Furthermore, there is an urgent need to develop and evaluate interventions for supporting women and partners living with this chronic and often debilitating condition.

23. Fawole, A. O., Bello, F. A., Ogunbode, O., Odukogbe, A. T. A., Nkwocha, G. C., Nnoaham,

K. E., Zondervan, K., Akintan, A., Abdus-Salam, R., Okunlola, M. A. (2015). Endometriosis and associated symptoms among Nigerian women. *International Journal of Gynecology & Obstetrics*, 130(2), 190-194. <https://doi.org/10.1016/j.ijgo.2015.02.030>

Abstract: OBJECTIVE: To determine the prevalence of endometriosis and identify associated symptoms among Nigerian women.

METHODS: A cross-sectional study was conducted at a center in Ibadan, Nigeria, between October 2008 and December 2010. All women aged 18-45 years scheduled for their first diagnostic laparoscopy for gynecologic indications were enrolled. Participants completed a previously validated self-administered questionnaire. Endometriosis was diagnosed on the basis of visual evidence.

RESULTS: Among 239 women analyzed, 115 (48.1%) had endometriotic lesions. Endometriosis was more common among women reporting dysmenorrhea and pelvic pain than among those not reporting these symptoms (20/28 [71.4%] vs 95/211 [45.0%]; $P=0.009$). Women who reported dysmenorrhea were significantly more likely to have endometriosis than were those without dysmenorrhea (90/171 [52.6%] vs 25/68 [36.8%]; $P=0.027$). The risk of endometriosis was not significantly increased in women with one pain symptom (odds ratio [OR] 1.69; 95% confidence interval [CI] 0.67-4.27), but was significantly increased in women with two (OR 2.70; 95% CI 1.13-6.52) or three (OR 4.87; 95% CI 1.88-12.82) pain symptoms (χ^2 trend=15.5; $P<0.001$). In a multivariate logistic regression model, only pain other than dysmenorrhea or dyspareunia independently predicted endometriosis ($P=0.017$).

CONCLUSION: Endometriosis is fairly common among Nigerian women. Efforts to increase the awareness of endometriosis among the public, researchers, and clinicians are needed.

24. Kagia, A., Gichuhi, J. W., & Karanja, J. (2018). Prevalence of pain symptoms suggestive of endometriosis among adolescents in Kenya. *East African Medical Journal*, 95(8), 1818-1826. <https://www.ajol.info/index.php/eamj/article/view/192076>

Abstract: OBJECTIVE: To determine the prevalence of pain symptoms suggestive of Endometriosis among adolescent Kenyans and their impact on quality of life.

STUDY DESIGN: Analytical cross-sectional study

SETTING: Dual centered study at Githunguri Girls High School (Rural) and Moi Girls High School Nairobi (Urban).

SUBJECTS: Three hundred and thirteen adolescents were interviewed with even distribution between rural (50.8%) and urban (49.2%) schools.

OUTCOME MEASURE: The primary outcome measure was the prevalence of pain symptoms suggestive of endometriosis.

RESULTS: Dysmenorrhea was the most prevalent symptom at 72% with severe dysmenorrhea reported at 29%. Regular absenteeism was reported at 4% in those with dysmenorrhea, 1% was due to acyclic pelvic pain and 1% reported intermenstrual pain limiting their daily activities. In the students' interviewed, 94% had not heard of endometriosis, of whom 70% were interested to know more about it. The dysmenorrhea and pelvic pain that interfered with ordinary chores was most likely due to endometriosis.

CONCLUSION: Majority of adolescent girls with chronic pelvic pain, not corresponding to conventional therapy have endometriosis. Endometriosis appearing in adolescence is more

likely to progress and if not treated, may progress beyond pain to infertility. Endometriosis in adolescence is a hidden progressive and severe disease that deserves attention, not just compassion.

25. Kyama, C. M., Mwenda, J. M., Machoki, J., Mihalyi, A., Simsa, P., Chai, D. C., & D'Hooghe, T. M. (2007). Endometriosis in African women. *Women's Health*, 3(5), 629-635. <https://doi.org/10.2217/17455057.3.5.629>

Abstract: Endometriosis is a gynecological disorder characterized by the growth of endometrial tissue outside the uterine cavity. Although the prevalence of endometriosis is well documented in women living in developed countries, studies on the prevalence of this disease among African women are still wanting. The current view is that endometriosis rarely affects women of African descent. However, in African-American women in the USA, endometriosis is one of the common indications for major gynecological surgery and hysterectomy and is associated with a long hospitalization and high hospital charges. Endometriosis may be more commonly found in infertile Caucasian or African-American women than in African-Indigenous women, but it is likely that the true prevalence of endometriosis in African-Indigenous women is under reported owing to inadequate facilities and demands of specialized skills for adequate assessment of the pelvis and recognition of the various types and appearances of the disease. Understanding the prevalence of endometriosis among African women will be instrumental in proper management of this disease in the African continent.

26. Macer, M. L., & Taylor, H. S. (2012). Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. *Obstet Gynecol Clin North Am*, 39(4), 535-549. <https://doi.org/10.1016/j.ogc.2012.10.002>

Summary: This review details the evidence on the pathogenesis of endometriosis, its association with infertility and possible treatments for associated infertility. The exact pathogenesis of endometriosis is not known but the evidence base strongly supports an association with infertility. The authors note that while oral contraceptives are among the medications used to treat pain for endometriosis, they have not been shown to be an effective treatment for endometriosis-related infertility.

27. Nesbitt-Hawes, E. M., & Ledger, W. (2015). Endometriosis and Infertility. In M. Metwally & T.C. Li (Eds.), *Reproductive Surgery in Assisted Conception* (pp. 29-35). Springer-Verlag London. doi: 10.1007/978-1-4471-4953-8

Abstract: It seems likely that endometriosis has a negative effect on fertility. This may result from reduced frequency of intercourse due to dyspareunia, from anatomical distortion in more severe cases of endometriosis or from more subtle alterations in the intra-ovarian and tubo-peritoneal environments. Medical treatment of endometriosis can waste time, resulting in loss of fertility due to ageing, and does not seem to improve fertility post-treatment. Surgical intervention holds more promise, but may have negative as well as positive impact on fertility. ART remains the mainstay of management of endometriosis-associated infertility, but treatment programs should be individualized and outcomes may be less favorable than seen for age-matched couples with other reasons for need for ART.

- 28. Nnoaham, K. E., Sivananthan, S., Hummelshoj, L., Jenkinson, C., Webster, P., Kennedy, S. H., & Zondervan, K. T. (2010). O-021 Global study of women's health: a multi-centre study of the global impact of endometriosis. *Human Reproduction*, 25(Suppl_1), i9-i11. <http://doi.org/10.1093/humrep/de.25.s1.5>**

Introduction: Endometriosis is known to influence quality of life, but little is known about its personal and societal impact across the world. We designed the Global Study of Women's Health (GSWH), a multicentre study of women attending for their first laparoscopic investigation to examine the global impact of endometriosis and associated symptoms. Materials and Methods: The GSWH prospectively recruited pre-menopausal 18-45 year old women having a laparoscopy in 16 centres across 10 countries. Women with a previous surgical diagnosis of endometriosis are excluded. Prior to surgery, women complete a comprehensive, multi-lingual questionnaire incorporating validated instruments. Surgeons subsequently complete a standardised questionnaire on laparoscopic findings. The GSWH recruited over 18 months from August 2008 to January 2010. A six-week pilot study in Oxford, UK, established the feasibility of the study protocols (response rate 84.4%). Results: By end of January 2010, a total of 1,459 women had been recruited. Interim analyses showed diagnostic incidence rates of endometriosis varying from 26.4% (95% CI: 20-32.7%) in African to 54.5% (95% CI: 44.2-64.7%) in South-American countries. Mean age of women varied significantly ($p < 0.001$) from 27.5 (SD: 5.6) in Africa to 34.8 (SD: 5.9) in Europe, as did their reported reason for surgery (e.g. infertility: 84.6% in Africa vs. 31.7% in South America), highlighting substantial differences in patient characteristics. Loss of work productivity among employed women with endometriosis averaged 10 hours/week vs. 7 hours/week in those without ($p < 0.01$). This difference was explained by increased levels of pelvic pain among women with endometriosis. Reduced productivity resulted from reduced effectiveness on the job rather than work absence. Conclusions: The GSWH is the first large-scale study assessing the impact of endometriosis in countries across the world, using a standardised research protocol. Recruitment ceased in January 2010 and final results from the study will be presented.

- 29. Tanmahasamut, P., Rattanachaiyanont, M., Angsuwathana, S., Techatraisak, K., Indhavivadhana, S., & Leerasiri, P. (2012). Postoperative levonorgestrel-releasing intrauterine system for pelvic endometriosis-related pain: a randomized controlled trial. *Obstet Gynecol*, 119(3), 519-526. <https://doi.org/10.1097/aog.0b013e31824264c3>**

Abstract: OBJECTIVES: To estimate the effectiveness of a postoperative levonorgestrel-releasing intrauterine system for relieving pelvic pain in patients with endometriosis.

METHODS: A double-blind randomized controlled trial was conducted in 55 patients with endometriosis and moderate-to-severe dysmenorrhea (visual analog scale, greater than 50 mm) undergoing laparoscopic conservative surgery. After surgery, patients were randomized to a levonorgestrel-releasing intrauterine system ($n=28$) or expectant management ($n=27$) group. Primary outcome was the change of dysmenorrhea visual analog scale. Secondary outcomes included changes of pelvic pain and dyspareunia visual analog scale, Short Form-36 score, and adverse effects.

RESULTS: The two groups were comparable in age, body mass index, parity, and baseline pain scores. At 12 months, the levonorgestrel-releasing intrauterine system group had a significantly lower median value of dysmenorrhea and noncyclic pelvic pain score. Compared with the

control group, the levonorgestrel-releasing intrauterine system group had greater reduction in dysmenorrhea visual analog scale (-81.0 compared with -50.0 mm, P=.006) and pelvic pain visual analog scale (-48.5 compared with -22.0 mm, P=.038) but a comparable reduction in dyspareunia visual analog scale (-15.0 compared with -19.0 mm, P=.831). Two patients in levonorgestrel-releasing intrauterine system group (7.4%) and nine in the expectant management group (39.1%) had recurrent dysmenorrhea within 1 year postoperatively (P=.014). Number-needed-to-treat to prevent one case with recurrent dysmenorrhea within the first year was three cases. The Short Form-36 scores improved in the levonorgestrel-releasing intrauterine system group but did not change in the expectant management group. There was no serious adverse event during the study period.

CONCLUSION: The levonorgestrel-releasing intrauterine system is effective and well accepted for long-term therapy after conservative surgery for patients with moderate to severe pain related to endometriosis. It can improve the patient's quality of life, including physical and mental health.

30. Walch, K., Unfried, G., Huber, J., Kurz, C., van Trotsenburg, M., Pernicka, E., & Wenzl, R. (2009). Implanon® versus medroxyprogesterone acetate: effects on pain scores in patients with symptomatic endometriosis - a pilot study. *Contraception, 79*(1), 29–34. <https://doi.org/10.1016/j.contraception.2008.07.017>

Abstract: BACKGROUND: Implanon® has been reported to be effective in the treatment of dysmenorrhea. We compared the therapeutic efficacies of depot medroxyprogesterone acetate (DMPA) and Implanon® with regard to pain relief in women with endometriosis.

STUDY DESIGN: In a clinical research center at a university hospital, 41 patients with dysmenorrhea, nonmenstrual pelvic pain and dyspareunia associated with histologically proven endometriosis were included in an open, prospective, randomized, controlled clinical trial. Twenty-one women were assigned by computer-generated randomization to receive Implanon®, and 20 women to receive DMPA. As main outcome measures of this pilot study, we evaluated pain improvement quantified according to visual analog scale score, side effects, vaginal bleeding patterns, withdrawal rate and overall degree of satisfaction.

RESULTS: During a follow-up period of 1 year, we ascertained a clear improvement in pain intensity for both treatment options. After 6 months, the average decrease in pain was 68% in the Implanon® group and 53% in the DMPA group. The side-effects profile and the overall degree of satisfaction after study termination were comparable for both treatment options.

CONCLUSION: Concerning pain relief, the therapeutic efficacy of the contraceptive implant Implanon® is not inferior to that of DMPA in symptomatic endometriosis.

31. Zorbas, K. A., Economopoulos, K. P., & Vlahos, N. F. (2015). Continuous versus cyclic oral contraceptives for the treatment of endometriosis: a systematic review. *Arch Gynecol Obstet, 292*(1), 37-43. <https://doi.org/10.1007/s00404-015-3641-1>

Abstract: PURPOSE: Recurrence of endometriosis after conservative surgery has been observed in 40–50 % of patients within the first 5 years. A variety of regimens such as combined oral contraceptives, GnRH agonists, danazol, and progestins have been used postoperatively to reduce recurrence rates. Oral contraceptives (oCP) have been used either in a cyclic or in a continuous (no pill-free interval) fashion. The purpose of this article was to summarize the

existing evidence on the efficacy and patient compliance for the use of oCP in a continuous versus cyclic fashion following conservative surgery for endometriosis.

METHODS: A systematic search of Medline identified four eligible studies. Studies were considered eligible, if they have evaluated oCP therapy, either in a cyclic or continuous regimen, after conservative surgery for endometriosis. Specifically, studies (1) reporting on women with endometriosis who were treated postoperatively with both continuous oCP and cyclic oCP, (2) written in English, (3) with minimum 6 months duration of medical treatment, and (4) with minimum 12 months duration of follow-up were considered eligible for our systematic review. Outcome measures of these eligible studies were tabulated and then analyzed cumulatively. A purely descriptive approach was adopted concerning all variables.

RESULTS: Postoperative use of continuous oCP was associated with a reduction in the recurrence rate of dysmenorrhea, delay in the presentation of dysmenorrhea, reduction in nonspecific pelvic pain, and reduction in the recurrence rate for endometrioma.

CONCLUSIONS: Use of OCP in a continuous fashion following conservative surgery for endometriosis is more beneficial to cyclic use.

Heavy Menstrual Bleeding

- 32. Abdelmoty, H. I.; Youssef, M. A.; Abdallah, S.; Abdel-Malak, K.; Hashish, N. M.; Samir, D.; Abdelbar, M.; Hosni, A. N.; Abd-El-Ghafar, M.; Khamis, Y.; Seleem, M. (2001). Menstrual patterns and disorders among secondary school adolescents in Egypt. A cross-sectional survey. *BMC Women's Health*, 15(70). <https://doi.org/10.1186/s12905-015-0228-8>**

Abstract: To our knowledge, no large population - based studies have been performed on the topic of menstrual patterns among Egyptian adolescent in recent years. The aims of this study were to identify menstrual patterns and associated disorders as well as the sources of menstrual health knowledge among Egyptian adolescents. A cross-sectional survey. A total of 800 questionnaires were administered to post-menarcheal Egyptian adolescents attending secondary schools in Giza, Egypt, from September 1, 2012, to December 1, 2013. Participants were asked to respond to a semi-structured questionnaire on menstrual health awareness. The questionnaire included items on girl's socio-demographic and menstrual pattern characteristics, concerning their age at menarche, menstrual cycle length and regularity, duration and amount of flow, type and severity of pain related to menstruation, need for analgesia; and symptoms suggestive of premenstrual syndrome (PMS) Main Outcome Measure: description of menstrual patterns, disorders and source of knowledge. Four hundred twelve (51.5 %) out of 800 adolescents completed the questionnaire. The mean age of the girls was 14.67 ± 1.7 years. Mean age at menarche was 12.49 ± 1.20 years. 382 respondents reported various menstrual disorders, giving a prevalence rate of 95 %. Dysmenorrhea was the most prevalent (93 %) menstrual disorder in our sample, followed by PMS (65 %), and abnormal cycle lengths (43 %). Menstrual disorders interfered with social and academic life of 33 and 7.7 % of respondents respectively. Most participants lacked menstrual health knowledge and only 8.9 % of girls reported consulting a physician. To the best of our knowledge, this is one of the largest studies on menstrual pattern and disorders among Egyptian adolescent girls. Our findings of the present study are consistent with other studies

and reported higher than expected prevalence of menstrual disorders.

- 33. Abid, M., Hashmi, A. A., Malik, B., Haroon, S., Faridi, N., Edhi, M. M., & Khan, M. (2014). Clinical pattern and spectrum of endometrial pathologies in patients with abnormal uterine bleeding in Pakistan: need to adopt a more conservative approach to treatment. *BMC Women's Health*, 14(1), 132. <https://doi.org/10.1186/s12905-014-0132-7>**

Abstract: BACKGROUND: Abnormal uterine bleeding (AUB) is one of the most common debilitating

menstrual problems and has remained one of the most frequent indications for hysterectomy in developing countries. Approximately in 40% of hysterectomy specimens, no definite organic pathology could be established. The problem is common worldwide but causes may vary from one region to another. This study may help gynecologists in our population to improve their therapeutic strategies by promoting minimally invasive uterus sparing modalities such as endometrial ablation and hysteroscopic resection of early proliferative lesions.

METHODS: It was a prospective, cross-sectional study conducted at Liaquat National Hospital from 15th January 2010 till 14th July 2011 over a period of 18 months. Women who underwent dilatation and curettage for endometrial sampling with complaints of AUB were included in the study and histopathologic spectrum was determined.

RESULTS: Polymenorrhea was the most common presenting pattern (30%, 72/241) with reproductive age women being the most susceptible (49.3%, 119/241). The commonest histopathological spectrum was normal menstrual pattern (34%, 82/241) and the commonest pathology was hormonal imbalance (27%, 65/241), followed by endometrial polyp (14%, 34/241), chronic endometritis (12%, 28/241), atrophic endometrium (6%, 15/241), endometrial hyperplasia (5%, 12/241), and endometrial carcinoma (2%, 5/241). Chronic endometritis was commonly seen in reproductive age (18%, 21/119); hormonal imbalance (45%, 35/77) and endometrial hyperplasia (6.5%, 5/77) in perimenopausal age; endometrial polyp (35.5%, 16/45) and endometrial carcinoma (9%, 4/45) in postmenopausal age.

CONCLUSION: Frequency of benign endometrial pathology is quite high in AUB, 236 participants (98%, 236/241). Histopathological spectrum in patients with AUB is quite variable with respect to age. The most common pattern of AUB was polymenorrhea. The most common pathology was hormonal imbalance. It is suggested that age was associated with more progressive lesions found in peri and postmenopausal age group such as endometrial hyperplasia and endometrial carcinoma. Yet endometrial polyp was the most common pathology found in postmenopausal women. Therefore, the management strategy should be individualized, as in most cases a restrictive approach is appropriate in order to avoid unnecessary hysterectomies.

- 34. Duckitt, K., & Collins, S. (2012). Menorrhagia. *BMJ Clinical Evidence*, 2012(1), 0805.**

Abstract: INTRODUCTION: Menorrhagia limits normal activities, and causes anaemia in two-thirds of women with objective menorrhagia (loss of 80 mL blood per cycle). Prostaglandin disorders may be associated with idiopathic menorrhagia, and with heavy bleeding due to fibroids, adenomyosis, or use of intrauterine devices (IUDs). Fibroids have been found in 10% of women with menorrhagia overall, and in 40% of women with severe menorrhagia; but half of

women having a hysterectomy for menorrhagia are found to have a normal uterus.

METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of medical treatments for menorrhagia? What are the effects of surgical treatments for menorrhagia? What are the effects of endometrial thinning before endometrial destruction in treating menorrhagia? We searched: Medline, Embase, The Cochrane Library, and other important databases up to June 2011 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organizations, such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA).

RESULTS: We found 39 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions.

CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following medical interventions: combined pill, danazol, etamsylate, gonadorelin analogues, intrauterine progesterone, non-steroidal anti-inflammatory drugs (NSAIDs), progestogens, and the following surgical interventions: dilatation and curettage, endometrial destruction, and hysterectomy.

35. Fraser, I. S., Mansour, D., Breyman, C., Hoffman, C., Mezzacasa, A., & Petraglia, F. (2015). Prevalence of heavy menstrual bleeding and experiences of affected women in a European patient survey. *Int J Gynaecol Obstet*, 128(3), 196-200. <https://doi.org/10.1016/j.ijgo.2014.09.027>

Abstract: **OBJECTIVE:** To examine the prevalence and impact of heavy menstrual bleeding (HMB) among women in Europe, and their experience of HMB assessment and management. **METHODS:** An internet-based survey was conducted among women (aged 18-57 years) in five European countries between January and February 2012. The prevalence of HMB among the general population was determined in a short survey, and women who had been diagnosed with HMB were then asked to complete an extended survey about their diagnosis and symptoms.

RESULTS: Overall, 4506 women responded, of whom 1225 (27.2%) had experienced two or more predefined HMB symptoms within the previous year. Of these women, 564 (46.0%) had never consulted a physician. Among 330 women who completed the detailed survey, 208 (63.0%) had ever been diagnosed with iron deficiency or iron-deficiency anemia. Symptoms associated with iron deficiency were used to help confirm a diagnosis in 83 (39.9%) women. Only 152 (46.1%) of the 330 patients with confirmed HMB had received prescription medication for iron deficiency.

CONCLUSION: Many women affected by HMB do not seek medical help, and few of those who do consult physicians report that they have received appropriate treatment. HMB continues to be underdiagnosed and poorly treated.

36. Gursel, T., Biri, A., Kaya, Z., Sivaslioglu, S., & Albayrak, M. (2014). The Frequency of Menorrhagia and Bleeding Disorders in University Students. *Pediatric Hematology and Oncology*, 31(5), 467-474. <https://doi.org/10.3109/08880018.2014.886316>

Abstract: STUDY OBJECTIVE: Menorrhagia is an important health problem in women of reproductive age. The aims of this study were to assess the prevalence of menorrhagia and hemostatic abnormalities associated with menorrhagia in university students. METHODS: The pictorial blood assessment chart (PBAC) was used to identify students with menorrhagia. Those with a PBAC score > 100 were examined by pelvic ultrasound and laboratory tests including complete blood count, levels of clotting factors, von Willebrand factor antigen, and ristocetin cofactor activity and Platelet Function Analyser-100 (PFA-100). Platelet aggregation was studied in students with prolonged PFA-100 closure time. RESULTS: Menorrhagia was identified in 82 (21.8%) of 376 students. Six of 82 students who had pelvic pathologies were excluded. Eleven (14.5%) of the remaining 76 students were found to have bleeding disorders, including von Willebrand disease in five (6.5%), platelet function disorder in four (5.2%), and clotting factor deficiencies in two (2.6%). CONCLUSIONS: Menorrhagia is a common but mostly unrecognized and untreated problem among university students. Underlying bleeding disorders are not rare and require comprehensive hemostatic evaluation for identification.

37. Haththotuwa, R., Goonewardene, M., Desai, S., Senanayake, L., Tank, J., & Fraser, I. (2011). Management of Abnormal Uterine Bleeding in Low- and High-Resource Settings: Consideration of Cultural Issues. *Seminars in Reproductive Medicine*, 29(05), 446–458. <https://doi.org/10.1055/s-0031-1287668>

Abstract: In non-industrialized countries the incidence of heavy menstrual bleeding (HMB) appears to be similar to that of industrialized countries, although data is scanty. In low-resource settings, women with abnormal uterine bleeding (AUB) often delay seeking medical care because of cultural beliefs that a heavy red menstrual bleed is healthy. Efforts to modify cultural issues are being considered. A detailed history and a meticulous examination are the important foundations of a definitive diagnosis and management in low-resource settings but are subject to time constraints and skill levels of the small numbers of health professionals. Women's subjective assessment of blood loss should be combined, if possible, with a colorimetric hemoglobin assessment, if full blood count is not possible. Outpatient endometrial sampling, transvaginal sonography, and hysteroscopy are available in some non-industrialized countries but not in the lowest resource settings. After exclusion of serious underlying pathology, hematinics should be commenced and antifibrinolytic or nonsteroidal anti-inflammatory drugs considered during menses to control the bleeding. Intrauterine or oral progestogens or the combined oral contraceptive are often the most cost-effective long-term medical treatments. When medical treatment is inappropriate or has failed, the surgical options available most often are myomectomy or hysterectomy. Hysteroscopic endometrial resection or newer endometrial ablation procedures are available in some centers. If hysterectomy is indicated the vaginal route is the most appropriate in most low-resource settings. In low-resource settings, lack of resources of all types can lead to empirical treatments or reliance on the unproven therapies of traditional healers. The shortage of human resources is often compounded by a limited availability of operative time. Governments and specialist medical organizations have rarely included attention to AUB and HMB in their health programs. Local guidelines and attention to training of doctors, midwives, and traditional health workers are critical for prevention and improvement in management of HMB and its consequences for iron deficiency anemia and postpartum hemorrhage, the major

killer of young women in developing countries.

38. Hemalatha, K., & Shruthi, S. (2018). Menstrual problem among adolescent girls regarding school absenteeism: a cross-sectional study. *Journal of Evolution of Medical and Dental Sciences*, 7(21), 2527–2530. <https://doi.org/10.14260/jemds/2018/568>

Abstract: BACKGROUND: Menstrual problems in adolescent girls are very common in this age group. Identification of abnormal menstrual problems is essential and correction is needed. In this study, we have attempted to study the frequency of menstrual problems and its impact on school and college attendance.

MATERIALS AND METHODS: In this study, 300 girls in the age group of 14 - 19 years who attained menarche were non-randomly selected for convenience. This study was carried out in a school and three colleges in Chengalpattu. Many criteria were applied and critically analysed.

RESULTS: Dysmenorrhoea was the commonest menstrual problem noticed, followed by irregular cycle pattern. There was a statistically significant association between school absenteeism and menstrual disorders.

CONCLUSION: Adolescent girls school health programme should include a provision for screening of adolescent girls for menstruation related problems, clearing misconception and offer them possible treatment options.

39. Katiyar, K., Chopra, H., Garg, S.K., Bajpai, S.K., Bano, T., Jain, S., Kumar, A. (2013). KAP study of menstrual problems in adolescent females in an urban area of Meerut. *Indian Journal of Community Health*, 25(3), 217–220. <https://www.iapsmupuk.org/journal/index.php/IJCH/article/view/317>

Abstract: BACKGROUND: Menstruation is an important milestone that results in development of sexual and reproductive capacity of girls. Adolescent girls do not have adequate knowledge about the abnormalities and healthy practices to be followed during menstruation.

OBJECTIVE: To find out the knowledge, attitude, practices regarding menstruation and treatment seeking behaviour for menstrual problems in adolescent females.

MATERIAL & METHODS: The present cross sectional study was carried out in an urban field practice area of Department of Community Medicine, LLRM Medical College, Meerut on adolescent girls. A sample of 384 was derived and girls were selected by systematic random sampling technique. Detailed information was collected on a predesigned and pretested questionnaire.

RESULTS: 38.5% girls were aware of menstruation prior to its onset out of which 66.9% learned from their mother. Only 14.6% of the menstruating girls were aware of at least one menstrual disorder. Dysmenorrhoea was found to be the most frequently occurring problem (58.4%), followed by oligomenorrhoea (16.2%), menorrhagia (13.9%), premenstrual tension (13.6%), infrequent menstruation (12.3%) and polymenorrhoea (12.2%). Out of the 226(72.7%) girls having menstrual problems 77.9% did not seek any treatment for their problems. 55.2% of the menstruating girls were using sanitary pads during menstruation.

CONCLUSION: The adolescent girls are not well prepared and do not have adequate information regarding menstruation which is an important event of life.

**40. Omran, A.R., Standley, C.C. (1981) *Family Formation Patterns and Health: Further Studies: An International Collaborative Study in Columbia, Egypt, Pakistan, and the Syrian Arab Republic* (pp. 271– 302). World Health Organization.
<https://apps.who.int/iris/handle/10665/37198>**

Summary: In the late 1970s, the World Health Organization (WHO) conducted a multi-country cross sectional survey of Family Formation Patterns and Health. Information on the prevalence of menstrual complaints in the past three months was obtained in seven countries. These data permit cross national comparisons in so far as similar questions with a similar time reference were asked. However, no definitions were provided and considerable variation in the interpretation of questions among individuals and across cultures is likely.

**41. Oni, T. H., Tshitangano, T. G. (2015). Prevalence of menstrual disorders and its academic impact amongst Tshivenda Speaking Teenagers in Rural South Africa. *Journal of Human Ecology, 51*(1-2), 214-219.
<https://doi.org/10.1080/09709274.2015.11906915>**

Abstract: This paper investigated the prevalence of menstrual disorders and its impact amongst Tshivenda speaking teenagers in rural South Africa. The paper adopted a quantitative approach using a descriptive survey design. Data were collected from a total of 173 randomly selected females, age 14-18 years from 10 secondary schools that makes up a rural Vhumbedzi circuit in the Limpopo province using a self-administered questionnaire. Validity and reliability of the instrument was ensured. Permission to enter the schools was obtained from the circuit manager. Parents/learners informed consent was obtained prior to data collection. Statistical package for Social Sciences was used to analyse data in terms of frequency and percentages. This study revealed high prevalence of undiagnosed menstrual disorders such as dysmenorrhea, heavy flow periods, irregular period and premenstrual syndrome, which are under-treated. The paper recommends screening for and school health education about menstrual problems to minimise the academic impact amongst teenagers.

**42. Rama Ravi; Shah, P. B.; Shanthi Edward; Palani Gopal; Sathiyasekaran, B. W. C. (2017). Social impact of menstrual problems among adolescent school girls in rural Tamil Nadu. *International Journal of Adolescent Medicine and Health, 30*(5).
<https://doi.org/10.1515/ijamh-2016-0088>.**

Abstract: BACKGROUND: Adolescence is a period of physiological, psychological and social transition between childhood and adulthood and is characterized by the onset of menstruation in girls. A adolescent girls are naïve about menstruation and they take time to adapt to these changes both socially and psychologically. This study was carried out to assess the psychosocial impact of menstrual problems among school going adolescent girls.

METHODS: This study is a cross-sectional study carried out in 350 school going adolescent girls in the year 2012 in the Thiruvallur district of Tamil Nadu. Girls who attained menarche 1 year prior to the data collection were included in the study. Data regarding background characteristics and psychosocial impact of menstrual problems were collected. Data was analyzed using SPSS ver. 15 software. The χ^2 -test was carried out to assess the statistical significance at the 95% level of significance.

RESULTS: The mean age of the participants was 14.7 years. In this study, 87.7% of the girls had

at least one menstrual problem. Among these, 78.5% could not attend school during menstruation, 51.1% were unable to perform household/sports activities ($p < 0.001$). It was observed that dysmenorrhea and menorrhagia were at increased risk of absenting the girls from school ($p < 0.05$).

CONCLUSION: The key to a sound adolescent health programme is a holistic approach which also focuses on the psychological and social domain of health. This could be achieved by involving all the stakeholders like parents, teachers, etc. to work as a team. It is also essential to develop adolescent friendly health services at the grassroots level.

43. Randhawa, J. K. . K. M. A. G. (2016). Menstrual disorders among young females of Amritsar. *Journal of Experimental Zoology, India, 19(1), 123-125.*
<https://www.cabdirect.org/cabdirect/abstract/20163131597>

Abstract: Menstruation is an important part of female reproductive cycle. The young adult female students are more exposed to stress as compared to any other age group. The different types of stress and its gravity are related to their jobs, studies, social and economic factors. Therefore, they are more prone to develop menstrual problems. The present study has been conducted to assess the menstrual pattern and associated factors like nutritional status and anemia among randomly selected young working females of Amritsar. A total of 100 young working females and college students were interviewed for common menstrual problems and out of 100, 76.00% girls have regular cycle while 24.00% have irregular cycle. The most prevalent disorder seen among them is dysmenorrhea, menorrhagia were 94.00% and 68.00%, while metorrhagia and oilgomenorrhoea were 11.00% and 13.00%. The most common PMS reported were backache, irritability, stress, headache, depression, and anxiety. Menstrual Problems are present among majority of the young females. The prevalence of menstrual problems in Amritsar girls is high and causes significant disruption to their daily activities which highlights the need for proper professional counseling.

44. Santos, I. S., Minten, G. C., Valle, N. C., Tuerlinckx, G. C., Silva, A. B., Pereira, G. A., & Carriconde, J. F. (2011). Menstrual bleeding patterns: A community-based cross-sectional study among women aged 18-45 years in Southern Brazil. *BMC Women's Health, 11(1), 26.*
<https://doi.org/10.1186/1472-6874-11-26>

Abstract: **BACKGROUND:** Population variation in the duration and amount of menstrual bleeding has received little attention in the literature. This study describes these characteristics and investigates the distribution of self-perceived amount of menstrual bleeding according to socio-demographic, behavioral, and reproductive characteristics.

METHODS: A community-based cross-sectional study was conducted among 18-45 years old women users of the 31 primary health care (PHC) facilities in Pelotas city (Brazil). Interviews with structured questionnaire were carried out in the waiting rooms during two work shifts. Heaviness of menstrual bleeding was determined through the answer to the question: "Usually how much blood do you lose in every period?" Crude and adjusted analyses through Poisson regression took into account the aggregation per PHC facility.

RESULTS: A total of 865 women were enrolled. Prevalence of heavy menstrual flow was 35.3% (95% CI 32.1-38.6%). In adjusted analyses, heavy menstrual bleeding was higher among the older, less educated and obese women, with higher number of pregnancies and who reported

longer menstrual periods, extra-menstrual bleeding and clots in the flow. Use of hormonal contraceptive methods was protective against heavy menses.

CONCLUSION: Heavy menstrual bleeding is highly prevalent at the community level, and is associated with socio-demographic and anthropometric women's characteristics, as well as with duration of menstruation, extra-bleeding and presence of clots.

45. Sommer, M., Phillips-Howard, P. A., Mahon, T., Zients, S., Jones, M., & Caruso, B. A. (2017). Beyond menstrual hygiene: addressing vaginal bleeding throughout the life course in low and middle-income countries. *BMJ Global Health*, 2(2), e000405. doi:10.1136/bmjgh-2017-000405

Abstract: Girls and women experience numerous types of vaginal bleeding. These include healthy reproductive processes, such as menstruation and bleeding after childbirth, but also bleeding related to health conditions, such as fibroids or cancer. In most societies, the management of menstruation is handled covertly, something girls are often instructed about at menarche. The management of other vaginal bleeding is often similarly discreet, although behaviors are not well documented. In many societies, cultural taboos frequently hinder open discussion around vaginal bleeding, restricting information and early access to healthcare. Additionally, the limited availability of clean, accessible water and sanitation facilities in many low and middle-income countries augments the challenges girls and women face in conducting daily activities while managing vaginal bleeding, including participating in school or work, going to the market or fetching water. This paper aims to highlight the key vaginal bleeding experiences throughout a woman's life course and the intersection of these bleeding experiences with their access to adequate water and sanitation facilities, information and education sources, and supplies. The aim is to address the silence around girls and women's vaginal bleeding and their related social, physical and clinical management needs across the life course; and highlight critical gaps that require attention in research, practice and policy around this neglected topic of health and gender equality.

46. Walraven, G., Ekpo, G., Coleman, R., Scherf, C., Morison, L., & Harlow, S. D. (2002). Menstrual disorders in rural Gambia. *Studies in Family Planning*, 33(3), 261–268. <http://www.ncbi.nlm.nih.gov/pubmed/12385087>

Abstract: As part of a community-based reproductive morbidity survey in rural Gambia, the prevalence and association of menstrual disorders with sociodemographic characteristics and other reproductive morbidities, and with knowledge, attitudes, and beliefs concerning menstrual problems were assessed. A questionnaire was administered by a field-worker and by a gynecologist, who also examined the women. Semistructured interviews were conducted to assess knowledge, attitudes, and beliefs in a subsample. Of 607 menstruating women not using hormonal contraceptives, 16 percent complained to the gynecologist of irregular cycles, 14 percent of dysmenorrhea, 8 percent of spotting, and 4 percent of heavy or prolonged bleeding. Each complaint was associated with other reproductive morbidities. A minority of women with menstrual problems had sought health care, and menstruation was revealed to be a highly personal and secretive topic in this population. Menstrual disorders constitute an important unaddressed area of reproductive health service needs in developing countries for which relatively simple and inexpensive therapies are often available. Information, education,

and support combined with clinical management of menstrual problems should be core elements of reproductive health programs.

Treatment of Menstrual Disorders

- 1. Azizkhani, M.; Dastjerdi, M. V.; Arani, M. T.; Pirjani, R.; Sepidarkish, M.; Ghorat, F.; Karimi, M. (2018). Traditional Dry Cupping Therapy Versus Medroxyprogesterone Acetate in the Treatment of Idiopathic Menorrhagia: A Randomized Controlled Trial. *Iran Red Crescent Med J*, 20(20), e60508. doi: 10.5812/ircmj.60508**

Abstract: BACKGROUND: Dry cupping has been used as a treatment for abnormal uterine bleeding in Iranian traditional medicine.

OBJECTIVES: The present study aimed at evaluating the usefulness of dry cupping on excessive menstrual blood loss in menorrhagia with a well- validated menstrual pictogram compared to medroxyprogesterone acetate.

METHODS: A total of 162 women with menorrhagia were enrolled in this prospective, randomized, controlled trial in Iran from 2015 to 2016. Written informed consent was obtained, then, patients were randomly allocated into dry cupping (three sessions of interrupted and kinetic dry cupping during menstrual bleeding) or medroxyprogesterone acetate (10 mg/day throughout the luteal period) groups using a random number sequence. The number of bleeding days and objective estimation of menstrual blood loss using a pictorial blood loss assessment chart (PBAC) were recorded before the intervention and at specific intervals (one and 3-months post-intervention).

RESULTS: At one and 3-months, PBAC scores were significantly lower in women treated with cupping compared with women treated with medroxyprogesterone acetate. These reductions in PBAC score were 214.9 mL with 95% CI (120.5 to 309.2) greater than medroxyprogesterone acetate at one month and 237.3 with 95% CI (143.0 to 331.7) at 3- month follow- up period. Reduction in the number of bleeding days in the cupping group for almost one day was better than the control groups at one and 3-months follow- up (Mean difference:-1.03, 95% CI (-1.78 to -0.26), P = 0.007).

CONCLUSIONS: Dry cupping is an effective treatment in reducing the intensity of bleeding during the menstrual period compared to medroxyprogesterone acetate.

- 2. Bahamondes, L., Ilza Monteiro, M., & Arlete Fernandes, F. (2010). Treatment of heavy menstrual bleeding with a new combination of estradiol valerate and dienogest.**

***Open Access Journal of Contraception*, 1, 119. <https://doi.org/10.2147/OAJC.S7943>**

Abstract: The first combined oral contraceptive (OC) was launched in the US 50 years ago and was followed by another formulation introduced in Germany one year later. The most common estrogen component in current formulations is ethinylestradiol; however, many concerns have been raised with respect to this estrogen. Although the natural estrogen produced by the ovary, 17-beta estradiol, is the most potent of the estrogens, it is poorly absorbed orally, and previous attempts to use it in combined OCs have been unsuccessful due to the occurrence of irregular bleeding. Recently, a new combined OC was developed containing a natural estrogen, estradiol valerate, and a new progestin, dienogest, in a dynamic 26-day, four-phasic (estrogen

stepdown and progestin stepup) scheme of administration. In clinical trials, its contraceptive performance was excellent, with good cycle control and bleeding patterns compared with other combined OCs or with placebo. This review focuses predominantly on the use of an estradiol valerate-dienogest combined OC for the treatment of heavy menstrual bleeding. The findings of two large, randomized, controlled trials have shown that this combined OC constitutes an effective treatment for women with heavy menstrual bleeding, representing a new therapeutic option to reduce menstrual blood loss. Further studies are necessary to confirm these data.

3. Cetin, N. N., Karabacak, O., Korucuoglu, U., & Karabacak, N. (2009). Gonadotropin-releasing hormone analog combined with a low-dose oral contraceptive to treat heavy menstrual bleeding. *International Journal of Gynecology & Obstetrics*, 104(3), 236–239. <https://doi.org/10.1016/j.ijgo.2008.10.032>

Abstract: OBJECTIVE: To compare the effects of low-dose oral contraceptives used alone and in combination with a gonadotropin-releasing hormone (GnRH) analog to treat heavy menstrual bleeding.

METHODS: Fifty-eight patients with heavy menstrual bleeding were prospectively randomized into two treatment groups to receive either a low-dose oral contraceptive alone (group 1), or combined with a GnRH analog (group 2) for 6 months. The patients' hormonal profiles, and hemoglobin and hematocrit levels were measured at the beginning and at the end of the treatment period.

RESULTS: Hemoglobin and hematocrit levels significantly improved in both groups after 6 months of treatment ($P < 0.05$ and $P < 0.01$, respectively). Even in the first month of the study, the number of pads used and the duration of menstruation were significantly decreased in both groups and markedly lower in group 2 ($P < 0.01$).

CONCLUSION: The addition of a GnRH analog to low-dose oral contraceptive treatment for heavy menstrual bleeding resulted in better control of vaginal bleeding, even in the first month of therapy.

4. Helal, A. S., Abdel-Hady, E.-S., Mashaly, A. E.-M., Shafaie, M. El, & Sherif, L. (2011). Modified thermal balloon endometrial ablation in low resource settings: a cost-effective method using Foley's catheter. *Archives of Gynecology and Obstetrics*, 284(3), 671–675. <https://doi.org/10.1007/s00404-010-1744-2>

Abstract: OBJECTIVE: To assess the efficacy of a modified Foley's catheter endometrial ablation in the treatment of abnormal uterine bleeding in low resource settings.

METHODS: Four hundred and thirty premenopausal women with abnormal uterine bleeding were subjected to thermal balloon endometrial ablation using modified Foley's catheter. The primary outcome measure was patient satisfaction regarding menstrual blood loss. Secondary measures included improvement in quality of life scores and failure rates.

RESULTS: Three hundred and three patients were available for evaluation at 3-year follow up. 270/303 (89.1%) reported their satisfaction as indicated by reduction in days of menstrual flow per cycle (4.2 vs. 8.8 days, $p < 0.0001$). There was a significant improvement in quality of life scores ($p < 0.0001$). The rate of failure varies according to the interval of follow up from 15.6% at 6 months to 10.9% at 3 years.

CONCLUSION: Modified Foley's catheter endometrial ablation is a cost effective alternative to other thermal endometrial ablation techniques in the treatment of abnormal uterine bleeding in low resource settings.

5. Karimian, Z.; Sadat, Z.; Bahrami, N.; Kafaie, M. (2015). Comparison of chamomile and mefenamic acid capsules in hemorrhage of menstruation. *Iranian Journal of Obstetrics, Gynecology and Infertility*, 18(157), 11-17.
<https://dx.doi.org/10.22038/ijogi.2015.4780>

Abstract: INTRODUCTION: Menstrual disorders can cause many problems for women at different periods, and sometimes diagnosis and treatment of these disorders manifests as a problem in clinical medicine. Due to the high prevalence of menstrual disorders and fewer side effects of herbal medicines than chemical drugs, this study was performed with aim to compare the effects of chamomile and mefenamic acid capsules in hemorrhage of menstruation.

METHODS: This triple-blind randomized clinical trial study was performed on 90 students living in dormitories of Kashan University of Medical Sciences. They were randomly divided into two groups of chamomile and mefenamic acid. 45 cases received 250 mg of chamomile and 45 cases received 250 mg mefenamic acid per 8 hour for two cycles. Data collection tool was questionnaire, and Higgam standard test was used to determine bleeding. Data was analyzed by SPSS statistical software (version 16), and Chi-square test, T-test, Fisher and paired t-test.

RESULTS: The amount of bleeding was significantly decreased in both treatment groups compared to pre-treatment ($P < 0.05$), but the difference between two groups was not significant ($P > 0.05$). Decreased amount of bleeding caused by chamomile and mefenamic acid was not different in the second cycle compared to first cycle ($P > 0.05$).

CONCLUSION: The use of chamomile capsule can decrease hemorrhage in menstruation, so its consumption is recommended to treat this disorder in women. © 2015, Mashhad University of Medical Sciences. All rights reserved.

6. Kapur, K., Joneja, G.S., Biswa, M. (2007). Uterine balloon therapy: An alternative therapy for menorrhagia. *Medical Journal Armed Forces India*, 63(1), 36-39.
[https://doi.org/10.1016/S0377-1237\(07\)80105-5](https://doi.org/10.1016/S0377-1237(07)80105-5)

Abstract: BACKGROUND: Menorrhagia is a common problem in women of reproductive age. Its aetiology in the absence of organic pathology, hormonal or haematological disorders remains largely unknown. Traditional medical therapy may not be beneficial in the long run.

Hysterectomy for this condition is an invasive over treatment. First generation endometrium ablation techniques aimed at destroying the endometrium, were associated with life threatening complications. The second generation endometrial ablation techniques like uterine thermal balloon therapy have reduced these problems.

METHODS: Fifty patients were selected for the procedure between 2002 and 2005. The patients qualified for the procedure if they had completed their family, had normal pelvic ultrasound findings, benign endometrial histology, normal PAP smear and clinically a normal size or bulky uterus.

RESULTS: 50% patients were in the age group of 35-45 years. 28(56%) procedures were done under local anaesthesia and 22(44%) under general anaesthesia. The patients were followed

up for a period of 3 to 29 months (median 16 months). Seven(14%) had amenorrhoea and 40(80%) had normal periods or hypomenorrhoea. Three(6%) patients continued to have menorrhagia and were considered failures. 94% patients were satisfied with the procedure and there were no complications in this series. Conclusions : Uterine balloon therapy is a simple, safe and effective method for the treatment of menorrhagia in selected patients.

7. Mandal, D., Hazra, A., Maity, T., Parmanik, S., Surana, S., & Mandal, S. (2014).

Comparative study of low-dose oral contraceptive pill and ormeloxifene in the treatment of dysfunctional uterine bleeding. *International Journal of Health & Allied Sciences*, 3(4), 225. doi: 10.4103/2278-344X.143056

Abstract: BACKGROUND: Role of oral contraceptive pill (OCP) and ormeloxifene (ORM) in dysfunctional uterine bleeding (DUB) is still in an exploring level. Aim: The aim was to observe the improvement of the menstrual bleeding pattern in terms of the amount, regularity, and hemoglobin (Hb) status of the women. Setting: Study was conducted in the Department of Obstetrics and Gynecology of IPGMER and SSKM Hospital, Kolkata a tertiary care teaching hospital. Design: Prospective randomized study with patients having subjective complaints of menorrhagia.

MATERIALS AND METHODS: A total of 36 women was treated with ORM 60 mg and OCP containing 30 [micro]g ethinyl estradiol and 150 [micro]g desogestrel was given to 34 women. Pictorial blood loss assessment chart (PBAC) was applied to assess the amount of bleeding. Statistical Analysis Used: Data were compared using a t-test (paired and unpaired) and Mann-Whitney U-test for numerical variables and McNemar's Chi-square test for categorical variables.

RESULTS: The primary outcome showed a comparable PBAC score of ORM in first posttreatment cycle and significantly better in following two cycles (PBAC - postC1: 0.118, PBAC - postC2: 0.016, and PBAC - postC3: 0.04). Group receiving OCP was observed to have good cycle regularity in comparison to ORM (P = 0.006). Hb rise in both groups was almost similar, OCP group revealed an improvement in mean Hb concentration of 0.65 g%, whereas ORM showed a rise of 0.72 g%. Secondary outcomes were adverse reactions, satisfaction level, and poor responders in both groups.

CONCLUSION: ORM is effective in treating DUB in almost in all aspects and can be considered as nonsteroidal option of therapy.

8. Qaraaty, M.; Kamali, S. H.; Dabaghian, F. H.; Zafarghandi, N.; Mokaberinejad, R.; Mobli, M.; Amin, G.; Naseri, M.; Kamalinejad, M.; Amin, M.; Ghaseminejad, A.; HosseiniKhabiri, S. J.; Talei, D. (2014). Effect of myrtle fruit syrup on abnormal uterine bleeding: a randomized double-blind, placebo-controlled pilot study. *Daru*, 22(1), 45. doi: 10.1186/2008-2231-22-45

Abstract: BACKGROUND: Myrtle (*Myrtus communis* L.) has been used in the Iranian Traditional Medicine as a treatment for abnormal uterine bleeding-menometrorrhagia. The main aim of this study is to evaluate the effect of myrtle fruit syrup on abnormal uterine bleeding-menometrorrhagia.

METHODS: A randomized, double-blind, placebo-controlled pilot study was conducted on 30 women suffering from abnormal uterine bleeding-menometrorrhagia. Treatment comprised of

giving 15 ml oral myrtle syrup daily (5 ml three times a day) for 7 days starting from the onset of bleeding. The myrtle syrup along with placebo was repeated for 3 consecutive menstrual periods. Menstrual duration and number of used pads were recorded by the Pictorial Blood loss Assessment Chart at the end of each menstrual period. The quality of life was also evaluated using the menorrhagia questionnaire.

RESULTS: The mean number of bleeding days significantly declined from 10.6 ± 2.7 days to 8.2 ± 1.9 days after 3 months treatment with the syrup ($p = 0.01$) and consequently the participants in the intervention group used fewer pads after 3 months (16.4 ± 10.7) compared with the number of pads used at the beginning of the treatment (22.7 ± 12.0 , $p = 0.01$). Bleeding days and number of pads used by the participants in the placebo group did not change significantly. Also significant changes of quality of life scores were observed in the intervention group after 3 months compared to the baseline.

CONCLUSION: Myrtle syrup is introduced as a potential remedy for abnormal uterine bleeding-menometrorrhagia.

- 9. Rajith, N. P.; Ambily, D. V.; Dan, V. M.; Devi, P. S.; George, V.; Pushpangadan, P. (2012). A survey on ethnomedicinal plants used for menstrual disorders in Kerala. *Indian Journal of Traditional Knowledge*, 11(3), 453-460.**
<http://nopr.niscair.res.in/bitstream/123456789/14386/1/IJTK%2011%283%29%20453-460.pdf>

Abstract: There are distinct biological and gender related differences between man and woman. Because of their special reproductive role, women are at risk of some distinctly gender related disorders. A survey of ethnomedicinal plants used in the rural areas of Kerala gave valuable ethnomedico-botanical information regarding plants used for menstrual disorders. The present study enumerates 19 plant species against Menorrhagia, 26 plant species against Dysmenorrhoea, 25 plant species against Oligomenorrhoea, 5 plant species against Hypomenorrhoea, 4 plant species for Amenorrhoea and 18 plant species which can be included in food during menstrual cycle.

- 10. Vidyasagar, G. M.; Siddalinga, S. M. M. (2010). Ethnomedicinal plants used to treat menstrual disorders by tribal people in Bellary district of Karnataka, India. *International Journal of Pharmacy & Life Sciences*, 3(7), 1871-1876. ISSN: 0976-7126. Available [here](#).**

Abstract: An ethnobotanical survey of Bellary district, comprising seven taluks was conducted during May 2009 to July 2011. The main purpose of this survey was to document the traditional use of medicinal plants for the treatment of menstrual disorders of women in Bellary district. Twenty six species of folk drug plants belonging to 24 genera and 21 families were found to be used as a remedy for this problem by the tribal and rural women. The scientific name, family and local names of these medicinal plants along with habit, part used and mode of their administrations are provided.

- 11. van Andel, T., de Boer, H. J., Barnes, J., & Vandebroek, I. (2014). Medicinal plants used for menstrual disorders in Latin America, the Caribbean, sub-Saharan Africa, South and Southeast Asia and their uterine properties: A review. *Journal of***

Ethnopharmacology, 155(2), 992–1000. <https://doi.org/10.1016/j.jep.2014.06.049>

Abstract: ETHNOPHARMACOLOGICAL RELEVANCE: Menstrual disorders are generally not perceived as major health concerns by global health organizations, despite being disruptive to women's daily activities, particularly when access to sanitary facilities or analgesics is limited. Improving menstrual health requires access to safe and effective medication, but many women in Latin America, Africa or Asia prefer traditional medicine above modern remedies (such as contraceptives), as they can cause physical symptoms associated with fertility loss. Many medicinal plants are used for menstrual disorders, but few have been examined for their pharmacological activities related to traditional uses. Plants that have a smooth muscle-relaxant effect could ease menstrual cramps, but there are indications that dysmenorrhea in low-income countries is commonly treated with emmenagogues. This review aims to assess the most salient plants used to treat menstrual morbidity in Latin America and the Caribbean, sub-Saharan Africa, South and Southeast Asia, their uterine properties and adverse effects. To test whether plants used for painful menstruation could have uterine contracting properties, we recorded whether these species were also used to ease birth, induce menstruation, abortion or expel the afterbirth, as these suggest spasmogenic activities.

MATERIALS AND METHODS: We reviewed the literature documenting traditional plant use in the study area for dysmenorrhea, regulating or inducing menstruation, uterine cleansing, uterine fibroids, expelling the placenta and lochia and for easing childbirth. Thirty genera (59 species) used in at least two continents or frequently throughout one continent, were shortlisted from the 90 most salient plant species emerging from our literature review. Using Medline, we searched for pharmacological properties and/or mechanisms of action relevant to their traditional uses of the shortlisted species. We searched VigiBase™, the WHO global individual case safety report database, on reported adverse drug reactions associated with these species.

RESULTS: More than 2000 plant species are used for menstrual disorders in the study area. The most salient uses are to treat painful menstruation, induce or regulate menses, and induce abortion. Around half (29) of the 59 most salient species have been tested for their pharmacological effects, of which 48% act as uterine spasmolytics and 31% as uterine spasmogenics. Several frequently used species contain toxic constituents, which may put women and their unborn children at serious risk. VigiBase™ listed adverse drug reactions for 18 of these species, but few reports came from the study area.

CONCLUSIONS: Research into the risks and benefits of medicinal plants for menstrual complaints should be given a higher priority in reproductive health programs that respect traditional knowledge and practices. Increased data collection is needed on adverse drug reactions among women using herbal medicines for reproductive health, especially in countries with limited reproductive health facilities.

12. Yassin, S. A. T. (2012). Herbal remedy used by rural adolescent girls with menstrual disorders. *Journal of American Science*, 8(1), 467-473. ISSN: 1545-1003

Abstract: The study aimed to determine the herbal remedy used by rural adolescent girls with menstrual disorders. The study comprised 900 adolescent students (aged 12-18years old) from preparatory and secondary schools in rural village in Elbehira governorate, Egypt. An interview schedule was developed and used to collect the necessary data. The results revealed that

89.9% of the adolescent girls had suffered from dysmenorrhea. 78% of them had used herbal remedy for treatment. Premenstrual syndrome (PMS) was experienced by 77.7% of the study subjects 72.7% of them had used herbal remedy for treatment. The type of herbs used in management of PMS and dysmenorrhea were fenugreek, peppermint and aniseed which were effective among almost all of the study subjects. Green tea, cinnamon and basil were moderately effective. Fenugreek, chamomile and cinnamon were effective in the management of amenorrhea. In spite of its high prevalence and enormous impact on their lives girls believed that dysmenorrhea is a normal part of the female menstrual cycle and only 16.1% sought medical treatment. A great number of adolescents obtained information from their mothers (62.7%) and peers (46.7%). These findings imply the need for educating adolescent girls on effective management of dysmenorrhea. Education should be extended to parents and school peer leaders to address the reproductive health needs of adolescents.

Urogenital Tract Infections and Linkages with Menstruation

1. Atashili, J., Poole, C., Ndumbe, P. M., Adimora, A. A., & Smith, J. S. (2008). Bacterial vaginosis and HIV acquisition: A meta-analysis of published studies. *AIDS (London, England)*, 22(12), 1493–1501. <https://doi.org/10.1097/qad.0b013e3283021a37>

Abstract: OBJECTIVES: To assess and summarize the published literature on the extent to which bacterial vaginosis may increase the risk of HIV acquisition. Design: Meta-analysis of published studies. METHODS: Medline and other electronic databases were systematically searched for eligible publications. The association between bacterial vaginosis and incident HIV was separately analyzed from that between bacterial vaginosis and prevalent HIV. The latter was further analyzed, stratified by bacterial vaginosis diagnostic method, HIV risk profile of the study population, and whether or not adjusted estimates were presented.

RESULTS: Twenty-three eligible publications were identified, including a total of 30,739 women. Bacterial vaginosis was associated with an increased risk of HIV acquisition in HIV-incidence studies (relative risk = 1.6, 95% confidence interval: 1.2, 2.1). All but one of 21 HIV-prevalence studies reported estimates above the null. The latter results were heterogeneous and showed some evidence of funnel plot asymmetry, precluding the estimation of a single summary measure. The association between bacterial vaginosis and HIV in prevalence studies appeared stronger for women without high-risk sexual behavior.

CONCLUSION: Bacterial vaginosis was consistently associated with an increased risk of HIV infection. High bacterial vaginosis prevalence may result in a high number of HIV infections being attributable to bacterial vaginosis. More prospective studies are needed to accurately evaluate the role of bacterial vaginosis in HIV acquisition in low-risk versus high-risk women. Furthermore, randomized clinical trials may be worth considering to determine the effect of bacterial vaginosis control measures on HIV acquisition.

2. Das, P., Baker, K. K., Dutta, A., Swain, T., Sahoo, S., Das, B. S., et al. (2015). Menstrual Hygiene Practices, WASH Access and the Risk of Urogenital Infection in Women from Odisha, India. *PLoS One*, 10(6), e0130777. <https://dx.doi.org/10.1371/journal.pone.0130777>

Abstract: Menstrual hygiene management (MHM) practices vary worldwide and depend on the individual's socioeconomic status, personal preferences, local traditions and beliefs, and access

to water and sanitation resources. MHM practices can be particularly unhygienic and inconvenient for girls and women in poorer settings. Little is known about whether unhygienic MHM practices increase a woman's exposure to urogenital infections, such as bacterial vaginosis (BV) and urinary tract infection (UTI). This study aimed to determine the association of MHM practices with urogenital infections, controlling for environmental drivers. A hospital-based case-control study was conducted on 486 women at Odisha, India. Cases and controls were recruited using a syndromic approach. Vaginal swabs were collected from all the participants and tested for BV status using Amsel's criteria. Urine samples were cultured to assess UTI status. Socioeconomic status, clinical symptoms and reproductive history, and MHM and water and sanitation practices were obtained by standardized questionnaire. A total of 486 women were recruited to the study, 228 symptomatic cases and 258 asymptomatic controls. Women who used reusable absorbent pads were more likely to have symptoms of urogenital infection (AdjOR=2.3, 95%CI1.5-3.4) or to be diagnosed with at least one urogenital infection (BV or UTI) (AdjOR=2.8, 95%CI1.7-4.5), than women using disposable pads. Increased wealth and space for personal hygiene in the household were protective for BV (AdjOR=0.5, 95%CI0.3-0.9 and AdjOR=0.6, 95%CI0.3-0.9 respectively). Lower education of the participants was the only factor associated with UTI after adjusting for all the confounders (AdjOR=3.1, 95%CI1.2-7.9). Interventions that ensure women have access to private facilities with water for MHM and that educate women about safer, low-cost MHM materials could reduce urogenital disease among women. Further studies of the effects of specific practices for managing hygienically reusable pads and studies to explore other pathogenic reproductive tract infections are needed.

3. Phillips-Howard, P. A., Nyothach, E., ter Kuile, F. O., Omoto, J., Wang, D., Zeh, C., et al. (2016). Menstrual cups and sanitary pads to reduce school attrition, and sexually transmitted and reproductive tract infections: a cluster randomised controlled feasibility study in rural Western Kenya. *BMJ Open*, 6(11), e013229. <https://doi.org/10.1136/bmjopen-2016-013229>

Abstract: OBJECTIVES: Conduct a feasibility study on the effect of menstrual hygiene on schoolgirls' school and health (reproductive/sexual) outcomes.

DESIGN: 3-arm single-site open cluster randomized controlled pilot study. Setting: 30 primary schools in rural western Kenya, within a Health and Demographic Surveillance System.

PARTICIPANTS: Primary schoolgirls 14–16 years, experienced 3 menses, no precluding disability, and resident in the study area.

INTERVENTIONS: 1 insertable menstrual cup, or monthly sanitary pads, against 'usual practice' control. All participants received puberty education preintervention, and hand wash soap during intervention. Schools received hand wash soap. Primary and secondary outcome measures: Primary: school attrition (drop-out, absence); secondary: sexually transmitted infection (STI) (*Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoea*), reproductive tract infection (RTI) (bacterial vaginosis, *Candida albicans*); safety: toxic shock syndrome, vaginal *Staphylococcus aureus*. Results: Of 751 girls enrolled 644 were followed-up for a median of 10.9 months. Cups or pads did not reduce school dropout risk (control=8.0%, cups=11.2%, pads=10.2%). Self-reported absence was rarely reported and not assessable. Prevalence of STIs in the end-of-study survey among controls was 7.7% versus 4.2% in the cups

arm (adjusted prevalence ratio (aPR) 0.48, 0.24 to 0.96, $p=0.039$), 4.5% with pads (aPR=0.62; 0.37 to 1.03, $p=0.063$), and 4.3% with cups and pads pooled (aPR=0.54, 0.34 to 0.87, $p=0.012$). RTI prevalence was 21.5%, 28.5% and 26.9% among cup, pad and control arms, 71% of which were bacterial vaginosis, with a prevalence of 14.6%, 19.8% and 20.5%, per arm, respectively. Bacterial vaginosis was less prevalent in the cups (12.9%) compared with pads (20.3%, aPR=0.65, 0.44 to 0.97, $p=0.034$) and control (19.2%, aPR=0.67, 0.43 to 1.04, $p=0.075$) arm girls enrolled for 9 months or longer. No adverse events were identified.

CONCLUSIONS: Provision of menstrual cups and sanitary pads for ~1 school-year was associated with a lower STI risk, and cups with a lower bacterial vaginosis risk, but there was no association with school dropout. A large-scale trial on menstrual cups is warranted.

4. Reichelderfer, P. S., Coombs, R. W., Wright, D. J., Cohn, J., Burns, D. N., Cu-Uvin, S., et al. (2000). Effect of menstrual cycle on HIV-1 levels in the peripheral blood and genital tract. *AIDS*, 14(14), 2101–2107. <https://doi.org/10.1097/00002030-200009290-00005>

Abstract: OBJECTIVE: To assess the variation in HIV-1 over the menstrual cycle, including RNA levels in the female genital tract, plasma HIV-1-RNA levels, CD4 cell counts, and culturable virus. Design: A prospective analysis of 55 HIV-1-infected women.

METHODS: Blood and genital tract specimens were collected weekly over 8 weeks, spanning two complete menstrual cycles. Applying repeated-measures models that used menses as the reference level, the variation in viral RNA levels was compared in endocervical canal fluid and cells (collected by Sno-strips and cytobrush, respectively) and ectocervicovaginal lavage (CVL) fluid. Repeated-measures models were also used to assess the variation in plasma CD4 cell counts and viral load.

RESULTS: Shedding patterns differed among the three sampling methods, independent of genital tract co-infections. Genital tract HIV-1-RNA levels from CVL fluid and endocervical canal cytobrush specimens were highest during menses and lowest immediately thereafter ($P = 0.001$ and $P = 0.04$). The HIV-1-RNA level in endocervical canal fluid was highest in the week preceding menses ($P = 0.003$). The menstrual cycle had no effect on blood levels of RNA ($P = 0.62$), culturable virus ($P = 0.34$), or CD4 cell counts ($P = 0.55$). HIV-1-RNA levels were higher in endocervical canal fluid than in peripheral blood plasma during the late luteal phase ($P = 0.03$). CONCLUSION: HIV-1-RNA levels vary with the menstrual cycle in the female genital tract but not the blood compartment. HIV-1-RNA levels are higher in endocervical canal fluid than in blood plasma. These findings may have important implications for sex-specific pathogenesis, heterosexual transmission, and contraceptive hormone interventions in HIV-1-infected women.

5. Sumpter, C., & Torondel, B. (2013). A Systematic Review of the Health and Social Effects of Menstrual Hygiene Management. *PLoS One*, 8(4), e62004. <https://doi.org/10.1371/journal.pone.0062004>

Abstract: BACKGROUND: Differing approaches to menstrual hygiene management (MHM) have been associated with a wide range of health and psycho-social outcomes in lower income settings. This paper systematically collates, summarizes and critically appraises the available evidence. METHODS: Following the PRISMA guidelines a structured search strategy was used to identify articles investigating the effects of MHM on health and psycho-social outcomes. The search was conducted in May 2012 and had no date limit. Data was (sic) extracted and quality

of methodology was independently assessed by two researchers. Where no measure of effect was provided, but sufficient data were available to calculate one, this was undertaken. Meta-analysis was conducted where sufficient data were available.

RESULTS: 14 articles were identified which looked at health outcomes, primarily reproductive tract infections (RTI). 11 articles were identified investigating associations between MHM, social restrictions and school attendance. MHM was found to be associated with RTI in 7 papers. Methodologies however varied greatly and overall quality was low. Meta-analysis of a subset of studies found no association between confirmed bacterial vaginosis and MHM (OR: 1.07, 95% CI: 0.52–2.24). No other substantial associations with health outcomes were found. Although there was good evidence that educational interventions can improve MHM practices and reduce social restrictions there was no quantitative evidence that improvements in management methods reduce school absenteeism.

CONCLUSION: The management of menstruation presents significant challenges for women in lower income settings; the effect of poor MHM however remains unclear. It is plausible that MHM can affect the reproductive tract but the specific infections, the strength of effect, and the route of transmission, remain unclear. There is a gap in the evidence for high quality randomized intervention studies which combine hardware and software interventions, in particular for better understanding the nuanced effect improving MHM may have on girls' attendance at school.

6. Villanueva, J. M., Ellerbrock, T. V., Lennox, J. L., Bush, T. J., Wright, T. C., Pratt- Palmore, M., et al. (2002). The Menstrual Cycle Does Not Affect Human Immunodeficiency Virus Type 1 Levels in Vaginal Secretions. *The Journal of Infectious Diseases*, 185(2), 170-177. <https://doi.org/10.1086/338447>

Abstract: To determine whether the menstrual cycle affects human immunodeficiency virus (HIV) type 1 levels in vaginal secretions, vaginal lavage samples were collected at 7, 14, and 21 days after initiation of menses, to compare virus levels during the follicular, ovulatory, and luteal phases. During 33 menstrual cycles in 25 women, HIV-1 RNA levels in vaginal secretions ranged from ,1000 to 5.3E 107 copies per lavage, and weekly changes ranged from ,0.5 to 2.5 log10 copies per lavage. HIV-1 RNA levels in vaginal lavage samples from days 7, 14, and 21 were not significantly different. No discernible pattern was found in changes of vaginal virus loads (VVLs) during the menstrual cycle. VVLs were not correlated with plasma estradiol or progesterone levels (P . .05). These results suggest that hormonal changes during the menstrual cycle do not have a significant effect on HIV-1 RNA levels in vaginal secretions.

Relevant Articles Cross-Referenced from Other Sections

In Programmatic Interventions

Juma, J., Nyothach, E., Laserson, K. F., Oduor, C., Arita, L., Ouma, C., et al. (2017). Examining the safety of menstrual cups among rural primary school girls in western Kenya: observational studies nested in a randomised controlled feasibility study. *BMJ Open*, 7(4), e015429. <https://doi.org/10.1136/bmjopen-2016-015429>

CONTRACEPTIVE-INDUCED MENSTRUAL CHANGES (CIMCs)

Frequency of Contraceptive-Induced Menstrual Changes (CIMCs)

1. Bachmann, G., & Korner, P. (2007). Bleeding patterns associated with oral contraceptive use: a review of the literature. *Contraception*, 76(3), 182-189.
<https://doi.org/10.1016/j.contraception.2007.05.081>

Abstract: The regulation of vaginal bleeding is an important effect impacting the choice of contraceptive methods. However, comparing vaginal bleeding control and disturbance between various contraceptive studies is often limited by the lack of uniformity in the analysis and reporting of the bleeding patterns. In 1986, the World Health Organization (WHO) issued recommendations for the standardized collection, analysis and reporting of bleeding associated with contraceptives based on 90-day reference periods. We systematically reviewed MEDLINE and EMBASE for all articles reporting bleeding data by reference periods in healthy women using oral contraception. Overall, 17 publications between 1986 and September 2006 were included for review. There was marked variability in the reporting of bleeding data with most studies reporting a few selected bleeding parameters. However, these studies showed, in general, that oral contraceptive users have the greatest bleeding (i.e., results in the highest number of bleeding/spotting days) during the first reference period which decreases by Reference Period 4. Reporting of the bleeding/spotting data using the WHO recommendations may be useful in objectively comparing vaginal bleeding patterns among different oral contraceptive products.

2. Beckert, V., Ahlers, C., Frenz, A.-K., Gerlinger, C., Bannemerschult, R., & Lukkari-Lax, E. (2019). Bleeding patterns with the 19.5 mg LNG-IUS, with special focus on the first year of use: implications for counselling. *European Journal of Contraceptive and Reproductive Healthcare*, 24(4), 251–259.
<https://doi.org/10.1080/13625187.2019.1630817>

Abstract: **OBJECTIVE:** The aim of the study was to provide an additional, detailed description of early bleeding patterns with the 19.5 mg levonorgestrel-releasing intrauterine system (LNG-IUS). **METHODS:** We conducted a pooled analysis of the bleeding diaries of participants in a previously reported phase II randomised controlled study ($n = 741$) and a phase III study ($n = 2904$), with 2-year extension phase ($n = 707$), of the 19.5 mg LNG-IUS. Main outcome measures were the median number of bleeding and/or spotting days per 30-day reference period for 12 months and the influence of the previous contraceptive method and levonorgestrel dose on bleeding patterns.

RESULTS: The pooled analysis comprised 1697 women. There was a progressive decline in the number of bleeding and/or spotting days from month 1: the proportion of women with ≤ 4 bleeding and/or spotting days per month increased from 6.2% in month 1 to 15.8% in month 2, 26.0% in month 3, 39.3% in month 6 and 54.1% in month 12. The median number of bleeding and/or spotting days in month 1 was lowest in women who had previously been using an LNG-IUS.

CONCLUSION: Analysis of bleeding diaries using 30-day reference periods provides detailed insight into bleeding changes in the first months following placement of the 19.5 mg LNG-IUS.

This insight may prove useful when counselling women about contraceptive choice and method continuation.

3. Cheng Toh, Y., Jain, J., Rahunny, M. H., Bode, F. R., & Ross, D. (2004). Suppression of ovulation by a new subcutaneous depot medroxyprogesterone acetate (104 mg/0.65 ml) contraceptive formulation in Asian women. *Clinical Therapeutics*, 26(11), 1845–1854. <https://doi.org/10.1016/j.clinthera.2004.11.013>

Abstract: BACKGROUND: A new progestin-only, nondaily depot medroxyprogesterone acetate (DMPA) SC injectable contraceptive suspension (104 mg/0.65 mL) has been developed. Clinical trials (including dose-ranging, pharmacokinetic/pharmacodynamic, and contraceptive efficacy studies) indicating the effectiveness of this new formulation were conducted primarily in white women. However, results of an early study by the World Health Organization suggested that in Thai women, medroxyprogesterone acetate (MPA) may be metabolized in $<91 \pm 7$ days (the range for effective suppression of ovulation established in clinical trials), resulting in a faster return to ovulation in this population.

Objectives: This study was designed to determine the duration of ovulation suppression and investigate the pharmacokinetic profile of MPA after a single SC injection of DMPA 104 mg/0.65 mL in Asian women. It also assessed the effect of ethnicity and injection site on the duration of ovulation suppression.

METHODS: This was a single-center, single-dose, open-label outpatient trial conducted in Singapore in Asian women aged 18 to 40 years. After 1 control cycle, women with confirmed ovulation were randomized in a 1:1 ratio to receive an SC injection of DMPA 104 mg/0.65 mL in either the anterior thigh or the abdomen. Serum concentrations of MPA, progesterone, estradiol, luteinizing hormone, and follicle-stimulating hormone were measured during the 91-day dosing interval and for an additional 15 days thereafter.

RESULTS: Twenty-four Asian women (mean [SD] age, 33.8 [43] years; range, 22.7–40.1 years; mean [SD] body mass index, 22.4 [3.0] kg/m²) belonging to 5 ethnic groups (Chinese, Filipino, Indian, Malaysian, and Thai) were included in the study. Ovulation suppression was maintained throughout the 91-day dosing interval, regardless of ethnicity or injection site. Ovulation was suppressed for at least 112 days after injection in 23 (95.8%) women, as evidenced by maintenance of serum progesterone concentrations <4.7 ng/mL. The pharmacokinetic parameters for MPA in these Asian women were similar to those previously reported in white women. The most frequently reported adverse events were flulike symptoms and headache, all of mild to moderate intensity. No serious adverse events were reported.

CONCLUSIONS: In this study, SC DMPA 104 mg/0.65 mL provided effective suppression of ovulation for at least 91 days in Asian women. Ethnicity and injection site had no effect on MPA profiles.

4. Creinin, M. D., Jansen, R., Starr, R. M., Gobburu, J., Gopalakrishnan, M., & Olariu, A. (2016). Levonorgestrel release rates over 5 years with the Liletta® 52-mg intrauterine system. *Contraception*, 94(4), 353–356. <https://doi.org/10.1016/j.contraception.2016.04.010>

Abstract: OBJECTIVE: To understand the potential duration of action for Liletta®, we conducted this study to estimate levonorgestrel (LNG) release rates over approximately 5½ years of product use.

METHODS: Clinical sites in the U.S. Phase 3 study of Liletta collected the LNG intrauterine systems (IUSs) from women who discontinued the study. We randomly selected samples within 90-day intervals after discontinuation of IUS use through 900 days (approximately 2.5 years) and 180-day intervals for the remaining duration through 5.4 years (1980 days) to evaluate residual LNG content. We also performed an initial LNG content analysis using 10 randomly selected samples from a single lot. We calculated the average ex vivo release rate using the residual LNG content over the duration of the analysis.

RESULTS: We analyzed 64 samples within 90-day intervals (range 6–10 samples per interval) through 900 days and 36 samples within 180-day intervals (6 samples per interval) for the remaining duration. The initial content analysis averaged 52.0 ± 1.8 mg. We calculated an average initial release rate of 19.5 mcg/day that decreased to 17.0, 14.8, 12.9, 11.3 and 9.8 mcg/day after 1, 2, 3, 4 and 5 years, respectively. The 5-year average release rate is 14.7 mcg/day.

CONCLUSION: The estimated initial LNG release rate and gradual decay of the estimated release rate are consistent with the target design and function of the product. The calculated LNG content and release rate curves support the continued evaluation of Liletta as a contraceptive for 5 or more years of use.

5. Edelman A, Micks E, Gallo MF, Jensen JT, Grimes DA. (2014). Continuous or extended cycle vs. cyclic use of combined hormonal contraceptives for contraception. *Cochrane database Syst Rev.* 2014(7), CD004695. doi:10.1002/14651858.CD002695.pub3

Abstract: BACKGROUND: The avoidance of menstruation through continuous or extended (greater than 28 days) administration of combination hormonal contraceptives (CHCs) has gained legitimacy through its use in treating endometriosis, dysmenorrhea, and menstruation-associated symptoms. Avoidance of menstruation through extended or continuous use of CHCs for reasons of personal preference may have additional advantages to women, including improved compliance, greater satisfaction, fewer menstrual symptoms, and less menstruation-related absenteeism from work or school.

OBJECTIVES: To determine the differences between continuous or extended-cycle CHCs (pills, patch, ring) in regimens of greater than 28 days of active hormone compared with traditional cyclic dosing (21 days of active hormone and 7 days of placebo, or 24 days of active hormones and 4 days of placebo). Our hypothesis was that continuous or extended-cycle CHCs have equivalent efficacy and safety but improved bleeding profiles, amenorrhea rates, adherence, continuation, participant satisfaction, and menstrual symptoms compared with standard cyclic CHCs.

SEARCH METHODS: We searched computerized databases (Cochrane Central Register of Controlled Trials, PUBMED, EMBASE, POPLINE, LILACS) for trials using continuous or extended CHCs (oral contraceptives, contraceptive ring and patch) during the years 1966 to 2013. We also searched the references in review articles and publications identified for inclusion in the protocol. Investigators were contacted regarding additional references.

Selection criteria: All randomized controlled trials in any language comparing continuous or extended-cycle (greater than 28 days of active hormones) versus traditional cyclic administration (21 days of active hormones and 7 days of placebo, or 24 days of active hormones and 4 days of placebo) of CHCs for contraception.

Data collection and analysis: Titles and abstracts identified from the literature searches were assessed for potential inclusion. Data were extracted onto data collection forms and then entered into RevMan 5. Peto odds ratios with 95% confidence intervals were calculated for all outcomes for dichotomous outcomes. Weighted mean difference was calculated for continuous outcomes. The trials were critically appraised by examining the following factors: study design, blinding, randomization method, group allocation concealment, exclusions after randomization, loss to follow-up, and early discontinuation. Because the included trials did not have a standard treatment (type of CHC formulation, route of delivery, or time length for continuous dosing), we could not aggregate data into meta-analysis.

MAIN RESULTS: Twelve randomized controlled trials met our inclusion criteria. Study findings were similar between 28-day and extended or continuous regimens in regard to contraceptive efficacy (i.e., pregnancy rates) and safety profiles. When compliance was reported, no difference between 28-day and extended or continuous cycles was found. Participants reported high satisfaction with both dosing regimens, but this was not an outcome universally studied. Overall discontinuation and discontinuation for bleeding problems were not uniformly higher in either group. The studies that reported menstrual symptoms found that the extended or continuous group fared better in terms of headaches, genital irritation, tiredness, bloating, and menstrual pain. Eleven out of the twelve studies found that bleeding patterns were either equivalent between groups or improved with extended or continuous cycles over time. Endometrial lining assessments by ultrasound and/or endometrial biopsy were done in some participants and were all normal after cyclic or extended CHC use.

AUTHORS' CONCLUSIONS: The 2014 update yielded four additional trials but unchanged conclusions. Evidence from existing randomized control trials comparing continuous or extended-cycle CHCs (greater than 28 days of active combined hormones) to traditional cyclic dosing (21 days of active hormone and 7 days of placebo, or 24 days of active hormone and 4 days of placebo) is of good quality. However, the variations in type of hormones and time length for extended-cycle dosing make a formal meta-analysis impossible. Future studies should choose a previously described type of CHC and dosing regimen. More attention needs to be directed towards participant satisfaction, continuation, and menstruation-associated symptoms.

6. Gemzell-Danielsson, K., Schellschmidt, I., & Apter, D. (2012). A randomized, phase II study describing the efficacy, bleeding profile, and safety of two low-dose levonorgestrel-releasing intrauterine contraceptive systems and Mirena. *Fertility and Sterility*, 97(3). 616-622.e3. <https://doi.org/10.1016/j.fertnstert.2011.12.003>

Abstract: OBJECTIVE: To identify an appropriate dose for a new contraceptive levonorgestrel intrauterine system (LNG-IUS).

DESIGN: Randomized, open-label, three-arm, phase II study.

SETTING: Thirty-seven centers in five European countries.

PATIENT(S): Parous or nulliparous women aged 21–40 years.

Intervention(s): Treatment with LNG-IUSs with initial in vitro release rates of 12 or 16 µg/d (LNG-IUS12/16) or 20 µg/d (Mirena).

MAIN OUTCOME MEASURE(S): Pearl index, bleeding profile, ease/pain of placement/removal, adverse events.

RESULT(S): A total of 738 subjects had an LNG-IUS placed (LNG-IUS12, n = 239; LNG-IUS16, n = 245; Mirena, n = 254). One, 5, and 0 pregnancies occurred in the LNG-IUS12, LNG-IUS16, and Mirena groups, respectively (3-year unadjusted Pearl indices: 0.17, 0.82, and 0). The bleeding profiles were similar in all groups, although total bleeding and spotting days decreased with increasing LNG dose. During 3 years, 10 subjects in the LNG-IUS12 (2 women), LNG-IUS16 (3 women), and Mirena (5 women) groups reported serious adverse events, possibly related to study treatment. Placement of LNG-IUS12 and LNG-IUS16 was considered easy in 94% versus 86.2% in the Mirena group and 72.3% in the LNG-IUS12/LNG-IUS16 group reported either “no pain” or only “mild pain” during placement versus 57.9% in the Mirena group.

CONCLUSION(S): LNG-IUS12 and LNG-IUS16 provided effective contraception, acceptable bleeding patterns, and were well tolerated compared with Mirena.

7. Goldthwaite, LM, Creinin, MD. Comparing bleeding patterns for the levonorgestrel 52 mg, 19.5 mg, and 13.5 mg intrauterine systems. *Contraception*, 100(2), 128-131. doi: [10.1016/j.contraception.2019.03.044](https://doi.org/10.1016/j.contraception.2019.03.044)

Abstract: OBJECTIVE: Compare bleeding patterns for levonorgestrel 52 mg, 19.5 mg, and 13.5 mg intrauterine system (IUS) products using the World Health Organization Belsey definitions. STUDY DESIGN: We extracted available data on bleeding patterns from published sources. Lower dose products had published data at 1 and 3 years; the 52 mg IUS had available data for 1, 2 and 3 years for amenorrhea and 1 and 2 years for other bleeding patterns. We interpolated 2-year data for the lower dose products based on 1- and 3-year data and compared bleeding pattern rates using Fisher exact testing.

RESULTS: The studies evaluated bleeding patterns in 1700, 1566 and 1531 women using levonorgestrel 52 mg, 19.5 mg and 13.5 mg products, respectively. Amenorrhea rates were greater by 180 days after insertion for 52 mg IUS users (11%) as compared to 19.5 mg (5%, $p < .0001$) and 13.5 mg (3%, $p < .0001$). Infrequent bleeding rates were higher for 52 mg users by the end of year 1 (31%) compared to 19.5 mg (26%, $p = .01$) and 13.5 mg (20%, $p < .0001$). Irregular bleeding rates were higher with the lower dose products by 90 days after insertion with continued lower rates at the end of year 1 for 52 mg users (6%) compared 19.5 mg (17%, $p < .0001$) and 13.5 mg (23%, $p < .0001$). Frequent and prolonged bleeding patterns were similar over the first 2 years for all products, although the rates were statistically higher for levonorgestrel 13.5 mg IUS users compared to 19.5 mg and 52 mg IUS users ($p \leq .03$ for all time points after 90-days post-insertion).

CONCLUSIONS: Levonorgestrel 52 mg IUS users have more amenorrhea and infrequent bleeding and less irregular bleeding compared to women using lower dose levonorgestrel IUS products.

8. Hickey, M., Krikun, G., Kodaman, P., Schatz, F., Carati, C., & Lockwood, C. J. (2006). Long-term progestin-only contraceptives result in reduced endometrial blood flow and oxidative stress. *Journal of Clinical Endocrinology and Metabolism*, 91(9), 3633–3638. <https://doi.org/10.1210/jc.2006-0724>

Abstract: CONTEXT: Because of their safety and efficacy, long-term progestin-only contraceptives (LTPOCs) are well-suited for women with restricted access to health care. However, abnormal uterine bleeding (AUB) causes half of all users to discontinue therapy

within 12 months. Endometria of LTPOC-treated patients display aberrant angiogenesis with abnormally enlarged, thin-walled, fragile blood vessels, inflammation, and focal hemorrhage. In this study, similar effects were observed with a new third-generation implantable LTPOC. OBJECTIVE: We hypothesized that LTPOC reduces uterine and endometrial blood flow, leading to hypoxia/reperfusion, which triggers the generation of reactive oxygen species. The latter induce aberrant angiogenesis, causing AUB.

DESIGN: Endometrial perfusion was measured by laser-Doppler fluxmetry in women requesting LTPOCs. Endometrial biopsies were obtained for in vivo and in vitro experiments.

SETTING: The study was conducted in the Yale University School of Medicine and Family-Planning Center in Western Australia.

PATIENTS: Seven women 18 yr or older requesting implantable LTPOCs were recruited in Western Australia.

INTERVENTION: Women received etonorgestrel implants.

MAIN OUTCOME: LTPOC treatment resulted in reduced endometrial perfusion and increased endometrial oxidative damage.

CONCLUSIONS: We propose that LTPOCs result in hypoxia reperfusion, which leads to aberrant angiogenesis resulting in AUB.

9. Hidalgo, M., Bahamondes, L., Perrotti, M., Diaz, J., Dantas-Monteiro, C., & Petta, C. (2002). Bleeding patterns and clinical performance of the levonorgestrel-releasing intrauterine system (Mirena) up to two years. *Contraception*, 65(2), 129–132. [https://doi.org/10.1016/S0010-7824\(01\)00302-X](https://doi.org/10.1016/S0010-7824(01)00302-X)

Abstract: The objectives of this study were to evaluate the bleeding patterns and clinical performance during the first 2 years of use of an intrauterine system releasing 20 µg/day of levonorgestrel (LNG-IUS, Mirena). Two-hundred-fifty-six women accepted use of Mirena from April 1998 through September 1998. The gross cumulative discontinuation rate due to pregnancy and expulsion were significantly higher in women who used the device because of heavy bleeding. There was one pregnancy at the 15th month of use after an inadvertent expulsion of the device. The continuation rate was 66.2 at the end of the second year. Forty-four percent of women reported amenorrhea at the 6th month of use. This rate maintained stability at 50% after 12 and 24 months of use. Spotting was present in 25% of the users at 6 months, decreasing to 8% and 11% at 18 and 24 months, respectively. Oligomenorrhea was described by one-quarter of women and was similar at each observation period. Removals due to menstrual bleeding problems were concentrated in the first 6 months of use and mostly due to amenorrhea or menorrhagia. In conclusion, LNG-IUS showed a high contraceptive efficacy and a good continuation rate up to 2 years. In addition, a reduction of blood loss was observed a few months after insertion.

10. Hubacher, D., Lopez, L., Steiner, M. J., & Dorflinger, L. (2009). Menstrual pattern changes from levonorgestrel subdermal implants and DMPA: systematic review and evidence-based comparisons. *Contraception*, 80(2), 113–118. <https://doi.org/10.1016/j.contraception.2009.02.008>

Abstract: BACKGROUND: Many women want a lengthy duration of contraception but are wary of the menstrual changes from depot medroxyprogesterone acetate (DMPA). A subdermal

levonorgestrel (LNG) implant may be a reasonable alternative. However, information on menstrual changes from these methods has not been summarized and compared in an easy-to-understand form.

STUDY DESIGN: We systematically reviewed the published literature on these contraceptives to find research that used menstrual diaries and standard World Health Organization definitions. We attempted to find information on amenorrhea, number of bleeding or spotting episodes, number of bleeding or spotting days and normal patterns, as reported in four consecutive 90-day reference periods.

RESULTS: We found 16 published articles meeting our criteria and involving diaries of up to 1600 DMPA users and 2300 LNG implant users. We were able to compare the two methods on only three outcomes. For DMPA use, the weighted prevalence of amenorrhea at successive 90-day periods was 12%, 25%, 37% and 46%. The comparable estimates for the LNG implant were 11%, 13%, 9% and 13%. Levonorgestrel implant users experienced a higher average number of bleeding or spotting days compared to DMPA users, but this average was similar to what is expected naturally. At 12 months, normal menstrual patterns were experienced by 23% of LNG implant users compared to 11% of DMPA users.

CONCLUSIONS: Like most hormonal contraception, LNG implants usually produce menstrual changes; however, the changes do not appear to deviate from normal patterns as much as the changes from DMPA. Understanding these differences and other method attributes might help women make an informed choice about which contraceptive to use.

11. Hubacher D, Chen P-L, Park S. (2009). Side effects from the copper IUD: do they decrease over time? *Contraception*, 79(5), 356- 262. doi:10.1016/j.contraception.2008.11.012.

Abstract: BACKGROUND: The copper intrauterine device (IUD) can cause side effects in some women; increased uterine bleeding and pain may cause early removal. Because of simplified reporting from previous research, little is known about how side effects might change over time.

STUDY DESIGN: This is a secondary analysis of a prospective study of 1947 first-time copper IUD users. Over a 1-year period, we collected detailed information on side effects and looked for trends using generalized mixed-effects regression modeling.

RESULTS: During menses, most bleeding and pain side effects were found to decrease over time ($p < .05$). During intermenstrual intervals, overall spotting and pain complaints remained unchanged, but the number of days with these problems increased ($p < .05$). Serious side effects that prompted either a clinic visit or IUD removal had varied patterns over time, depending on the type of problem.

CONCLUSION: Side effects from the copper IUD can be troubling for both user and clinician. Some problems improve over time, while others do not. This information may be helpful in counseling women who are considering IUD use and current users who are contemplating IUD removal due to side effects.

12. Krattenmacher, R. (2000). Drospirenone: Pharmacology and pharmacokinetics of a unique progestogen. *Contraception*, 62(1), 29–38. [https://doi.org/10.1016/S0010-7824\(00\)00133-5](https://doi.org/10.1016/S0010-7824(00)00133-5)

Abstract: The pharmacology and pharmacokinetics of drospirenone, a unique progestogen, are reviewed in this paper. Unlike other progestogens, drospirenone, an analogue of spironolactone, has biochemical and pharmacologic profiles similar to endogenous progesterone, especially regarding antimineralocorticoid and antiandrogenic activities. Drospirenone counteracts the estrogen-induced stimulation of the renin-angiotensin-aldosterone system and blocks testosterone from binding to androgen receptors. Because of these characteristics, it has the potential to reduce body weight, blood pressure, and low-density lipoprotein levels and to enhance high-density lipoprotein levels. As a combination oral contraceptive, drospirenone with ethinyl estradiol is effective and has positive effects on weight and lipid levels. Additionally, it relieves menstrually related symptoms (e.g., negative affect and water retention) that are commonly observed with other combination oral contraceptives. Based on the biochemical and pharmacodynamic data, drospirenone appears to be a viable alternative to the currently available progestogens.

13. Lazorwitz A, Aquilante CL, Dinginer E, Harrison M, Sheeder J, Teal S. (2019).

Relationship between etonogestrel concentrations and bleeding patterns in contraceptive implant users. *Obstet. Gynecol*, 134(4), 807-813. doi. 10.1097/AOG.0000000000003452.

Abstract: OBJECTIVE: To estimate whether serum etonogestrel concentrations influence bleeding patterns and related side effects in contraceptive implant users.

METHODS: We conducted a prospective cross-sectional study with healthy, reproductive-aged women using etonogestrel implants for 12-36 months. Participants completed a brief questionnaire to assess their current bleeding pattern and any experience of abnormal bleeding with the implant. We then measured serum etonogestrel concentrations. We also reviewed the charts of participants to determine whether a prescription for oral contraceptive pills was ever given for treatment of implant-related bothersome bleeding. We performed multivariable logistic regression to test for associations between serum etonogestrel concentrations and both bleeding patterns and related side effects.

RESULTS: We enrolled 350 women, and 59.4% reported having experienced abnormal bleeding with the contraceptive implant. Only 14.9% of participants reported amenorrhea and 37.7% reported monthly periods. Among participants with reviewable medical records (n=253), roughly 20% had received a prescription for oral contraceptive pills during implant use. Increasing serum etonogestrel concentrations were significantly associated with increasing odds of reporting abnormal bleeding (adjusted odds ratio [aOR] 1.005, P=.015) and increasing odds of having received an oral contraceptive pill prescription (aOR 1.008, P=.002). For every 100 pg/mL increase in serum etonogestrel concentration, contraceptive implant users in this study had 1.6 times the odds of reporting abnormal bleeding and 2.3 times the odds of having received a prescription as treatment for bothersome bleeding.

CONCLUSION: We found both objective and subjective evidence that higher levels of progestin from the contraceptive implant were associated with bleeding side effects experienced by women in this study. Pharmacologic variation may influence the side effects women experience with a variety of hormonal contraceptive methods, in turn affecting patient satisfaction and discontinuation rates.

14. Maldonado LY, Sergison JE, Gao X, Hubacher D. Menstrual bleeding and spotting with the Legonorgestrel Intrauterine System (52 mg) during the first-year after insertion: a systematic review and meta-analysis. (2020). *Am J Obstet Gynecol*, 222(5), 451-468. <https://doi.org/10.1016/j.ajog.2019.09.044>

Abstract: BACKGROUND: Changes in menstrual bleeding concern many users of the 52 mg Levonorgestrel Intrauterine System. Prescribing information for Levonorgestrel Intrauterine System devices describe an overall decrease in bleeding and spotting days over time; however, estimates derived from a variety of existing clinical data are currently unavailable.

OBJECTIVE: The objective of the study was to systematically calculate the mean days of bleeding-only, spotting-only, and bleeding and/or spotting experienced by a population of reproductive-aged Levonorgestrel Intrauterine System users with normal regular menses prior to insertion during the first year of use.

DATA SOURCES: We identified clinical trials, including randomized controlled trials and randomized comparative trials, as well as cohort studies published in English between January 1970 and November 2018 through searching 12 biomedical and scientific literature databases including MEDLINE and ClinicalTrials.gov.

STUDY ELIGIBILITY CRITERIA: We considered studies that reported data on Levonorgestrel Intrauterine System devices releasing 20 µg of levonorgestrel per day, collected daily menstrual bleeding data for at least 90 consecutive days, defined bleeding and spotting per World Health Organization standards and evaluated participants with normal regular menses prior to insertion.

STUDY APPRAISAL AND SYNTHESIS METHODS: We assessed study quality using established guidelines. Two reviewers independently conducted all review stages and rated the quality of evidence for each article; any disagreements were resolved by a third. Where possible, we pooled data using a random-effects model.

RESULTS: Among 3403 potentially relevant studies, we included 7 in our meta-analysis. We calculated the mean days of bleeding-only, spotting-only, and bleeding and/or spotting for the first four 90 day intervals after Levonorgestrel Intrauterine System insertion. Combined menstrual bleeding and/or spotting days gradually decreased throughout the first year, from 35.6 days (95% confidence interval, 32.2-39.1) during the first 90 day interval to 19.1 (95% confidence interval, 16.6-21.5), 14.2 (95% confidence interval, 11.7-16.8), and 11.7 days (95% confidence interval, 9.7-13.7) in the second, third, and fourth intervals. Measures for bleeding-only and spotting-only days similarly decreased throughout the first year, with the greatest decreases occurring between the first and second intervals.

CONCLUSION: Our study provides 90 day reference period measures that characterize menstrual patterns for Levonorgestrel Intrauterine System users with normal regular menses prior to insertion during the first year of use. Our findings provide broader generalizability and more detail than patterns described in the prescribing information. These findings quantify an overall decrease in menstrual bleeding days with longer duration of use, with the greatest decrease occurring between months 3 and 6. Accurately establishing expectations with the Levonorgestrel Intrauterine System may improve informed selection and decrease discontinuation.

15. Mansour D, Korver T, Marintcheva-Petrova M, Fraser IS. (2008). The effects of Implanon

on menstrual bleeding patterns. *Eur J Contracept Reprod Health Care*, 13(Suppl 1), 13-28. <https://doi.org/10.1080/13625180801959931>

Abstract: OBJECTIVES: To evaluate an integrated analysis of bleeding patterns associated with use of the subdermal contraceptive implant Implanon (etonogestrel, Organon, part of Schering-Plough) and to provide physician guidance to optimize patient counselling. METHODS: Data from 11 clinical trials were reviewed (N = 923). Assessments included bleeding-spotting records, dysmenorrhoea, and patient-perceived reasons for discontinuation. Bleeding patterns were analysed via reference period (RP) analyses.

RESULTS: Implanon use was associated with the following bleeding irregularities: amenorrhoea (22.2%) and infrequent (33.6%), frequent (6.7%), and/or prolonged bleeding (17.7%). In 75% of RPs, bleeding-spotting days were fewer than or comparable to those observed during the natural cycle, but they occurred at unpredictable intervals. The bleeding pattern experienced during the initial phase predicted future patterns for the majority of women. The group of women with favourable bleeding patterns during the first three months tended to continue with this pattern throughout the first two years of use, whereas the group with unfavourable initial patterns had at least a 50% chance that the pattern would improve. Only 11.3% of patients discontinued owing to bleeding irregularities, mainly because of prolonged flow and frequent irregular bleeding. Most women (77%) who had baseline dysmenorrhoea experienced complete resolution of symptoms.

CONCLUSION: Implanon use is associated with an unpredictable bleeding pattern, which includes amenorrhoea and infrequent, frequent, and/or prolonged bleeding. The bleeding pattern experienced during the first three months is broadly predictive of future bleeding patterns for many women. Effective preinsertion counselling on the possible changes in bleeding patterns may improve continuation rates.

16. Mishell D.R., Guillebaud, J., Westhoff, C., Nelson A.L., Kaunitz, A.M., Trussell, J., Davis, A.J. (2007). Combined hormonal contraceptive trials: variable data collection and bleeding assessment methodologies influence study outcomes and physician perception. *Contraception*, 27(1), 4-10. doi: 10.1016/j.contraception.2006.08.008.

Abstract: Initially approved for use in the United States nearly 50 years ago, oral hormonal contraceptives containing both estrogen and progestin have undergone steady improvements in safety and convenience. Concurrent with improvements in safety associated with decreasing doses of both steroids, there has been an increased incidence of unscheduled bleeding and spotting. There exist no standards regarding data collection techniques and methods, and reporting and analysis of bleeding and spotting events during combined hormonal contraceptive (CHC) trials. For the regulatory review of hormonal contraceptives, data regarding the incidence of bleeding and spotting events are not included in either of the traditional categories of efficacy and safety. Standardization of methods for collecting and analyzing data about cycle control in all clinical trials of CHCs is long overdue. Until such standards are developed and implemented, clinicians need to familiarize themselves with the techniques used in each study in order to provide correct information to their patients about the frequency of bleeding and spotting associated with different formulations and delivery systems.

- 17. Mishell D.R., Guillebaud, J., Westhoff, C., Nelson A.L., Kaunitz, A.M., Trussell, J., Davis, A.J. (2007). Recommendations for standardization of data collection and analysis bleeding in combined hormonal contraceptive trials. *Contraception*, 27(1), 11-15. doi:10.1016/j.contraception.2006.08.012**

Abstract: Initially approved for use in the United States nearly 50 years ago, oral hormonal contraceptives containing both estrogen and progestin have undergone steady improvements in safety and convenience. Concurrent with improvements in safety associated with decreasing doses of both steroids, there has been an increased incidence of unscheduled bleeding and spotting. There exist no standards regarding data collection techniques and methods, and reporting and analysis of bleeding and spotting events during combined hormonal contraceptive (CHC) trials. For the regulatory review of hormonal contraceptives, data regarding the incidence of bleeding and spotting events are not included in either of the traditional categories of efficacy and safety. Standardization of methods for collecting and analyzing data about cycle control in all clinical trials of CHCs is long overdue. Until such standards are developed and implemented, clinicians need to familiarize themselves with the techniques used in each study in order to provide correct information to their patients about the frequency of bleeding and spotting associated with different formulations and delivery systems.

- 18. Roumen, F. J. M. E., Apter, D., Mulders, T. M. T., & Dieben, T. O. M. (2001). Efficacy, tolerability and acceptability of a novel contraceptive vaginal ring releasing etonogestrel and ethinyl oestradiol. *Human Reproduction*, 16(3), 469–475. <https://doi.org/10.1093/humrep/16.3.469>**

Abstract: A novel contraceptive vaginal ring releasing etonogestrel 120 µg and ethinyl oestradiol 15 µg daily over a period of 3 weeks was tested. Each ring was used for one cycle, comprising 3 weeks of ring use followed by a 1 week ring-free period. This 1 year, multicentre study assessed the contraceptive efficacy, cycle control, tolerability and acceptability of the contraceptive. Altogether, 1145 women were exposed to the vaginal ring for 12 109 cycles (928 woman-years). Six pregnancies occurred during treatment, giving a Pearl Index of 0.65 (95% confidence interval 0.24–1.41). Cycle control was very good, since irregular bleeding was rare (2.6–6.4% of evaluable cycles) and withdrawal bleeding (mean duration 4.7–5.3 days) occurred in 97.9–99.4% of evaluable cycles. Compliance to the prescribed regimen was high with criteria being fulfilled in 90.8% of cycles. The ring was well tolerated. The majority of women considered this new contraceptive method easy to use, and it offers an effective, convenient, well-accepted and novel method for hormonal contraception.

- 19. Rowe, P., Farley, T., Peregoudov, A., Piaggio, G., Boccard, S., Landoulsi, S., & Meirik, O. (2016). Safety and efficacy in parous women of a 52-mg levonorgestrel-medicated intrauterine device: a 7-year randomized comparative study with the TCu380A. *Contraception*, 94(3), 288. <https://doi.org/10.1016/j.contraception.2016.06.001>**

Abstract: Objectives: To compare rates of unintended pregnancy, method continuation and reasons for removal among women using the 52-mg levonorgestrel (daily release 20 microg) levonorgestrel IUD (LNG-IUD) or the copper T 380 A (TCu380A) intrauterine device.

Study design: This was an open-label 7-year randomized controlled trial in 20 centres, 11 of which in China. Data on 1884 women with interval insertion of the LNG-IUD and 1871 of the TCU380A were analysed using life tables with 30-day intervals and Cox proportional hazards models.

Results: The cumulative 7-year pregnancy rate of the LNG-IUD was 0.5 (standard error 0.2) per 100, significantly lower than 2.5 (0.4) per 100 of the TCU380A, cumulative method discontinuation rates at 7 years were 70.6 (1.2) and 40.8 (1.3) per 100, respectively. Dominant reasons for discontinuing the LNG-IUD were amenorrhea (26.1 [1.3] per 100) and reduced bleeding (12.5 [1.1] per 100), particularly in Chinese women and, for the TCU380A, increased bleeding (9.9 [0.9] per 100), especially among non-Chinese women. Removal rates for pain were similar for the two intrauterine devices (IUDs). Cumulative rates of removal for symptoms compatible with hormonal side effects were 5.7 (0.7) and 0.4 (0.2) per 100 for the LNG-IUD and TCU380A, respectively, and cumulative losses to follow-up at 7 years were 26.0 (1.4) and 36.9 (1.3) per 100, respectively.

Conclusion: The LNG-IUD and the TCU380A have very high contraceptive efficacy, with the LNG-IUD significantly higher than the TCU380A. Overall rates of IUD removals were higher among LNG-IUD users than TCU380A users. Removals for amenorrhea appeared culturally associated.

20. Rubin, S. L., & Robinson, J. A. (2017). Bleeding Associated with Hormonal Contraceptives: Understanding and Managing a Common Problem. *Current Obstetrics and Gynecology Reports*, 6, 198–206. <https://doi.org/10.1007/s13669-017-0219-x>

Abstract: Changes in menstrual bleeding are common with hormonal contraceptives, and unfavorable bleeding profiles are leading reasons for method dissatisfaction and discontinuation. Studies suggest that acceptance of menstrual disturbance is highly dependent on appropriate counseling. This review presents an overview of the pathophysiology of uterine bleeding related to hormonal contraceptive use, the expected bleeding profiles of the various hormonal contraceptives, and evidence supporting various management strategies for treatment of unscheduled bleeding. Recent Findings Published trials on treatments for bleeding with hormonal contraceptives are heterogeneous in methodology and outcome measures. Overall, data show mixed results and disappointingly small treatment effects for medications studied to manage unscheduled bleeding. Short courses of NSAIDs and oral estrogen may have modest benefits. Tranexamic acid and mifepristone require larger trials and additional study. Summary Treatment of bleeding associated with hormonal contraception hinges on understanding the bleeding profiles of the hormonal contraceptives, employing anticipatory counseling, and understanding the spectrum and limitations of treatment options for menstrual disturbance.

21. Sanders JN, Adkins DE, Kaur S, Storck K, Gawron LM, Turok DL. (2018). Bleeding, cramping and satisfaction among new copper IUD users: A prospective study. *PLoS One*, 13(11), e0199724. doi: 10.1371/journal.pone.0199724

Abstract: OBJECTIVE: We assess change in bleeding, cramping, and IUD satisfaction among new copper (Cu) IUD users during the first six months of use, and evaluate the impact of bleeding and cramping on method satisfaction.

METHODS: We recruited 77 women ages 18-45 for this prospective longitudinal observational cohort study. Eligible women reported regular menses, had no exposure to hormonal contraception in the last three months, and desired a Cu IUD for contraception. We collected data prospectively for 180 days following IUD insertion. Monthly, participants reported bleeding scores using the validated pictorial blood loss assessment chart (PBAC), IUD satisfaction using a five-point Likert scale, and cramping using a six-level ordinal scale. We used multiple imputation to address nonrandom attrition. Structural equation models for count and ordered outcomes were used to model bleeding, cramping, and IUD satisfaction growth curves over the six monthly repeated assessments.

RESULTS: Bleeding significantly decreased (approximately 23%) over the course of the study from an estimated PBAC = 195 at one month post-insertion to PBAC = 151 at six months ($t = -2.38$, $p < 0.05$). Additionally, IUD satisfaction improved over time ($t = 2.65$, $p < 0.01$), increasing from between "Neutral" and "Satisfied" to "Satisfied" over the six month study. Cramping decreased notably over the six month study from between biweekly and weekly, to once or twice a month ($t = -4.38$, $p < 0.001$). Finally, bleeding, but not cramping, was associated with IUD satisfaction across the study ($t = -2.31$, $p < 0.05$) and at study end ($t = -2.81$, $p < 0.01$).

CONCLUSIONS: New Cu IUD users reported decreasing bleeding and cramping, and increasing IUD satisfaction, over the first six months. Method satisfaction was negatively associated with bleeding.

22. Sergison, J. E., Maldonado, L. Y., Gao, X., & Hubacher, D. (2019). Levonorgestrel intrauterine system associated amenorrhea: a systematic review and metaanalysis. *American Journal of Obstetrics and Gynecology*, 220(5), 440-448.e8. <https://doi.org/10.1016/j.ajog.2018.12.008>

Abstract: OBJECTIVE DATA: Amenorrhea is a polarizing noncontraceptive effect of the levonorgestrel intrauterine system. Composite amenorrhea prevalence estimates that summarize all clinical data for the first-year after insertion currently are not available. The purpose of this study was to investigate the validity of existing prevalence estimates by the systematic calculation of amenorrhea measures for a general population of levonorgestrel intrauterine system users and to provide 90-day interval point estimates for the first year of use.

STUDY: We identified clinical trials, randomized controlled trials, and randomized comparative trials that were published in English between January 1970 and September 2017 through electronic searches of 12 biomedical and scientific literature databases that included MEDLINE and ClinicalTrials.gov.

STUDY APPRAISAL AND SYNTHESIS METHODS: We considered studies that clearly defined amenorrhea per World Health Organization standards (the complete cessation of bleeding for at least 90 days), collected data from written daily bleeding diaries (the gold standard data collection technique on menstrual bleeding changes), and evaluated levonorgestrel intrauterine system devices that released 20 µg of levonorgestrel per day. We assessed study quality using guidelines established by the US Preventive Services Task Force and Cochrane handbook for systematic reviews of interventions. Two reviewers independently conducted all review stages; disagreements were resolved by a third reviewer. Where possible, data were pooled with the use of a random-effects model.

RESULTS: Of 2938 potentially relevant studies, we included 9 in our meta-analysis. We calculated amenorrhea prevalence, which was weighted for inter- and intrastudy variance, for 4 90-day intervals and months 0–12. Our results demonstrated few levonorgestrel intrauterine system users (0.2%; 95% confidence interval, 0.0–0.4) experienced amenorrhea during the first 90 days after insertion; however, prevalence increased to 8.1% (95% confidence interval, 6.6–9.7) on days 91–180. Finally, 18.2% (95% confidence interval, 14.9–21.5) of users experienced amenorrhea for at least 1 90-day interval during the first year. Although interstudy heterogeneity limited reliability of days 181–271 and 272–365 measures, prevalence increased from 13.6% (95% confidence interval, 9.3–18.0) to 20.3% (95% confidence interval, 13.5–27.0), respectively.

CONCLUSION: Approximately 20% of levonorgestrel intrauterine system users experience amenorrhea during at least 1 90-day interval by the first year after insertion. This composite estimate is consistent with the product labeling and demonstrates that most users do not experience amenorrhea during the first year. These results provide accurate summary measures to facilitate counselling and informed method selection.

23. Sereepapong, W., Chotnopparatpattara, P., Taneepanichsku, S., Markham, R., Russell, P., & Fraser, I. S. (2004). Endometrial progesterone and estrogen receptors and bleeding disturbances in depot medroxyprogesterone acetate users. *Human Reproduction*, 19(3), 547–552. <https://doi.org/10.1093/humrep/deh123>

Abstract: BACKGROUND: Depot medroxyprogesterone acetate (DMPA) is a very popular hormonal contraceptive. Unpredictable bleeding disturbances are the main reasons for discontinuation and may be mediated through endometrial hormone receptors. This study was aimed to compare the expression of progesterone and estrogen receptors in the endometrium of bleeding DMPA users with that of amenorrhoeic DMPA users.

METHODS: Subjects were recruited between April 2000 and January 2001. On the day of the third DMPA injection, 42 amenorrhoeic DMPA users and 42 DMPA users who had frequent or prolonged endometrial bleeding and were bleeding on that day were matched by age and body mass index. Endometrial biopsies were collected for immunohistochemical study of progesterone receptor A plus B (PRAB) and B alone (PRB) and estrogen receptor α (ER α) and β (ER β) expression.

RESULTS: There were 23 adequate endometrial samples from each group. There were no differences in any of a series of comparisons of PRAB, PRB, ER α and ER β expression in glands or stroma between the groups. Serum estradiol and progesterone levels were also not different between the groups.

CONCLUSIONS: Endometrial PRAB, PRB, ER α and ER β expression in glands and stroma was not different between DMPA users who had frequent or prolonged bleeding and amenorrhoeic DMPA users.

24. Zigler, R. E., & McNicholas, C. (2017). Unscheduled vaginal bleeding with progestin-only contraceptive use. *American Journal of Obstetrics and Gynecology*, 216(5), 443–450. <https://doi.org/10.1016/j.ajog.2016.12.008>

Summary: Nearly 20% of women using contraception are using progestin-only contraception, including progestin-only pills, depot-medroxyprogesterone acetate, subdermal etonogestrel

implants, and levonorgestrel intrauterine devices. This number will continue to grow with the increased provision of long-acting reversible contraception. Although overall satisfaction among women using progestin-only contraception is high, dissatisfaction and discontinuation may be associated with unscheduled bleeding and spotting. The exact etiology of irregular bleeding associated with progestin-containing contraceptives is not completely understood, yet several mechanisms have been suggested. Several therapies targeting these mechanisms have been evaluated with mixed results. This paper will review the physiology and management of unscheduled bleeding with progestin-containing contraceptives.

Acceptability and User Experiences

- 1. Brunie A, Callahan RL, Mackenzie A, Kibira SPS, Wayack-Pambè M. (2019). Developing acceptable contraceptive methods: Mixed-method findings on preferred method characteristics from Burkina Faso and Uganda. *Gates Open Research*, 3, 1205. doi:10.12688/gatesopenres.12953.2**

Abstract: BACKGROUND: Unmet need remains high in developing regions. New contraceptive technologies may improve uptake and use. This study examines desirable product characteristics.

METHODS: We added a module to the female questionnaire of the PMA2020 surveys in Burkina Faso and Uganda and conducted 50 focus group discussions (FGDs) with women, 10 FGDs with men, and 37 in-depth interviews (IDIs) with providers across the two countries. FGDs with women and IDIs with providers included a semi-structured ranking exercise on pre-selected product characteristics.

RESULTS: Effectiveness, duration, few side effects, cost, and access were the characteristics most commonly reported as important in choosing a method by survey respondents across both countries. Half or more of women surveyed in each country would like a method that lasts at least one year, while 65% in Burkina Faso and 40% in Uganda said they would use a method causing amenorrhea. Qualitative findings show that women want methods with minimal and predictable side effects. Reactions to increased bleeding were negative, especially in Burkina Faso, but perspectives on reduced bleeding were more mixed. Women and providers preferred methods that are discreet and not user-dependent, and associate duration with convenience of use. Some women in Uganda expressed concerns about the invasive nature of long-acting methods, and cost was an important consideration in both countries. In the ranking exercise, discreet use and few side effects often ranked high, while causing amenorrhea and not requiring a pelvic exam often ranked low.

CONCLUSION: Product development should consider user preferences for success in these settings.

- 2. Brunie A, Callahan RL, Godwin CL, Bajpai J, OlaOlorun FM. (2019). User preferences for a contraceptive microarray patch in India and Nigeria: Qualitative research on what women want. *PloS one*, 14(6), e0216797. doi:10.1371/journal.pone.0216797**

Abstract: BACKGROUND: A new contraceptive microarray patch (MAP) for women is in development. Input on this method from potential end-users early in the product development process is important to guide design decisions. This paper presents the qualitative component of a broader study exploring initial acceptability of the MAP and selected product features. The

qualitative research was intended to identify product features that are most salient to end-users and to contextualize preferences around them with subsequent research planned to assess quantitatively the relative importance of those features.

METHODS: We conducted 16 focus group discussions and 20 in-depth interviews with women and 20 IDIs with family planning providers in New Delhi, India, and Ibadan, Nigeria. Input from the MAP developer served to identify plausible features of the MAP to include in the focus group discussions and in-depth interviews. Interviews were audio-recorded, transcribed into English, coded, and analyzed to examine key dimensions of MAP features.

RESULTS: Many participants viewed the MAP as potentially easy to use. Interest in self-application after learning correct use was high, especially in India. Participants favored formulations affording protection from pregnancy for three or six months, if not longer. Interest in a shorter-acting MAP was particularly low in Nigeria. Non-desirable MAP features included a potential localized skin rash and pain at application. Views on patch size and location of application were related to the potential for rash and pain, with a desire to permit discreet use and minimize pain. Results indicate that the side effect profile, effectiveness, and pricing are also important factors for acceptability and uptake of a future product.

CONCLUSION: Study findings indicate that a contraceptive MAP is of potential interest to women and that specific MAP attributes will be important to acceptability.

3. Callahan RL, Brunie A, Mackenzie ACL, Wayack-Pambè M, Guiella G, Kibira SPS, Makumbi F. Potential user interest in new long-acting contraceptives: Results from a mixed methods study in Burkina Faso and Uganda. (2019). *PloS one*, 14(5), e0217333. doi: 10.1371/journal.pone.0217333;

Abstract: Method-related concerns represent an important cause of contraceptive non-use and discontinuation. User preferences must be incorporated into the design of new contraceptive technologies to ensure product success and improve family planning outcomes. We assessed preferences among potential users in Burkina Faso and Uganda for six contraceptive methods currently under development or ready for introduction: a new copper intra-uterine device (IUD), a levonorgestrel intra-uterine system, a new single-rod implant, a biodegradable implant, a longer-acting injectable, and a method of non-surgical permanent contraception. Questions were added to nationally-representative PMA2020 household surveys that asked 2,743 and 2,403 women in Burkina Faso and Uganda, respectively, their interest in using each new method. We assessed factors associated with interest through multivariable logistic regression models. We conducted qualitative interviews and focus groups with 398 women, 78 men, and 52 family planning providers and key informants to explore perceived advantages and disadvantages of the methods. Respondents expressed interest in using all new methods, with greatest interest in the longer-acting injectable (77% in Burkina Faso, 61% in Uganda), followed by a new single-rod implant. Least interest was expressed in a new copper IUD (26% Burkina Faso, 15% in Uganda). In both countries, women with less education had higher odds of interest in a longer-acting injectable. Interest in most new methods was associated with desiring a method lasting longer than one year and acceptance of lack of menstrual bleeding as a contraceptive side effect. Perceived advantages and disadvantages were similar between countries, including concerns about menstrual side effects and fear of the biodegradable nature of the biodegradable implant. Potential users, their

partners, and providers are interested in new longer-acting methods, however, familiar forms including the injectable and implant may be the most immediately acceptable. A biodegradable implant will require clear counseling messages to allay potential fears.

- 4. Castle, S. & Askew, I. (2015). *Contraceptive Discontinuation: Reasons, Challenges, and Solutions*. Population Council & FP2020.**
<https://www.familyplanning2020.org/resources/contraceptive-discontinuation-reasons-challenges-and-solutions>

Summary: In this review of the evidence base on contraceptive discontinuation, the authors propose a theory of change to limit unnecessary discontinuation. They report that method-induced side effects, including bleeding changes such as amenorrhea, are one of the main reasons for discontinuation. Interventions to address these concerns include allowing women to talk about their side effects, engaging male partners, ensuring confidentiality, addressing misconceptions, and counselling women who are amenorrheic. Other reasons emerge from problems within the health system and service and sociocultural environment. Their theory of change involves evidence-based pathways for interventions to address these components.

- 5. Castle, S. (2003). Factors influencing young Malians' reluctance to use hormonal contraceptives. *Studies in Family Planning*, 34(3), 186–199.**
<https://doi.org/10.1111/j.1728-4465.2003.00186.x>

Abstract: During a qualitative evaluation of three peer-education programs in urban Mali, young people stated that they were wary of using either the pill or injectable contraceptives because they believed that these methods would make them sterile. Unmarried women's contraceptive decisionmaking was not primarily driven by a current need to limit fertility, but rather by a future need to maximize it in order to gain status through childbearing in their marital households. Further interviews explored notions of conception, menstruation, and the perceived action of hormonal methods on the reproductive system. Findings revealed that menstrual disruption (in the form of amenorrhea or prolonged bleeding) appeared to have dire repercussions, including accusations of witchcraft and immoral behavior that could result in a woman's being divorced or in her husband's acquiring an additional wife. The social consequences of side effects were perceived to be more important than their biological manifestations, and together with the fear of sterility, resulted in a preference for the condom.

- 6. D'Arcangues, C., Jackson, E., Brache, V., & Piaggio, G. (2011). Women's views and experiences of their vaginal bleeding patterns: An international perspective from Norplant users. *European Journal of Contraception and Reproductive Health Care*, 16(1), 9–17. <https://doi.org/10.3109/13625187.2010.535871>**

Abstract: OBJECTIVES: Contraceptive-induced vaginal bleeding changes may be an undesired side effect, or a welcome opportunity to alter menstrual patterns. In Europe and the US, such changes are increasingly accepted; this study explores the perceptions of women around the globe.

METHODS: Norplant users from five countries (Chile, China, the Dominican Republic, Indonesia and Tunisia; N = 486) were surveyed at entry into a contraceptive clinical trial regarding preferred frequency of menstruation, menses-associated symptoms, and activities during

menses.

RESULTS: Most women preferred once-monthly menstruation (81%); women in Chile, younger women, women neither married nor cohabitating, Christian women, and women experienced with hormonal contraception were more likely to accept alternative bleeding patterns. Women in Tunisia and Chile reported more symptoms associated with menses, while women in Beijing reported very few; decreased energy (32%), headaches (26%), abdominal pain (23%) and depression (22%) were most common. Avoidance of activities during menses such as physical work, sports, praying and entering religious sites, was closely tied to study centre. Across all sites, women (90%) avoided sexual intercourse during menses.

CONCLUSIONS: Despite growing acceptance of altering bleeding patterns, women in this study preferred monthly vaginal bleeding. Understanding sociocultural contexts and individual preferences is important when addressing this issue with women from diverse backgrounds.

7. Fiala, C., Chabbert-Buffet, N., Häusler, G., Jamin, C., Lete, I., Lobo, P., et al. (2017).

Women's preferences for menstrual bleeding frequency in 12 European countries: the Inconvenience Due to Women's Monthly Bleeding (ISY) survey. *The European Journal of Contraception & Reproductive Health Care*, 22(4), 268-273. Available [here](#).

Objectives: Our aim was to assess the level of inconvenience associated with menstrual bleeding and determine how many women across 12 European countries would prefer a bleeding frequency of less than once a month and what would motivate their choice.

Methods: A 15-min quantitative online survey was conducted in two waves among 5728 women aged between 18 and 45 years, with an equal distribution of women using a combined hormonal contraceptive (CHC group, n = 2739) and women using a non-hormonal contraceptive or no contraceptive (non-HC group, n = 2989). The first wave was carried out in Austria, Belgium, France, Italy, Poland and Spain, in February 2015, and the results have been published. The second wave was conducted in the Czech Republic, Germany, Hungary, Portugal, Latvia and the Netherlands, between August and September 2015. Results: The menstrual period was significantly longer (5.0 versus 4.6 days) and heavier (15 versus 7%) in non-HC users than in CHC users ($p < .0001$). Given the choice, ~60% of women would like less frequent menstrual bleeding. There was heterogeneity in the preference across countries. Sexuality, social life, work and sporting activities were key factors affecting women's preference.

Conclusion: The majority of women in the 12 European countries would prefer to reduce the frequency of menstrual periods. Quality of life was the main factor affecting their preference.

8. Glasier, A. F., Smith, K. B., Van der Spuy, Z. M., Ho, P. C., Cheng, L., Dada, K., et al. (2003). Amenorrhea associated with contraception - An international study on acceptability. *Contraception*, 67(1), 1-8. [https://doi.org/10.1016/s0010-7824\(02\)00474-2](https://doi.org/10.1016/s0010-7824(02)00474-2)

Abstract: Surveys undertaken in the 1970s and 1980s suggested that amenorrhea was unacceptable to most women, especially in developing countries. More recent research suggests that increasing numbers of women in the developed world prefer to menstruate less often. In a questionnaire survey of 1001 women attending family-planning clinics and 290 contraceptive providers in China, South Africa, Nigeria and Scotland, only among black women in Africa did the majority like having periods. In all other groups, most women disliked periods, which were

“inconvenient” and associated with menstrual problems. Given the choice, the majority of Nigerian women would prefer to bleed monthly. Elsewhere, women would opt to bleed only once every 3 months, or not at all. In all except the Chinese centers, the majority of women would be willing to try a contraceptive which induced amenorrhea. Providers tended to overestimate the importance of regular menstruation to their clients. This is an important observation for scientists and funding agencies involved in developing new methods of contraception.

9. Halpern, V., Lopez, L. M., Grimes, D. A., Stockton, L. L., & Gallo, M. F. (2013). Strategies to improve adherence and acceptability of hormonal methods of contraception.

Cochrane Database of Systematic Reviews, 2013(10), CD004317.

<https://doi.org/10.1002/14651858.CD004317.pub4>

Abstract: BACKGROUND: Worldwide, hormonal contraceptives are among the most popular reversible contraceptives. Despite their high theoretical effectiveness, typical use results in much lower effectiveness. In large part, this disparity reflects difficulties in adherence to the contraceptive regimen and low rates for long-term continuation.

OBJECTIVES: The intent was to determine the effectiveness of ancillary counseling techniques to improve adherence to, and continuation of, hormonal methods of contraception.

Search methods: Through August 2013, we searched computerized databases for randomized controlled trials (RCTs) comparing client-provider interventions with standard family planning counseling. Sources included CENTRAL, MEDLINE, EMBASE, POPLINE, ClinicalTrials.gov and ICTRP. Earlier searches also included LILACS, PsycINFO, Dissertation Abstracts, African Index Medicus, and IMEMR.

SELECTION CRITERIA: We included RCTs of an intensive counseling technique or other client-provider intervention compared to routine family planning counseling. Interventions included group motivation; structured, peer, or multi-component counseling; and intensive reminders of appointments or next dosing. Outcome measures were discontinuation, reasons for discontinuation, number of missed pills or on-time injections, and pregnancy.

Data collection and analysis: One author evaluated the titles and abstracts from the searches to determine eligibility. Two authors extracted data from the included studies. We calculated the Mantel-Haenszel odds ratio (OR) for dichotomous outcomes. For continuous variables, the mean difference (MD) was computed; RevMan uses the inverse variance approach. For all analyses, 95% confidence intervals (CI) were also computed. Since the studies identified differed in both interventions and outcome measures, we did not conduct a meta-analysis.

MAIN RESULTS: Nine RCTs met our inclusion criteria. Five involved direct counseling; of those, two also provided multiple contacts by telephone. Four other trials provided intensive reminders, two of which also provided health education information. Three trials showed some benefit of the experimental intervention. In a counseling intervention, women who received repeated structured information about the injectable depot medroxyprogesterone acetate (DMPA) were less likely to discontinue the method by 12 months (OR 0.27; 95% CI 0.16 to 0.44) than women who had routine counseling. The intervention group was also less likely to discontinue due to menstrual disturbances (OR 0.20; 95% CI 0.11 to 0.37). Another trial showed a group with special counseling plus phone calls was more likely than the special-counseling group to report consistent use of oral contraceptives (OC) at 3 months (OR 1.41;

95% CI 1.06 to 1.87), though not at 12 months. The group with only special counseling did not differ significantly from those with standard care for any outcome. The third trial compared daily text-message reminders about OCs plus health information versus standard care. Women in the text-message group were more likely than the standard-care group to continue OC use by six months (OR 1.54; 95% CI 1.14 to 2.10). The text-message group was also more likely to avoid an interruption in OC use longer than seven days (OR 1.53; 95% CI 1.13 to 2.07).
AUTHORS' CONCLUSIONS: Only three trials showed some benefit of strategies to improve adherence and continuation. However, several had small sample sizes and six had high losses to follow up. The overall quality of evidence was considered moderate. The intervention type and intensity varied greatly across the studies. A combination of intensive counseling and multiple contacts and reminders may be needed to improve adherence and acceptability of contraceptive use. High-quality RCTs with adequate power and well-designed interventions could help identify ways to improve adherence to, and continuation of, hormonal contraceptive methods.

- 10. Jain, A., Reichenbach, L., Ehsan, I., & Rob, U. (2017). Side effects affected my daily activities: a qualitative exploration of the impact of contraceptive side effects in Bangladesh. *Open Access Journal of Contraception*, 8, 45–52.
<https://doi.org/10.2147/oajc.s140214>**

Abstract: PURPOSE: In a country like Bangladesh that has made great progress in contraceptive use with one of the lowest levels of fertility and highest levels of contraceptive use, understanding what factors influence women's decisions to discontinue a contraceptive method and not switch to a new method is critical in designing interventions and programs that will help enable Bangladesh to reach its FP2020 goals. Research on side effects has focused on physical manifestations like headaches, moodiness, abdominal pain, and menstrual irregularities. While physical effects alone may stop women from continuing a contraceptive method, less is known about how side effects influence women's daily activities and lives. The purpose of this study is to understand the ways that side effects affect Bangladeshi women's participation in different social settings.

METHODS: Thirty-five in-depth interviews with married women who recently discontinued or switched to a different contraceptive method were conducted in Sylhet and Khulna Divisions. Interviews explored reasons for discontinuation including experience of side effects and impact of side effects on women's lives.

RESULTS: Key themes emerged including that side effects are not only experienced physically but are barriers to women's participation in many aspects of their lives. The spheres of life that most commonly appeared to be influenced by side effects include religion, household, and sexual intimacy irrespective of method used or residence.

CONCLUSION: Family planning providers need to be aware of these additional consequences associated with contraceptive side effects to provide tailored counseling that recognizes these issues and helps women to mitigate them. For Bangladesh to achieve its FP2020 goals, understanding the broader context in which family planning decisions are made vis-à-vis side effects is critical to design programs and interventions that meet all the needs of women beyond just their fertility intentions.

- 11. Kibira, S. P. S., Muhumuza, C., Bukenya, J. N., & Atuyambe, L. M. (2015). "I Spent a Full Month Bleeding, I Thought I Was Going to Die..." A Qualitative Study of Experiences of Women Using Modern Contraception in Wakiso District, Uganda. *PLOS ONE*, 10(11), e0141998. <https://doi.org/10.1371/journal.pone.0141998>**

Abstract: INTRODUCTION: There is high unmet need for family planning (FP) in Uganda as well as high contraceptive discontinuation rates. These contribute to the high fertility rates that in part are due to unplanned pregnancies. There are gaps in knowledge about experiences that couples go through while using contraceptives in their lives. This study explored women's experiences during the course of their contraceptive use.

METHODS: We conducted a qualitative study involving 30 women who had used modern contraception for at least one year in Wakiso district, central Uganda. We used in-depth interviews to obtain their personal accounts. Index women were approached through health officers at four health centres in the district. All ethical approvals and informed consent were obtained. We used conventional content analysis; identifying codes through open coding, on which basis categories were developed and grouped into overarching themes.

RESULTS: Women's accounts were summarised in the following themes: negative experiences with modern contraceptive use, motivation to continue using FP in spite of these negative experiences, the role of influential people, and discontinuation of use. Negative accounts dominated the experiences of most women but they expressed strong desire to continue using modern contraception even amidst all challenges. Health workers emerged as the most influential people that played a vital role in women's decisions.

CONCLUSION: Varied negative experiences with modern contraception and misperceptions exist amidst a determination to continue use. Partner engagement, health service strengthening to improve side effects management and health worker skills, and engaging older women that have successfully used contraception as community champions, are potential strategies to support women's contraceptive decisions.

- 12. Li W, Tang J, Terry RN, Li S, Brunie A, Callahan RL, Noel RK, Rodríguez CA, Schwendeman SP, Prausnitz MR. Long-acting reversible contraception by effervescent microneedle patch. *Science advances*. 2019;5(11):eaaw8145. doi:10.1126/sciadv.aaw8145**

Abstract: To increase access to long-acting contraception, we developed a reversible contraceptive microneedle patch that is simple-to-administer, slowly releases contraceptive hormone (levonorgestrel) for >1 month, and generates no biohazardous sharps waste. After manually pressing the patch to skin for 1 min, microneedles rapidly separate from the patch within the skin due to effervescence triggered by contact with skin's interstitial fluid, as demonstrated in rats and human participants. Long-acting contraception is achieved by formulating microneedles with a biodegradable polymer [poly(lactic-co-glycolic) acid] that slowly releases levonorgestrel for ~1 month in vitro. In rats, the patch maintained levonorgestrel concentration above the human contraceptive threshold level for >1 month, and a placebo microneedle patch was well-tolerated in human participants. Women of reproductive age in three continents demonstrated interest in and preference for long-acting contraception by microneedle patch. These studies indicate that an effervescent microneedle patch could facilitate greater access to long-acting contraception.

- 13. Liu, Z., Doan, Q. V., Blumenthal, P., & Dubois, R. W. (2007). A systematic review evaluating health-related quality of life, work impairment, and health-care costs and utilization in abnormal uterine bleeding. *Value in Health*, 10(3), 183–194. <https://doi.org/10.1111/j.1524-4733.2007.00168.x>**

Abstract: OBJECTIVES: Abnormal uterine bleeding (AUB) impacts women's health-related quality of life (HRQoL) and puts a heavy economic burden on society. To date, this burden has not been systematically studied. We conducted a systematic review of the medical literature to evaluate the impact of AUB on HRQoL and to quantify the economic burden of AUB from a societal perspective.

METHODS: We searched the PubMed and Cochrane databases, and article bibliographies for the period up to July 2005. Teams of two reviewers independently abstracted data from studies that reported outcomes of interest: prevalence, HRQoL, work impairment, and health-care utilization and costs associated with AUB.

RESULTS: The search yielded 1009 English-language articles. Ninety-eight studies (including randomized controlled trials, observational studies, and reviews) that met the inclusion and exclusion criteria underwent a full-text review. The prevalence of AUB among women of reproductive age ranged from 10% to 30%. The HRQoL scores from the 36-item Short-Form Health Survey Questionnaire (SF-36) suggested that women with AUB have HRQoL below the 25th percentile of that for the general female population within a similar age range. The conservatively estimated annual direct and indirect economic costs of AUB were approximately \$1 billion and \$12 billion, respectively. These figures do not account for intangible costs and productivity loss due to presenteeism.

CONCLUSIONS: The burden of AUB needs further and more thorough investigation. Additional research should prospectively evaluate the impact of AUB and the value of treatment provided to help guide future health resource allocation and clinical decision-making.

- 14. Polis, C. B., Hussain, R., & Berry, A. (2018). There might be blood: a scoping review on women's responses to contraceptive-induced menstrual bleeding changes. *Reproductive Health*, 15(114). Available [here](#).**

Abstract: INTRODUCTION: Concern about side effects and health issues are common reasons for contraceptive non-use or discontinuation. Contraceptive-induced menstrual bleeding changes (CIMBCs) are linked to these concerns. Research on women's responses to CIMBCs has not been mapped or summarized in a systematic scoping review.

METHODS: We conducted a systematic scoping review of data on women's responses to CIMBCs in peer-reviewed, English-language publications in the last 15 years. Investigator dyads abstracted information from relevant studies on pre-specified and emergent themes using a standardized form. We held an expert consultation to obtain critical input. We provide recommendations for researchers, contraceptive counselors, and product developers.

RESULTS: We identified 100 relevant studies. All world regions were represented (except Antarctica), including Africa (11%), the Americas (32%), Asia (7%), Europe (20%), and Oceania (6%). We summarize findings pertinent to five thematic areas: women's responses to contraceptive-induced non-standard bleeding patterns; CIMBCs influence on non-use, dissatisfaction or discontinuation; conceptual linkages between CIMBCs and health; women's responses to menstrual suppression; and other emergent themes. Women's preferences for

non-monthly bleeding patterns ranged widely, though amenorrhea appears most acceptable in the Americas and Europe. Multiple studies reported CIMBCs as top reasons for contraceptive dissatisfaction and discontinuation; others suggested disruption of regular bleeding patterns was associated with non-use. CIMBCs in some contexts were perceived as linked with a wide range of health concerns; e.g., some women perceived amenorrhea to cause a buildup of “dirty” or “blocked” blood, in turn perceived as causing blood clots, fibroids, emotional disturbances, weight gain, infertility, or death. Multiple studies addressed how CIMBCs (or menstruation) impacted daily activities, including participation in domestic, work, school, sports, or religious life; sexual or emotional relationships; and other domains.

CONCLUSIONS: Substantial variability exists around how women respond to CIMBCs; these responses are shaped by individual and social influences. Despite variation in responses across contexts and sub-populations, CIMBCs can impact multiple aspects of women’s lives. Women’s responses to CIMBCs should be recognized as a key issue in contraceptive research, counseling, and product development, but may be underappreciated, despite likely – and potentially substantial – impacts on contraceptive discontinuation and unmet need for modern contraception.

15. Snow, R., Hardy, E., Kneuper, E., Hebling, E. M., & Hall, G. (2007). Women’s responses to menses and nonbleeding intervals in the USA, Brazil and Germany.

***Contraception*, 76(1), 23–29. <https://doi.org/10.1016/j.contraception.2007.03.008>**

Abstract: BACKGROUND: Studies from several countries suggest women differ in their preferred length of nonbleeding intervals, yet studies to date have not explored the social determinants of such preferences.

METHOD: We report results from a menstrual preference and social survey of 1207 healthy women in three age groups (18-20, 25-34 and 45-49 years) and two educational strata (high and low educational attainment), from Campinas (Brazil), Heidelberg (Germany) and Ann Arbor (USA) (400 women from each country).

RESULTS: Women's preferred length of nonbleeding intervals differed significantly between countries. In Ann Arbor, only 15.5% of women preferred to bleed monthly, vs. 30.2% in Heidelberg. In both Ann Arbor and Campinas, approximately one-third of women preferred to never have menses, compared to 8.2% in Heidelberg. Multivariate analyses indicated that country, church attendance, stress and menstrual pain were significant predictors of women's preferences.

CONCLUSION: The most common preference among women was to bleed once every 3 months, but preferences varied substantially by country groups. Preferences for nonbleeding intervals were, in part, explained by personal experiences of stress or menstrual pain, but unexplained cultural differences persist between country groups.

16. Szarewski, A., von Stenglin, A., & Rybowski, S. (2012). Women's attitudes towards monthly bleeding: results of a global population-based survey. *Eur J*

***Contracept Reprod Health Care*, 17(4), 270-283. Available [here](#).**

Abstract: OBJECTIVE: Monthly bleeding can be uncomfortable and inconvenient. Fifty years after the introduction of the pill, one wonders whether women still want to bleed every month.

METHODS: Cross-national online survey of women aged 15–49 years (N = 4039) who were

currently using, had used or would consider using a hormonal contraceptive. The survey was conducted in eight countries across Europe, North America and Latin America to assess attitudes towards monthly bleeding.

RESULTS: Almost one-third of women reported that bleeding had a severe negative impact on their daily life, particularly with respect to sexual life and sports activities. Approximately 60% of women would, at least sometimes, like to postpone their bleeding and 50% wished they had the flexibility to determine when their menstrual bleeding starts. Overall, 34% of women would change the frequency of their bleeding to once every two or three months.

CONCLUSIONS: Past, current or future users of hormonal contraception reported that bleeding has a severe negative impact on daily life. Given the choice, most women surveyed would reduce the frequency of their bleeding.

17. Tolley, E., Loza, S., Kafafi, L., & Cummings, S. (2005). The Impact of Menstrual Side Effects on Contraceptive Discontinuation: Findings from a Longitudinal Study in Cairo, Egypt. *International Family Planning Perspectives*, 31(1), 15-23. Available [here](#).

Context: Although many research studies have documented the relationship between menstrual side effects of contraceptives and discontinuation of use, few have sought to identify factors that predispose women to discontinue because of changes in bleeding patterns. Such information is important to enable family planning providers to better help women and couples choose appropriate methods and use them successfully.

Methods: Forty-eight women participating in six focus group discussions described their experiences using the IUD, the hormonal implant or the three-month injectable. Subsequently, 259 women using one of these methods for the first time were followed for up to 18 months to determine patterns of menstrual bleeding and perceptions of menstrual cycle change over time. Multivariable analytical methods were used to examine the associations between selected measures and method discontinuation.

Results: Contraceptive discontinuation differed by method: Nearly 70% of injectable users had stopped using their chosen method after one year, compared with 34% of IUD users and 10% of implant users. Before initiating a method, women reported an average of five bleeding days per cycle. During the first six months of use, IUD users reported an average of six days of bleeding per cycle; injectable and implant users reported 11–12. In multivariable models, each additional day of bleeding was significantly associated with a 2–4% increase in discontinuation, depending on method type. Among IUD users, women whose husbands knew that they had visited a clinic to initiate a method were less likely than others to discontinue method use (hazard ratio, –1.9). Age was significantly associated with decreased discontinuation among implant users.

Conclusion: Counseling about bleeding and other side effects should be tailored to women's personal contexts and contraceptive experiences

18. Zimmerman LA, Sarnak D, Karp C, Wood S, Ahmed S, Makumbi F, Kibira S. (2020). Impact of Experiencing Specific Side-Effects on Contraceptive Switching and Discontinuation in Uganda: Results from a Longitudinal PMA Survey. *Reproductive Health*. Under review. doi:10.21203/rs.3.rs-47447/v1

Abstract: BACKGROUND: There is substantial evidence that contraceptive side-effects are a

major deterrent to consistent use of contraception but few studies in low- or middle-income countries explore the role that specific side-effects, rather than “side-effects and health concerns”, have on contraceptive dynamics. This study used population-based, longitudinal data to explore the effect that specific side-effects had on contraceptive continuation, discontinuation, and switching in Uganda.

METHODS: Data for this study come from two rounds of PMA2020 data collection in Uganda PMA2020 Uganda’s sixth cross-sectional survey and a follow-up survey conducted one year later. The main outcomes of interest were discontinuation and switching among modern users of hormonal contraceptive methods and the IUD at baseline (n=550). Multivariable multinomial logistic regressions assessed the association of reporting experiencing specific side-effects (more bleeding, less bleeding, irregular bleeding, increased dryness/reduced libido, and physical discomfort) with discontinuation and switching one year later, adjusting for socio-demographic characteristics, type of method, and length of use.

RESULTS: One-third of hormonal contraceptive users reported experiencing side-effects at baseline. Reporting more bleeding increased the risk of discontinuation by 2.39 times (95% CI: 0.01-4.72). Experiencing irregular bleeding decreased the risk of switching by a factor of 0.40 (95% CI: 0.17-0.93). Vaginal dryness/reduced libido and physical discomfort were both marginally associated with increased relative risk of switching, increasing the risk of switching by a factor of 3.10 (95% CI : 0.97-9.10) and 1.75 (95% CI: 0.95-3.24), respectively. Wealth was significantly negatively associated with discontinuation while education was marginally significantly and positively associated with switching.

CONCLUSIONS: Greater attention should be paid to understanding the unique contributions of side-effects to contraceptive behavior using population-based data. Not all side-effects are associated with contraceptive discontinuation and switching, despite the experience of side-effects being common. The experience of physical discomfort and vaginal dryness/reduced libido, largely ignored in other research, were shown to affect use. Providing greater individualized care that includes information about common side-effects and how they may impact daily life is necessary.

Treatment and Prevention of CIMCs

1. Abdel-Aleem, H., Shaaban, O. M., Amin, A. F., & Abdel-Aleem, A. M. (2005). Tamoxifen treatment of bleeding irregularities associated with Norplant use. *Contraception*, 72(6), 432–437. <https://doi.org/10.1016/j.contraception.2005.05.015>

Abstract: OBJECTIVES: To evaluate the possible role of tamoxifen (selective estrogen receptor modulators, SERM) in treating bleeding irregularities associated with Norplant contraceptive use.

MATERIAL AND METHODS: Randomized clinical trial including 100 Norplant users complaining of vaginal bleeding irregularities. The trial was conducted in the Family Planning Clinic of Assiut University Hospital. Women were assigned at random to receive tamoxifen tablets (10 mg) twice daily for 10 days or similar placebo. Women were followed-up for 3 months. The end points were percentage of women who stopped bleeding during treatment, bleeding/spotting days during the period of follow-up, effect of treatment on their lifestyle, and side effects and discontinuation of contraception.

RESULTS: There was good compliance with treatment. At the end of treatment, a significantly higher percentage of tamoxifen users stopped bleeding in comparison to the control group (88% vs. 68%, respectively; $p=.016$). Women who used tamoxifen had significantly less bleeding and/or spotting days than women who used placebo, during the first and second months. During the third month, there were no significant differences between the two groups. Women who used tamoxifen reported improvement in performing household activities, religious duties and in sexual life, during the first 2 months. In the third month, there were no differences between the two groups. There were no significant differences between tamoxifen and placebo groups in reporting side effects. In the group who used tamoxifen, two women discontinued Norplant use because of bleeding vs. nine women in the placebo group. **CONCLUSION:** Tamoxifen use at a dose of 10 mg twice daily orally, for 10 days, has a beneficial effect on vaginal bleeding associated with Norplant use. In addition, the bleeding pattern was better in women who used tamoxifen for the following 2 months after treatment. However, these results have to be confirmed in a larger trial before advocating this line of treatment.

2. Bahamondes, L., Bahamondes, M. V., & Shulman, L. P. (2015). Non-contraceptive benefits of hormonal and intrauterine reversible contraceptive methods. *Hum Reprod Update*, 21(5), 640- 651. <https://doi.org/10.1093/humupd/dmv023>

Abstract: **BACKGROUND:** Most contraceptive methods present benefits beyond contraception; however, despite a large body of evidence, many healthcare professionals (HCPs), users and potential users are unaware of those benefits. This review evaluates the evidence for non-contraceptive benefits of hormonal and non-hormonal contraceptive methods. **METHODS:** We searched the medical publications in PubMed, POPLINE, CENTRAL, EMBASE and LILACS for relevant articles, on non-contraceptive benefits of the use of hormonal and intrauterine reversible contraceptive methods, which were published in English between 1980 and July 2014. Articles were identified using the following search terms: ‘contraceptive methods’, ‘benefits’, ‘cancer’, ‘anaemia’, ‘heavy menstrual bleeding (HMB)’, ‘endometrial hyperplasia’, ‘endometriosis’ and ‘leiomyoma’.

RESULTS: We identified, through the literature search, evidence that some combined oral contraceptives have benefits in controlling HMB and anaemia, reducing the rate of endometrial, ovarian and colorectal cancer and ectopic pregnancy as well as alleviating symptoms of premenstrual dysphoric disorder. Furthermore, the use of the levonorgestrel-releasing intrauterine system also controls HMB and anaemia and endometrial hyperplasia and cancer, reduces rates of endometrial polyps in users of tamoxifen and alleviates pain associated with endometriosis and adenomyosis. Depot medroxyprogesterone acetate controls crises of pain associated with sickle cell disease and endometriosis. Users of the etonogestrel-releasing contraceptive implant have the benefits of a reduction of pain associated with endometriosis, and users of the copper intrauterine device have reduced rates of endometrial and cervical cancer.

CONCLUSIONS: Despite the high contraceptive effectiveness of many hormonal and intrauterine reversible contraceptive methods, many HCPs, users and potential users are concerned mainly about side effects and safety of both hormonal and non-hormonal contraceptive methods, and there is scarce information about the many benefits that these methods offer beyond contraception.

3. Bahamondes, M. V., de Lima, Y., Teich, V., Bahamondes, L., & Monteiro, I. (2012). Resources and procedures in the treatment of heavy menstrual bleeding with the levonorgestrel-releasing intrauterine system (LNG-IUS) or hysterectomy in Brazil. *Contraception*, 86(3), 244–250.

<https://doi.org/10.1016/j.contraception.2011.12.005>

Abstract: BACKGROUND: Heavy menstrual bleeding (HMB) is the most common complaint of women seeking gynecological care. Treatments included surgical or medical options including hysterectomy and the levonorgestrel-releasing intrauterine system (LNG-IUS) due to the profound suppression of endometrial growth that intrauterine LNG exerts which results in amenorrhea or in a reduction of blood loss.

OBJECTIVE: The study was conducted to evaluate the resources and procedures involved in inserting an LNG-IUS compared to performing hysterectomy in women with HMB in a public sector hospital in Brazil.

STUDY DESIGN: Two cohorts of women were studied: women who accepted an LNG-IUS (n=124) and matched women who underwent hysterectomy on the same day (n=122). We evaluate the number of procedures carried out in each group of women, including those performed before the decision was made to insert an LNG-IUS or to perform hysterectomy, the insertion of the device itself and the surgical procedure, in addition to the procedures and complications registered up to 1 year after LNG-IUS insertion or hysterectomy.

RESULTS: Age and the duration of HMB were significantly lower in the LNG-IUS acceptors than women at the hysterectomy group. The numbers of gynecological consultations and Pap smears were similar in both groups; however, women in the hysterectomy group also underwent laboratory tests, ultrasonography, chest X-ray and electrocardiogram. In the hysterectomy group, the main complications were hemorrhage (six), bladder/bowel perforation (four), complications with anesthesia (one), ureteral reimplantation required (one) and abdominal pain (two). At 1 year, HMB was controlled in 83.1% of women in the LNG-IUS group, and 106 women continued with the device.

CONCLUSIONS: Both treatments were effective in HMB control. Fewer resources and complications were observed in LNG-IUS acceptors when compared to hysterectomy. The LNG-IUS represents a good strategy for reducing the number of hysterectomies and the resources required for women with HMB.

4. Bayer, L. L., & Hillard, P. J. (2013). Use of levonorgestrel intrauterine system for medical indications in adolescents. *J Adolesc Health*, 52(4 Suppl), S54-58.

<https://doi.org/10.1016/j.jadohealth.2012.09.022>

Abstract: The levonorgestrel intrauterine system (LNG-IUS) is an underused contraceptive method in adolescent populations. In addition to being a highly effective, reversible, long-acting contraception, the LNG-IUS has many noncontraceptive health benefits including reduced menstrual bleeding, decreased dysmenorrhea and pelvic pain related to endometriosis, and menstruation suppression in teens with physical or developmental disabilities. The LNG-IUS can also provide endometrial protection in teens with chronic anovulation, and may be used to treat endometrial hyperplasia and cancer. This review examines the evidence supporting the use of the LNG-IUS in adolescents for these noncontraceptive benefits.

5. Brenner, R. M., Slayden, O. D., & Critchley, H. O. D. (2002). Anti-proliferative effects of progesterone antagonists in the primate endometrium: A potential role for the androgen receptor. *Reproduction*, 124(2), 167-172.

<https://doi.org/10.1530/rep.0.1240167>

Abstract: In women and non-human primates, treatment with anti-progestins suppresses oestrogen-dependent mitotic activity in the endometrial glands. This anti-proliferative effect is paradoxical, because anti-progestins do not bind to the oestrogen receptor. Although this phenomenon has been termed a 'non-competitive anti-oestrogenic effect', it does not occur in all species or in other regions of the primate reproductive tract, so is best referred to as an 'endometrial anti-proliferative effect'. The abundance of androgen receptors is greatly increased by anti-progestin treatment, especially in the glandular epithelium in non-human primates and women. Such an increase could lead to an enhancement of androgen action in the endometrium. As androgens suppress oestrogen-dependent endometrial proliferation, the increased abundance of androgen receptors could mediate the anti-proliferative effects of anti-progestin treatment. This brief review evaluates the implications of these findings.

6. Cohen, M. A., Simmons, K. B., Edelman, A. B., & Jensen, J. T. (2019). Tamoxifen for the prevention of unscheduled bleeding in new users of the levonorgestrel 52-mg intrauterine system: a randomized controlled trial. *Contraception*, 100(5), 391–396.

<https://doi.org/10.1016/j.contraception.2019.06.009>

Abstract: OBJECTIVE: To determine if a course of oral tamoxifen initiated following placement of a levonorgestrel 52-mg intrauterine system (IUS) reduces bleeding/spotting days over 30 days.

STUDY DESIGN: In this single-center, double-blind, placebo-controlled trial, we recruited women ages 15–45 years initiating the levonorgestrel 52-mg IUS. We randomized eligible women to tamoxifen 10 mg or placebo twice daily for 7 days starting 21 days after levonorgestrel 52-mg IUS insertion. Participants tracked bleeding/spotting days via daily electronic diaries for 30 days after starting drug treatment. We assessed participant satisfaction with their bleeding pattern and the IUS using a visual analog scale (0–100 mm). A sample size of 42 provided 80% power to detect a difference of 7 bleeding/spotting days in 30 days by two-sample *t* test, accounting for an expected 20% dropout rate.

RESULTS: From September 2016 to January 2018, 42 women enrolled. A total of 34 women provided complete bleeding/spotting data, and 30 women provided satisfaction data. Mean bleeding/spotting days over 30 days did not differ between tamoxifen (12.0±5.8 days) and placebo users (16.8±9.0 days), *p*=.08. We found no significant differences in mean satisfaction with bleeding profiles (51 mm tamoxifen vs. 59 mm placebo, *p*=.48) or with the IUS (83 mm vs. 75 mm, *p*=.36) between groups. Both groups reported similar rates of adverse events, with no serious adverse events reported.

CONCLUSION: A course of oral tamoxifen did not improve early breakthrough bleeding or satisfaction in new users of the levonorgestrel 52-mg IUS.

IMPLICATIONS: Although tamoxifen treatment caused a trend toward modest bleeding/spotting day reduction in new levonorgestrel 52-mg IUS

7. Grimes DA, Hubacher D, Lopez LM, Schulz KF. Non-steroidal anti-inflammatory drugs for heavy bleeding or pain associated with intrauterine-device use. (2006). *Cochrane database Syst Rev*, 4:CD006034. doi:10.1002/14651858.CD006034.pub2

Abstract: BACKGROUND: Heavy bleeding and pain are the most common reasons why women discontinue IUDs. Non-steroidal anti-inflammatory drugs, which inhibit prostaglandin synthesis, have been shown to be effective in reducing menstrual bleeding and pain in women without IUDs.

OBJECTIVES: This review summarizes all randomized controlled trials studying use of nonsteroidal anti-inflammatory drugs for treatment of bleeding or pain associated with IUD use. Trials of prophylactic use of these drugs around the time of IUD insertion were also included.

SEARCH STRATEGY: We performed searches of PubMed, CENTRAL, POPLINE, EMBASE, LILACS, and CINAHL for relevant trials. We also wrote to the authors of all trials identified to seek other published or unpublished trials.

SELECTION CRITERIA: We included all randomized controlled trials in any language that tested one or more nonsteroidal anti-inflammatory drugs for treatment or prevention of bleeding or pain associated with IUD insertion or use.

DATA COLLECTION AND ANALYSIS: Two authors independently abstracted data from relevant trials, and we entered data into RevMan for analysis.

MAIN RESULTS: We found 15 trials from 10 countries; the total number of participants was 2702. Nonsteroidal anti-inflammatory drugs (naproxen, suprofen, mefenamic acid, ibuprofen, indomethacin, flufenamic acid, alclufenac, and diclofenac) were effective in reducing menstrual blood loss associated with IUD use. This held true for women with and without complaints of heavy bleeding. Similarly, these drugs were effective in reducing pain associated with IUD use. In contrast, prophylactic use of nonsteroidal anti-inflammatory drugs had mixed results; studies with ibuprofen found no effect on pain after insertion on IUD discontinuation. No important differences emerged in the one trial comparing the effect of different NSAIDs on bleeding.

AUTHORS' CONCLUSIONS: Nonsteroidal anti-inflammatory drugs reduce bleeding and pain associated with IUD use. NSAIDs should be considered first-line therapy; if NSAIDs are ineffective, tranexamic acid may be considered as second-line therapy. Prophylactic ibuprofen administration with the first six menses after insertion appears unwarranted.

**8. Grow, D. R., & Reece, M. T. (2000). The role of selective oestrogen receptor modulators in the treatment of endometrial bleeding in women using long-acting progestin contraception. *Human Reproduction*, 15, 30 - 38.
https://doi.org/10.1093/humrep/15.suppl_3.30**

Abstract: This paper explores the concept that endometrial breakthrough bleeding results from the stimulatory effects of oestrogen in the endometrium. Though 'progestin-only' contraceptive regimens have long been associated with user dissatisfaction because of unpredictable vaginal bleeding, it is likely that the substantial contribution of endogenous ovarian oestradiol during such treatments predisposes the bleeding problems. Oestrogen causes endometrial proliferation, hyperplasia and neoplasia if unopposed. Oestrogen allows production of growth factors supporting angiogenesis which results in an abundance of dilated

or fragile endothelial surface blood vessels, predisposing this tissue to bleeding when these vessels lose competence.

9. Guiahi, M., McBride, M., Sheeder, J., & Teal, S. (2015). Short-Term Treatment of Bothersome Bleeding for Etonogestrel Implant Users Using a 14-Day Oral Contraceptive Pill Regimen: A Randomized Controlled Trial. *Obstetrical and Gynecological Survey*, 70(12), 763-764.

<https://doi.org/10.1097/01.ogx.0000473158.94049.6e>

Abstract: The etonogestrel contraceptive implant is one of the most effective contraceptives available, with a failure rate of 0.05%. Approved for 3 years of use, it has a high 2-year continuation rate (53%–90%). Up to 11.3% of women in clinical trials discontinued use of this implant before 3 years because of bothersome bleeding (prolonged bleeding and frequent episodes). This double-blind randomized, placebo-controlled trial was designed to determine whether 14 days of treatment with a combination of oral contraceptive pills (OCPs) would stop bleeding in users of the implant with bothersome bleeding. The OCP regimen was a low-dose combination of levonorgestrel and ethinyl estradiol. The primary study outcome was the proportion of women in each group who stopped bleeding during treatment and continued to report no bleeding at the end of 14 days of therapy. Prespecified secondary outcomes included number of days until temporary cessation of bleeding, number of days without bleeding during therapy, and number of days to recurrence of bleeding after therapy was discontinued. The investigators hypothesized that the intervention would result in temporary interruption of bleeding in 80% of the treatment group compared with 20% in the control group; using 80% power, a sample size of 26 women (13 in each group) was required. The study was performed according to the intention-to-treat principle. Most subjects (78%) were young white women. Baseline characteristics of groups were similar. Mean age was 21 to 22 years (range, 18–44 years). A total of 66 women were screened between November 2013 and December 2014; 32 of these were randomized to an OCP group or to a placebo group. Users of the etonogestrel implant with bothersome bleeding episodes for at least 7 consecutive days were randomized to receive 14 pills of combined OCPs (150 µg levonorgestrel and 30 µg ethinyl estradiol, n = 16, or an identical-appearing placebo, n = 16). Significantly, more women in the OCP group than in the placebo group were likely to have a temporary interruption of bleeding during the study period (14 of 16 [87.5% ± 16.2%] in the OCP group vs 6 of 16 [37.5% ± 23.7%] in the placebo group); the odds ratio was 11.7, with a 95% confidence interval of 1.9 to 70.2 (P < 0.01). Among women who had a temporary interruption of bleeding during OCP therapy, 85.7% had bleeding recurrence within 10 days after treatment ended. Use of a low-dose combination OCP in etonogestrel implant users who had reported bothersome bleeding before treatment usually stops bleeding within 14 days. However, bleeding resumes in most patients within 10 days of treatment cessation.

10. Guttmacher Institute. (2011). *Beyond Birth Control: The Overlooked Benefits Of Oral Contraceptive Pills* | Guttmacher Institute. Retrieved November 24, 2020, from <https://www.guttmacher.org/report/beyond-birth-control-overlooked-benefits-oral-contraceptive-pills>

Introduction: Oral contraceptive pills (OCPs) are primarily intended to prevent pregnancy. But

they also offer a number of additional and immediate health benefits, particularly for women who experience menstrual-related disorders. According to the American College of Obstetrics and Gynecology (ACOG), OCPs help relieve or reduce the symptoms of severe menstrual pain (dysmenorrhea), which is experienced by up to 40% of all adult women¹ and can lead to absences from work and school. The pill (as well as other hormonal contraceptives) is useful in treating excessive menstrual bleeding (menorrhagia), which can lead to anemia, and it also has the potential to reduce acne and excess hair growth (hirsutism). Other noncontraceptive uses include prevention of menstrual-related migraines, and treatment of pelvic pain that accompanies endometriosis and of bleeding due to uterine fibroids. Additional benefits identified by ACOG are normalization of irregular periods and suppression of menstruation. For some women, predicting when they will have their period or avoiding it altogether may be a matter of convenience; for others, menstrual regulation may help prevent migraines and other painful “side effects” of menstruation. To date, little is known about the extent to which women use OCPs for purposes other than pregnancy prevention. To help fill this gap, we use national data from the 2006–2008 National Survey of Family Growth (NSFG) to examine how frequently women use the pill for noncontraceptive reasons. This information will provide a broader understanding of how women balance the different reasons for method use and the extent to which they overlap, and how the uses vary among women of different ages and by sexual activity.

11. Hubacher, D., & Grimes, D. A. (2002). Noncontraceptive Health Benefits of Intrauterine Devices: A Systematic Review. *Obstetrical & Gynecological Survey, 57*(2), 120-128. <https://doi.org/10.1097/00006254-200202000-00024>

Abstract: Most women and their clinicians are unaware that IUDs confer important noncontraceptive health benefits. This review summarizes the evidence from published articles on this topic. We conducted a series of systematic literature searches to identify articles on the noncontraceptive health benefits of IUD use. We reviewed the potentially pertinent ones for content, grouped them according to type of IUD, and evaluated them using the U.S. Preventive Services Task Force rating system. Over 500 titles were identified and several hundred abstracts were reviewed. Use of nonhormonal IUDs (plastic and copper) was associated with a decrease in endometrial cancer. The levonorgestrel intrauterine system can treat a variety of gynecological disorders, including menorrhagia and anemia. The levonorgestrel system has also been used successfully as part of hormone replacement therapy, as adjuvant therapy with tamoxifen, and as an alternative to hysterectomy for women with bleeding problems. Like oral contraceptives, intrauterine contraceptives confer important noncontraceptive health benefits.

12. Hurskainen, R., Teperi, J., Rissanen, P., Aalto, A. M., Grenman, S., Kivelä, A., Kujansuu, E., Vuorma, S., Yliskoski, M., & Paavonen, J. (2004). Clinical Outcomes and Costs with the Levonorgestrel-Releasing Intrauterine System or Hysterectomy for Treatment of Menorrhagia: Randomized Trial 5-Year Follow-up. *Journal of the American Medical Association, 291*(12), 1456–1463. <https://doi.org/10.1001/jama.291.12.1456>

Abstract: CONTEXT: Because menorrhagia is often a reason for seeking medical attention, it is important to consider outcomes and costs associated with alternative treatment modalities.

Both the levonorgestrel-releasing intrauterine system (LNG-IUS) and hysterectomy have proven effective for treatment of menorrhagia but there are no long-term comparative studies measuring cost and quality of life.

OBJECTIVE: To compare outcomes, quality-of-life issues, and costs of the LNG-IUS vs hysterectomy in the treatment of menorrhagia.

DESIGN, SETTING, AND PARTICIPANTS: Randomized controlled trial conducted between October 1, 1994, and October 6, 2002, and enrolling 236 women (mean [SD] age, 43 [3.4] years) referred to 5 university hospitals in Finland for complaints of menorrhagia.

Interventions: Participants were randomly assigned to treatment with the LNG-IUS (n = 119) or hysterectomy (n = 117) and were monitored for 5 years.

MAIN OUTCOME MEASURES: Health-related quality of life (HRQL) as measured by the 5-Dimensional EuroQol and the RAND 36-Item Short-Form Health Survey, other measures of psychosocial well-being (anxiety, depression, and sexual function), and costs.

RESULTS: After 5 years of follow-up, 232 women (99%) were analyzed for the primary outcomes. The 2 groups did not differ substantially in terms of HRQL or psychosocial well-being. Although 50 (42%) of the women assigned to the LNG-IUS group eventually underwent hysterectomy, the discounted direct and indirect costs in the LNG-IUS group (\$2817 [95% confidence interval, \$2222-\$3530] per participant) remained substantially lower than in the hysterectomy group (\$4660 [95% confidence interval, \$4014-\$5180]). Satisfaction with treatment was similar in both groups.

CONCLUSIONS: By providing improvement in HRQL at relatively low cost, the LNG-IUS may offer a wider availability of choices for the patient and may decrease costs due to interventions involving surgery.

13. Kaunitz, A. M., Bissonnette, F., Monteiro, I., Lukkari-Lax, E., Desanctis, Y., & Jensen, J. (2012). Levonorgestrel-releasing intrauterine system for heavy menstrual bleeding improves hemoglobin and ferritin levels. *Contraception, 86*(5), 452–457. <https://doi.org/10.1016/j.contraception.2012.07.018>

Abstract: BACKGROUND: We compared the effects of the levonorgestrel-releasing intrauterine system (LNG-IUS) with cyclic oral medroxyprogesterone acetate (MPA) on hemoglobin and serum ferritin levels in women with heavy menstrual bleeding (HMB).

STUDY DESIGN: This was a multicenter, randomized study assessing the efficacy of the LNG-IUS and oral MPA (10 mg/day for 10 days) in women with confirmed HMB over 6 cycles of treatment. We previously reported that treatment with the LNG-IUS resulted in greater menstrual blood loss reduction than MPA. In this analysis, hemoglobin and serum ferritin levels were assessed at baseline, Cycle 3, and at Cycle 6, and the relative improvement on treatment was subjectively rated by investigators and women.

RESULTS: One hundred and sixty-five women were randomized (82 LNG-IUS/83 MPA). Increases in median hemoglobin levels from baseline to Cycle 6 (7.5% vs. 1.9%; $p < .001$) and median serum ferritin levels (68.8% vs. 14.3%; $p < .001$) were greater in the LNG-IUS group than in the oral MPA group. Baseline median hemoglobin and ferritin levels were 12.4 g/dL and 19.0 mcg/L with the LNG-IUS and 12.2 g/dL and 19.0 mcg/L with oral MPA, respectively. At Cycle 6, the corresponding medians were 13.4 g/dL and 34.0 mcg/L with the LNG-IUS and 12.6 g/dL and 21.0 mcg/L with oral MPA. At Cycle 6, the proportion of women who rated their bleeding as

'improved' was higher with the LNG-IUS than with oral MPA, both according to investigator assessment (93.6% vs. 61.0%) and self-assessment (93.6% vs. 67.1%).

CONCLUSIONS: Women treated with the LNG-IUS had greater increases in median hemoglobin and serum ferritin levels, and higher rates of subjective improvement than women treated with oral MPA.

14. Lee, B. S., Ling, X., Asif, S., Kraemer, P., Hanisch, J. U., & Inki, P. (2013). Levonorgestrel-releasing intrauterine system versus conventional medical therapy for heavy menstrual bleeding in the Asia-Pacific region. *International Journal of Gynecology & Obstetrics*, 121(1), 24–30. <https://doi.org/10.1016/j.ijgo.2012.10.028>

Abstract: OBJECTIVE: To compare clinical outcomes, including cumulative continuation rate (CCR), in the treatment of idiopathic heavy menstrual bleeding (HMB) with the levonorgestrel-releasing intrauterine system (LNG-IUS) and with conventional medical therapies (CMTs), including combined oral contraceptives, oral progestins, and antifibrinolytics, either alone or in combination, in the Asia-Pacific region.

METHODS: In a prospective observational cohort study conducted between September 2008 and December 2010, 647 women (LNG-IUS, n = 483; CMTs, n = 164), aged 18–45 years and diagnosed with HMB, were recruited from 8 countries and followed for up to 1 year. The primary outcome was the CCR at 12 months. Secondary outcomes included bleeding pattern, an assessment of treatment efficacy by the treating physician, and safety.

RESULTS: The CCR at 12 months was significantly higher for LNG-IUS than for CMTs (87.6% vs 56.3% P < 0.05). Compared with CMTs, LNG-IUS offered a better reduction in both subjectively assessed menstrual blood loss and the number of bleeding days, and had better efficacy for HMB, as determined by the physician's final evaluation.

CONCLUSION: The present study provides information on the real-life patterns of treatment of HMB in the Asia-Pacific region. The efficacy of CMTs was inferior compared with LNG-IUS in the clinical outcomes measured.

15. Madden, T., Proehl, S., Allsworth, J. E., Secura, G. M., & Peipert, J. F. (2012). Naproxen or estradiol for bleeding and spotting with the levonorgestrel intrauterine system: A randomized controlled trial. *American Journal of Obstetrics and Gynecology*, 206(2), 129.e1-129.e8. <https://doi.org/10.1016/j.ajog.2011.09.021>

Abstract: OBJECTIVE: The purpose of this study was to evaluate whether oral naproxen or transdermal estradiol decreases bleeding and spotting in women who are initiating the levonorgestrel-releasing intrauterine system.

STUDY DESIGN: We conducted a randomized controlled trial of naproxen, estradiol, or placebo that was administered over the first 12 weeks of levonorgestrel-releasing intrauterine system use. Participants completed a written bleeding diary. We imputed missing values and performed an intention-to-treat analysis.

RESULTS: There were 129 women who were assigned randomly to naproxen (n = 42 women), estradiol (n = 44 women), or placebo (n = 43 women). The naproxen group was more likely to be in the lowest quartile of bleeding and spotting days compared with placebo (42.9% vs 16.3%; P = .03). In the multivariable analysis, the naproxen group had a 10% reduction in bleeding and spotting days (adjusted relative risk, 0.90; 95% confidence interval, 0.84–0.97)

compared with placebo. More frequent bleeding and spotting was observed in the estradiol group (adjusted relative risk, 1.25; 95% confidence interval, 1.17–1.34).

CONCLUSION: The administration of naproxen resulted in a reduction in bleeding and spotting days compared with placebo.

16. Narvekar, N., Critchley, H. O. D., Cheng, L., & Baird, D. T. (2006). Mifepristone-induced amenorrhoea is associated with an increase in microvessel density and glucocorticoid receptor and a decrease in stromal vascular endothelial growth factor. *Human Reproduction*, 21(9), 2312–2318. <https://doi.org/10.1093/humrep/del182>

Abstract: BACKGROUND: We have previously shown that the progesterone antagonist mifepristone is a contraceptive when given in a dose of 2 or 5 mg per day. The majority of women experience amenorrhoea rather than the irregular break through bleeding usually occurring with other estrogen-free contraceptive pills, such as progestogen-only pill (POP). We investigated the effects of low-dose mifepristone on endometrial parameters which may be associated with changes in endometrial function, such as microvasculature, vascular endothelial growth factor (VEGF) and glucocorticoid receptor (GR) content.

METHODS AND RESULTS: Endometrial biopsies were collected from 16 women before (late proliferative phase) and 60 and 120 days after taking 2 or 5 mg mifepristone daily for 120 days. Seven of the eight women who received 2 mg mifepristone and all eight women who received 5 mg were amenorrhoeic during the study. Mean estradiol (E2) concentrations remained in the mid-proliferative range, and the majority (9/16) of women showed proliferative endometrial histology at 60 and 120 days following treatment. There was a significant increase in the density of the endometrial stroma ($P < 0.05$) and microvessels ($P < 0.01$) following 120 days of treatment. Immunocytochemistry showed that GR, hitherto localized specifically in endometrial stroma, was up-regulated in the nuclei of glands ($P < 0.05$) and surface (luminal) epithelium ($P < 0.01$) by 60 days and maintained at 120 days. There was a significant reduction in stromal VEGF protein expression by day 120 of treatment ($P \leq 0.01$). CONCLUSION: The high incidence of amenorrhoea in women taking mifepristone may be related to changes in the regulation of vascular function.

17. Qui J., Cheng, J, Wang, Q., Hua, J. (2014). Levonorgestrel-Releasing Intrauterine System versus Medical Therapy for Menorrhagia: A Systematic Review and Meta-Analysis. *Medical Science Monitor*, 20, 1700–1713. <https://doi.org/10.12659/MSM.892126>

BACKGROUND: The aim of this study was to compare the effects of the levonorgestrel-releasing intrauterine system (LNG-IUS) with conventional medical treatment in reducing heavy menstrual bleeding.

MATERIAL/METHODS: Relevant studies were identified by a search of MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and clinical trials registries (from inception to April 2014). Randomized controlled trials comparing the LNG-IUS with conventional medical treatment (mefenamic acid, tranexamic acid, norethindrone, medroxyprogesterone acetate injection, or combined oral contraceptive pills) in patients with menorrhagia were included.

RESULTS: Eight randomized controlled trials that included 1170 women (LNG-IUS, n=562; conventional medical treatment, n=608) met inclusion criteria. The LNG-IUS was superior to

conventional medical treatment in reducing menstrual blood loss (as measured by the alkaline hematin method or estimated by pictorial bleeding assessment chart scores). More women were satisfied with the LNG-IUS than with the use of conventional medical treatment (odds ratio [OR] 5.19, 95% confidence interval [CI] 2.73–9.86). Compared with conventional medical treatment, the LNG-IUS was associated with a lower rate of discontinuation (14.6% vs. 28.9%, OR 0.39, 95% CI 0.20–0.74) and fewer treatment failures (9.2% vs. 31.0%, OR 0.18, 95% CI 0.10–0.34). Furthermore, quality of life assessment favored LNG-IUS over conventional medical treatment, although use of various measurements limited our ability to pool the data for more powerful evidence. Serious adverse events were statistically comparable between treatments. CONCLUSIONS: The LNG-IUS was the more effective first choice for management of menorrhagia compared with conventional medical treatment. Long-term, randomized trials are required to further investigate patient-based outcomes and evaluate the cost-effectiveness of the LNG-IUS and other medical treatments.

18. Sanghera, S., Roberts, T. E., Barton, P., Frew, E., Daniels, J., Middleton, L., Gennard, L., Kai, J., & Gupta, J. K. (2014). Levonorgestrel-releasing intrauterine system vs. usual medical treatment for menorrhagia: An economic evaluation alongside a randomised controlled trial. *PLoS ONE*, 9(3). <https://doi.org/10.1371/journal.pone.0091891>

Abstract: OBJECTIVE: To undertake an economic evaluation alongside the largest randomised controlled trial comparing Levonorgestrel-releasing intrauterine device ('LNG-IUS') and usual medical treatment for women with menorrhagia in primary care; and compare the cost-effectiveness findings using two alternative measures of quality of life.

METHODS: 571 women with menorrhagia from 63 UK centres were randomised between February 2005 and July 2009. Women were randomised to having a LNG-IUS fitted, or usual medical treatment, after discussing with their general practitioner their contraceptive needs or desire to avoid hormonal treatment. The treatment was specified prior to randomisation. For the economic evaluation we developed a state transition (Markov) model with a 24 month follow-up. The model structure was informed by the trial women's pathway and clinical experts. The economic evaluation adopted a UK National Health Service perspective and was based on an outcome of incremental cost per Quality Adjusted Life Year (QALY) estimated using both EQ-5D and SF-6D.

RESULTS: Using EQ-5D, LNG-IUS was the most cost-effective treatment for menorrhagia. LNG-IUS costs £100 more than usual medical treatment but generated 0.07 more QALYs. The incremental cost-effectiveness ratio for LNG-IUS compared to usual medical treatment was £1600 per additional QALY. Using SF-6D, usual medical treatment was the most cost-effective treatment. Usual medical treatment was both less costly (£100) and generated 0.002 more QALYs.

CONCLUSION: Impact on quality of life is the primary indicator of treatment success in menorrhagia. However, the most cost-effective treatment differs depending on the quality of life measure used to estimate the QALY. Under UK guidelines LNG-IUS would be the recommended treatment for menorrhagia. This study demonstrates that the appropriate valuation of outcomes in menorrhagia is crucial.

19. Silva-Filho, A. L., Pereira, F. de A. N., de Souza, S. S., Loures, L. F., Rocha, A. P. C., Valadares, C. N., Carneiro, M. M., Tavares, R. L. C., & Camargos, A. F. (2013). Five-year follow-up of levonorgestrel-releasing intrauterine system versus thermal balloon ablation for the treatment of heavy menstrual bleeding: a randomized controlled trial. *Contraception*, *87*(4), 409–415.

<https://doi.org/10.1016/j.contraception.2012.11.004>

Abstract: BACKGROUND: The study was conducted to compare 5-year follow-up of levonorgestrel-releasing intrauterine system (LNG-IUS) or thermal balloon ablation (TBA) for the treatment of heavy menstrual bleeding (HMB).

STUDY DESIGN: A prospective, randomized controlled trial comparing LNG-IUS (n=30) and TBA (n=28) was performed. Hysterectomy rates, hemoglobin level, bleeding pattern, well-being status and satisfaction rates were assessed. Comparisons between groups were performed by 2 test and by unpaired and paired t tests.

RESULTS: After 5 years of follow-up, women treated with a TBA had higher rates of hysterectomy (24%) compared to the LNG-IUS group (3.7%) due to treatment failure (p=.039). Use of LNG-IUS resulted in higher mean hemoglobin (\pm SD) levels in comparison to the TBA group (14.1 \pm 0.3 vs 12.7 \pm 0.4 g/dL, p=.009). Menstrual blood loss was significantly higher in the TBA when compared to the LNG-IUS group (45.5% vs 0.0% p<.001). The psychological general well-being index scores were similar. Patient acceptability, perceived clinical improvement and overall satisfaction rates were significantly higher in women using LNG-IUS.

CONCLUSION: Five-year follow-up of HMB treatment with LNG-IUS was associated with higher efficacy and satisfaction ratings compared to TBA.

20. Simmons, K. B., Edelman, A. B., Fu, R., & Jensen, J. T. (2017). Tamoxifen for the treatment of breakthrough bleeding with the etonogestrel implant: a randomized controlled trial. *Contraception*, *95*(2), 198–

204. <https://doi.org/10.1016/j.contraception.2016.10.001>

Abstract: OBJECTIVE: The etonogestrel (ENG) subdermal implant can cause frequent breakthrough bleeding in some users. The objective of this study was to evaluate whether a short course of tamoxifen reduces bleeding/spotting days compared to placebo in ENG implant users.

STUDY DESIGN: In this double-blind trial, we randomized ENG implant users with frequent or prolonged bleeding or spotting to tamoxifen 10 mg or placebo twice daily for 7 days, to be started after 3 consecutive days of bleeding/spotting. Treatment was repeated as needed up to three times in 180 days. Subjects completed a daily text message bleeding diary. A sample size of 56 provided 80% power to detect a difference of 6 days of bleeding/spotting per 30 days by two-sample t test. Ovulation was monitored by urinary metabolites of progesterone.

RESULTS: From March 2014 to February 2015, 56 women enrolled. Fifty-one completed at least 30 days of follow up, and 34 completed 180 days. Compared to women randomized to placebo, women randomized to tamoxifen reported 5 fewer days of bleeding/spotting over 30 days (95% confidence interval [CI] -9.9 to -0.05, p=.05), and 15.2 more continuous bleeding-free days (95% CI 2.8–27.5 days, p=.02) after first use of study drug. Conclusions could not be drawn after 30 days due to higher-than-expected dropout. No ovulation was detected.

CONCLUSION: First use of tamoxifen by ENG implant users reduces bleeding/spotting days and provides a longer cessation of bleeding/spotting than placebo, without compromising ovulation suppression. Further study is needed to determine whether this effect is maintained with repeat use.

IMPLICATIONS: Women with frequent ENG implant-related breakthrough bleeding may experience a reduction in bleeding/spotting days and an increase in continuous bleeding-free days in the month following first use of tamoxifen. This short course of tamoxifen was well tolerated with bleeding cessation noted within a median of 5 days.

21. Sørdal, T., P., Draeby, J., O'Flynn, M., & Schmelter, T. (2013). Management of Initial Bleeding or Spotting After Levonorgestrel-Releasing Intrauterine System Placement. *Obstetrics & Gynecology*, 121(5), 934–941. <https://doi.org/10.1097/aog.0b013e31828c65d8>

Abstract: OBJECTIVE: To assess the efficacy of tranexamic acid or mefenamic acid in the management of the initial “nuisance” bleeding or spotting in the period immediately after placement of the levonorgestrel-releasing intrauterine system.

METHODS: Women were randomized after levonorgestrel-releasing intrauterine system placement to oral tranexamic acid (500 mg), mefenamic acid (500 mg), or placebo three times daily during bleeding or spotting episodes over a 90-day treatment period. Treatment was initiated from onset of a bleeding or spotting episode and continued until the first day after bleeding or spotting stopped and restarted with a new bleeding or spotting episode. The primary efficacy variable was reduction in the number of bleeding or spotting days.

Tranexamic acid and mefenamic acid were compared with placebo using a one-sided Wilcoxon rank-sum test. Bonferroni-Holm adjustment was used to account for multiple testing.

RESULTS: A total of 204 women were screened; 187 were randomized to tranexamic acid (n=63), mefenamic acid (n=63), or placebo (n=61). The median number of bleeding or spotting days experienced during treatment was 25, 29, and 33 days in the three groups, respectively.

The median number of bleeding or spotting days was reduced by 6 days (95% confidence interval [CI] –14.0 to 1.0, P=.049) with tranexamic acid and by 3 days (95% CI –11.0 to 5.0, P=.229) with mefenamic acid compared with placebo. The relative risk of bleeding or spotting compared with placebo with tranexamic acid and mefenamic acid was 0.82 (95% CI 0.65–1.03) and 0.89 (95% CI 0.71–1.11), respectively. Most women (85% or more) were satisfied with the levonorgestrel-releasing intrauterine system across the groups.

CONCLUSIONS: Tranexamic acid and mefenamic acid during the first 90 days after levonorgestrel-releasing intrauterine system placement do not alleviate “nuisance” bleeding or spotting.

22. Tantiwattanakul, P., & Taneepanichskul, S. (2004). Effect of mefenamic acid on controlling irregular uterine bleeding in {DMPA} users. *Contraception*, 70(4), 277–279. <https://doi.org/10.1016/j.contraception.2004.04.003>

Abstract: The objective of this double-blind, placebo-controlled study was to evaluate the effect of mefenamic acid and placebo on controlling irregular uterine bleeding in depot-medroxyprogesterone acetate (DMPA) users. A total of 48 DMPA users attending the Family Planning Clinic, Chulalongkorn Hospital were studied, all had abnormal bleeding. These

participants were randomly divided into two groups. A total of 23 users received mefenamic acid, 500 mg, twice a day for 5 days, and placebos were given to the other 25 in the same manner. Total days of bleeding and spotting and percentage of women in whom bleeding was stopped were analyzed in the first and the fourth week. Percentage of subjects in whom bleeding was stopped during the first week after initial treatment was significantly higher in the mefenamic acid group than the placebo group (69.6%, 40.0%; $p < 0.05$). During the follow-up period (4 weeks after initial treatment), the mean of the bleeding-free interval during 28 days was found to be 16.1 days in the subjects treated with mefenamic acid and 12.39 days in the placebo group. However, the difference was not statistically significant. From the results of the study, we concluded that mefenamic acid was effective in very short-term control of bleeding during DMPA use, but not effective long-term.

23. Upawi, S. N., Ahmad, M. F., Abu, M. A., & Ahmad, S. (2020). Management of bleeding irregularities among etonogestrel implant users: Is combined oral contraceptives pills or nonsteroidal anti-inflammatory drugs the better option? *Journal of Obstetrics and Gynaecology Research*, 46(3), 479–484. <https://doi.org/10.1111/jog.14195>

Abstract: AIM: This study is to evaluate whether unacceptable bleeding among the etonogestrel implant user could be better alleviated using combined oral contraceptive pills (COCP) or nonsteroidal anti-inflammation drugs (NSAID).

METHODS: This is a prospective randomized study for evaluation of 84 etonogestrel implant (Implanon) users with prolonged or frequent bleeding. They were assigned to either receiving a COCP containing 20 mcg ethinyl estradiol/150 mg desogestrel for two continuous cycle or NSAID; mefenamic acid 500 mg TDS for 5 days, 21 days apart for two cycles. Bleeding pattern during the treatment was recorded and analyzed.

RESULTS: A total of 32 women (76.2%) in COCP group and 15 women (35.7%) in NSAID group stop bleeding within 7 days after the initiation of treatment which was statistically significant ($P < 0.05$). The mean duration of bleeding and spotting days in women treated with COCP was significantly lesser compared to NSAID group (7.29 ± 3.16 vs 10.57 ± 4.14 days ($P < 0.05$)).

CONCLUSION: We conclude that COCP is more efficient compared to NSAID in managing bleeding irregularities among etonogestrel implant users.

Relevant Articles Cross-Referenced from Other Sections

In Biological Mechanisms of the Menstrual Cycle

Critchley, H. O. D., Brenner, R. M., Henderson, T. A., Williams, K., Nayak, N. R., Slayden, O. D., Millar, M. R., & Saunders, P. T. K. (2001). Estrogen Receptor β , But Not Estrogen Receptor α , Is Present in the Vascular Endothelium of the Human and Nonhuman Primate Endometrium¹. *The Journal of Clinical Endocrinology & Metabolism*, 86(3), 1370–1378. <https://doi.org/10.1210/jcem.86.3.7317>

In Treatment and Prevention of CIMCs

Sanghera, S., Roberts, T. E., Barton, P., Frew, E., Daniels, J., Middleton, L., Gennard, L., Kai, J., & Gupta, J. K. (2014). Levonorgestrel-releasing intrauterine system vs. usual medical treatment for menorrhagia: An economic evaluation alongside a randomised controlled trial. *PLoS ONE*, 9(3). <https://doi.org/10.1371/journal.pone.0091891>

In Treatment of Menstrual Disorders

Mandal, D., Hazra, A., Maity, T., Parmanik, S., Surana, S., & Mandal, S. (2014). Comparative study of low-dose oral contraceptive pill and ormeloxifene in the treatment of dysfunctional uterine bleeding. *International Journal of Health & Allied Sciences*, 3(4), 225. <https://doi.org/10.4103/2278-344X.143056>

In Menstrual Disorders

Harlow, S. D., & Campbell, O. M. R. (2004). Epidemiology of menstrual disorders in developing countries: a systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology*, 111(1), 6-16.

PROGRAMMATIC INTERVENTIONS

Menstrual Health Interventions

- 1. Averbach, S., Sahin-Hodoglugil, N., Musara, P., Chipato, T., & van der Straten, A. (2009). *Duet® for menstrual protection: a feasibility study in Zimbabwe. Contraception, 79(6), 463–468. <https://doi.org/10.1016/j.contraception.2008.12.002>***

Abstract: BACKGROUND: Managing menses is a challenge for women in developing countries. Duet® is a cervical barrier being developed for contraception and STI prevention. We explored the hypothetical acceptability of using Duet as a menstrual cup, among Zimbabwean women. STUDY DESIGN: A survey and focus group discussions (FGD) were conducted with 43 women aged 18–45 years to gain information about their menstrual practices and attitudes regarding the use of Duet for menstrual protection.

RESULTS: All 43 women reported that if Duet were available, they would “definitely” try it, and that it was “very important” that Duet is low cost and easy to clean; 86% reported that using it would make a difference in their lives. FGD findings highlighted unhygienic practices due to the lack of affordable options for menstrual management and a genuine interest in Duet, including its potential use for multiple purposes (contraception, disease prevention and menstrual protection).

CONCLUSIONS: Accessing affordable and hygienic menstrual protection was a problem for these Zimbabwean women. Duet appeared acceptable and it would be feasible to conduct a user-acceptability study of Duet as a menstrual cup in Zimbabwe.

- 2. Crofts, T., & Fisher, J. (2012). *Menstrual hygiene in Ugandan schools: An investigation of low-cost sanitary pads. Journal of Water Sanitation and Hygiene for Development, 2(1), 50–58. <https://doi.org/10.2166/washdev.2012.067>***

Abstract: Menstrual hygiene management (MHM) is a largely overlooked issue in the water,

sanitation and hygiene (WASH) sector. Every day, millions of menstruating girls and women in low-income countries struggle to find clean water for washing, private places for changing and adequate blood absorbing materials. This study aims to explore the difficulties experienced by schoolgirls in Uganda in managing menstrual hygiene and investigates the extent to which low-cost sanitary pads are part of the solution. Low-cost sanitary pads, either re-usable or disposable, are a timely, simple and innovative means of improving menstrual hygiene and of addressing a broader set of problems related to MHM in schools. Other factors highlighted are: pain relief, education, safe water provision, clean and private latrines, hygienic and secure bathing facilities, use of soap, sealed waste disposal points, private drying places, anal cleansing materials and effective facility operation and management strategies.

3. Dongre, A. R., Deshmukh, P. R., & Garg, B. S. (2007). The Effect of Community-Based Health Education Intervention on Management of Menstrual Hygiene among Rural Indian Adolescent Girls. *World Health & Population*, 9(3), 48-54.
<https://doi.org/10.12927/whp.2007.19303>

Abstract: OBJECTIVE: To study the effect of a community-based health education intervention on awareness and behavior change of rural adolescent girls regarding their management of menstrual hygiene.

MATERIALS AND METHOD: A participatory-action study was undertaken in Primary Health Centres in 23 villages in Anji, in the Wardha district of Maharashtra state. Study subjects were unmarried rural adolescent girls (12–19 years). We conducted a needs assessment for health messages with this target audience, using a triangulated research design of quantitative (survey) and qualitative (focus group discussions) methods. Program for Appropriate Technology for Health (PATH) guidelines were used to develop a pre-tested, handmade flip book containing needs-based key messages about the management of menstrual hygiene. The messages were delivered at monthly meetings of village-based groups of adolescent girls, called Kishori Panchayat. After 3 years, the effect of the messages was assessed using a combination of quantitative (survey) and qualitative (trend analysis) methods.

RESULTS: After 3 years, significantly more adolescent girls (55%) were aware of menstruation before its initiation compared with baseline (35%). The practice of using ready-made pads increased significantly from 5% to 25% and reuse of cloth declined from 85% to 57%. The trend analysis showed that adolescent girls perceived a positive change in their behavior and level of awareness.

CONCLUSION: The present community health education intervention strategy could bring significant changes in the awareness and behavior of rural adolescent girls regarding management of their menstrual hygiene.

4. Fakhri, M., Hamzehgardeshi, Z., Hajikhani Golchin, N. A., & Komili, A. (2012). Promoting menstrual health among Persian adolescent girls from low socioeconomic backgrounds: a quasi-experimental study. *BMC Public Health*, 12(1), 193.
<https://doi.org/10.1186/1471-2458-12-193>

Abstract: BACKGROUND: Research in the past decade has revealed average to poor menstrual health among many Iranian girls. The present study investigated the effectiveness of a health promotion project on improving menstrual health in adolescent girls in Iran.

METHODS: A quasi-experimental study was conducted to evaluate the effectiveness of the health intervention program. A total of 698 students (study participants and controls) in several schools in Mazandaran province, Iran were included. The project comprised 10 two-hour educational sessions. Educational topics included the significance of adolescence, physical and emotional changes during adolescence, pubertal and menstruation health and premenstrual syndrome. A self-administered questionnaire measuring demographic characteristics, behaviors during menstruation, menstrual patterns, sources of information about menstruation and personal health data was administered. The questionnaire was administered to all participating students after the experimental group received the training.

RESULTS: Among the most significant results was the impact of educational sessions on bathing and genital hygiene. A total of 61.6% in the experimental group compared with 49.3% in the control group engaged in usual bathing during menstruation ($p = 0.002$). Individual health status was significantly statistically correlated with menstrual health. Attitude towards menstruation was also significantly related to menstrual health.

CONCLUSIONS: The present study confirms that educational interventions, such as the health promotion project in this study, can be quite effective in promoting menstrual health.

5. Girod, C., Ellis, A., Andes, K. L., Freeman, M. C., & Caruso, B. A. (2017). Physical, Social, and Political Inequities Constraining Girls' Menstrual Management at Schools in Informal Settlements of Nairobi, Kenya. *Journal of Urban Health*, 94(6), 835–846. <https://doi.org/10.1007/s11524-017-0189-3>

Abstract: Access to adequate water and sanitation is limited in informal settlements, contributing to girls' challenges managing menstruation at school, especially when they cannot access materials to absorb menstrual blood and appropriate facilities for hygiene. This study documents differences between girls' experience of menstruation at public schools (where the Kenyan government provides menstrual pads) and private schools (where pads are not provided) in two informal settlements of Nairobi, Kenya. Results showed that supply chains to public schools were not reliable, and equitable pad provision was not assured. Girls in private schools struggled to access pads because they were not provided. Sanitation facilities were physically available, but Muslim girls were unable to practice ablution due to the design of toilets in our study schools. Girls experienced fear and anxiety due to harassment from male peers and had incomplete information about menstruation from teachers. Findings suggest that practitioners and policy-makers should acknowledge the diversity of school populations and monitor programs to ensure efforts do not contribute to inequity.

6. Hennegan, J., & Montgomery, P. (2016). Do Menstrual Hygiene Management Interventions Improve Education and Outcomes for Women and Girls in Low and Middle-Income Countries? A Systematic Review. *PLoS One*, 11(2), e0146985. <https://doi.org/10.1371/journal.pone.0146985>

Abstract: BACKGROUND: Unhygienic and ineffective menstrual hygiene management has been documented across low resource contexts and linked to negative consequences for women and girls.

OBJECTIVES: To summarize and critically appraise evidence for the effectiveness of menstruation management interventions in improving women and girls' education, work and

psychosocial wellbeing in low and middle-income countries. Methods: Structured systematic searches were conducted in peer-reviewed and grey literature to identify studies evaluating education and resource provision interventions for menstruation management. Individual and cluster randomized controlled trials were eligible for inclusion, as were non-randomized controlled trials. Study characteristics, outcomes and risk of bias were extracted using a piloted form. Risk of bias was independently assessed by two researchers.

RESULTS: Eight studies described in ten citations were eligible for inclusion. Studies were highly heterogeneous in design and context. Six included assessment of education-only interventions, and three provided assessment of the provision of different types of sanitary products (menstrual cups, disposable sanitary pads, and reusable sanitary pads). A moderate but non-significant standardized mean difference was found for the two studies assessing the impact of sanitary pad provision on school attendance: 0.49 (95%CI -0.13, 1.11). Included studies were heterogeneous with considerable risk of bias. Trials of education interventions reported positive impacts on menstrual knowledge and practices, however, many studies failed to assess other relevant outcomes. No trials assessed or reported harms.

CONCLUSIONS: There is insufficient evidence to establish the effectiveness of menstruation management interventions, although current results are promising. Eight trials have been conducted, but a high risk of bias was found and clinical heterogeneity precluded synthesis of most results. Whilst trials provided some indication of positive results, further research is needed to establish the role of menstruation hygiene management in education performance, employment and other psychosocial outcomes. This review provides a concise summary of present trials and highlights improvements for future work.

7. Juma, J., Nyothach, E., Laserson, K. F., Oduor, C., Arita, L., Ouma, C., et al. (2017).

Examining the safety of menstrual cups among rural primary school girls in western Kenya: observational studies nested in a randomised controlled feasibility study. *BMJ Open*, 7(4), e015429. <https://doi.org/10.1136/bmjopen-2016-015429>

Abstract: OBJECTIVE: Examine the safety of menstrual cups against sanitary pads and usual practice in Kenyan schoolgirls.

DESIGN: Observational studies nested in a cluster randomized controlled feasibility study.

SETTING: 30 primary schools in a health and demographic surveillance system in rural western Kenya.

PARTICIPANTS: Menstruating primary schoolgirls aged 14–16 years participating in a menstrual feasibility study.

INTERVENTIONS: Insertable menstrual cup, monthly sanitary pads or 'usual practice' (controls). Outcome measures *Staphylococcus aureus* vaginal colonization, *Escherichia coli* growth on sampled used cups, toxic shock syndrome or other adverse health outcomes.

RESULTS: Among 604 eligible girls tested, no adverse event or TSS was detected over a median 10.9 months follow-up. *S. aureus* prevalence was 10.8%, with no significant difference over intervention time or between groups. Of 65 *S. aureus* positives at first test, 49 girls were retested and 10 (20.4%) remained positive. Of these, two (20%) sample isolates tested positive for toxic shock syndrome toxin-1; both girls were provided pads and were clinically healthy. Seven per cent of cups required replacements for loss, damage, dropping in a latrine or a poor fit. Of 30 used cups processed for *E. coli* growth, 13 (37.1%, 95% CI 21.1% to 53.1%) had

growth. E. coli growth was greatest in newer compared with established users (53%vs22.2%, $p=0.12$).

CONCLUSIONS: Among this feasibility sample, no evidence emerged to indicate menstrual cups are hazardous or cause health harms among rural Kenyan schoolgirls, but large-scale trials and post-marketing surveillance should continue to evaluate cup safety.

8. Montgomery, P., Hennegan, J., Dolan, C., Wu, M., Mbizvo, L., & Scott, L. (2016). Menstruation and the Cycle of Poverty: A Cluster Quasi-Randomised Control Trial of Sanitary Pad and Puberty Education Provision in Uganda. *PLoS One*, 11(12), e0166122. <https://dx.doi.org/10.1371%2Fjournal.pone.0166122>

Abstract: BACKGROUND: Poor menstrual knowledge and access to sanitary products have been proposed as barriers to menstrual health and school attendance. In response, interventions targeting these needs have seen increasing implementation in public and private sectors. However, there has been limited assessment of their effectiveness.

OBJECTIVES: Assess the impact of providing reusable sanitary pads and puberty education on girls' school attendance and psychosocial wellbeing outcomes.

METHODS: A cluster quasi-randomised controlled trial was conducted across 8 schools, including 1124 girls, in rural Uganda. Schools were allocated to one of four conditions: the provision of puberty education alone; reusable sanitary pads alone; puberty education and reusable sanitary pads; and a control (no intervention). The primary outcome was school attendance. Secondary outcomes reflected psychosocial wellbeing.

RESULTS: At follow-up, school attendance had worsened for girls across all conditions. Per-protocol analysis revealed that this decline was significantly greater for those in the control condition $d = 0.52$ (95%CI 0.26–0.77), with those in control schools having a 17.1% (95%CI: 8.7–25.5) greater drop in attendance than those in any intervention school. There were no differences between the intervention conditions. High rates of school drop-out and transfer meant the trial suffered from substantial participant drop-out. Intention-to-treat analyses using two different imputation strategies were consistent with the main results, with mean differences of 5.2% attendance in best-case and 24.5% in worst-case imputations. Results were robust to adjustments for clustering. There was no impact of the interventions on girls' self-reported shame or insecurity during menstruation.

CONCLUSION: Results of the trial support the hypothesized positive impact of providing sanitary pads or puberty education for girls' school attendance in a developing country context. Findings must be interpreted with caution in light of poor participant retention, intervention fidelity, and the attendance measures used

9. Montgomery, P., Ryus, C. R., Dolan, C. S., Dopson, S., & Scott, L. M. (2012). Sanitary Pad Interventions for Girls' Education in Ghana: A Pilot Study. *PLoS One*, 7(10), e48274. <https://doi.org/10.1371/journal.pone.0048274>

Abstract: BACKGROUND: Increased education of girls in developing contexts is associated with a number of important positive health, social, and economic outcomes for a community. The event of menarche tends to coincide with girls' transitions from primary to secondary education and may constitute a barrier for continued school attendance and performance. Following the MRC Framework for Complex Interventions, a pilot controlled study was conducted in Ghana to

assess the role of sanitary pads in girls' education.

METHODS: A sample of 120 schoolgirls between the ages of 12 and 18 from four villages in Ghana participated in a nonrandomized trial of sanitary pad provision with education. The trial had three levels of treatment: provision of pads with puberty education; puberty education alone; or control (no pads or education). The primary outcome was school attendance.

RESULTS: After 3 months, providing pads with education significantly improved attendance among participants, (λ 0.824, $F=3.760$, $p,.001$). After 5 months, puberty education alone improved attendance to a similar level ($M=91.26$, $SD=7.82$) as sites where pads were provided with puberty education (Rural $M=89.74$, $SD=9.34$; Periurban $M=90.54$, $SD=17.37$), all of which were higher than control ($M=84.48$, $SD=12.39$). The total improvement through pads with education intervention after 5 months was a 9% increase in attendance. After 3 months, providing pads with education significantly improved attendance among participants. The changes in attendance at the end of the trial, after 5 months, were found to be significant by site over time. With puberty education alone resulting in a similar attendance level.

CONCLUSION: This pilot study demonstrated promising results of a low-cost, rapid-return intervention for girls' education in a developing context. Given the considerable development needs of poorer countries and the potential of young women there, these results suggest that a large-scale cluster randomized trial is warranted.

10. Nanda, G., Lupele, J., & Tharaldson, J. (2016). *Menstrual Hygiene Management among Schoolgirls in Eastern Province of Zambia: Qualitative research final report.*

<http://www.washplus.org/resources/reports/2016/05/01/menstrual-hygiene-management-among-schoolgirls-eastern-province-zambia.html>

Summary: Menstruation is a natural physiological process for adolescent girls and women of reproductive age in which blood is discharged through the uterus and flows out through the vagina monthly for approximately two to seven days. The practical challenge of managing menstruation in low-income settings is compounded with socio-cultural factors that include negative perceptions of menses. For far too long, the subject of poor menstrual hygiene in these settings has been neglected and overlooked, not only by the water sector, but by the health and education sectors as well (House et al 2013). Although the topic is finally gaining traction in the international development community, the lives of girls and women continue to be adversely affected by a range of barriers that inhibit their ability to practice acceptable menstrual hygiene management.

11. Oster, E., & Thornton, R. (2009). *Menstruation and education in Nepal. NBER Working Paper Series.* Retrieved from: <http://www.nber.org/papers/w14853>.

Abstract: This paper presents the results from a randomized evaluation that distributed menstrual cups (menstrual sanitary products) to adolescent girls in rural Nepal. Girls in the study were randomly allocated a menstrual cup for use during their monthly period and were followed for fifteen months to measure the effects of having modern sanitary products on schooling. While girls were 3 percentage points less likely to attend school on days of their period, we find no significant effect of being allocated a menstrual cup on school attendance. There were also no effects on test scores, self-reported measures of self-esteem or gynecological health. These results suggest that policy claims that barriers to girls' schooling

and activities during menstrual periods are due to lack of modern sanitary protection may not be warranted. On the other hand, sanitary products are quickly and widely adopted by girls and are convenient in other ways, unrelated to short-term schooling gains.

12. Sommer, M. (2011). An Early Window of Opportunity for Promoting Girls' Health: Policy Implications of the Girl's Puberty Book Project in Tanzania. *International Electronic Journal of Health Education*, 14, 77–92. <https://eric.ed.gov/?id=EJ946325>

Abstract: The onset of puberty, and specifically menstruation, is an opportune moment for reaching girls as they transition into adolescence and young womanhood. Despite the importance of this transitional period, the reproductive health community has tended to overlook the onset of menstruation and early puberty in global, national and local policy and practice in low-income countries. This paper will describe one response to this gap in attention, the Tanzania girl's puberty book project, which was developed through participatory research conducted with Tanzanian girls in 2006-2007. An initial pilot distribution and evaluation of the girl's book was followed by sustained efforts with local stakeholders that led to the girl's puberty book being integrated into government level policy in education and WASH in schools, and over 140,000 copies being disseminated. The Tanzania girl's puberty book project has implications for girls' health and education policy across low-income countries, and is being adapted for Ghana, with plans for developing an Ethiopia book in 2012.

Counseling Including on CIMCs

1. Allen, R., & Villavicencio, J. (2016). Unscheduled bleeding and contraceptive choice: increasing satisfaction and continuation rates. *Open Access Journal of Contraception*, 7, 4 <https://doi.org/10.2147/OAJC.S85565>

Abstract: Approximately half (51%) of the 6.6 million pregnancies in the US each year are unintended and half of those pregnancies (54%) occur among women not using contraception. Many women discontinue their contraceptives due to method dissatisfaction. Bothersome unscheduled bleeding is one of the main reasons cited by women for stopping a birth control method. Improving counseling and management of these side effects will aide in increasing satisfaction with contraceptive methods. The following review will discuss the bleeding profiles associated with the contraceptive options available in the US. A valuable resource from the Centers for Disease Control and Prevention, the US Selected Practice Recommendations for Contraceptive Use, will be introduced. Definitions of the types of unscheduled bleeding are included, as well as strategies for treatment for each contraceptive method. The evidence whether or not anticipatory counseling increases continuation rates will also be reviewed.

2. Cavallaro FL, Benova L, Owolabi OO, Ali M. (2019). A systematic review of the effectiveness of counselling strategies for modern contraceptive methods: what works and what doesn't? *BMJ Sexual & Reproductive Health*, 46(4), 254-269. doi:10.1136/bmjshr-2019-200377

Abstract: AIM: The aim of this systematic review was to synthesise the evidence on the comparative effectiveness of different counselling strategies for modern contraception on

contraceptive behaviour and satisfaction, and to examine their advantages and disadvantages. METHODS: Six electronic databases (Medline, Embase, Global Health, Popline, CINAHL Plus, and Cochrane Library) were searched to identify publications comparing two or more contraceptive counselling strategies and reporting quantitative results on contraceptive use, uptake, continuation or switching, or client satisfaction. Studies of women or couples from any country, published in English since 1990 were considered.

RESULTS: A total of 63 publications corresponding to 61 studies met the inclusion criteria. There was substantial heterogeneity in study settings, interventions and outcome measures. Interventions targeting women initiating a method (including structured counselling on side effects) tended to show positive effects on contraceptive continuation. In contrast, the majority of studies of provider training and decision-making tools for method choice did not find evidence of an effect. Additional antenatal or postpartum counselling sessions were associated with increased postpartum contraceptive use, regardless of their timing in pregnancy or postpartum. Dedicated pre-abortion contraceptive counselling was associated with increased use only when accompanied by broader contraceptive method provision. Male partner or couples counselling was effective at increasing contraceptive use in two of five studies targeting non-users, women initiating implants or seeking abortion. High-quality evidence is lacking for the majority of intervention types.

CONCLUSIONS: The evidence base and quality of studies are limited, and further research is needed to determine the effectiveness of many counselling interventions in different settings.

3. Modesto, W., Bahamondes, M. V., & Bahamondes, L. (2014). A randomized clinical trial of the effect of intensive versus non-intensive counselling on discontinuation rates due to bleeding disturbances of three long-acting reversible contraceptives. *Human Reproduction*, 29(7), 1393–1399. <https://doi.org/10.1093/humrep/deu089>

Abstract: STUDY QUESTION: Does intensive counselling before insertion and throughout the first year of use have any influence on discontinuation rates due to unpredictable menstrual bleeding in users of three long-acting reversible contraceptives (LARCs)?

SUMMARY ANSWER: Intensive counselling had a similar effect to routine counselling in terms of discontinuation rates due to unpredictable menstrual bleeding in new users of the contraceptives.

WHAT IS KNOWN ALREADY: Contraceptive efficacy and satisfaction rates are very high with LARCs, including the etonogestrel (ENG)-releasing implant, the levonorgestrel-releasing intrauterine system (LNG-IUS) and the TCU380A intrauterine device (IUD). However, unpredictable menstrual bleeding constitutes the principal reason for premature discontinuation, particularly in the cases of the ENG-implant and the LNG-IUS.

STUDY DESIGN, SIZE, DURATION: A randomized clinical trial was conducted between 2011 and 2013, and involved 297 women: 98 ENG-implant users, 99 LNG-IUS users and 100 TCU380A IUD users.

PARTICIPANTS, SETTING, METHODS: Women accepting each contraceptive method were randomized into two groups after the women chose their contraceptive method. Group I received routine counselling at the clinic, including information on safety, efficacy and side effects, as well as what to expect regarding bleeding disturbances. Group II received 'intensive counselling'. In addition to the information provided to those in Group I, these women also

received leaflets on their chosen method and were seen by the same three professionals, the most experienced at the clinic, throughout the year of follow-up. These three professionals went over all the information provided at each consultation. Women in both groups were instructed to return to the clinic after 45 (± 7) days and at 6 and 12 (± 1) months after insertion. They were instructed to record all bleeding episodes on a menstrual calendar specifically provided for this purpose. Additionally, satisfaction with the method was evaluated by a questionnaire completed by the women after 12 months of use of the contraceptive method.

MAIN RESULTS AND THE ROLE OF CHANCE: There were no significant differences between the intensive and routine counselling groups on the discontinuation rates due to unpredictable menstrual bleeding of the three contraceptives under evaluation. The 1-year cumulative discontinuation rates due to menstrual bleeding irregularities were 2.1, 2.7 and 4.0% and the continuation rates were 82.6, 81.0 and 73.2%, for the ENG-implant, the LNG-IUS or the TCu380A IUD users, respectively. The main reasons for discontinuation of the methods were weight gain in users of the ENG-implant and expulsion of the TCu380A.

LIMITATIONS, REASONS FOR CAUTION: The main limitations are that we cannot assure generalization of the results to another settings and that the routine counselling provided by our counsellors may already be appropriate for the women attending the clinic and so consequently intensive counselling including written leaflets was unable to influence the premature discontinuation rate due to unpredictable menstrual bleeding. Additionally, counselling could discourage some women from using the LARC methods offered in the study and consequently those women may have decided on other contraceptives.

WIDER IMPLICATIONS OF THE FINDINGS: Routine counselling may be sufficient for many women to help reduce premature discontinuation rates and improve continuation rates and user satisfaction among new users of LARC methods.

4. Punzi, M. C., & Hekste O. *Technical brief for the Integration of Menstrual Health in SRHR*. Retrieved September 28, 2020. Available [here](#).

Abstract: Menstrual health is an entry point and essential lens to understand and approach women's sexual and reproductive health journeys. The menstrual cycle accompanies girls and women from the beginning of puberty until menopause and is an important predictor and indicator of health (American College of Obstetricians and Gynecologists, 2016). Despite its importance, global health practitioners have often overlooked the value of menstruation. As a consequence, girls and women don't receive appropriate education about their menstrual cycle and fertility, contributing to a lack of confidence and ownership of their own bodies, which are essential elements to make informed decisions throughout their sexual and reproductive health journeys. In December 2018, building on previous projects, PSI-Europe partnered with The Case for Her, a funding collaborative investing in early stage markets within women's and girls' health, with the aim to understand the role menstrual health plays in PSI's network members' programs and its potential to strengthen and improve Sexual and Reproductive Health and Rights (SRHR) interventions. With this technical brief, the authors hope to support the SRHR work in-country, providing a technical brief for integrating menstrual health in existing SRHR programs

5. Rademacher, K. H., Sergison, J., Glish, L., Maldonado, L. Y., Mackenzie, A., Nanda, G., & Yacobson, I. (2018). *Menstrual bleeding changes are NORMAL: Proposed counseling tool to address common reasons for non-use and discontinuation of*

contraception. *Global Health Science and Practice*, 6(3), 603–610. doi: [10.9745/GHSP-D-18-00093](https://doi.org/10.9745/GHSP-D-18-00093)

Abstract: BACKGROUND: Evidence shows that menstrual bleeding changes associated with contraceptive use contribute to both discontinuation rates and non-use of contraception. Helping women understand the typical bleeding changes associated with modern contraceptive methods could lead to greater acceptance of these changes, increased method uptake, improved satisfaction, and higher continuation rates.

METHODS: In order to better understand what current guidance is available to health care providers on how to counsel women about menstrual bleeding changes and contraceptive use, we reviewed counseling, training, and reference materials developed and commonly used by international family planning programs. The information was evaluated for 4 contraceptive methods—implants, injectables, the copper intrauterine device (IUD), and the levonorgestrel intrauterine system (LNG IUS).

FINDINGS AND DISCUSSION: A key finding from the assessment was that menstrual bleeding changes are insufficiently addressed in the resources reviewed. To address gaps in existing guidance and training materials, a multidisciplinary project team from FHI 360 and Population Services International (PSI) developed the “NORMAL” tool which uses the simple mnemonic device —Normal, Opportunities, Return, Methods, Absence of Menses, and Limit—to help practitioners remember brief messages about menstrual bleeding changes and address typical concerns and questions women often have. Further research and stakeholder engagement is needed before use of the tool is implemented on a wide scale.

6. Schivone, G. B., & Glish, L. L. (2017). Contraceptive counseling for continuation and satisfaction. *Current Opinion in Obstetrics and Gynecology*, 29(6), 443–448 doi: [10.1097/GCO.0000000000000408](https://doi.org/10.1097/GCO.0000000000000408)

Abstract: PURPOSE OF REVIEW: Quality contraceptive counseling has been identified as a potential means to reduce unintended pregnancy and to increase contraceptive continuation and satisfaction. Past approaches that focused on autonomous decision making and directive counseling have not been shown to meet these goals consistently. Women’s health organizations globally are calling for improved counseling through more thorough discussion of side-effects and bleeding changes, and renewed focus on shared decision making and patient-centered care.

RECENT FINDINGS: Reproductive life planning can help initiate contraceptive counseling but does not resonate with all patients. A client-centered approach using shared decision making, building trust, and eliciting client preferences has been shown to increase satisfaction and continuation. Patient preferences vary widely and may or may not prioritize extremely high effectiveness. Decision support tools have mixed results, but generally can help improve the method choice process when they are well designed.

SUMMARY: Clinicians should strive for good interpersonal relationships with patients and elicit patient experiences and preferences to tailor their counseling to each individual’s needs. Shared decision making with input from both the patient and clinician is preferred by many women, and clinicians should be cognizant of perceptions of pushing any method too strongly, especially among marginalized populations. More research on long-term satisfaction and continuation linked to different counseling practices is needed

Relevant Articles Cross-Referenced from Other Sections

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