

Review

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Review

The Menstrual Cycle as a Vital Sign: A Comprehensive Review

Running title: Menstrual Cycle as a Vital Sign

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Abstract: Some medical professional organizations have advocated for including the menstrual cycle as a vital sign in adolescence, but not in adulthood. However, documenting menstrual cycle patterns is not routine clinical or research practice. Vital signs are used to predict health outcomes, indicate needed treatment, and monitor a clinical course. They can help identify pathologies, affirm wellness, and are responsive to exposures. Here we review the scientific evidence showing how the menstrual cycle meets these criteria and should therefore be treated as a vital sign. Using key words and controlled vocabulary terms, we carried out multiple literature searches, prioritizing the inclusion of systematic reviews, meta-analyses, and clinical practice guidelines. This review describes how the menstrual cycle is a health indicator, can cyclically impact health conditions, and its associations with long-term post-menopausal health outcomes. We review exposures influencing the menstrual cycle, evidence underlying its use to optimize wellness, and available tools for documenting cycles. Supplementary materials include patient handouts on menstrual cycle tracking, and an index of related clinical practice guidelines and reviews by subject. The menstrual cycle is a vital sign from menarche through menopause, an underutilized but powerful tool for understanding gynecological and general health.

Keywords: menstrual cycle; menstruation; vital signs; menstrual cycle tracking; menstrual health

Introduction

In 2006, the American College of Obstetricians and Gynecologists (ACOG) and American Academy of Pediatrics (AAP) advocated using the menstrual cycle as a vital sign for girls and adolescents, allowing early identification of health conditions with abnormal menstrual patterns and early interventions to improve adult health outcomes (1, 2). ACOG reaffirmed its opinion in 2015 and 2021. Since these committee opinions were published, smartphone cycle tracking applications proliferated (3); menstrual equity laws were passed to address period poverty and improve menstrual product accessibility, affordability, and safety (4); and thousands of individuals reported COVID-19 mRNA vaccines seemed to impact their cycles, spurring research and highlighting the fact that cycle information is rarely collected in vaccine trials (5). Menstrual health is of critical public health importance, directly impacting the health and wellbeing of people who menstruate, and requiring the education and involvement of those who do not experience the menstrual cycle (6, 7). The Global Menstrual Collective defines menstrual health as “a state of physical, mental, and social well-being and not merely the absence of disease or infirmity, in relation to the menstrual cycle” (7). Treating the menstrual cycle as a vital sign has the potential to increase access to accurate information

across the lifespan and improve timely diagnosis and treatment of menstrual health-related conditions (7). Yet, documenting the menstrual cycle as a vital sign is still not routine clinical practice.

In this review, we assess the evidence for treating the menstrual cycle as a vital sign from menarche to menopause. We describe how the menstrual cycle is a health indicator, associated with long-term health outcomes, and used to optimize wellness. We review exposures that can influence the menstrual cycle, and health conditions that can vary with it. We also summarize available tools for documenting cycles. While ACOG and AAP advocated using the menstrual cycle as a vital sign for children and adolescents, based on the evidence we argue it should be considered a vital sign through menopause. In this review, we use the inclusive terms “menstruator” (8) and “people with a menstrual cycle”.

Methods

For each of the review’s core terms and main subsections, we developed a list of concept terms and used key word and controlled vocabulary searches in the PubMed database to search for current systematic reviews, meta-analyses, or clinical practice guidelines published since 2020 covering the topic. If such literature was unavailable, we searched for original research published since 2020 and earlier reviews from 2010-2020. Concept terms, MeSH terms, and search strategies for each subsection are included in Supplementary Materials. Articles were screened using title and abstract, and were also identified through bibliographic review. During full text review, we also screened for study type, prioritizing the inclusion of high-quality systematic reviews, meta-analyses, clinical practice guidelines, and sentinel research studies. Practice guidelines and reviews with a clinical practice emphasis included in this review are also listed by subject in Supplementary Table S1 for further clinical reference.

Vital Signs

Vital signs are patient features used to predict health outcomes, indicate need for treatment, and monitor a clinical course (9-11). They help identify pathologies, affirm wellness, and are responsive to exposures. Vital signs are dynamic. The classic vital signs – pulse, temperature, respiratory rate, and blood pressure – change over seconds to minutes. The menstrual cycle has a longer timeframe of days to months, but is also dynamic. Although information from a single point in time can be useful, trends over time are key to interpreting vital signs (9, 10). The same is true of the menstrual cycle: although information from a single cycle can be useful, it cannot capture variability or patterns over time (12). Just as the classic vital signs regularly are altered with, for example, antihypertensives and exercise, the menstrual cycle is also routinely altered with medications and hormones.

The Menstrual cycle

The menstrual cycle is a series of interdependent cyclic physiologic events. In a typical cycle, the hypothalamus releases pulses of gonadotropin-releasing hormone (GnRH), leading to the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary gland (13). During the follicular phase, FSH stimulates the growth of ovarian follicles. As the follicles develop, they secrete increasing levels of estradiol which stimulates endometrial proliferation (14). At the same time, rising estradiol leads to a mid-cycle LH surge, which triggers ovulation. The luteal phase begins as the ruptured follicle becomes the corpus luteum which secretes multiple hormones, especially progesterone which stimulates decidualization of the endometrium. With corpus luteum involution, progesterone declines triggering menstruation and the start of a new menstrual cycle (13-15).

Commonly tracked external indicators reflecting the internal hormonal changes of the menstrual cycle include vaginal bleeding, basal body temperature (BBT), cervical fluid or mucus, and urinary levels of LH, and estradiol, progesterone, and their metabolites (14). BBT is measured upon waking at approximately the same time each day (16). It is approximately 0.5 °F (0.3 °C) lower in the follicular than the luteal phase (14, 15). After ovulation, increasing progesterone raises BBT until 1-2 days before menses, when BBT falls. Daily BBT tracking can be used to confirm ovulation retrospectively.

Changes to cervical fluid across the menstrual cycle are easily observed at the vulva and cervix (17). In ovulatory cycles, cervical fluid changes in sensation (from dry, to moist, to wet, to slippery), color (from white/yellow to clear), and consistency (from tacky, to creamy, to stretchy) (18, 19). It is produced most abundantly in the days just before ovulation, and the last day of clear, stretchy (at least 1 inch), and slippery cervical fluid occurs within about 24 hours of ovulation in 75% of menstrual cycles (18, 20). As estrogen levels fall after ovulation and progesterone rises, cervical fluid disappears and menstruators experience dry days for the rest of the luteal phase (15, 20). See Supplementary Materials for educational handouts on tracking the menstrual cycle.

Non-Reproductive Physiologic Changes across the Menstrual Cycle

The menstrual cycle impacts an array of non-reproductive physiologic processes in the body (Table 1). The classic vital signs – temperature, heart rate, respiratory rate, blood pressure – all measurably increase in the luteal phase before declining with the onset of menstruation (21-26). The implications of these changes for other physiologic functions are not well known, but at minimum are connected to cyclic changes in thermoregulation, fluid regulation, and metabolism.

Table 1. Non-reproductive physiologic changes across the menstrual cycle.

Physiologic parameter process	or	Menstrual cycle phase			References
		Menses	Follicular phase	Luteal phase	
<i>Vital signs</i>					
Temperature	↓			↑ 0.5-0.8 °C	(23, 25)
Heart rate	↓			↑ 3 bpm/3-5%	(21, 25, 26)
Heart rate variability			↑ variability	↓ variability	(26)
Respiratory rate	↓			↑ 0.8 breaths/minute	(26)
Blood pressure	↓			↑ 3mmHg	(22, 24)
<i>Thermoregulation</i>					
Sweating				↑ 0.5 °C response threshold compared to follicular phase	(22, 23)
Skin vasodilation				↑ 0.5 °C response threshold compared to follicular phase	(22, 23, 27)
Shivering				↑ 0.5 °C response threshold compared to follicular phase	(22, 23, 27)
<i>Fluid regulation</i>					
Thirst threshold		↓ threshold, ↓ thirst stimulation	↑↑ threshold, ↑ stimulation	↓ thirst	(28, 29)
Arginine vasopressin		↑ production, ↓ threshold release	↓ for ↓ release		(28, 29)
Aldosterone		↓ production	↑ production		(28, 29)
Interstitial fluid			↑ compared to follicular phase		(28, 29)
Plasma volume		↑ with preovulation peak	↓ up to 8%		(28, 29)
Plasma osmolality		↓	↑		(28, 29)
<i>Metabolism</i>					
Basal metabolic rate			↑ 5-9% compared to follicular phase		(21)
Energy intake		↓, with nadir at ovulation	↑		(30)

Glycogen storage	↑ compared to follicular phase	(30)
Fat metabolism	↑ compared to follicular phase	(30)
Protein metabolism	↑ compared to follicular phase	(30)
<i>Sleep</i>		
REM episodes	↓ compared to follicular phase	(35)
Sleep spindles	↑ compared to follicular phase	(35)
<i>Circadian rhythms</i>		
Temperature	↓ amplitude of change compared to follicular phase	(34, 37)
Cortisol	↓ amplitude of change compared to follicular phase	(34)
Thyroid stimulating hormone	↓ amplitude of change compared to follicular phase	(34)
<i>Immune system</i>		
C-reactive protein	↑ compared to follicular and luteal phases	(31)
Regulatory T-cells	↑ number	↓ number (32)
<i>Hemostatic factors</i>		
von Willebrand's factor	↓ compared to follicular or luteal phase	(38)
Platelets	↓ compared to follicular or luteal phase	(38)
<i>Microbiome</i>		
Vaginal microbiome	↑ species diversity	↓ species diversity with <i>Lactobacillus</i> spp. dominance (39)

Thermoregulation keeps body temperature stable across varying environments and activities. Increased luteal phase BBT increases the temperature thresholds triggering skin vasodilation, sweating, and shivering (22, 23, 27). Because large volumes of blood are moved to and from skin circulation as part of the body’s responses to heat and cold, blood pressure regulation is intertwined with thermoregulation. Cyclic blood pressure changes are thought to be linked to levels of estradiol – a vasodilator – and the sympathetic nervous system, which is more active in the luteal phase as evidenced by decreased heart rate variability (22, 24, 26).

Estrogen and progesterone also influence fluid. Estrogen decreases the threshold for arginine vasopressin (AVP) release; when AVP levels are higher, more water is resorbed by the kidneys rather than excreted in urine, resulting in lower plasma osmolality without water retention (28, 29). Progesterone is thought to increase aldosterone concentration, which promotes sodium reabsorption and water retention (28, 29). The implications of elevated luteal phase estrogen and progesterone for fluid dynamics is not completely understood, but in the luteal phase, plasma volume has been observed to decline up to 8%, and plasma osmolality and interstitial fluid are elevated (28, 29). Energy intake and the basal metabolic rate also increase in the luteal phase, accompanied by changes to carbohydrate, fat, and protein metabolism (21, 30).

Interactions between the immune system and the menstrual cycle are not yet fully understood. Although research on immune cells fluctuations across the cycle is scant, regulatory T cells appear to be lower in the luteal phase, and C-reactive protein (CRP), an indicator of general inflammation, is elevated during menses (31, 32). This aligns with observations that some autoimmune disorders have cyclic flare-ups, typically worsening premenstrually and during menses (32). Additionally, immune responses occurring with some vaccines, like the COVID-19 mRNA vaccines, are hypothesized to impact the HPO axis, causing temporary changes to cycle length (33).

Circadian rhythms, hemostatic factors, and the vaginal microbiome also vary across the menstrual cycle. The amplitude of several circadian rhythms, including body temperature and cortisol levels, decreases during the luteal phase (34, 35). Circadian rhythms interact with the menstrual cycle in complex ways, including via the suprachiasmatic nucleus, the circadian pacemaker, which contains estrogen and progesterone receptors and interacts with GnRH across the menstrual cycle (36, 37). The complex neuroendocrine interplay between the menstrual cycle and circadian rhythms has primarily been studied in rodents and is not fully understood in humans. Although most hemostatic factors do not appear to fluctuate cyclically, evidence does support changes to von Willebrand factor and platelets, which are lowest during menses and the early follicular phase (38). Composition of the vaginal microbiome strongly varies across the menstrual cycle, with more species diversity during menses. As the cycle progresses, microbial composition stabilizes, with *Lactobacillus* spp. dominance in the luteal phase (39).

Our understanding of these cyclic changes is limited as menstruators are underrepresented in physiologic research and menstrual cycle data is infrequently documented. Despite this, cyclic fluctuations of diverse physiologic parameters and processes have been observed, underscoring the importance and value of collecting menstrual cycle data and accounting for cycle phase in research.

The Menstrual Cycle as Health Indicator

The menstrual cycle responds to diverse health conditions (Table 2). Observed over time, it can serve as an indicator for endocrine diseases, bleeding disorders, structural anomalies of the reproductive tract, neoplasms, infections, and infertility (40, 41). While providing detailed clinical practice guidelines on using menstrual cycle characteristics to diagnose health conditions is beyond the scope of this review, practice guidelines and reviews with a clinical practice emphasis related to the menstrual cycle and cited in this review are listed by topic in Table S1 for ease of further reference.

Table 2. Health conditions and the menstrual cycle.

Health condition	Associated changes to menstrual cycle	References
<i>Endocrine disorders</i>		
Polycystic ovarian syndrome (PCOS)	Irregular, infrequent bleeding; long cycles; variable volume and duration of bleeding; amenorrhea	(42, 45*, 46*)
Hypothalamic amenorrhea	Amenorrhea	(43*)
Primary or premature ovarian insufficiency	Infrequent bleeding; amenorrhea	(48, 49*)
Ovulatory dysfunction	Irregular bleeding; amenorrhea	(12*, 50*)
Diabetes (types 1 and 2)	Long cycles; infrequent bleeding; variability in menstrual cycle length; prolonged and heavy bleeding; amenorrhea; later menarche and earlier menopause (type 1 diabetes)	(42, 44*)
Hypothyroidism	Irregular and infrequent bleeding; heavy or prolonged bleeding; amenorrhea	(42, 47)
Hyperthyroidism	Infrequent or frequent bleeding; low volume of bleeding; amenorrhea	(42, 47)
<i>Bleeding disorders</i>		

von Willebrand’s disease	Heavy or prolonged bleeding	(56*, 57*)
Platelet dysfunction	Heavy or prolonged bleeding	(56*, 57*)
Structural anomalies and pathologies		
Congenital structural anomalies	Amenorrhea, increasing dysmenorrhea after menarche, acyclic or cyclic pelvic/abdominal pain	(62*, 63, 64*)
Fibroids (uterine leiomyomas)	Heavy or prolonged bleeding	(40*)
Adenomyosis	Heavy or prolonged bleeding	(40*)
Endometrial polyps	Intermenstrual bleeding	(40*)
Cervical polyps	Intermenstrual bleeding	(40*)
Endometriosis	Heavy or prolonged menstrual bleeding	(40*)
Cancers of the reproductive tract	Heavy or prolonged menstrual bleeding, intermenstrual bleeding, dysmenorrhea	(40*)
Cervical dysplasia or cancer	Intermenstrual bleeding	(40*)
Infections		
Vaginitis, cervicitis	Intermenstrual bleeding	(65*)
Sexually transmitted infections (i.e., chlamydia, gonorrhea)	Intermenstrual bleeding	(40*, 41*, 65*)
Physiologic changes across the lifespan		
Menarche and development of ovulatory cycles	Cycle length of 21-45 days, with increasing regularity and fewer anovulatory cycles over time; cycle length of 21-34 days by 3 years after menarche; heavy menstrual bleeding is never normal; menses last 2-7 days	(70)
Pregnancy	Amenorrhea	(69)
Postpartum return of the ovarian cycle	Amenorrhea, anovulatory cycles, short luteal phase	(69)
Lactational amenorrhea	Amenorrhea, anovulation, infrequent bleeding	(69)
Perimenopause/menopausal transition	Regular bleeding with increased frequency, shorter cycle length, anovulatory cycles	(69)
Health condition	Condition changes across the menstrual cycle	References
Neurological conditions		
Migraine	Migraines more common in premenstrual phase, during menses, and around ovulation	(71, 72, 73*)
Seizures	Increased seizures in premenstrual phase, during menses, around ovulation, during luteal phase in anovulatory cycles, and during perimenopause; seizures least likely during luteal phase of ovulatory cycles	(71, 74*, 75*)
Autoimmune conditions		
Systemic lupus erythematosus	Symptoms worse in premenstrual phase	(32)
Multiple sclerosis (MS)	Symptoms worse in luteal and premenstrual phases	(74*)
Rheumatoid arthritis	Symptoms better during luteal phase, worse during menses	(71, 76)
Chronic pain conditions		
Fibromyalgia	Pain and symptoms worse in premenstrual phase and during menses	(76)

Musculoskeletal pain	Pain worse in premenstrual phase and during menses	(76)
Temporomandibular disorder	Pain worse in premenstrual phase, during menses, and occasionally around ovulation	(76)
Mental health disorders		
Psychotic disorders	Symptoms worse in premenstrual phase and during menses	(77)
Depression	Symptoms worse in premenstrual phase and during menses	(77)
Panic disorder	Symptoms worse in premenstrual phase and during menses	(77)
Eating disorders	Symptoms worse in premenstrual phase and during menses	(77)
Borderline personality disorder	Symptoms worse in premenstrual phase and during menses	(77)
Bipolar disorder	Symptoms worse in premenstrual phase, during menses, and occasionally around ovulation	(77)
Other conditions		
Asthma	Symptoms worse in premenstrual phase and during menses, with decreased lung function	(71, 78)
Irritable bowel syndrome	Pain and symptoms worse in premenstrual phase and during menses (diarrhea/loose stool) and post-ovulation (constipation)	(71, 76)

* Reference is a clinical practice guideline or review with clinical practice emphasis. See Supplementary Table S1 for a full reference list of practice guidelines and clinical reviews cited in this paper.

Irregular cycle length, variable volume and duration of bleeding, and amenorrhea indicate disturbances to the endocrine system and the hypothalamic-pituitary-ovarian (HPO) axis (42, 43). Endocrine conditions that can perturb the menstrual cycle include type 1 and 2 diabetes (44), polycystic ovarian syndrome (PCOS) (45, 46), thyroid diseases (47), primary or premature ovarian insufficiency (48, 49), and ovulatory disorders (12, 50). Documenting menstrual cycle patterns can help assess, diagnose, and treat infertility, guiding clinical testing and fertility treatment timing (14).

Approximately 27%-53% of menstruators experience heavy menstrual bleeding (HMB) (51, 52), or bleeding that affects quality of life (53). HMB can cause iron deficiency, anemia, fatigue, and hemodynamic instability (54, 55). It is often the sentinel symptom of a bleeding disorder (56, 57): studies found 29%-47% of menstruators with HMB have a bleeding disorder, most commonly von Willebrand’s disease or platelet dysfunction (58, 59). While rare, menstruators with bleeding disorders can experience hemorrhage during ovulation (60). A systematic review of hemostatic factors across the menstrual cycle found evidence for cyclic variation of platelets and von Willebrand factor, with lowest levels during menstruation and the early follicular phase (38). Anovulatory cycles from ovulation disorders such as PCOS also increase the risk of HMB, as prolonged estrogen exposure causes increased endometrial build-up and uncontrolled bleeding (61).

The menstrual cycle can indicate congenital structural/obstructive anomalies of the reproductive tract, with symptoms including amenorrhea, increasing dysmenorrhea after menarche, and pelvic or abdominal pain (cyclic and non-cyclic) from menstrual blood retention (62-64). Because structural differences are rarely externally visible, these symptoms during puberty often provide the first clue of an underlying condition (62). Other structural abnormalities causing HMB, dysmenorrhea, and intermenstrual bleeding are polyps, adenomyosis, fibroids, and neoplasms of the reproductive tract ranging from cervical dysplasia to uterine cancers (40).

Abnormal uterine bleeding like spotting and intermenstrual bleeding can signal sexually transmitted infections (40, 41). Chlamydia and gonorrhea, often asymptomatic, commonly cause

cervicitis (65). Left untreated, they can develop into pelvic inflammatory disease (66, 67), increasing the risk of infertility, ectopic pregnancy, and chronic pelvic pain (65, 68).

Shifts in menstrual cycle patterns can also signal physiologic changes such as pregnancy, the postpartum return of the ovarian cycle, lactational amenorrhea, perimenopause, and menopause (69, 70). When people are familiar with their menstrual cycle patterns, these changes can be detected earlier and better understood.

Menstrual Cycle Impacts on Health Conditions

Hormonal fluctuations across the menstrual cycle can cause cyclic changes in neurological, chronic pain, mental health, gastrointestinal, and other conditions (Table 1) (71). Migraine headaches and seizures are more common perimenstrually and around ovulation. Estrogen withdrawal is thought to contribute to migraines, as estrogen receptors are found throughout the brain, including along pain-processing and migraine pathways (72, 73). Estrogen-progesterone ratios may impact menstrual-related epilepsy, increasing perimenstrual seizures: estrogen is a proconvulsant while progesterone has an anticonvulsant effect (74, 75).

Several autoimmune diseases exhibit cyclic symptom fluctuations. Systemic lupus erythematosus may have premenstrual flare-ups (32). Multiple sclerosis symptoms also worsen premenstrually, with an increased lesion size observed in the luteal phase. These changes are hypothesized to be linked to increased luteal phase BBT, as temperature elevations can exacerbate neurological symptoms in demyelinating conditions (74). In contrast, rheumatoid arthritis symptoms typically improve during the luteal phase when estrogen and progesterone are high, with increased pain and stiffness during menses and the early follicular phase (71, 76). Chronic pain associated with fibromyalgia musculoskeletal conditions, and temporomandibular disorder also can worsen perimenstrually when estrogen, involved along pain pathways, is low (76).

Some mental health disorders can be exacerbated by the menstrual cycle. Symptoms of depression and eating, panic, borderline personality, bipolar, and psychotic disorders all may worsen during the perimenstrual phase, possibly due to some individuals’ increased sensitivity to hormone fluctuations (77). Asthma worsens perimenstrually, possibly related to declining progesterone, although the etiology remains largely unknown (71, 78). In irritable bowel syndrome, progesterone relaxes sphincters and delays gastric emptying, with constipation after ovulation when progesterone is high, and perimenstrual loose stool when levels fall (71).

Menstrual Cycle Characteristics and Long-Term Health

Menstrual cycle characteristics – especially long and irregular cycles – are associated with long-term health outcomes, including cancer, diabetes, cardiovascular disease (CVD), fracture, and premature mortality (Table 3).

Table 3. Long-term health outcomes associated with menstrual cycle characteristics.

Health outcome	Participant s, n	Menstrual cycle characteristic	Age at menstrual cycle assessment	Comparison group	Age at outcome assessment	Health outcome risk estimate (95% CI)	References
Cancer – cycle regularity							
a) Any cancer b) Obesity-related cancer ^a	78,943	Always irregular or no menses (self-report)	29-46 yr	Very regular cycles (±3 d)	Incident cases over 22 years of follow-up	a) HR=1.11 (1.02, 1.21) b) HR=1.23 (1.09, 1.39)	(79)
Ovarian cancer	15,528	Irregular cycles (self-reported, diagnosed, or cycle length >35 d)	Median 26 yr	Regular cycles	70 yr	HR=2.26 (1.20, 4.26)	(80)

Obesity-related cancer ^a	78,943	Change from regular (±7 d) to always irregular or no menses (self-report)	18-22 yr (regular), 29-46 yr (irregular)	No change in regular cycles	Incident cases over 22 years of follow-up	HR=1.36 (1.09, 1.69)	(79)
<i>Cancer – cycle length</i>							
a) Any cancer b) Obesity-related cancer ^a	78,943	Long cycles (≥40 d)	29-46 yr	26-31 d cycles	Incident cases over 22 years of follow-up	a) HR=1.22 (1.09, 1.37) b) HR=1.37 (1.17, 1.59)	(79)
<i>Diabetes – cycle regularity</i>							
Type 2 diabetes	704,743	Irregular cycles (medical record, variation >20 d over 12 months)	18-40 yr (median 27 yr)	Regular cycles (variation 2-20 d over 12 months), age-matched Regular cycles (self-report, includes never, rarely, or sometimes irregular cycles)	Incident cases over 26 yr after enrollment	HR=1.37 (1.29, 1.45)	(81)
Type 2 diabetes	13,714	Often irregular cycles (self-report)	45-50 yr (mean 48 yr)		Incident cases over 20 yr follow-up	HR=1.17 (1.00, 1.38)	(84)
Type 2 diabetes	75,546	Always irregular or no menses (self-report)	a) 14-17 yr b) 18-22 yr c) 29-46 yr	Very regular cycles (±4 d)	Incident cases over 24 yr follow-up	a) HR=1.32 (1.22, 1.44) b) HR=1.41 (1.23, 1.62) c) HR=1.66 (1.49, 1.84)	(82)
Type 2 diabetes	75,546	Change from regular (±7 d) to irregular (self-report)	a) 14-17 yr (regular), 29-46 yr (irregular) b) 18-22 yr (regular), 29-46 yr (irregular)	No change in regular cycles	Incident cases over 24 years of follow-up	a) HR=1.28 (1.14, 1.43) b) HR=1.34 (1.13, 1.60)	(82)
a) Prediabetes b) Type 1 diabetes c) Type 2 diabetes	21,213	Irregular cycles (self-reported as unpredictable)	At study enrollment, mean age 34.5 yr	Regular cycles (self-reported as predictable)	Mean age: a) 38.4 yr b) 19.1 yr c) 39.6 yr	a) POR=1.47 (1.28, 1.67) b) POR=1.13 (0.75, 1.66) c) POR=1.46 (1.18, 1.81)	(85)
a) Prediabetes b) Type 1 diabetes c) Type 2 diabetes	37,707	Prolonged time to cycle regularity (>5 yr after menarche)	Within 5 yr of menarche	Cycle regularity within 4 yr of menarche	Mean age: a) 38.4 yr b) 19.1 yr c) 39.6 yr	a) POR=1.20 (1.08, 1.32) b) POR=1.47 (1.13, 1.89) c) POR=1.24 (1.05, 1.33)	(85)
Gestational diabetes	10,906 (14,418 pregnancies)	Always irregular or no menses (self-report)	29-46 yr	Very regular cycles (±4 d)	Incident cases over 16 years of follow-up	RR=1.65 (1.21, 2.25)	(83)

Gestational diabetes	10,906 (14,418 pregnancies)	Change from regular to irregular (self-report)	18-22 yr (regular), 29-46 yr (irregular)	No change in regular cycles	Incident cases over 16 years of follow-up	RR=1.68 (0.93, 3.01)	(83)
<i>Diabetes – cycle length</i>							
Type 2 diabetes	704,743	Short (<24 d) or long (>38 d) cycles (medical record)	18-40 yr (median 27 yr)	24-38 d cycle, age-matched	Incident cases over 26 yr after enrollment	HR=1.74 (1.52, 1.98)	(81)
Type 2 Diabetes	75,546	Long cycles (≥40 d)	a) 18-22 yr b) 29-46 yr	26-31 d cycles	Incident cases over 24 yr follow-up	a) HR=1.37 (1.19, 1.57) b) HR=1.50 (1.36, 1.65)	(82)
Type 2 Diabetes	75,546	Change in cycle length from <32 d to ≥32 d	18-22 yr (<32 d), 29-46 yr (≥32 d)	<32 d maintained	Incident cases over 24 yr follow-up	HR=1.62 (1.39, 1.88)	(82)
Gestational diabetes	10,906 (14,418 pregnancies)	Long cycles (≥32 d)	29-46 yr	26-31 d cycles	Incident cases over 16 years of follow-up	RR=1.42 (1.15, 1.75)	(83)
Gestational diabetes	10,906 (14,418 pregnancies)	Change in cycle length from <32 d to ≥32 d	18-22 yr (<32 d), 29-46 yr (≥32 d)	<32 d maintained	Incident cases over 24 yr follow-up	RR=1.98 (1.24, 2.92)	(83)
<i>Cardiovascular disease – cycle regularity</i>							
CVD ^b	80,630	Always irregular or no menses (self-report)	a) 14-17 yr b) 18-22 yr c) 29-46 yr	Very regular cycles (±4 d)	Incident cases over 24 years of follow-up	a) HR=1.15 (0.99, 1.34) b) HR=1.36 (1.06, 1.75) c) HR=1.40 (1.14, 1.71)	(87)
CVD ^c	704,743	Irregular cycles (medical record, variation >20 d over 12 months)	18-40 yr (median 27 yr)	Regular cycles (variation 2-20 d over 12 months), age-matched	Incident cases over 26 yr after enrollment	a) HR=1.08 (1.00, 1.19)	(81)
CVD ^d	58,056	Irregular cycles (self-report, ≤21 d or ≥35 d)	40-69 yr (median 46 yr)	Regular cycles (22-34 d)	Incident cases over 10-14 yr follow-up	HR=1.19 (1.07, 1.31)	(86)
CVD ^e	13,714	Often irregular cycles (self-report)	45-50 yr (mean 48 yr)	Regular cycles (self-report, includes never, rarely, or sometimes irregular cycles)	Incident cases over 20 yr follow-up	HR=1.20 (1.01, 1.43)	(84)
CVD ^b	80,630	Change from regular (±7 d) to irregular (self-report)	14-17 yr (regular), 29-46 yr (irregular)	No change in regular cycles	Incident cases over 24 years of follow-up	HR=1.43 (1.11, 1.63)	(87)

a) Hypertension						a) POR=1.25 (1.12, 1.35)	
b) Arrhythmia						b) POR=1.28 (1.08, 1.51)	
c) Transient ischemic attack	21,213	Irregular cycles (self-reported as unpredictable)	At study enrollment, mean age 34.5 yr	Regular cycles (self-reported as predictable)	Mean age: a) 37.1 yr b) 32.3 yr c) 39.5 yr d) 43.5 yr	c) POR=1.63 (1.12, 2.32)	(85)
d) Heart attack						d) POR=1.68 (0.97, 2.79)	
a) Hypertension						a) POR=1.08 (1.00, 1.17)	
b) Arrhythmia						b) POR=1.25 (1.11, 1.40)	
c) Transient ischemic attack	37,707	Prolonged time to cycle regularity (>5 yr after menarche)	Within 5 yr of menarche	Cycle regularity within 4 yr of menarche	Mean age: a) 37.1 yr b) 32.3 yr c) 39.5 yr d) 40.5 yr e) 39.0	c) POR=1.37 (1.05, 1.76)	(85)
d) Stroke						d) POR=1.49 (1.11, 1.98)	
e) Congestive heart failure						e) POR=1.40 (1.00, 1.92)	

Cardiovascular disease – cycle length

CVD ^b	80,630	Long cycles (≥40 d)	a) 18-22 yr b) 29-46 yr	26-31 d cycles	Incident cases over 24 years of follow-up	a) HR=1.44 (1.13, 1.84) b) HR=1.30 (1.09, 1.57)	(87)
CVD ^c	704,743	Short (<24 d) or long (>38 d) cycles (medical record)	18-40 yr (median 27 yr)	24-38 d cycles, age-matched	Incident cases over 26 yr after enrollment	a) HR=1.24 (1.02, 1.52)	(81)
CVD ^d	58,056	a) Short cycles, ≤21 d b) Long cycles, ≥35 d (self-report)	40-69 yr (median 46 yr)	28-34 d cycles	Incident cases over 10-14 yr follow-up	a) HR=1.29 (1.11, 1.50) b) HR=1.11 (0.98, 1.56)	(86)

Fracture

Hip fracture	33,434	a) Always irregular cycles (>±5 d, self-report) b) Variable length of menses (not usually same number of d, self-report) c) Always irregular cycles and variable bleeding duration	Postmenopausal report of lifetime menstrual cycle history (study enrollment at 55-69 yr)	a) Never irregular cycles b) Length of menses not variable c) Regular cycles and regular bleeding duration	Self-reported cases over 11 years	a) RR=1.36 (1.03, 1.78) b) RR=1.40 (1.10, 1.78) c) RR=1.82 (1.55, 2.15)	(92)
Wrist fracture	832	a) Late menarche (14-18 yr) b) Long cycle length (>30.5 d) c) Long bleeding duration (>6 d)	28-32 yr	a) Menarche at 12-13 yr b) Cycle length 26.6-30.5 d	Fracture history questionnaire at mean age 73 yr	a) OR=3.29 (1.73, 6.23) b) OR=2.23 (1.02, 4.89) c) OR=1.66 (0.89, 3.13)	(93)

c) Bleeding duration 4.7-6 d						
Premature mortality						
Premature mortality (<70 yr)	79,505	Always irregular or no menses (self-report)	a) 14-17 yr b) 18-22 yr c) 29-46 yr	Very regular cycles (±4 d)	Deaths over 24 yr follow-up	a) HR=1.18 (1.02, 1.37) b) HR=1.37 (1.09, 1.73) c) HR=1.39 (1.14, 1.70) (96)
Premature mortality (<70 yr)	79,505	Long cycles (≥40 d)	a) 18-22 yr b) 29-46 yr	26-31 d cycles	Deaths over 24 yr follow-up	a) HR=1.34 (1.06, 1.69) b) HR=1.40 (1.17, 1.68) (96)

Notes: CI, confidence interval; CVD, cardiovascular disease; d, days; HR, hazard ratio; OR, odds ratio; POR, prevalence odds ratio; RR, relative risk; yr, years. a. Obesity-related cancers include colorectal, gallbladder, kidney, multiple myeloma, thyroid, pancreatic, esophageal, gastric, liver, endometrial, ovarian and postmenopausal breast cancer. b. Cardiovascular disease included fatal and nonfatal coronary heart disease, myocardial infarction, coronary revascularization, and stroke. c. Cardiovascular disease included ischemic heart disease, heart failure, and cerebrovascular disease (stroke or transient ischemic attack). d. Cardiovascular disease included coronary heart disease, myocardial infarction, heart failure, atrial fibrillation, and stroke. e. Cardiovascular disease included myocardial infarction and angina.

Prolonged estrogen and decreased progesterone exposure, as may occur with long, irregular cycles and amenorrhea, might increase the risk of cancer (79). Two prospective cohort studies (n=94,471) found that compared to participants with regular cycles, those with irregular cycles had 11% (95% CI: 2%, 21%) increased risk of any cancer, 23% (95% CI: 9%, 39%) increased risk of obesity-related cancer (79), and were more than twice as likely to develop ovarian cancer starting at age 70 (HR=2.26; 95% CI: 1.20, 4.26) (80). Menstruators with long cycles also had a 22% (95% CI: 9%, 27%) increased risk of any cancer compared to those with 26- to 31-day cycles (79).

Five cohort studies (n=842,616) examined associations between menstrual cycle characteristics and diabetes (81-84). In irregular and long cycles, FSH and LH stimulate ovarian androgen production, which increases insulin resistance and may lead to diabetes (82). Compared to participants with regular cycles, those with irregular cycles had 17%-66% increased risk of developing type 2 diabetes (81, 82, 84, 85), and were 1.5 times more likely to develop gestational diabetes (83). Menstruators whose cycles took more than 5 years to reach regularity after menarche had a 47% (95% CI: 13%, 89%) increased risk of type 1 diabetes and a 24% (95% CI: 5%, 33%) risk of type 2 diabetes compared to those whose cycles were regular within 4 years of menarche (85). Long cycles were associated with 37%-50% increased risk of type 2 diabetes (82), and 42% (95% CI: 15%, 75%) increased risk of gestational diabetes (83).

Studies within the same cohorts (n=894,850) examined associations between the menstrual cycle and CVD (81, 84-87), as cycle dysfunction can impact glucose homeostasis leading to hyperinsulinemia and elevated testosterone levels, CVD risk factors (81). Additionally, because estrogen reduces vascular inflammation, cycles with lower estrogen levels could contribute to atherosclerotic CVD (81). Compared to regular cycles, irregular cycles were associated with 8%-40% increased risk of CVD (81, 84, 86, 87), and cycle length extremes (long or short cycles) were associated with 11-44% increased risk of CVD (81, 86, 87). While conditions like PCOS could help explain associations between menstrual cycle characteristics and CVD (88), one study including information about PCOS diagnosis found that irregular cycles were associated with CVD and diabetes even among participants without PCOS (85).

Many of the same neuro-endocrine pathways regulating ovarian function also impact bone remodeling and homeostasis (89). Estrogen inhibits bone resorption, reducing bone remodeling, while progesterone stimulates bone formation (89, 90). In estrogen-deficient states – such as functional hypothalamic amenorrhea with low estrogen – bone resorption outpaces bone production,

accelerating bone loss (89, 90). Because 90% of bone mass is achieved by age 18, amenorrhea and low estrogen during adolescence can irreversibly impair bone density, increasing risks of osteoporosis and fracture (90, 91). Irregular cycles, long cycles, variable bleeding duration, and age at menarche are all associated with increased risk of postmenopausal fracture (92, 93). Reviews on lactational amenorrhea indicate that bone mineral density declines during lactation to provide calcium for the breastfeeding infant but recovers after breastfeeding is finished (94, 95), and breastfeeding duration is not associated with increased postmenopausal fracture risk (94).

Only one study (n=79,505) has examined cycle characteristics and premature mortality (<70 years) (96). Irregular and long cycles were associated with 18%-40% increased risk of death depending on the age when the cycle characteristic was observed, with higher risk for older menstruators.

Collectively, evidence indicates cycle characteristics are associated with long-term health outcomes, with the potential to inform preventive screening and behavior modifications to address long-term health risks. Notably, cycle phenotype transitions from regular to irregular or normal to longer cycles from young- to mid-adulthood were associated with increased risks of cancer, CVD, diabetes, and gestational diabetes (79, 82, 83, 87), underscoring the importance of tracking cycle characteristics over time.

Optimizing Wellness with the Menstrual Cycle

Numerous self-help books and popular press articles frame menstruation as natural, manageable, and potentially empowering: by understanding and aligning their menstrual cycles with their lifestyle, diet, and exercise, menstruators can improve their physical and emotional wellbeing (97). In this section, we review evidence for using the menstrual cycle to optimize reproductive health, exercise, and nutrition.

The primary reasons menstruators report cycle tracking include optimizing reproductive health through conceiving or avoiding pregnancy, improving body literacy, and informing conversations with healthcare providers (98). Menstrual cycle tracking application (app) use increases conception rates for pregnancy planners, particularly when combined with additional fertility indicators like BBT or cervical fluid (99, 100). Cycle tracking is also used for contraception. Only the Natural Cycles app is FDA-approved as a contraceptive device and currently available, with a 13-cycle typical use pregnancy probability of 7.2% (95% CI: 6.4%, 8.1%) (101).

Hormonal fluctuations across the menstrual cycle influence metabolism, thirst, fluid regulation, and thermoregulation, offering a plausible physiologic basis for efforts to optimize nutrition and exercise across the cycle (Table 1). Evidence suggests daily energy intake is lowest during the late follicular phase and ovulation and increases during the luteal phase (30, 102). Estrogen may promote muscle strength by increasing glycogen uptake and has antioxidant properties that could protect against exercise-induced muscle damage and inflammation (103), potentially improving follicular phase resistance training efficacy (104).

However, data are lacking to support cycle phase-specific nutritional and exercise interventions at the population level (102, 105). A meta-analysis of 78 studies found exercise performance might be slightly reduced during menses compared to other menstrual cycle phases ($ES_{0.5} = -0.06$; 95% CrI: $-0.16, 0.04$) (103). Hypotheses that high pre-ovulatory estrogen concentrations could contribute to ligament laxity and increased mid-cycle injuries are not supported by high quality research (106). Reviews on athlete nutrition concluded that simply having adequate energy intake was crucial, as inadequate intake can cause functional hypothalamic amenorrhea (105, 107).

While generalized recommendations related to menstrual cycle phase, physical exercise, and nutrition are not currently supported by scientific literature, surveys of athletes found that nearly 1/3 reported their menstrual cycle impacted training and performance (108). Accordingly, individuals can track their cycles along with training, recovery, and other symptoms to determine personal patterns, needs, and strategies (107). The lack of data supporting cycle-related nutrition and exercise interventions reflects an underrepresentation of menstruators and a lack of menstrual cycle data

collection in nutrition and exercise studies, leading to gaps in basic knowledge about the whole-body impact of menstrual cycles (30, 103, 107).

Exposures Influence the Menstrual Cycle

The menstrual cycle responds to diverse environmental exposures, lifestyle factors, and intrinsic characteristics (Table 4) – including age, air pollution, and night-shift work – that interact with neuro-endocrine pathways.

Table 4. External exposures and associated changes to the menstrual cycle.

Exposure	Associated changes to menstrual cycle	References
<i>Intrinsic characteristics</i>		
Age	↓ cycle length at age 30-40, ↑ cycle length and ↑ cycle variability at perimenopause, ↓ peak cervical fluid at age ≥35	(20, 109, 110)
Body mass index (BMI)	↑ cycle length with high BMI, ↑ cycle length variability with low BMI	(109, 111)
<i>Environmental exposures</i>		
Per- and polyfluoroalkyl substances (PFAS)	↑ cycle length, ↑ cycle irregularity	(114)
Bisphenol A (BPA)	↓ luteal phase length	(115, 116)
Butyl paraben	↓ luteal phase length	(109, 115, 116)
Select phthalates	↓ luteal phase length	(115)
Polybrominated diphenyl ethers (PBDEs)	↓ luteal phase length	(109)
Pesticides (pyrethroids, organochlorines, organophosphates)	↑ cycle length, ↑ cycle irregularity	(109)
Cadmium	↓ cycle length	(109)
Selenium	↓ cycle length	(109)
Copper	↑ cycle length	(109)
Mercury	↑ cycle irregularity	(117)
Lead	↑ cycle irregularity	(117)
Air pollution	↑ cycle irregularity, ↑ follicular phase length, ↓ luteal phase length	(109, 116)
<i>Lifestyle factors</i>		
Low vitamin D	↑ cycle length, ↑ cycle irregularity	(118-120)
Nightshift work	↑ cycle disruption (cycle length shorter or longer than usual)	(121)
Low physical activity	↑ cycle irregularity	(122)
High alcohol consumption	↑ cycle irregularity, ↓ cycle length, ↑ menstrual bleeding	(122, 123)
Smoking	↓ cycle length, ↑ menstrual bleeding	(109, 122, 123)
Caffeine	↓ cycle length, ↑ menstrual bleeding	(122)
<i>COVID-19 pandemic exposures</i>		
COVID-19 vaccination	↑ cycle length (1-2 days), ↑ long cycles (>38d), rapid return to pre-vaccination cycle length	(33, 124)
COVID-19 infection	↓ menstrual bleeding, ↑ cycle length	(125, 126)
Lockdown conditions	↑ cycle disruption (cycle length shorter or longer than usual)	(127)

General pandemic conditions	↑ cycle variability, ↑ menstrual bleeding, ↑ dysmenorrhea	(126)
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The menstrual cycle varies with intrinsic characteristics, notably age and body mass index (BMI). Cycle length decreases during a menstruator’s 30s and early 40s and increases and becomes more variable with perimenopause (109, 110). Menstruators ≥35 years old also have fewer days of peak quality cervical fluid (20). Higher BMI (30-50 kg/m²) is associated with longer cycles, especially BMI >50 kg/m², and lower BMI (<18.5 kg/m²) with increased cycle length variability (109, 111).

Endocrine-disrupting chemicals (EDCs) interfere with endocrine system function via multiple pathways. Common exposure sources include personal care products, food, water, dust, industrial chemicals, and pesticides (112, 113). Recent reviews found per- and polyfluoroalkyl substances (PFAS) were associated with longer, more irregular cycles (114), while bisphenol A (BPA), butyl paraben, select phthalates, and flame retardant polybrominated diphenyl ethers (PBDEs) were associated with a shorter luteal phase (109, 115, 116). Metals also can have endocrine-disrupting effects: cadmium and selenium are associated with decreased cycle length, copper with increased cycle length, and mercury and lead with irregular cycles (109, 117). Air pollution has been observed to increase irregular cycles and follicular phase length and decrease luteal phase length (109, 116).

Lifestyle factors also influence menstrual cycles. Low vitamin D has been associated with prolonged and irregular menstrual cycles, even in those with no history of PCOS (118-120). Vitamin D is obtained from supplements or synthesized in the skin with sunlight exposure. A meta-analysis of 8 studies (n=28,479) found night-shift work disrupted circadian rhythms, increasing the odds of cycle disruption (OR 1.15; 95% CI 1.01, 1.31) (121). Sedentary behavior and high alcohol consumption were associated with increased cycle irregularity (122), and smoking, caffeine, and high alcohol intake with shorter cycles and HMB (109, 122, 123).

Recently, studies have examined menstrual cycle responses to COVID-19-related exposures. A meta-analysis of 4 studies (n=25,054) compared cycle characteristics before and after COVID-19 vaccination; vaccinated menstruators were more likely to report temporary cycle changes (OR=1.91, 95% CI 1.76, 2.07) (124). A large cohort study (n=9,652, 128,094 cycles) found vaccination was associated with a 1-2 day increase in cycle length and an increased odds of a long cycle (>38 days), especially with the Johnson & Johnson vaccine; cycles quickly returned to pre-vaccination lengths (33). Two systematic reviews found COVID-19 infection was associated with longer cycles and a possible decrease in menstrual bleeding, but the reviewed studies were small and lacked pre-infection data for comparison (125, 126). Pandemic conditions also were associated with cycle changes: a meta-analysis of 7 studies (n=21,729) found that compared to non-lockdown times, lockdowns were associated with an increased odds of changes in menstrual cycle length (OR=9.14; 95% CI 3.16, 26.5) (127). Another review of 17 studies found that during the pandemic, menstruators reported increased menstrual irregularities, cycle variability, heavier bleeding, and dysmenorrhea, with participants reporting higher levels of anxiety, stress, and depression more likely to experience cycle changes (126).

Documenting the Menstrual Cycle as a Vital Sign

Clinicians and researchers should ask patients about their menstrual cycle at least once to identify unusual cycles or acute issues. Ideally, information should be documented over multiple cycles. While data from a single cycle can be used to address an acute issue, patterns over time offer additional insights, as with other vital signs. Clinicians and researchers should educate patients in basic menstrual cycle biology and tracking skills so they can track, observe, and identify patterns in their own cycles over time (see Supplementary Materials, educational handouts, menstrual cycle tracking chart). By tracking their cycles, menstruators have a powerful tool to understand and optimize their own health and wellness, and to access timely treatment and preventative care.

Tracking the menstrual cycle is simple and involves noting dates and intensity of vaginal bleeding. This allows determination of cycle length and bleeding duration and intensity. When multiple cycles are documented, cycle regularity and variability can also be observed. Signs such as

BBT and cervical fluid can allow retrospective identification of ovulation and calculation of follicular and luteal phase lengths. Other symptoms (mood, pain, headaches), activities (sex, travel, exercise), and information (diet, medications) can also be recorded to understand how the menstrual cycle may be impacting health conditions, and how activities might impact menstrual cycle patterns.

The menstrual cycle can be documented on calendars, special charts (see Supplementary Materials, educational handouts, menstrual cycle tracking chart), or using smartphone-based apps. Apps range from simple calendars to proprietary algorithms predicting menses onset, the fertile window, and ovulation. Many apps allow users to document symptoms and activities (128). Users report apps improve self-knowledge, health management, and information-sharing with healthcare providers (98, 129).

Despite tracking app popularity, reviews have found their algorithms for next cycle or fertile window prediction to be inaccurate, particularly for users with irregular cycles, and that 20% of reviewed apps contained incorrect clinical information (3, 130-132). Few available apps incorporate evidence-based fertility awareness methods, even though 33% are marketed for contraception and 15% for conception (132).

Data privacy is a growing concern, as many apps allow third-party access to users’ personal information (133), which can be used without consent for advertising, research, and insurance purposes, or shared with employers (134). Health apps’ data collection and privacy practices are not regulated unless they are considered medical devices (134). In the wake of the United States Supreme Court’s 2022 *Dobbs v. Jackson Women’s Health Organization* decision, which eliminated the constitutional right to abortion, some app users were concerned that information from period tracking apps could be used to prosecute illegal abortions, especially self-managed at-home abortions which are clinically indistinguishable from miscarriages. However, based on case reviews and experience, several legal experts suggest that texts, emails, and search/website histories are more likely to be used than apps as digital evidence in abortion prosecutions (135). Apps that store data locally on smartphones are more secure (135).

Development of a standardized menstrual history questionnaire could improve care and facilitate research (136). In primary care settings, menstrual histories should include an assessment of bleeding characteristics, associated symptoms, impacts on quality of life, and a comprehensive medical history (Table 5) (136). Cycle tracking could complement history-taking. In preparation for a routine health visit, patients could track their cycles for 3-6 months, with charts reviewed at the visit. Alternatively, patients could track their cycles after a visit when potential health concerns or goals have been identified and discuss in follow-up care.

Table 5. Key components of a menstrual history in a primary care setting.

Menstrual history components	Additional information
1. Bleeding characteristics	
a) Frequency of menses	Frequent, normal, infrequent, absent
b) Regularity of menstrual cycle (month-to-month)	Regular, irregular
c) Duration of bleeding	Short, normal, prolonged
d) Flow or volume of bleeding	Light, normal, heavy; for volume assessment techniques see (136)
2. Symptoms associated with menstrual cycle and bleeding	Questions to identify the symptoms most concerning to the patient, and determine etiology of bleeding or symptoms
3. How bleeding and symptoms impact quality of life	Whether work or social plans are missed because of bleeding
4. Comprehensive medical history	

Notes: Table adapted from Matteson et al., 2011 (136).

Conclusion

Documenting the menstrual cycle as well as consideration of symptoms in relation to the menstrual cycle can inform the diagnosis, assessment, and management of health conditions commonly encountered in primary and specialized care settings. However, research gaps and challenges in integrating its documentation into clinical practice remain.

While much evidence supports the menstrual cycle as a vital sign, more research is needed on its associations with long-term outcomes, external exposures, and wellness. Research suggests strong connections between cycle characteristics and long-term health outcomes, but the etiology is not well understood. Future work could explore using cycle characteristics as biomarkers of future risk, guiding preventive care strategies (137). Menstruators already use cycle self-knowledge to improve their health and wellbeing. Research comprehensively characterizing the menstrual cycle's influences on physiologic processes throughout the body (138) and high-quality studies on wellness-oriented interventions are needed.

Although apps abound, tools for cycle tracking are not integrated into clinical practice. A standardized menstrual history tool incorporating cycle tracking capabilities into electronic medical record systems and simple ways for patients to share app data with providers would facilitate menstrual cycle documentation. As a start, providers can share the tracking and educational tool included in the Supplementary Materials with their patients.

Because of its broad scope, this review has limitations. For example, discussing the impact of exposures for which there is in vivo evidence or few studies, but no systematic reviews, is beyond this paper's scope. Additionally, like other vital signs, the menstrual cycle is frequently altered. Discussion of interventions altering or suppressing the menstrual and ovarian cycles such as hormonal contraceptives, gender-affirming hormone treatment, and ovary-sparing hysterectomy is beyond the scope of this review. Given the high importance of such interventions, research focusing on, for example, post-hysterectomy ovarian function (139) and menstrual cycle responses to hormone therapy (140) is warranted.

Treating and documenting the menstrual cycle as a vital sign has the potential to transform research and clinical care, promoting menstrual health equity and, most fundamentally, improving the health and wellbeing of people who menstruate.

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References

1. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 651: Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign. *Obstet Gynecol.* 2015;126(6):e143-e6. Epub 2015/11/26. doi: 10.1097/AOG.0000000000001215. PubMed PMID: 26595586.
2. American Academy of Pediatrics. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. *Pediatrics.* 2006;118(5):2245-50. Epub 2006/11/03. doi: 10.1542/peds.2006-2481. PubMed PMID: 17079600.

3. Zwingerman R, Chaikof M, Jones C. A Critical Appraisal of Fertility and Menstrual Tracking Apps for the iPhone. *J Obstet Gynaecol Can.* 2020;42(5):583-90. Epub 2019/12/29. doi: 10.1016/j.jogc.2019.09.023. PubMed PMID: 31882289.
4. Casola AR, Lubner K, Riley AH, Medley L. Menstrual Health: Taking Action Against Period Poverty. *American Journal of Public Health.* 2022;112(3):374-7.
5. Male V. COVID-19 vaccination and menstruation. *Science.* 2022;378(6621):704-6. doi: <https://doi.org/10.1126/science.ade1051>.
6. Babbar K, Martin J, Ruiz J, Parrray AA, Sommer M. Menstrual health is a public health and human rights issue. *Lancet Public Health.* 2022;7(1):e10-e1. Epub 2021/11/01. doi: 10.1016/S2468-2667(21)00212-7. PubMed PMID: 34717798; PubMed Central PMCID: PMC8552814.
7. Hennegan J, Winkler IT, Bobel C, Keiser D, Hampton J, Larsson G, et al. Menstrual health: a definition for policy, practice, and research. *Sex Reprod Health Matters.* 2021;29(1):1911618. Epub 2021/04/30. doi: 10.1080/26410397.2021.1911618. PubMed PMID: 33910492; PubMed Central PMCID: PMC8098749.
8. Chrisler JC, Gorman JA, Manion J, Murgo M, Barney A, Adams-Clark A, et al. Queer periods: attitudes toward and experiences with menstruation in the masculine of centre and transgender community. *Cult Health Sex.* 2016;18(11):1238-50. Epub 2016/05/24. doi: 10.1080/13691058.2016.1182645. PubMed PMID: 27212580.
9. Kellett J. The Assessment and Interpretation of Vital Signs. *Textbook of Rapid Response Systems* 2017. p. 63-85.
10. Brekke IJ, Puntervoll LH, Pedersen PB, Kellett J, Brabrand M. The value of vital sign trends in predicting and monitoring clinical deterioration: A systematic review. *PLoS One.* 2019;14(1):e0210875. Epub 2019/01/16. doi: 10.1371/journal.pone.0210875.
11. Kellett J, Sebat F. Make vital signs great again - A call for action. *Eur J Intern Med.* 2017;45:13-9. Epub 2017/09/25. doi: 10.1016/j.ejim.2017.09.018. PubMed PMID: 28941841.
12. Munro MG, Balen AH, Cho S, Critchley HOD, Diaz I, Ferriani R, et al. The FIGO ovulatory disorders classification system. *Int J Gynaecol Obstet.* 2022;159(1):1-20. Epub 2022/08/20. doi: 10.1002/ijgo.14331. PubMed PMID: 35983674.
13. Blackburn ST. *Maternal, Fetal, and Neonatal Physiology: A Clinical Perspective.* 3 ed. Philadelphia, PA: Saunders Elsevier; 2007.
14. Duane M, Stanford JB, Porucznik CA, Vigil P. Fertility Awareness-Based Methods for Women's Health and Family Planning. *Front Med (Lausanne).* 2022;9:858977. Epub 2022/06/11. doi: 10.3389/fmed.2022.858977. PubMed PMID: 35685421; PubMed Central PMCID: PMC9171018.
15. Simmons RG, Jennings V. Fertility awareness-based methods of family planning. *Best Pract Res Clin Obstet Gynaecol.* 2020;66:68-82. Epub 2020/03/15. doi: 10.1016/j.bpobgyn.2019.12.003. PubMed PMID: 32169418.
16. Pyper CM. Fertility awareness and natural family planning. *Eur J Contracept Reprod Health Care.* 1997;2(2):131-46. Epub 1997/06/01. doi: 10.3109/13625189709167468. PubMed PMID: 9678103.
17. Han L, Taub R, Jensen JT. Cervical mucus and contraception: what we know and what we don't. *Contraception.* 2017;96(5):310-21. Epub 2017/08/13. doi: 10.1016/j.contraception.2017.07.168. PubMed PMID: 28801053.
18. Ecochard R, Boehringer H, Rabilloud M, Marret H. Chronological aspects of ultrasonic, hormonal, and other indirect indices of ovulation. *British Journal of Obstetrics and Gynaecology.* 2001;108(August):822-9.
19. Ecochard R, Duterque O, Leiva R, Bouchard T, Vigil P. Self-identification of the clinical fertile window and the ovulation period. *Fertil Steril.* 2015;103(5):1319-25 e3. Epub 2015/03/01. doi: 10.1016/j.fertnstert.2015.01.031. PubMed PMID: 25724738.
20. Najmabadi S, Schliep KC, Simonsen SE, Porucznik CA, Egger MJ, Stanford JB. Cervical mucus patterns and the fertile window in women without known subfertility: a pooled analysis of three cohorts. *Hum Reprod.* 2021;36(7):1784-95. Epub 2021/05/16. doi: 10.1093/humrep/deab049. PubMed PMID: 33990841; PubMed Central PMCID: PMC8487651.
21. Baker FC, Siboza F, Fuller A. Temperature regulation in women: Effects of the menstrual cycle. *Temperature (Austin).* 2020;7(3):226-62. Epub 2020/10/31. doi: 10.1080/23328940.2020.1735927. PubMed PMID: 33123618; PubMed Central PMCID: PMC7575238.
22. Charkoudian N, Hart ECJ, Barnes JN, Joyner MJ. Autonomic control of body temperature and blood pressure: influences of female sex hormones. *Clin Auton Res.* 2017;27(3):149-55. Epub 20170509. doi: 10.1007/s10286-017-0420-z. PubMed PMID: 28488202.
23. Charkoudian N, Stachenfeld N. Sex hormone effects on autonomic mechanisms of thermoregulation in humans. *Auton Neurosci.* 2016;196:75-80. Epub 20151130. doi: 10.1016/j.autneu.2015.11.004. PubMed PMID: 26674572.
24. Lutsenko OI, Kovalenko SO. Blood pressure and hemodynamics: Mayer waves in different phases of ovarian and menstrual cycle in women. *Physiol Res.* 2017;66(2):235-40. Epub 2016/12/17. doi: 10.33549/physiolres.933313. PubMed PMID: 27982674.

25. Pierson E, Althoff T, Thomas D, Hillard P, Leskovec J. Daily, weekly, seasonal and menstrual cycles in women's mood, behaviour and vital signs. *Nat Hum Behav.* 2021;5(6):716-25. Epub 2021/02/03. doi: 10.1038/s41562-020-01046-9. PubMed PMID: 33526880.
26. Tenan MS, Brothers RM, Tweedell AJ, Hackney AC, Griffin L. Changes in resting heart rate variability across the menstrual cycle. *Psychophysiology.* 2014;51(10):996-1004. Epub 2014/06/20. doi: 10.1111/psyp.12250. PubMed PMID: 24942292.
27. Greenfield AM, Charkoudian N, Alba BK. Influences of ovarian hormones on physiological responses to cold in women. *Temperature (Austin).* 2022;9(1):23-45. Epub 20210914. doi: 10.1080/23328940.2021.1953688. PubMed PMID: 35655670; PubMed Central PMCID: PMC9154773.
28. Giersch GEW, Charkoudian N, Stearns RL, Casa DJ. Fluid Balance and Hydration Considerations for Women: Review and Future Directions. *Sports Med.* 2020;50(2):253-61. doi: 10.1007/s40279-019-01206-6. PubMed PMID: 31641955.
29. Rodriguez-Giustiniani P, Rodriguez-Sanchez N, Galloway SDR. Fluid and electrolyte balance considerations for female athletes. *Eur J Sport Sci.* 2022;22(5):697-708. Epub 20210617. doi: 10.1080/17461391.2021.1939428. PubMed PMID: 34121620.
30. Rogan MM, Black KE. Dietary energy intake across the menstrual cycle: a narrative review. *Nutr Rev.* 2023;81(7):869-86. doi: 10.1093/nutrit/nuac094. PubMed PMID: 36367830; PubMed Central PMCID: PMC10251302.
31. Alvergne A, Hogqvist Tabor V. Is Female Health Cyclical? Evolutionary Perspectives on Menstruation. *Trends Ecol Evol.* 2018;33(6):399-414. Epub 20180516. doi: 10.1016/j.tree.2018.03.006. PubMed PMID: 29778270.
32. Oertelt-Prigione S. Immunology and the menstrual cycle. *Autoimmun Rev.* 2012;11(6-7):A486-92. Epub 20111203. doi: 10.1016/j.autrev.2011.11.023. PubMed PMID: 22155200.
33. Gibson EA, Li H, Fruh V, Gabra M, Asokan G, Jukic AMZ, et al. Covid-19 vaccination and menstrual cycle length in the Apple Women's Health Study. *NPJ Digit Med.* 2022;5(1):165. Epub 20221102. doi: 10.1038/s41746-022-00711-9. PubMed PMID: 36323769; PubMed Central PMCID: PMC9628464.
34. Baker FC, Driver HS. Circadian rhythms, sleep, and the menstrual cycle. *Sleep Med.* 2007;8(6):613-22. Epub 2007/03/27. doi: 10.1016/j.sleep.2006.09.011. PubMed PMID: 17383933.
35. Baker FC, Lee KA. Menstrual Cycle Effects on Sleep. *Sleep Med Clin.* 2018;13(3):283-94. Epub 2018/08/14. doi: 10.1016/j.jsmc.2018.04.002. PubMed PMID: 30098748.
36. Alvord VM, Kantra EJ, Pendergast JS. Estrogens and the circadian system. *Semin Cell Dev Biol.* 2022;126:56-65. Epub 20210509. doi: 10.1016/j.semcdb.2021.04.010. PubMed PMID: 33975754; PubMed Central PMCID: PMC8573061.
37. Miller BH, Takahashi JS. Central circadian control of female reproductive function. *Front Endocrinol (Lausanne).* 2013;4:195. Epub 20140122. doi: 10.3389/fendo.2013.00195. PubMed PMID: 24478756; PubMed Central PMCID: PMC3898595.
38. Knol HM, Kemperman RF, Kluin-Nelemans HC, Mulder AB, Meijer K. Haemostatic variables during normal menstrual cycle. A systematic review. *Thromb Haemost.* 2012;107(1):22-9. Epub 2011/12/14. doi: 10.1160/TH11-07-0481. PubMed PMID: 22159564.
39. Holdcroft AM, Ireland DJ, Payne MS. The Vaginal Microbiome in Health and Disease-What Role Do Common Intimate Hygiene Practices Play? *Microorganisms.* 2023;11(2). Epub 20230123. doi: 10.3390/microorganisms11020298. PubMed PMID: 36838262; PubMed Central PMCID: PMC9959050.
40. Munro MG, Critchley HOD, Fraser IS, Committee FMD. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet.* 2018;143(3):393-408. Epub 2018/09/11. doi: 10.1002/ijgo.12666. PubMed PMID: 30198563.
41. Singh S, Best C, Dunn S, Leyland N, Wolfman WL. No. 292-Abnormal Uterine Bleeding in Pre-Menopausal Women. *J Obstet Gynaecol Can.* 2018;40(5):e391-e415. Epub 2018/05/08. doi: 10.1016/j.jogc.2018.03.007. PubMed PMID: 29731212.
42. Saei Ghare Naz M, Rostami Dovom M, Ramezani Tehrani F. The Menstrual Disturbances in Endocrine Disorders: A Narrative Review. *Int J Endocrinol Metab.* 2020;18(4):e106694. Epub 2021/02/23. doi: 10.5812/ijem.106694. PubMed PMID: 33613678; PubMed Central PMCID: PMC7887462.
43. Shufelt CL, Torbati T, Dutra E. Hypothalamic Amenorrhea and the Long-Term Health Consequences. *Semin Reprod Med.* 2017;35(3):256-62. Epub 2017/06/29. doi: 10.1055/s-0037-1603581. PubMed PMID: 28658709; PubMed Central PMCID: PMC6374026.
44. Thong EP, Codner E, Laven JSE, Teede H. Diabetes: a metabolic and reproductive disorder in women. *Lancet Diabetes Endocrinol.* 2020;8(2):134-49. Epub 2019/10/23. doi: 10.1016/S2213-8587(19)30345-6. PubMed PMID: 31635966.
45. Walker K, Decherney AH, Saunders R. Menstrual Dysfunction in PCOS. *Clinical Obstetrics and Gynecology.* 2021;64(1):119-25.

46. Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Eur J Endocrinol.* 2023;189(2):G43-G64. doi: 10.1093/ajendo/lvad096. PubMed PMID: 37580861.
47. Krassas GE, Markou KB. The impact of thyroid diseases starting from birth on reproductive function. *Hormones (Athens).* 2019;18(4):365-81. Epub 2019/11/18. doi: 10.1007/s42000-019-00156-y. PubMed PMID: 31734887.
48. Li M, Zhu Y, Wei J, Chen L, Chen S, Lai D. The global prevalence of premature ovarian insufficiency: a systematic review and meta-analysis. *Climacteric.* 2023;26(2):95-102. Epub 2022/12/16. doi: 10.1080/13697137.2022.2153033. PubMed PMID: 36519275.
49. Stuenkel CA, Gompel A. Primary Ovarian Insufficiency. *N Engl J Med.* 2023;388(2):154-63. Epub 2023/01/12. doi: 10.1056/NEJMcp2116488. PubMed PMID: 36630623.
50. American College of Obstetricians and Gynecologists. Practice Bulletin No. 136: Management of abnormal uterine bleeding associated with ovulatory dysfunction. *Obstet Gynecol.* 2013;122:176-85.
51. Fraser IS, Mansour D, Breyman C, Hoffman C, Mezzacasa A, Petraglia F. Prevalence of heavy menstrual bleeding and experiences of affected women in a European patient survey. *Int J Gynaecol Obstet.* 2015;128(3):196-200. Epub 2015/01/30. doi: 10.1016/j.ijgo.2014.09.027. PubMed PMID: 25627706.
52. Schoep ME, Nieboer TE, van der Zanden M, Braat DDM, Nap AW. The impact of menstrual symptoms on everyday life: a survey among 42,879 women. *Am J Obstet Gynecol.* 2019;220(6):569 e1- e7. Epub 2019/03/20. doi: 10.1016/j.ajog.2019.02.048. PubMed PMID: 30885768.
53. Baldwin MK, Ahmadzia HK, Bartlett DL, Bensen-Kennedy D, Desai V, Haley KM, et al. Building the foundation for a community-generated national research blueprint for inherited bleeding disorders: research to advance the health of people with inherited bleeding disorders with the potential to menstruate. *Expert Rev Hematol.* 2023;16(sup1):71-86. Epub 2023/03/16. doi: 10.1080/17474086.2023.2175660. PubMed PMID: 36920864; PubMed Central PMCID: PMC10020871.
54. Borzutzky C, Jaffray J. Diagnosis and Management of Heavy Menstrual Bleeding and Bleeding Disorders in Adolescents. *JAMA Pediatr.* 2020;174(2):186-94. Epub 2019/12/31. doi: 10.1001/jamapediatrics.2019.5040. PubMed PMID: 31886837.
55. Munro MG, Mast AE, Powers JM, Kouides PA, O'Brien SH, Richards T, et al. The relationship between heavy menstrual bleeding, iron deficiency, and iron deficiency anemia. *Am J Obstet Gynecol.* 2023. Epub 2023/01/28. doi: 10.1016/j.ajog.2023.01.017. PubMed PMID: 36706856.
56. Curry N, Bowles L, Clark TJ, Lowe G, Mainwaring J, Mangles S, et al. Gynaecological management of women with inherited bleeding disorders. A UK Haemophilia Centres Doctors' Organisation Guideline. *Haemophilia.* 2022;28(6):917-37. Epub 2022/08/18. doi: 10.1111/hae.14643. PubMed PMID: 35976756.
57. Adeyemi-Fowode O, Simms-Cendan J, Comm Adolescent Hlth C. Screening and Management of Bleeding Disorders in Adolescents With Heavy Menstrual Bleeding. *Obstet Gynecol.* 2019;134(3):E71-E83. doi: 10.1097/aog.0000000000003411. PubMed PMID: WOS:000512783100002.
58. Knol HM, Mulder AB, Bogchelman DH, Kluin-Nelemans HC, van der Zee AG, Meijer K. The prevalence of underlying bleeding disorders in patients with heavy menstrual bleeding with and without gynecologic abnormalities. *Am J Obstet Gynecol.* 2013;209(3):202 e1-7. Epub 2013/06/04. doi: 10.1016/j.ajog.2013.05.059. PubMed PMID: 23727521.
59. Philipp CS, Faiz A, Dowling N, Dilley A, Michaels LA, Ayers C, et al. Age and the prevalence of bleeding disorders in women with menorrhagia. *Obstet Gynecol.* 2005;105(1):61-6. Epub 2004/12/31. doi: 10.1097/01.AOG.0000148889.15061.fb. PubMed PMID: 15625143.
60. van Galen K, Lavin M, Skouw-Rasmussen N, Fischer K, Noone D, Pollard D, et al. European principles of care for women and girls with inherited bleeding disorders. *Haemophilia.* 2021;27(5):837-47. doi: 10.1111/hae.14379. PubMed PMID: WOS:000680555200001.
61. Luiro K, Holopainen E. Heavy Menstrual Bleeding in Adolescent: Normal or a Sign of an Underlying Disease? *Semin Reprod Med.* 2022;40(01/02):23-31. doi: 10.1055/s-0041-1739309. PubMed PMID: WOS:000714203100001.
62. Dietrich JE, Millar DM, Quint EH. Obstructive reproductive tract anomalies. *J Pediatr Adolesc Gynecol.* 2014;27(6):396-402. Epub 2014/12/03. doi: 10.1016/j.jpjag.2014.09.001. PubMed PMID: 25438708.
63. Patel V, Gomez-Lobo V. Obstructive anomalies of the gynecologic tract. *Curr Opin Obstet Gynecol.* 2016;28(5):339-44. Epub 2016/07/28. doi: 10.1097/GCO.0000000000000300. PubMed PMID: 27454849.
64. American College of Obstetricians and Gynecologists. Committee Opinion No. 779: Management of Acute Obstructive Uterovaginal Anomalies. *Obstet Gynecol.* 2019;133:e363-71.
65. Shroff S. Infectious Vaginitis, Cervicitis, and Pelvic Inflammatory Disease. *Med Clin North Am.* 2023;107(2):299-315. Epub 2022/12/26. doi: 10.1016/j.mcna.2022.10.009. PubMed PMID: 36759099.
66. Price MJ, Ades AE, De Angelis D, Welton NJ, Macleod J, Soldan K, et al. Risk of pelvic inflammatory disease following Chlamydia trachomatis infection: analysis of prospective studies with a multistate model. *Am J Epidemiol.* 2013;178(3):484-92. Epub 2013/06/27. doi: 10.1093/aje/kws583. PubMed PMID: 23813703; PubMed Central PMCID: PMC3727337.

67. Reekie J, Donovan B, Guy R, Hocking JS, Kaldor JM, Mak DB, et al. Risk of Pelvic Inflammatory Disease in Relation to Chlamydia and Gonorrhea Testing, Repeat Testing, and Positivity: A Population-Based Cohort Study. *Clin Infect Dis*. 2018;66(3):437-43. doi: 10.1093/cid/cix769. PubMed PMID: 29136127.
68. Curry A, Williams T, Penny ML. Pelvic Inflammatory Disease: Diagnosis, Management, and Prevention. *American Family Physician*. 2019;100(6):357-64.
69. Brown JB. Types of ovarian activity in women and their significance: the continuum (a reinterpretation of early findings). *Hum Reprod Update*. 2011;17(2):141-58. Epub 20101005. doi: 10.1093/humupd/dmq040. PubMed PMID: 20923873; PubMed Central PMCID: PMC3039221.
70. Adams Hillard PJ. Menstruation in adolescents: what do we know? And what do we do with the information? *J Pediatr Adolesc Gynecol*. 2014;27(6):309-19. Epub 2014/12/03. doi: 10.1016/j.jpap.2013.12.001. PubMed PMID: 25438706.
71. Case AM, Reid RL. Effects of the Menstrual Cycle on Medical Disorders. *Archives of Internal Medicine*. 1998;158.
72. Nappi RE, Tiranini L, Sacco S, De Matteis E, De Icco R, Tassorelli C. Role of Estrogens in Menstrual Migraine. *Cells*. 2022;11(8). Epub 20220415. doi: 10.3390/cells11081355. PubMed PMID: 35456034; PubMed Central PMCID: PMC9025552.
73. Cupini LM, Corbelli I, Sarchelli P. Menstrual migraine: what it is and does it matter? *J Neurol*. 2021;268(7):2355-63. Epub 20200128. doi: 10.1007/s00415-020-09726-2. PubMed PMID: 31989282.
74. Roeder HJ, Leira EC. Effects of the Menstrual Cycle on Neurological Disorders. *Curr Neurol Neurosci Rep*. 2021;21(7):34. Epub 2021/05/11. doi: 10.1007/s11910-021-01115-0. PubMed PMID: 33970361.
75. Maguire MJ, Nevitt SJ. Treatments for seizures in catamenial (menstrual-related) epilepsy. *Cochrane Database Syst Rev*. 2021;9(9):Cd013225. Epub 20210916. doi: 10.1002/14651858.CD013225.pub3. PubMed PMID: 34528245; PubMed Central PMCID: PMC8444032.
76. Hassan S, Muere A, Einstein G. Ovarian hormones and chronic pain: A comprehensive review. *Pain*. 2014;155(12):2448-60. Epub 20140827. doi: 10.1016/j.pain.2014.08.027. PubMed PMID: 25172822.
77. Nolan LN, Hughes L. Premenstrual exacerbation of mental health disorders: a systematic review of prospective studies. *Arch Womens Ment Health*. 2022;25(5):831-52. Epub 20220722. doi: 10.1007/s00737-022-01246-4. PubMed PMID: 35867164.
78. Sanchez-Ramos JL, Pereira-Vega AR, Alvarado-Gomez F, Maldonado-Perez JA, Svanes C, Gomez-Real F. Risk factors for premenstrual asthma: a systematic review and meta-analysis. *Expert Rev Respir Med*. 2017;11(1):57-72. Epub 2016/12/10. doi: 10.1080/17476348.2017.1270762. PubMed PMID: 27935742.
79. Wang S, Wang YX, Sandoval-Insausti H, Farland LV, Shifren JL, Zhang D, et al. Menstrual cycle characteristics and incident cancer: a prospective cohort study. *Hum Reprod*. 2022;37(2):341-51. Epub 2021/12/12. doi: 10.1093/humrep/deab251. PubMed PMID: 34893843; PubMed Central PMCID: PMC8804333.
80. Cirillo PM, Wang ET, Cedars MI, Chen LM, Cohn BA. Irregular menses predicts ovarian cancer: Prospective evidence from the Child Health and Development Studies. *Int J Cancer*. 2016;139(5):1009-17. Epub 20160429. doi: 10.1002/ijc.30144. PubMed PMID: 27082375; PubMed Central PMCID: PMC6917033.
81. Okoth K, Smith WP, Thomas GN, Nirantharakumar K, Adderley NJ. The association between menstrual cycle characteristics and cardiometabolic outcomes in later life: a retrospective matched cohort study of 704,743 women from the UK. *BMC Med*. 2023;21(1):104. Epub 2023/03/22. doi: 10.1186/s12916-023-02794-x. PubMed PMID: 36941638; PubMed Central PMCID: PMC10029324.
82. Wang YX, Shan Z, Arvizu M, Pan A, Manson JE, Missmer SA, et al. Associations of Menstrual Cycle Characteristics Across the Reproductive Life Span and Lifestyle Factors With Risk of Type 2 Diabetes. *JAMA Netw Open*. 2020;3(12):e2027928. Epub 2020/12/22. doi: 10.1001/jamanetworkopen.2020.27928. PubMed PMID: 33346844.
83. Wang YX, Wang S, Mitsunami M, Manson JE, Rich-Edwards JW, Wang L, et al. Pre-pregnancy menstrual cycle regularity and length and the risk of gestational diabetes mellitus: prospective cohort study. *Diabetologia*. 2021;64(11):2415-24. Epub 2021/08/15. doi: 10.1007/s00125-021-05531-2. PubMed PMID: 34390365; PubMed Central PMCID: PMC8679096.
84. Kiconco S, Teede HJ, Earnest A, Loxton D, Joham AE. Menstrual cycle regularity as a predictor for heart disease and diabetes: Findings from a large population-based longitudinal cohort study. *Clin Endocrinol (Oxf)*. 2022;96(4):605-16. Epub 20211124. doi: 10.1111/cen.14640. PubMed PMID: 34817084.
85. Wang Z, Jukic AMZ, Baird DD, Wilcox AJ, Li H, Curry CL, et al. Irregular Cycles, Ovulatory Disorders, and Cardiometabolic Conditions in a US-Based Digital Cohort. *JAMA Netw Open*. 2024;7(5):e249657. Epub 20240501. doi: 10.1001/jamanetworkopen.2024.9657. PubMed PMID: 38700861; PubMed Central PMCID: PMC11069087.
86. Huang C, Lin B, Yuan Y, Li K, Xu B, Zhang P, et al. Associations of Menstrual Cycle Regularity and Length With Cardiovascular Diseases: A Prospective Study From UK Biobank. *J Am Heart Assoc*. 2023:e029020. Epub 20230524. doi: 10.1161/jaha.122.029020. PubMed PMID: 37222132.

87. Wang YX, Stuart JJ, Rich-Edwards JW, Missmer SA, Rexrode KM, Farland LV, et al. Menstrual Cycle Regularity and Length Across the Reproductive Lifespan and Risk of Cardiovascular Disease. *JAMA Netw Open*. 2022;5(10):e2238513. Epub 2022/10/26. doi: 10.1001/jamanetworkopen.2022.38513. PubMed PMID: 36282498.
88. Royal College of Obstetricians and Gynaecologists. Long-term Consequences of Polycystic Ovary Syndrome: Green-top Guideline No. 33. 2014.
89. Kalyan S, Prior JC. Bone changes and fracture related to menstrual cycles and ovulation. *Crit Rev Eukaryot Gene Expr*. 2010;20(3):213-33. doi: 10.1615/critreveukargeneexpr.v20.i3.30. PubMed PMID: 21175412.
90. Behary P, Comninou AN. Bone Perspectives in Functional Hypothalamic Amenorrhoea: An Update and Future Avenues. *Front Endocrinol (Lausanne)*. 2022;13:923791. Epub 20220620. doi: 10.3389/fendo.2022.923791. PubMed PMID: 35795153; PubMed Central PMCID: PMC9251506.
91. Indirli R, Lanzi V, Mantovani G, Arosio M, Ferrante E. Bone health in functional hypothalamic amenorrhea: What the endocrinologist needs to know. *Front Endocrinol (Lausanne)*. 2022;13:946695. Epub 20221011. doi: 10.3389/fendo.2022.946695. PubMed PMID: 36303862; PubMed Central PMCID: PMC9592968.
92. Nicodemus KK, Folsom AR, Anderson KE. Menstrual History and Risk of Hip Fractures in Postmenopausal Women The Iowa Women's Health Study. *American Journal of Epidemiology*. 2001;153(3):251-5. doi: 10.1093/aje/153.3.251.
93. Cooper GS, Sandler DP. Long-term effects of reproductive-age menstrual cycle patterns on peri- and postmenopausal fracture risk. *Am J Epidemiol*. 1997;145(9):804-9. doi: 10.1093/oxfordjournals.aje.a009173. PubMed PMID: 9143210.
94. Calik-Ksepka A, Stradczuk M, Czarnecka K, Grymowicz M, Smolarczyk R. Lactational Amenorrhea: Neuroendocrine Pathways Controlling Fertility and Bone Turnover. *Int J Mol Sci*. 2022;23(3). Epub 20220131. doi: 10.3390/ijms23031633. PubMed PMID: 35163554; PubMed Central PMCID: PMC8835773.
95. Chowdhury R, Sinha B, Sankar MJ, Taneja S, Bhandari N, Rollins N, et al. Breastfeeding and maternal health outcomes: a systematic review and meta-analysis. *Acta Paediatr*. 2015;104(467):96-113. Epub 2015/07/15. doi: 10.1111/apa.13102. PubMed PMID: 26172878; PubMed Central PMCID: PMC4670483.
96. Wang YX, Arvizu M, Rich-Edwards JW, Stuart JJ, Manson JE, Missmer SA, et al. Menstrual cycle regularity and length across the reproductive lifespan and risk of premature mortality: prospective cohort study. *BMJ*. 2020;371:m3464. Epub 2020/10/02. doi: 10.1136/bmj.m3464. PubMed PMID: 32998909; PubMed Central PMCID: PMC7526082.
97. Koskenniemi A. Taking Charge of the Menstrual Cycle: Discourses of Menstruation and the Menstruating Body in Self-Help Literature. *Women's Reproductive Health*. 2022;1-18. doi: 10.1080/23293691.2022.2085532.
98. Earle S, Marston HR, Hadley R, Banks D. Use of menstruation and fertility app trackers: a scoping review of the evidence. *BMJ Sex Reprod Health*. 2021;47(2):90-101. Epub 2020/04/08. doi: 10.1136/bmj.srh-2019-200488. PubMed PMID: 32253280.
99. Stanford JB, Willis SK, Hatch EE, Rothman KJ, Wise LA. Fecundability in relation to use of mobile computing apps to track the menstrual cycle. *Hum Reprod*. 2020;35(10):2245-52. doi: 10.1093/humrep/deaa176. PubMed PMID: 32910202; PubMed Central PMCID: PMC7518709.
100. Favaro C, Pearson JT, Rowland SP, Jukic AM, Chelstowska M, Berglund Scherwitzl E, et al. Time to Pregnancy for Women Using a Fertility Awareness Based Mobile Application to Plan a Pregnancy. *J Womens Health (Larchmt)*. 2021;30(11):1538-45. Epub 20210908. doi: 10.1089/jwh.2021.0026. PubMed PMID: 34495761; PubMed Central PMCID: PMC8917888.
101. Pearson JT, Chelstowska M, Rowland SP, Benhar E, Kopp-Kallner H, Berglund Scherwitzl E, et al. Contraceptive Effectiveness of an FDA-Cleared Birth Control App: Results from the Natural Cycles U.S. Cohort. *J Womens Health (Larchmt)*. 2021;30(6):782-8. Epub 20201223. doi: 10.1089/jwh.2020.8547. PubMed PMID: 33370220.
102. Wohlgemuth KJ, Arieta LR, Brewer GJ, Hoselton AL, Gould LM, Smith-Ryan AE. Sex differences and considerations for female specific nutritional strategies: a narrative review. *J Int Soc Sports Nutr*. 2021;18(1):27. Epub 20210401. doi: 10.1186/s12970-021-00422-8. PubMed PMID: 33794937; PubMed Central PMCID: PMC8015182.
103. McNulty KL, Elliott-Sale KJ, Dolan E, Swinton PA, Ansdell P, Goodall S, et al. The Effects of Menstrual Cycle Phase on Exercise Performance in Eumenorrhoeic Women: A Systematic Review and Meta-Analysis. *Sports Med*. 2020;50(10):1813-27. doi: 10.1007/s40279-020-01319-3. PubMed PMID: 32661839; PubMed Central PMCID: PMC7497427.
104. Kissow J, Jacobsen KJ, Gunnarsson TP, Jessen S, Hostrup M. Effects of Follicular and Luteal Phase-Based Menstrual Cycle Resistance Training on Muscle Strength and Mass. *Sports Med*. 2022;52(12):2813-9. Epub 2022/04/27. doi: 10.1007/s40279-022-01679-y. PubMed PMID: 35471634.
105. Holtzman B, Ackerman KE. Recommendations and Nutritional Considerations for Female Athletes: Health and Performance. *Sports Med*. 2021;51(Suppl 1):43-57. Epub 20210913. doi: 10.1007/s40279-021-01508-8. PubMed PMID: 34515972; PubMed Central PMCID: PMC8566643.

106. Randell RK, Clifford T, Drust B, Moss SL, Unnithan VB, De Ste Croix MBA, et al. Physiological Characteristics of Female Soccer Players and Health and Performance Considerations: A Narrative Review. *Sports Med.* 2021;51(7):1377-99. Epub 20210412. doi: 10.1007/s40279-021-01458-1. PubMed PMID: 33844195; PubMed Central PMCID: PMC8222040.
107. Sims ST, Kerksick CM, Smith-Ryan AE, Janse de Jonge XAK, Hirsch KR, Arent SM, et al. International society of sports nutrition position stand: nutritional concerns of the female athlete. *J Int Soc Sports Nutr.* 2023;20(1):2204066. doi: 10.1080/15502783.2023.2204066. PubMed PMID: 37221858; PubMed Central PMCID: PMC10210857.
108. Bruinvels G, Burden R, Brown N, Richards T, Pedlar C. The Prevalence and Impact of Heavy Menstrual Bleeding (Menorrhagia) in Elite and Non-Elite Athletes. *PLoS One.* 2016;11(2):e0149881. Epub 20160222. doi: 10.1371/journal.pone.0149881. PubMed PMID: 26901873; PubMed Central PMCID: PMC4763330.
109. Campbell LR, Scalise AL, DiBenedictis BT, Mahalingaiah S. Menstrual cycle length and modern living: a review. *Curr Opin Endocrinol Diabetes Obes.* 2021;28(6):566-73. Epub 2021/09/22. doi: 10.1097/MED.0000000000000681. PubMed PMID: 34545843; PubMed Central PMCID: PMC8631146.
110. Tatsumi T, Sampei M, Saito K, Honda Y, Okazaki Y, Arata N, et al. Age-Dependent and Seasonal Changes in Menstrual Cycle Length and Body Temperature Based on Big Data. *Obstet Gynecol.* 2020;136(4):666-74. Epub 2020/09/15. doi: 10.1097/AOG.0000000000003910. PubMed PMID: 32925608; PubMed Central PMCID: PMC7505142.
111. Grieger JA, Norman RJ. Menstrual Cycle Length and Patterns in a Global Cohort of Women Using a Mobile Phone App: Retrospective Cohort Study. *J Med Internet Res.* 2020;22(6):e17109. Epub 2020/05/23. doi: 10.2196/17109. PubMed PMID: 32442161; PubMed Central PMCID: PMC7381001.
112. Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, et al. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. *Endocr Rev.* 2015;36(6):E1-E150. Epub 20151106. doi: 10.1210/er.2015-1010. PubMed PMID: 26544531; PubMed Central PMCID: PMC4702494.
113. Giudice LC. Environmental impact on reproductive health and risk mitigating strategies. *Curr Opin Obstet Gynecol.* 2021;33(4):343-9. doi: 10.1097/GCO.0000000000000722. PubMed PMID: 34039883.
114. Rickard BP, Rizvi I, Fenton SE. Per- and poly-fluoroalkyl substances (PFAS) and female reproductive outcomes: PFAS elimination, endocrine-mediated effects, and disease. *Toxicology.* 2022;465:153031. Epub 2021/11/15. doi: 10.1016/j.tox.2021.153031. PubMed PMID: 34774661; PubMed Central PMCID: PMC8743032.
115. Cho YJ, Yun JH, Kim SJ, Kwon HY. Nonpersistent endocrine disrupting chemicals and reproductive health of women. *Obstet Gynecol Sci.* 2020;63(1):1-12. Epub 20191226. doi: 10.5468/ogs.2020.63.1.1. PubMed PMID: 31970122; PubMed Central PMCID: PMC6962585.
116. Hammer KC, Veiga A, Mahalingaiah S. Environmental toxicant exposure and menstrual cycle length. *Curr Opin Endocrinol Diabetes Obes.* 2020;27(6):373-9. Epub 2020/10/08. doi: 10.1097/MED.0000000000000579. PubMed PMID: 33027071; PubMed Central PMCID: PMC7647430.
117. Dutta S, Gorain B, Choudhury H, Roychoudhury S, Sengupta P. Environmental and occupational exposure of metals and female reproductive health. *Environ Sci Pollut Res Int.* 2022;29(41):62067-92. Epub 2021/09/25. doi: 10.1007/s11356-021-16581-9. PubMed PMID: 34558053.
118. Jukic AM, Steiner AZ, Baird DD. Lower plasma 25-hydroxyvitamin D is associated with irregular menstrual cycles in a cross-sectional study. *Reprod Biol Endocrinol.* 2015;13:20. Epub 20150311. doi: 10.1186/s12958-015-0012-5. PubMed PMID: 25879830; PubMed Central PMCID: PMC4359493.
119. Jukic AMZ, Upson K, Harmon QE, Baird DD. Increasing serum 25-hydroxyvitamin D is associated with reduced odds of long menstrual cycles in a cross-sectional study of African American women. *Fertil Steril.* 2016;106(1):172-9 e2. Epub 20160318. doi: 10.1016/j.fertnstert.2016.03.004. PubMed PMID: 26997249; PubMed Central PMCID: PMC4930882.
120. Jukic AMZ, Wilcox AJ, McConaughy DR, Weinberg CR, Steiner AZ. 25-Hydroxyvitamin D and Long Menstrual Cycles in a Prospective Cohort Study. *Epidemiology.* 2018;29(3):388-96. doi: 10.1097/EDE.0000000000000804. PubMed PMID: 29337846; PubMed Central PMCID: PMC5882585.
121. Kervezee L, Shechter A, Boivin DB. Impact of Shift Work on the Circadian Timing System and Health in Women. *Sleep Med Clin.* 2018;13(3):295-306. doi: 10.1016/j.jsmc.2018.04.003. PubMed PMID: 30098749.
122. Hahn KA, Wise LA, Riis AH, Mikkelsen EM, Rothman KJ, Banholzer K, et al. Correlates of menstrual cycle characteristics among nulliparous Danish women. *Clin Epidemiol.* 2013;5:311-9. Epub 20130819. doi: 10.2147/CLEP.S46712. PubMed PMID: 23983490; PubMed Central PMCID: PMC3751379.
123. Liu Y, Gold EB, Lasley BL, Johnson WO. Factors affecting menstrual cycle characteristics. *Am J Epidemiol.* 2004;160(2):131-40. doi: 10.1093/aje/kwh188. PubMed PMID: 15234934.
124. Chao MJ, Menon C, Elgendi M. Effect of COVID-19 vaccination on the menstrual cycle. *Front Med (Lausanne).* 2022;9:1065421. Epub 20221216. doi: 10.3389/fmed.2022.1065421. PubMed PMID: 36590952; PubMed Central PMCID: PMC9802578.

125. Lebar V, Lagana AS, Chiantera V, Kunic T, Lukanovic D. The Effect of COVID-19 on the Menstrual Cycle: A Systematic Review. *J Clin Med*. 2022;11(13). Epub 2022/07/10. doi: 10.3390/jcm11133800. PubMed PMID: 35807090; PubMed Central PMCID: PMC9267255.
126. Tayyaba Rehan S, Imran L, Mansoor H, Sayyeda Q, Hussain HU, Cheema MS, et al. Effects of SARS-CoV-2 infection and COVID-19 pandemic on menstrual health of women: A systematic review. *Health Sci Rep*. 2022;5(6):e881. Epub 2022/10/18. doi: 10.1002/hsr2.881. PubMed PMID: 36248348; PubMed Central PMCID: PMC9547349.
127. Chao M, Menon C, Elgendi M. Menstrual cycles during COVID-19 lockdowns: A systematic review and meta-analysis. *Front Reprod Health*. 2022;4:949365. Epub 2022/08/09. doi: 10.3389/frph.2022.949365. PubMed PMID: 36303682; PubMed Central PMCID: PMC9580671.
128. Adnan T, Coull BA, Jukic AM, Mahalingaiah S. The real-world applications of the symptom tracking functionality available to menstrual health tracking apps. *Curr Opin Endocrinol Diabetes Obes*. 2021;28(6):574-86. doi: 10.1097/med.0000000000000682. PubMed PMID: 34560714; PubMed Central PMCID: PMC8631160.
129. Hohmann-Marriott BE, Williams T, Girling JE. The role of menstrual apps in healthcare: provider and patient perspectives. *New Zealand Medical Journal*. 2023;136(1570):42-53.
130. Worsfold L, Marriott L, Johnson S, Harper JC. Period tracker applications: What menstrual cycle information are they giving women? *Womens Health (Lond)*. 2021;17:17455065211049905. Epub 2021/10/12. doi: 10.1177/17455065211049905. PubMed PMID: 34629005; PubMed Central PMCID: PMC8504278.
131. DeNicola N, Marko K. Connected Health and Mobile Apps in Obstetrics and Gynecology. *Obstet Gynecol Clin North Am*. 2020;47(2):317-31. doi: 10.1016/j.ogc.2020.02.008. PubMed PMID: 32451020.
132. Ford EA, Peters AE, Roman SD, McLaughlin EA, Beckett EL, Sutherland JM. A scoping review of the information provided by fertility smartphone applications. *Hum Fertil (Camb)*. 2022;25(4):625-39. Epub 2021/03/30. doi: 10.1080/14647273.2021.1871784. PubMed PMID: 33783305.
133. Kalampalikis A, Chatziioannou SS, Protopapas A, Gerakini AM, Michala L. mHealth and its application in menstrual related issues: a systematic review. *Eur J Contracept Reprod Health Care*. 2022;27(1):53-60. Epub 2021/10/07. doi: 10.1080/13625187.2021.1980873. PubMed PMID: 34615425.
134. Fowler LR, Morain SR. Schrodinger's App. *Am J Law Med*. 2020;46(2-3):203-18. doi: 10.1177/0098858820933495. PubMed PMID: 32659192.
135. Albert K, Delano M, Weil E. Okay, Fine, Let's Talk About Period Tracking: The Detailed Explainer [web page]. Medium2022 [cited 2024 June 5]. Available from: <https://medium.com/@maggied/okay-fine-lets-talk-about-period-tracking-the-detailed-explainer-2f45112eebb4>.
136. Matteson KA, Munro MG, Fraser IS. The structured menstrual history: developing a tool to facilitate diagnosis and aid in symptom management. *Semin Reprod Med*. 2011;29(5):423-35. Epub 2011/11/09. doi: 10.1055/s-0031-1287666. PubMed PMID: 22065328.
137. FDA-NIH Biomarker Working Group. BEST (Biomarkers, EndpointS, and other Tools) Resource. Silver Spring, MD: Food and Drug Administration; 2016-.
138. Critchley HOD, Babayev E, Bulun SE, Clark S, Garcia-Grau I, Gregersen PK, et al. Menstruation: science and society. *Am J Obstet Gynecol*. 2020;223(5):624-64. Epub 2020/07/25. doi: 10.1016/j.ajog.2020.06.004. PubMed PMID: 32707266; PubMed Central PMCID: PMC7661839.
139. Huang Y, Wu M, Wu C, Zhu Q, Wu T, Zhu X, et al. Effect of hysterectomy on ovarian function: a systematic review and meta-analysis. *J Ovarian Res*. 2023;16(1):35. Epub 2023/02/09. doi: 10.1186/s13048-023-01117-1. PubMed PMID: 36759829; PubMed Central PMCID: PMC9912518.
140. Bonnington A, Dianat S, Kerns J, Hastings J, Hawkins M, De Haan G, et al. Society of Family Planning clinical recommendations: Contraceptive counseling for transgender and gender diverse people who were female sex assigned at birth. *Contraception*. 2020;102(2):70-82. Epub 2020/04/15. doi: 10.1016/j.contraception.2020.04.001. PubMed PMID: 32304766.

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