Ek Rashtra - Ek Mission
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Har Ghar FOGSIAN

From Adolescence to Aging

Comprehensive Insights into Women's Health

FROM THE PRESIDENT'S DESK

Dr. Sunita Tandulwadkar

President, FOGSI 2025

"It gives me immense pleasure to present the FOGSI Focus document titled From Adolescence to Aging: Comprehensive Insights into Women's Health." This work reflects the essence of FOGSI's commitment to women's health at every stage of life—from the dawn of menarche to the transformative years of pregnancy and postpartum, and further into the transition of menopause and beyond.

Women's health is a continuum, intricately woven with biological, psychological, and social dimensions. At each stage of this journey, unique challenges arise—be it menstrual disorders in adolescence, the importance of preconception optimization, the complexities of pregnancy and childbirth, the resilience required in the postpartum period, or the holistic care essential during menopause. This document brings together evidence-based knowledge and practical recommendations, authored by experts, to empower clinicians in providing the highest standard of care to women across these milestones.

As President of FOGSI, I believe that such academic contributions strengthen our collective mission: Swasth Nari, Samruddha Vatan"—a healthy woman leads to a prosperous nation. By equipping healthcare professionals with comprehensive, guideline-based insights, we not only improve clinical outcomes but also create a healthier future for generations to come.

I congratulate the editors and contributors for their dedication and scholarly effort in curating this valuable resource. I am confident that this document will serve as a trusted companion to gynecologists and healthcare providers, guiding them in optimizing women's health at every age and stage."

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Chapter 1

Menarche
The Beginning of Reproductive Life

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Introduction to **Reproductive Life**

Reproductive health is a fundamental aspect of overall well-being throughout life and is considered essential for social, economic, and human development. In women, reproductive health broadly encompasses various aspects, including menarche and menstruation, fertility, pregnancy and childbirth, sexually transmitted infections, gynecological cancers, and sexual health and function.[1]
Menarche marks a significant milestone in a woman's reproductive journey. The onset of puberty, or menarche, is a critical phase characterized by the emergence and progressive development of secondary sexual characteristics, ultimately leading to full sexual maturation and reproductive capability. Globally, the age at which menarche occurs has progressively declined compared to previous decades.

The onset of puberty and its broader health implications

Puberty is a pivotal stage in human development, and growing evidence indicates a trend toward earlier onset. This phase plays a significant role in the development of metabolic disorders, primarily due to a sharp rise in insulin resistance. This increase can elevate the risk of type 2 diabetes. Additionally, hormonal changes during puberty may contribute to excessive weight gain, further heightening the likelihood of obesity.[2] An early onset of puberty has been associated with various physical and psychological challenges, as well as an increased risk of metabolic diseases.

Menarche: Influencing Factors, Physical and Psychological Health Outcome

Menarche, the first menstrual period, is commonly used in epidemiological studies as a key variable due to its distinct occurrence, ease of recall, and relatively late timing, typically between 12 and 13 years of age. It follows the onset of breast development and the adolescent growth spurt in girls. The timing of puberty is influenced by genetic and neuroendocrine factors, as well as overall health, nutrition, physical activity, and exposure to environmental chemicals.

The role of nutrient intake in childhood and early menarche onset

Among genetic and environmental risk factors, nutrition plays a key role in determining the timing of puberty. Excessive calorie intake can contribute to earlier menarche onset (EMO) by promoting body fat accumulation, which increases leptin levels—signaling the brain to initiate puberty. As a result, sexual maturation is highly responsive to nutritional regulation, emphasizing the need for a balanced diet to support healthy pubertal development.

Studies have shown that[3, 4]:

- High intakes of energy, protein, animal protein, and iron in childhood are related to EMO, whereas high fiber intake in childhood is likely associated with delayed menarche onset.
- High-fat diet might be linked to EMO as it accelerates the development of breast (the earliest secondary sexual characteristic in girls).
- Puberty onset is influenced by the prepubertal body composition because the estrogen formation from the androgen occurs in adipose tissue, which is a critical source of extragonadal estrogen.
- Healthy children often have insufficient zinc intake, a vital nutrient for growth. Studies have shown that zinc sulfate can promote bone formation in healthy premenarcheal girls in 4 weeks.

Key micronutrients and their role in pubertal health

Nutrient	Role in Menarche/Menstrual Health	Recommended Daily Allowance (RDA) [Adolescents]
Iron	Prevents anemia due to menstrual blood loss[5]	15.4 to 18.5 mg/day[6]
Vitamin B12	Supports red blood cell production and nerve health[7, 8]	2.4 mcg/day[9]
Vitamin D	Modulates immune function and influences pubertal timing[10]	600 IU/day[9]
Calcium	Essential for bone growth during puberty[11]	1300 mg/day[9]
Zinc	Supports hormonal regulation[12]	9 mg/day[13]
Magnesium	Helps reduce PMS symptoms[14]	360 mg/day[15]
Folate	Supports cell division, DNA synthesis, red blood cell formation and development during adolescence[16]	400 mcg/day[9]

- **Vitamin D supplementation and early menarche onset:** Vitamin D exists in four different forms: vitamin D3, vitamin D2, calcidiol, and calcitriol. Studies have substantiated that vitamin D deficiency is linked to changes in pubertal timing. Girls experiencing early puberty, menarche, and obesity often have insufficient vitamin D levels, necessitating appropriate clinical supplementation. Additionally, girls with short stature and even healthy girls may have some degree of deficiency, highlighting the need for increased prevention efforts.[10, 17]

Sedentary lifestyle

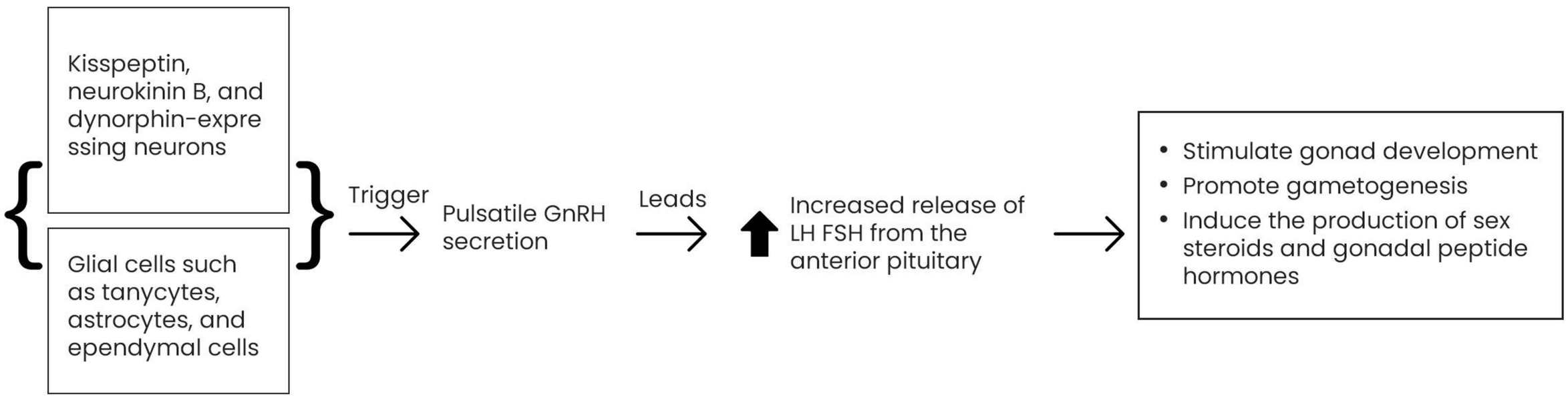
It is often referred to as 'couch potato syndrome', is increasingly recognized as a contributing factor to early menarche. Prolonged screen time, reduced physical activity, and high-calorie diets associated with this behavior promote adiposity and can accelerate pubertal timing. Encouraging physical exercise and reducing sedentary time are crucial interventions to delay early puberty onset.[18, 19]

Hormonal and genetic factors

Throughout the menstrual cycle, a woman's body undergoes various changes designed to create optimal conditions for conception and pregnancy. However, this intricate process can be easily disrupted by genetic abnormalities and hormonal imbalances.

- Puberty begins with the third activation of the hypothalamo–pituitary–gonadal (HPG) axis following a period of childhood quiescence. Hypothalamic GnRH-secreting neurons play a central role within a complex neuroendocrine network.

This network includes:



Puberty typically begins in girls about a year earlier than boys, with pubertal onset—marked by the transition from Tanner breast stage 1 to stage 2—occurring between 8 and 13 years of age in healthy individuals.[20]

- Recent advancements have led to significant insights into factors influencing normal pubertal timing. Various studies have identified single nucleotide polymorphisms (SNPs) associated with pubertal timing across both sexes and different ethnic groups. Puberty initiation is a highly polygenic process, with genes classified into three groups: puberty inhibitors, puberty-activating genes and genes with a dual effect. Certain polymorphic variants in genes biologically linked to gonadotropins and those encoding steroidogenesis enzymes may be associated with precocious puberty.

Table 1: **Genetic Causes of Puberty Disorders**[21]

Category	Genetic Causes	
Precocious puberty		
Central precocious puberty	Monogenic causes	Chromosomal abnormalities
	• Gain-of-function mutations in *KISS1R* and *KISS1* genes • Loss-of-function mutations in *MKRN3* gene • Loss-of-function mutations in *DLK1* gene	• 1p36 deletion • 9p distal deletion • 9q34.3 duplication (including the *NOTCH* gene) • Xp11.23–p11.22 duplication
Genetics of delayed puberty		
Constitutional delay of growth and puberty	Genetic background is unknown; pathogenic variants in the ***IGSF10*** gene are associated.	
Kallmann syndrome	**Mutated genes:** *KAL1, FGFR1, FGF8, FGF17, IL17RD, DUSP6, SPRY4, FLRT3, KLB, HS6ST1, CHD7, WDR11, SEMA3A, SEMA3E, IGSF10, SMCHD1, CCDC141, FEZF1, SOX10, PROKR2, PROK2*	
Normosmic idiopathic hypogonadotropic hypogonadism	**Mutated genes:** *CHD7, DAX1, FGF8, FGF17, FGFR1, HS6ST1, NSMF, LEP, LEPR, PROK2, PROKR2, WDR11, GNRH1, GNRHR, KISS1, KISS1R, SRA1, TAC3, TACR3*	

Category	Genetic Causes	
Hypogonadism hypergonadotropic	Monogenic causes	Chromosomal abnormalities
	• Enzymatic defects in testosterone biosynthesis: 17 α-hydroxylase, 3 β-hydroxysteroid dehydrogenase, 17,20-lyase, and 17β-hydroxysteroid dehydrogenase deficiency • Inactivating mutations in gonadotropin receptor genes • Polymalformative syndromes	• **Turner syndrome** • **Klinefelter syndrome**

Puberty's timing and progression are tightly regulated by genetic, epigenetic, and environmental factors. Much remains to be discovered about the signaling pathways governing prepubertal neuroendocrine development.

Metabolic and Cardiovascular Outcomes of Early Menarche

Age at menarche (AAM) is not only a biological marker for women but also an indicator of a population's quality of life. Due to population differences, there are no universal definitions for early and late menarche, though early menarche is generally considered before age 12. It is linked to a higher risk of chronic diseases, including cardiovascular disease, rheumatoid arthritis, and breast cancer. It has been found that women who experience menarche before 12 have a 23% higher risk of breast cancer than those who menstruate at 15 or later.[22]

Obesity risk[22]

Multiple studies suggest a link between early menarche, high BMI, and obesity, indicating that increased adiposity in girls may contribute to earlier puberty and menarche, making early menarche a risk factor for obesity.

- Studies have shown that females who experience early menarche are more likely to have a BMI of ≥ 25 kg/m² compared to those with a BMI below 25 kg/m².
- Females with late age at menarche show significantly lower BMI compared to their peers characterized by early onset of menarche.

Cardiometabolic and diabetes risks in adulthood linked to early menarche[2, 23]

Recent studies indicate that early menarche may elevate the risk of cardiometabolic, and it is also considered an independent risk factor for gestational diabetes and type 2 diabetes.

CVD

1. Studies have indicated that early puberty might increase the CVD risk, even after age and BMI adjustment.
2. The Women's Ischemia Syndrome Evaluation study highlighted a 4.53-fold higher risk of adverse CVD outcomes in women with early age at menarche (≤10 years).
3. Early puberty is also linked to a higher risk of diastolic blood pressure, stroke, triglycerides, and decreased high-density lipoprotein cholesterol.

Diabetes

1. Research has demonstrated that later age at menarche is related to a lower risk of T2DM/ impaired glucose tolerance risk, even after adjusting for adult adiposity.
2. Furthermore, girls with earlier menarche have a higher risk of developing gestational diabetes mellitus, which can have adversative effects on pregnancy outcomes.

Early menarche and increased risks of preeclampsia

Preeclampsia affects 2-8% of pregnancies globally and poses serious risks to both mothers and infants. Newborns of women who experienced menarche at or before age 12 have a higher likelihood of adverse neonatal outcomes.[24] Pregnant women who attained menarche at the age of ≤12 years are at increased risks of preeclampsia.

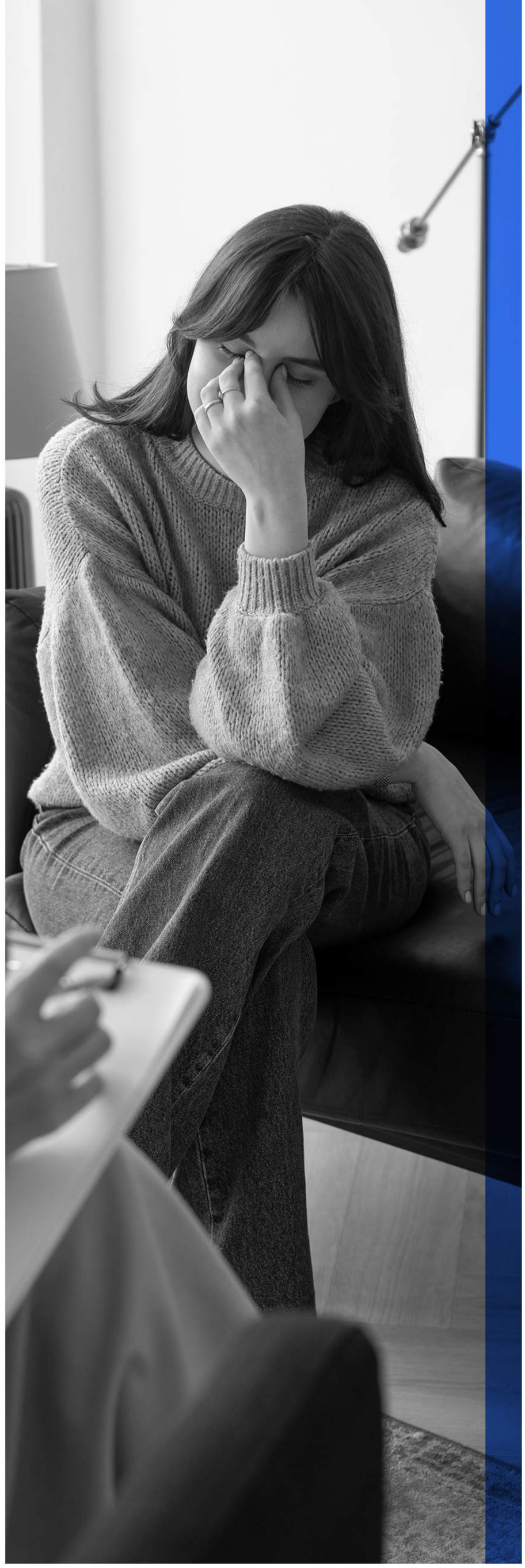
Mental health and psychosocial impacts of early menarche

Early menarche also has significant psychological implications. Girls who mature earlier than their peers often face heightened emotional and social challenges, including increased risk of anxiety, depression, low self-esteem, and poor body image. The mismatch between physical development and emotional maturity can lead to vulnerability to peer pressure, bullying, and engagement in risky behaviors. Therefore, timely psychological support and education are vital.[25-27]

Behavioral dysfunction and depression

Extensive research suggests that early puberty increases the risk of behavioral dysfunction. Adolescents who experience early menarche are more likely to engage in substance use, including cigarettes, alcohol, and marijuana, compared to their peers.

Drug abuse in the early menarche group displayed higher levels of:	Self-reported criminality
	Substance use problems
	Social isolation
	Early sexual behavior
	Psychiatric problems



Depression significantly affects overall health and well-being, contributing to more disability-adjusted life years than any other condition. Strong evidence suggests a negative association between pubertal timing and depression risk. Additionally, early puberty has been linked to an increased risk of bulimia nervosa, anxiety disorders, distress disorders, excessive psychosomatic symptoms, fear, and self-harm.

Studies linking early menarche to higher disordered eating behavior risks[28]

Disordered eating (DE) encompasses irregular eating or weight-control behaviors that do not meet the criteria for clinically diagnosed eating disorders. Epidemiological research suggests that DE is significantly more prevalent than clinical eating disorders. Findings from cross-sectional and certain longitudinal studies indicate that early pubertal timing may contribute to the development of DE symptoms.

- Early onset of menstruation has been linked to body dissatisfaction and binge eating in young adult women.
- Studies have shown a strong correlation between early menarche and behaviors such as self-induced vomiting, excessive weight loss, and body image distortion in girls.
- Previous research indicates that early menarche is associated with higher BMI and increased levels of DE, supporting the "maturation disparity hypothesis," which suggests that elevated BMI poses a greater risk for individuals undergoing early puberty.

PMS, Menstrual Migraine, and the Burden of **Iron Deficiency**

Premenstrual syndrome (PMS): A common disorder of reproductive age

Many women experience PMS, an amalgamation of physical and psychological symptoms occurring two weeks before menstruation and resolving afterward. The worldwide prevalence of PMS is estimated to be 47.8%, while its most severe form, premenstrual dysphoric disorder (PMDD), impacts approximately 3-8% of women of reproductive age.[29]

- Hormonal changes, stress, diet, and neurotransmitter imbalances are key risk factors.
- Common symptoms include irritability, anxiety, depression, bloating, breast tenderness, and headaches.

Cognitive behavioral therapy (CBT) A primary option for PMS

The majority of women of reproductive age experience at least one PMS symptom monthly, with around 5% facing significant impairment requiring medical support. Providing effective and long-term treatment is crucial. Pharmacological treatments may offer quicker relief, but their effects diminish once discontinued. However, based on the systematic literature review, there is sufficient evidence to recommend CBT as the primary approach for managing PMS.[30] To attain effective outcomes, women should change their mindset and mentally overcome PMS-related distress.

- Self-help programs, assisted by modern technology, is sufficient for most women to effectively manage PMS distress.
- One-to-one individual or group intervention may be necessary for those with most severe PMS forms.
- In the future research, male partners should be included for PMS treatment interventions.

Menstrual migraine (MM)

Menstrual migraine (MM), associated with hormonal changes during the menstrual cycle, affects around 4% to 8% (global prevalence) of women in their reproductive years. It is generally more severe, persists longer, and responds less effectively to treatment than other types of migraine.[31] Additionally, during menopause, migraine remains a concern, with prevalence rates ranging from 10% to 29%, highlighting the continued influence of hormonal changes on migraine patterns throughout a woman's life.[32] MM is classified as either pure menstrual migraines (PMMs), which occur only around the menstrual period, or menstrual-related migraines (MRMs), which occur during menstruation but also at other times of the month.[33] Multiple studies from various regions in India have reported that approximately 70% of women with menstrual migraine experience pure menstrual migraine (PMM), while around 30% present with menstrual-related migraine (MRM) linked to hormonal fluctuations during the menstrual cycle.[34, 35]

ICHD-3 classification of PMMs and MRMs[36]

Criteria	Pure Menstrual Migraine	Menstrually Related Migraine
A. Definition	Attacks, in a menstruating woman, fulfilling criteria for **migraine without aura**	Attacks, in a menstruating woman, fulfilling criteria for migraine without aura
B. Timing of Attacks	Occur **exclusively** on day **1 ± 2** of menstruation[a] (i.e., days -2 to +3)[b] in **≥2 of 3 cycles, and** at no **other time in the** cycle	Occur on **day 1 ± 2** of menstruation[a] (i.e., days -2 to +3)[b] in **≥2 of 3 cycles, and also** at other times in the cycle

[a]Definition of Menstruation
Endometrial bleeding due to **normal menstrual cycle or withdrawal of exogenous progestogens** (e.g., combined oral contraceptives or cyclical HRT)
Same as for pure menstrual migraine

[b]Cycle Day Clarification
Day 1 = first day of menstruation; day -1 = day before menstruation; no day 0
Same as for pure menstrual migraine

The treatment of MM is categorized into acute and preventive therapy.

Acute and prophylactic treatment of MM[37, 38]

Acute treatment (for severe, long, difficult-to-treat attacks)	Prophylactic treatment
Triptans (Almotriptan, Rizatriptan, Sumatriptan, Zolmitriptan)	NSAIDs
NSAIDs	Ergotamine derivatives
Paracetamol	Triptans (Sumatriptan, Zolmitriptan)
Opiates	Anticonvulsants (Topiramate, Divalproex sodium)
Combination analgesics	Beta-blockers (Propranolol, Timolol)
Ergotamine, Dihydroergotamine	Hormonal therapies (contraceptives)
Hormonal therapies (estrogen supplements, prostaglandin)	NSAIDs

Short-term prophylaxis for MM is beneficial for women on oral contraceptives or those with very regular menstrual cycles, in whom the period of maximum susceptibility to migraine is easily predictable. Triptans and NSAIDs have shown varying efficacy in mitigating MM. Additionally, hormonal therapies have also been studied for short-term prevention of MM. Dihydroergotamine mesylate has also demonstrated efficacy in reducing MM severity.

Iron deficiency and anemia in women

There is a varying risk of exposure to anemia during each stage of a woman's reproductive cycle. The global prevalence of anemia is 30% among non-pregnant women. The interplay of several factors, such as socioeconomic status, dietary deficiencies and parasitic infections, can contribute to anemia development. To address anemia, different interventions, including encouraging an iron-rich diet, improving access to iron supplements, familiarizing the public regarding reproductive health and enhancing antenatal care, can be implemented.[39]

Nutritional interventions: A focus on managing anemia[40-43]

HMB in women is characterized by a regular blood loss exceeding 80 ml per menstrual cycle, outpacing iron intake, and is the most common cause of iron deficiency (ID). Globally, ID affects over 2 billion people, with iron deficiency anemia (IDA) being the leading cause of anemia.

IDA can be managed by increasing iron-rich foods and enhancing iron absorption.
o Heme iron sources include lean meat and seafood.

- Since plant-based iron is less absorbable, the WHO recommends pairing it with enhancers like vitamin C, citric, or malic acid, with vitamin C being the most effective.
- Studies suggest that consuming vitamin A-rich foods and reducing high-fat, sugary foods may lower the risk of dysmenorrhea and irregular menstrual cycle, while regular exercise can help reduce PMS and IMC risk.
- Additionally, in anemic patients, oral iron should be continued until Hb normalizes (6-12 weeks), followed by at least three months of supplementation to restore iron stores (target ferritin >100 µg/L).

Emphasizing iron supplementation for ID/IDA

- Iron supplementation, available as oral and intravenous formulations, is essential for ID management. Oral iron, including ferrous and other iron salts, is widely used because of its safety and affordability. However, poor adherence remains a significant issue in treatment failure and recurrence.
- Novel oral formulations, with improved absorption and fewer GI side effects, such as ferric maltol, sucrosomial iron, ferric citrate, and iron hydroxide adipate tartrate (under trial for children in developing countries), offer more satisfactory tolerance.
- IV iron therapy provides an alternative for patients with GI issues, allowing higher doses and improved efficacy.
- The WHO recommends intermittent supplementation with 60 mg of elemental iron (which can be derived from 300 mg of ferrous sulfate, 180 mg of ferrous fumarate, or 500 mg of ferrous gluconate) and 2.8 mg of folic acid (at least once weekly for 3 months, administered twice a year or after the school semester) to help prevent anemia in menstruating adolescents (10-19 years) and women in regions where anemia prevalence exceeds 20%.[44, 45]

Menstrual Irregularities in Adolescents: Causes, Contributing Factors and Management

A normal menstrual period lasts between 2 and 7 days and occurs every 21 to 35 days. However, 14 to 25% of girls experience irregular cycles, which may involve unusually heavy or light bleeding, cycle lengths exceeding 35 days or falling below 21 days, or other symptoms like abdominal cramps.[46]

Menstrual irregularities also include:
- Bleeding or spotting between periods
- Bleeding or spotting after sex
- Menstrual cycle length varying by >7-9 days, and/or not having a period for 3-6 months

Altered progesterone and estrogen levels lead to irregular cycle.

Modifiable risk factors for irregular cycle:
- Obesity
- Stress
- Smoking

Common causes are:
- Birth control pills
- Breastfeeding
- Excessive exercise
- Intrauterine devices
- Hyperthyroidism or hypothyroidism

Additional causes of menstrual irregularities

Underlying medical conditions can significantly influence menstrual irregularities in adolescents:
- Polycystic Ovary Syndrome (PCOS): Characterized by irregular menstrual cycles, hyperandrogenism, and polycystic ovaries. It is often associated with insulin resistance and obesity. Cyproterone acetate, an anti-androgenic progestin, is often used in combination with estrogens to treat symptoms of PCOS such as hirsutism, acne, and menstrual irregularities. It blocks androgen receptors and reduces androgen production, making it effective for hyperandrogenic manifestations in PCOS.[47] Long-term use requires monitoring.[48]
- Genital Tuberculosis (TB): Particularly relevant in endemic areas, TB can affect the endometrium, leading to amenorrhea or infertility.[49]

- Von Willebrand Disease: A common hereditary bleeding disorder presenting as menorrhagia in adolescents.[50] Evaluation should include coagulation profiles and family history.[51]
- Other Coagulopathies: Platelet function disorders and hemophilia carriers may also experience excessive menstrual bleeding, necessitating hematologic assessment.[52, 53]

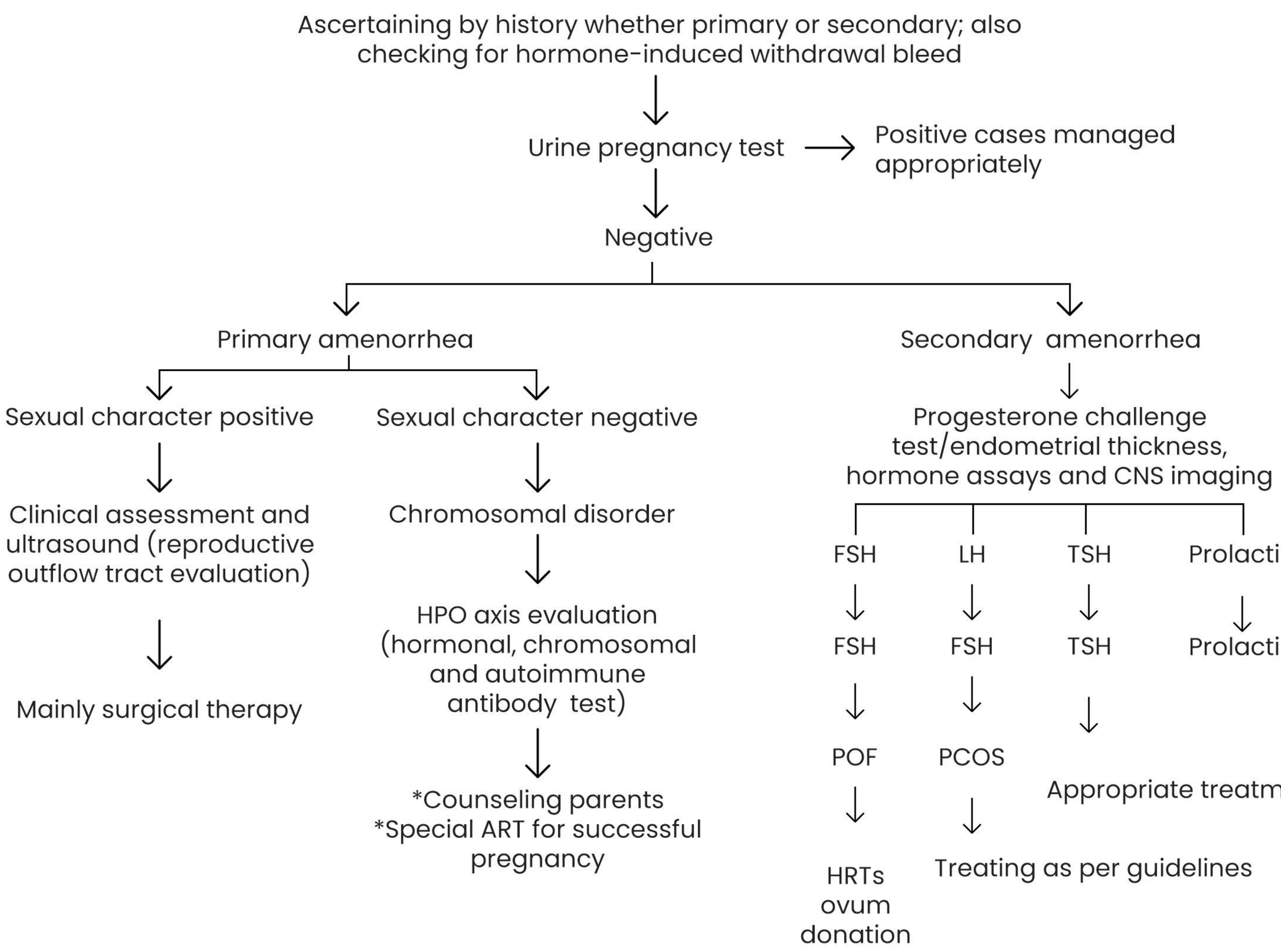
Common disorders and their management

Menstrual health plays a crucial role in the well-being and quality of life of adolescents. While cycle irregularities are common during the first two years after menarche due to the immaturity of the gonadal axis and anovulatory cycles, certain menstrual abnormalities are pathological. Early recognition of these conditions is essential to ensure appropriate treatment and monitoring for affected individuals.

- **Amenorrhea or Oligomenorrhea:**
  Primary amenorrhea refers to the absence of menarche by the age of 16. Secondary amenorrhea is characterised by the cessation of menstruation for over 90 days in individuals who previously had regular cycles. Oligomenorrhea is defined as infrequent menstrual cycles occurring more than 35 days apart. However, in adolescents, the definition may be broadened to include cycles exceeding 45 days in length for up to 2-3 years following menarche.[54]

  Treatment is guided by the underlying cause identified through the outlined workup protocol. It also considers the necessity of regular menstruation, future reproductive goals, including the desire for children, and contraceptive intentions in cases of amenorrhea.

Streamlined decision-making framework for assessing and managing amenorrhea[55]

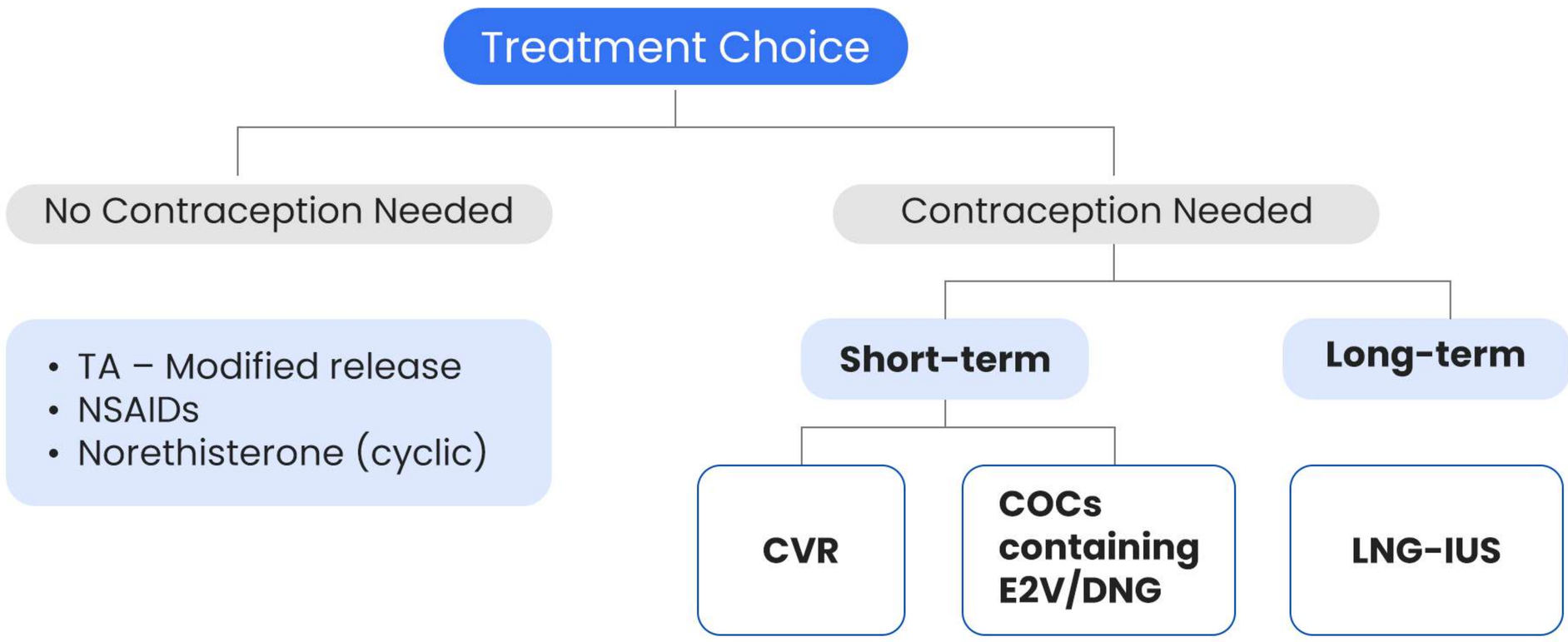


HRT: Hormone replacement therapy; POF: Premature ovarian failure.

- **Menorrhagia:**
  Heavy menstrual bleeding (HMB) or menorrhagia is a prevalent condition, affecting one in five females.[56]

For the majority of patients, medical management should be the first-line treatment. Available options include oral progestins, multidose regimens of combined oral contraceptives (COCs), and Tranexamic acid.

Medical management of acute HMB[57]



TA: Tranexamic acid; NSAIDs: Non-steroidal anti-inflammatory drugs; CVR: Combined contraceptive vaginal ring; COCs (E2V/DNG): Estradiol valerate/dienogest four-phasic combined oral contraceptive; LNG-IUS: Levonorgestrel-releasing intrauterine system

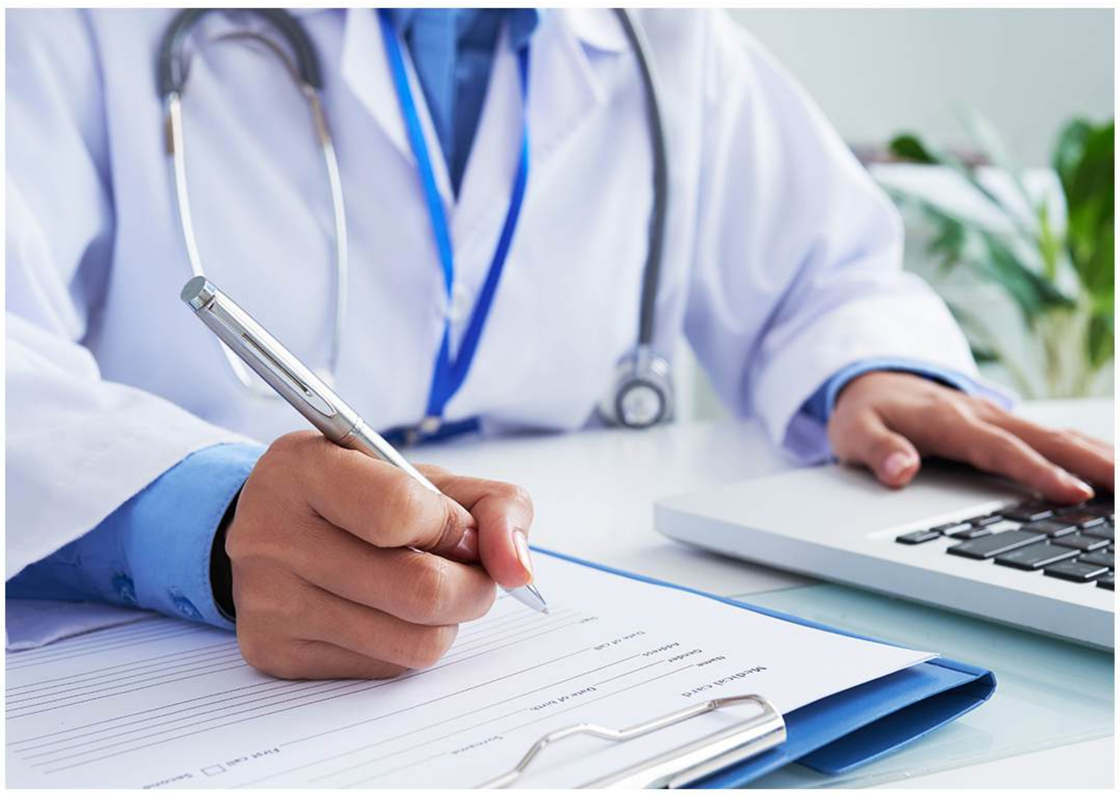
Abnormal uterine bleeding (AUB)

Menstrual bleeding is considered abnormal based on factors such as menstrual frequency, cycle regularity, duration of flow, and blood volume.

Cobalamin and B-complex on hypermenorrhea

Hypermenorrhea is characterized by excessive menstrual bleeding exceeding 90 ml/cycle while maintaining a normal duration. Research has shown that patients with prolonged bleeding experienced significant improvement when given a daily B-complex and B-12 ampule for 5 days, with most responding positively. This suggests that B-complex and B-12 may play a crucial role in managing hypermenorrhea.[58,59]

The American College of Obstetricians and Gynecologists (ACOG) Recommendations on Management of AUB [60]



Medical management

- Options: Multidose regimens of OCs or oral progestins, and Tranexamic acid.
- Decisions must be based on the patient's medical history and contraindications to therapies.

Surgical treatment

The need for surgery depends on the clinical stability of the patient, the bleeding severity, contraindications to medical management, the patient's lack of response to medical management, and the underlying medical condition of the patient.

Guideline-Based Hormonal Management of Menstrual Disorders and PMS[61-63]

Acute HMB
Monophasic OCPs (in 30-50 µg Ethinyl estradiol formulation) every 6-8 hours until cessation of bleeding

Dysfunction uterine bleeding
Moderate (mild anemia; no hemodynamic instability): Oral Norgestrel-ethinyl estradiol
Severe (Hb <90; unstable), High dose estrogen: Oral 50 µg Norgestrel-ethinyl estradiol every 4 hours with an antiemetic until bleeding decreases then every 6 hours, then every 8 hours; IV 25 mg estrogen every 4 hours with an antiemetic; iron supplementation then cycle with COCs for 3 months

PMS
Drospirenone-containing COCs represent effective treatment
Percutaneous estradiol combined with cyclical progestogens effective physical and psychological symptoms of severe PMS

HMB maintenance therapy
Combined hormonal contraceptives, oral and injectable progestins, and Levonorgestrel-releasing intrauterine devices (LNG-IUDs)

ACOG's updated guidelines recommend evidence-based treatments for premenstrual disorders[64]

Premenstrual disorders encompass a range of conditions, including PMS and PMDD. The American College of Obstetricians and Gynecologists (ACOG) offers evidence-based guidelines for managing these disorders, applicable to both adults and adolescents unless specified otherwise.

Routine exercise, patient education and acupuncture	CBT
NSAIDs	COCs
Calcium supplementation of 1,000-1,200 mg/day	GnRH agonists with combined hormonal add-back therapy (refractory symptoms)
SSRIs	

Combined Oral Contraceptives (COCs): Therapeutic Benefits Beyond Birth Control

COCs { They help reduce PMS severity and functional impairment. The only FDA-approved COC for treating PMDD in individuals requiring contraception is a Drospirenone-containing formulation (3 mg Drospirenone, 20 mcg Ethinyl estradiol) in a 24-day regimen.

COCs contain a combination of estrogen and progestin[65, 66]

Estrogen component: Current formulation ranges from 50 µg (high-dose) to 20 µg (ultra-low dose), while the most common doses being 30-35 µg (low-dose). Most combined contraceptives contain ethinyl estradiol (EE) as an estrogen component.
Progestin component: They are categorized based on their chronological development into different generations.

1st Generation: Estranes and Pregnanes > 2nd Generation: Gonanes, e.g. Levonorgestrel or Norgestrel > 3rd Generation: Gonanes, e.g. Gestodene, Desogestrel and Norgestimate > 4th Generation: 19-norpregnanes Estranes (non-ethinylated) Spironolactone derivative

Clinical use of progestins[67]

Progestins with or without estrogen are used to address irregular bleeding and also used for:

Dysmenorrhea	Secondary amenorrhea
Oligomenorrhea	Endometriosis
Polymenorrhea	Dysfunctional uterine bleeding
Hypermenorrhea	

Mechanism of action of COCs[68-70]

- **Contraceptive benefits:**
  - They suppress luteinizing hormone (LH) and follicle-stimulating hormone (FSH), preventing the mid-cycle LH surge.
  - COCs prevent ovulation by inhibiting gonadotropin-releasing hormone (GnRH) from the hypothalamus.
  - Estrogen plays a key role by suppressing FSH, blocking folliculogenesis.

- **Non-contraceptive benefits**
  - Benefits stem from ovulation suppression and local progestin effects on the endometrium and genital tissue.
  - Mechanisms involve anti-ovulatory effects (e.g., ovarian cancer prevention), progestogens' antiproliferative effect on endometrium (e.g., heavy menstrual bleeding, dysmenorrhea, and endometrial carcinoma prevention), or endocrine system modulation (acne prevention).

Hormonal and non-hormonal contraceptives were originally formulated for the prevention of unintended pregnancy. However, since the introduction of the first COC, numerous studies have highlighted its significant non-contraceptive benefits, particularly in menstrual disorders.

Menstrual cycle disorders	Though COCs are not a first-line therapy, they are employed for oligomenorrhea due to PCOS, AUB, MM, and PMS or PMDD.
Pelvic pain disorders	Women with endometriosis-related or chronic pelvic pain or dysmenorrhea can benefit from the hormonal/endometrial suppression related to COC use to reduce their symptoms.
Ovarian cysts	COCs are given to women with a history of painful ovarian cysts to suppress ovulation and the occurrence of new cysts.

Hyperandrogenism	The dermatologic manifestations of hyperandrogenism can be reduced by COCs which are particularly common in women with PCOS.
Cancer risk reduction	Women at high risk of ovarian and endometrial cancer can benefit from COC use to lessen cancer risk.
Bone health	Perimenopausal women using COCs have better bone mineral density (BMD) in comparison to non-users.

- **Benefits of COCs** [71-73]
  Currently, 40-60% of combined oral contraceptive pill (COCP) prescriptions are for non-contraceptive benefits, primarily to manage gynecological conditions. COCP use reduces endometrial proliferation, maintaining a thin, stable endometrium, which helps decrease menstrual blood loss and lowers the risk of IDA. Evidence suggests that over six months, COCs can reduce HMB to normal levels (PBAC score <100) in 12–77% of women, compared to 3% with placebo, though LNG-IUS remains more effective. COCs were initially prescribed to manage dysmenorrhea caused by uterine contractions. Their use reduces prostaglandin release during menstruation, leading to less painful periods.

- **Side effects of COCs**
  Side effects, such as abnormal menstrual bleeding, nausea, mood changes, weight gain, breast tenderness, and headache, are encountered during the first 3 months. Adequate counseling can help in enhancing compliance and prevent discontinuation.

- **Available COCs and their clinical non-contraceptive uses**[74-78]

Norgestrel + Ethinyl Estradiol

Studies support the following indications:
- Increased menstrual cycle regularity
- Decreased blood loss, IDA, and dysmenorrhea
- Decreased incidence of functional ovarian cysts and ectopic pregnancies
- Long-term use: Decreased incidence of fibroadenomas, breast fibrocystic disease, acute pelvic inflammatory disease, endometrial and ovarian cancer

Levonorgestrel/Ethinyl Estradiol

Most widely used and effective formulations in COCs
- Effective in long-term contraception
- Used off-label for treating menorrhagia, endometrial hyperplasia, endometriosis, and as a part of menopausal hormone therapy

Ethinyl Estradiol + Drospirenone

- Treat premenstrual dysphoric disorder (PMDD) symptoms for women on oral contraceptives for contraception
- Treat moderate acne for women at least 14 years old only if the patient desires an oral contraceptive for birth control

Medroxyprogesterone acetate

Indications:
- Secondary amenorrhea
- Prevents endometrial hyperplasia in non-hysterectomized postmenopausal women receiving conjugated estrogens
- Studies findings: 10-day cyclic regimen of MPA more effective in regulating the menstrual cycle and stopping AUB due to ovulatory dysfunction

Conclusion

In conclusion, menarche is not merely a biological milestone but a crucial indicator of a girl's overall health, future reproductive potential, and long-term metabolic and psychological well-being. Its timing is influenced by a complex interplay of genetic, hormonal, nutritional, and environmental factors. Early menarche, increasingly prevalent worldwide, has been linked to a heightened risk of obesity, type 2 diabetes, cardiovascular disease, preeclampsia, and mental health disorders, including depression and disordered eating. Understanding these associations underscores the importance of early-life nutritional interventions, hormonal assessments, and psychosocial support. Clinicians should adopt a holistic, evidence-based approach to monitoring pubertal development, recognizing deviations from normative timelines as potential early warnings for broader health concerns. Through timely screening and individualized care, we can mitigate the long-term consequences associated with early or abnormal pubertal onset, promoting healthier transitions into adolescence and beyond.

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Chapter 2

Pre-Pregnancy
Optimizing Health For Conception

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Introduction to **Pre-Conception Care**

The preceding three months before a pregnancy is the pre-conceptional period. Some define it as the period 1-2 years before the initiation of unprotected sexual intercourse. Pre-conception care is the provision of biomedical, behavioral, and social health interventions before conception occurs, aimed at improving the health status, and reducing behaviors and individual and environmental factors that could contribute to poor maternal and child health outcomes.[1, 2]

Pregnancies can be unplanned and organizations like World Health Organization (WHO) and the American College of Obstetricians and Gynaecologists (ACOG) recommend a healthy lifestyle in women planning pregnancies for an optimum outcome in pregnancy. The pre-pregnancy period will provide a window of opportunity to prepare for a successful pregnancy.[3, 4] The main recommendations for the pre-conception period are avoidance of substance use, attaining and retaining a normal body mass index (BMI), engaging in more than 150 minutes of moderate exercise per week, having a balanced diet, and multivitamin supplementation. Associations have been observed between pre-pregnancy lifestyle and maternal and child health outcomes.

Preconception Health Optimization
Role of Lifestyle and Nutrition

Nutrients needed in the pre-conception period[5-11]

The deficiencies of the micronutrients during the preconception period, including iron, folic acid, iodine, and vitamin D, can be very influential during the development of the fetus.

Essential nutrients[11]

Folic acid (FA) lowers the risk of neural tube, heart, urinary tract, and limb defects

- Women eligible for pregnancy: FA (0.4 mg) starting 8-12 weeks before conception and until 12 weeks after conception.
- Women with diabetes, on antiepileptic drugs or have had pregnancies affected by NTD: FA 0.8-5 mg daily during the periconception phase.

Iron

- Daily oral supplementation of 30 mg to 60 mg of elemental iron is recommended for pregnant women to prevent maternal anemia, puerperal sepsis, low birth

Vitamin D deficiency (circulating 25-OH-D levels <32 ng/mL)

- Women with vitamin D deficiency may benefit from supplementation:
  - 1,000 IU/day for levels between 30-49 nmol/L
  - 2,000 IU/day for levels below 30 nmol/L

Other nutrients

- The ATA recommends daily 150-200 µg of iodine for women planning a pregnancy, or currently pregnant or breastfeeding.
- DHA/omega-3 fatty acid reduces risk of PTB and early preterm birth (EPB).
- Calcium supplement can lower and prevent pregnancy-induced hypertension. At least 1000 mg daily of calcium carbonate is advisable.
- Multivitamin supplements with folic acid, iron, and other nutrients (B vitamins, A, D, E, omega-3s, and minerals) exert better impact on pregnancy outcomes.

A well-balanced and healthy diet plays a significant role in the prevention of malnutrition and health related risks. In the long term, it will also lessen the risk of developing diet-related non-communicable diseases (NCDs). The maternal nutritional status during the preconception period, is crucial and may influence the placenta function, pregnancy outcomes, and the offspring's health in later life. The intake of different foods should be based on the age, gender, weight, and physical activity of the individual. A combination of whole grains, cereals, and millets should be chosen. Vegetables which are fresh and locally produced should be preferred. Animal origin foods like meat, eggs, and milk should be partaken. Sugar should be less than 5% of the daily calorie intake.

A healthy lifestyle with adequate physical activity should be followed. Sedentary lifestyle should be avoided. Regular physical activity, yoga, and moderate intensity exercises are useful for maintaining muscle and bone health, and flexibility of joints.

ICMR guidelines have advised that for a 2000 kcal diet for a day, the person should consume cereals with 250 gm content, 400 gm of fresh vegetables, 100 gm of fresh fruit, 85 grams of pulses/eggs/flesh foods, 35 grams of nuts and 27 gm of fats and oils.[12]

Maternal over-nutrition:

Maternal over nutrition may cause an increased long-term vulnerability and induce a pathological response. Pre-pregnancy overweight and obesity can lead to gestational diabetes mellitus, micro-nutrient deficiency, impaired fertility, pre-term birth, co-morbidities, and even maternal mortality. In the fetus, it can cause macrosomia and alter the glucose and lipid metabolism. The long-term effects of maternal over nutrition are abdominal or generalized obesity across infancy and childhood, which can progress into adolescence and adulthood with related metabolic disorders; and asthma in predisposed children.

Gestational diabetes mellitus (GDM)

The risk of developing GDM increases significantly with increases in pre-pregnancy BMI. The presence of GDM increases the risk of either restricted or excess fetal growth, fetal adiposity, predisposition to obesity throughout life, impaired glucose tolerance, T2DM, and metabolic disorders in the infant.

Maternal obesity combined with multiple micronutrient deficiency

It is paradoxical, but obese pregnant women may have multiple nutrient deficiencies (with undernutrition from intake of micronutrient-poor foods).

Micronutrient deficiency and overweight or obesity are likely to overlap, and this conjunction may exacerbate the rise in transgenerational NCDs. This may lead to serious long-term health and societal consequences.

Management of obesity

Diet, exercise, and lifestyle management is the cornerstone for treatment of obesity in the pre-conception period. Some women will have problems with losing weight despite changes in the lifestyle. Bariatric surgery can be considered in the morbidly obese patient. Bariatric procedures have become less invasive and result in effective weight loss and the reversal of metabolic morbidities in some patients.

Patients who have undergone bariatric surgeries should not consider pregnancy for at least one year after the surgery because they can have nutritional deficiencies which can affect the fetus.
Newer emerging therapies, including twincretins, triple GLP-1 agonists, glucagon receptor antagonists, and imeglemin can also be considered for weight loss.[13, 14]

Pre-Pregnancy Care and Risk Management for Improved Maternal Outcomes[15-17]

Neonatal and birth disorders include a wide range of conditions that may have a lasting effect on both individuals and their families, preconception care has been linked to a lower risk of complications, including preterm birth, low birth weight, and congenital abnormalities such as neural tube defects.

Prevention of neural tube defects (NTDs)

Spina bifida, anencephaly, and encephalocele are the prevalent NTDs. Following factors can increase the risk of these conditions:

1. Low levels of folate during early pregnancy
2. Pre-existing and unregulated health conditions (diabetes mellitus)
3. Certain medications (Trimethoprim, Sulfasalazine, Methotrexate, and Triamterene)
4. Fever

5-MTHF: Essential for health and well-being[17]

5-MTHF, the biologically active form of folate, plays a crucial role in one-carbon metabolism, a pathway essential for DNA synthesis, repair, and methylation.

Alongside vitamin B12, 5-MTHF supports the conversion of homocysteine (Hcy) into methionine, helping to maintain cardiovascular health by preventing hyperhomocysteinemia (HCys), a condition linked to blood clots and heart disease.

Research has shown that supplementation with 5-MTHF is more effective than Folic acid in raising folate levels, making it a preferred choice for individuals with folate metabolism issues.

In reproductive health, adequate 5-MTHF levels are vital for fertility and pregnancy. Deficiencies, particularly in individuals with MTHFR gene polymorphisms, can increase the risk of pregnancy-related complications and NTDs.

High-dose Folic acid: In standard practice, high-dose folic acid is often recommended (1-5 mg/day) for pregnant women with epilepsy or diabetes, individuals with folate-deficiency anemia, or on Methotrexate for cancer or rheumatoid arthritis treatment.[18]

IMPORTANCE OF FOLIC ACID

The only form of folate confirmed to help prevent NTDs is folic acid. Administration of 400 µg of folic acid daily before and during early pregnancy can prevent an NTD.[13]

BUT

Dietary intake, genetic predisposition, and medicines interfering with the folate-homocysteine cycle are the 3 primary factors influencing folate levels in individuals.

Role of 5-Methyltetrahydrofolate (5-MTHF)	• Polymorphisms in genes coding for folate cycle enzymes are common. Polymorphisms of the *MTHFR* (5,10-*methylenetetrahydrofolate reductase*) gene are the most crucial. • Active folate 5-MTHF supplementation can bypasses the entire folate metabolization (impaired by *MTHFR* polymorphism), and 5-MTHF is directly absorbed to exert bioactivity.

**Thus, using 5-MTHF is strongly recommended for external supplementation as a food supplement instead of FA.

As per the WHO Recommendations, women who have had a foetus diagnosed as affected by a NTD or have given birth to a child with a NTD must be provided 5 mg Folic acid daily.[19]

- Serum folate level rise by 0.94 ng/mL for every 0.1 mg/day increase in folic acid intake in women aged 20-35 years, and about double in women aged 40-65.[20]
- Every doubling of serum folate level roughly halves the NTD risk.[21]
- An increase of 0·4 mg/day reduces risk by about 36%, whereas providing a 5-mg tablet daily reduces risk by about 85%.[22]

Remarks: Folic acid fortification levels must be increased and women in pre-conception period must have 5 mg folic acid tablets daily, instead of the 0·4 mg dose.

Managing pre-existing medical conditions

Pre-existing medical conditions can influence the outcome of the pregnancy; therefore, the identification and management of co-morbidities is crucial and is an important aspect of preconception care. The screening for illnesses, such as infections, thyroids disorders, diabetes, and hypertension, aims at early identification and implementation of management strategies like medication adjustments, lifestyle interventions, or referrals to specialists, to improve health before pregnancy.

Endometriosis

Endometriosis is a chronic condition that can compromise fertility in up to 30-50% of affected patients.[23] It is also associated with increased obstetrical complications, including small for gestational age, cesarean section, miscarriage, hemorrhage, low placental adhesion, and preterm delivery.[24] Contraception plays a vital role in preserving fertility and optimizing health status prior to planned pregnancy. Hormonal contraceptives are an effective treatment option for endometriosis.[25]

The primary treatment for endometriosis involves, progestins, with combined hormonal contraception being the first-line recommendation. However, while contraceptives pills help manage symptoms, they do not address infertility caused by endometriosis. The goal of progestins therapy is to induce anovulation and amenorrhea, thereby alleviating symptoms and controlling disease progression.

Combined oral contraceptives (COCs) containing ethinyl estradiol and various progestogens have long been used in the management of endometriosis-associated dysmenorrhea.

Multiple studies with COCs formulated with desogestrel, gestodene, norethisterone, drospirenone, and levonorgestrel (LNG) suggest that these combinations are generally effective in alleviating dysmenorrhea in most women with endometriosis.[26]

Anemia in the pre-conception period

One of the most prevalent causes of anemia is iron deficiency, which may be combined with deficiencies of folate, vitamin B12, riboflavin and/or vitamin A. Anemia during preconception and early gestation is associated with impaired fetal development, preterm delivery, and low birth weight.[27, 28]

Oral iron preparations are available for iron supplementation including ferrous sulfate, fumarate, gluconate, glutamate, succinate, lactate, and ferrous ascorbate. Ferrous ascorbate is preferred for treating IDA in pregnant women. The advantages are high bioavailability, fast response, safety, and good efficacy.[29]

Role of iron supplementation in IDA[29-33]

Ferrous fumarate is a preferred option due to its higher elemental iron (33%) content and the iron form is also stable. Similarly, ferrous ascorbate is also useful in IDA management. It has better bioavailability and utilization of iron in comparison to other iron preparations.

Research has shown a mean rise of >5.0 g/dL in Hb in 60 days and >2.0g/dL in 45 days with once-daily therapy of ferrous ascorbate. It is also considered more effective than ferrous sulfate or carbonyl iron for the IDA treatment.

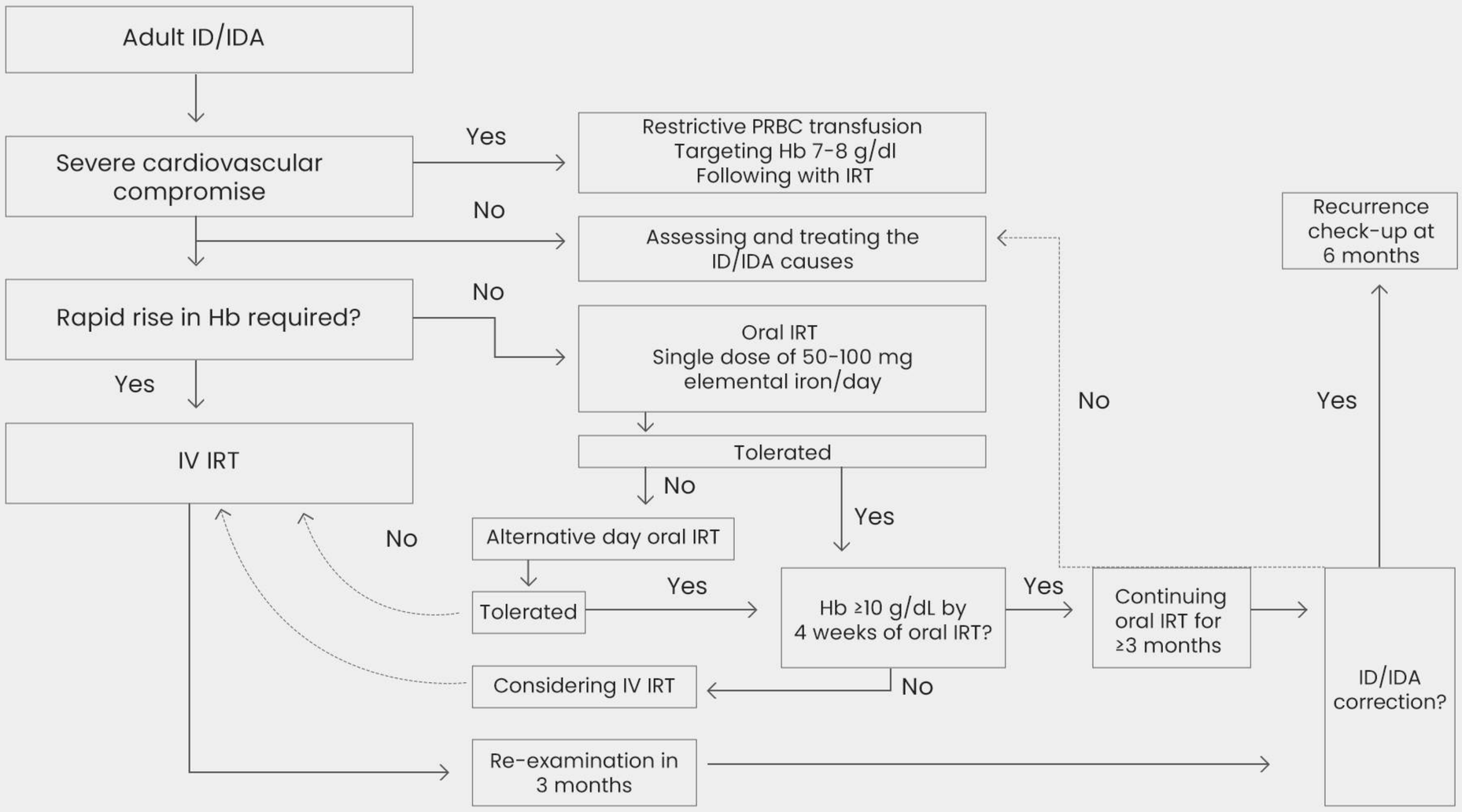
Several studies have established the relationship of zinc deficiency with IDA, particularly in preschool-aged children and women of reproductive age. Therefore, zinc concentration should be measured in such patients.

The primary mechanism is impaired iron absorption due to a decrease in zinc level, which is present in many enzymes that coordinate or catalyst the iron metabolism.

It is suggested that iron and zinc supplementation may be considered in cases of iron deficiency instead of only iron replacement, particularly in patients with severe epithelial dysfunctions.

Zinc supplementation, along with iron therapy, increases hemoglobin levels and improves iron indexes more than iron alone in pregnant women with anemia.

Potential treatment options for adult patients with ID or IDA[34]



IRT: Iron replacement therapy; PRBC: Packed red blood cells.

- Vital role of vitamin B12 in pregnancy: Vitamin B12 deficiency is common in India in pregnant women (50-70%). Cobalamin (vitamin B12), essential for RBC synthesis, nervous system function, cellular growth, and DNA synthesis, is present in active forms as hydroxo-, adenosyl- and methylcobalamin. Pre-conceptional vitamin B12 supplementation enhances maternal B12 levels, and studies have highlighted that supplementation of 50 µg/day oral B12 from 14 weeks of pregnancy until 6 weeks postpartum improved B12 level in breast milk, B12 vitamin status of infants at 6 weeks and infant cognitive function.[35, 36]

Maternal vitamin B (B6, B12) deficiency and hyperhomocysteinemia[33, 37, 38]

In India, there is limited awareness among practicing clinicians regarding the widespread prevalence of vitamin B12 deficiency. This deficiency has been linked to cognitive impairment, elevated homocysteine levels (hyperhomocysteinemia), and hippocampal atrophy.

Additionally, maternal vitamin B12 deficiency and hyperhomocysteinemia are associated with adverse pregnancy outcomes, fetal adiposity, and insulin resistance.

Research has demonstrated that supplementing with vitamin B12 (1500 µg/day) in individuals with low B12 levels leads to a reduction in homocysteine levels and improvements in cognitive function, regardless of hippocampal atrophy, at least in the short term.

Alongside vitamin B12, adequate pre-pregnancy vitamin B6 status is also crucial, as its deficiency can exacerbate hyperhomocysteinemia by impairing the transsulfuration pathway, further increasing the risk of neural tube defects and adverse pregnancy outcomes.

Non-Communicable Disease Management During the Preconception Period

Diabetes[39]

Optimizing diabetes prevention in the pre-pregnancy period involves a multi-faceted approach focusing on lifestyle modifications, early intervention, and medication adjustments. Key strategies include achieving and maintaining healthy blood glucose levels, ensuring adequate folic acid intake, managing pre-existing diabetes-related conditions, and discontinuing or adjusting medications that could harm the fetus.

Hypertension[40]

Optimizing hypertension management before pregnancy involves lifestyle changes, medication adjustments, and risk factor evaluation. Women with chronic hypertension should undergo pre-pregnancy counseling to discuss medication safety during pregnancy, lifestyle modifications, and potential risks. Specifically, ACE inhibitors and ARBs should be replaced with alternatives like Methyldopa. Additionally, low-dose Aspirin may be considered in women with risk of pre-eclampsia.

Thyroid disorders[41]

Optimizing thyroid disorders before pregnancy involves achieving and maintaining optimal thyroid hormone levels, typically aiming for a Thyroid Stimulating Hormone (TSH) level below 2.5 mIU/L. This can be achieved through medication adjustments, primarily with levothyroxine for hypothyroidism, and by monitoring thyroid function regularly. Additionally, ensuring adequate iodine intake is crucial for overall thyroid health during the pre-pregnancy period.

Epilepsy

Optimizing epilepsy management before pregnancy involves a multidisciplinary approach focusing on seizure control, minimizing the risks of foetal malformations, and ensuring adequate folic acid supplementation. This includes counseling, medication review, and seizure control strategies.[43, 44]

Mental health

Ensuring mental health of women supports and guides them towards a positive pregnancy experience and for children to be healthy and grow with optimal emotional and psychological parental bonding and wellbeing.[45]

Cardiac disorders

A patient with a diagnosed cardiac disorder should be thoroughly evaluated by a specialist before the patient can plan for a pregnancy. Necessary adjustments to medications, and lifestyle modifications are very important. The risk factors which can increase the severity of cardiac disease like high blood pressure, diabetes need to be controlled in the pre-conceptional period.[42]

Immunization and Vaccination Recommendations in Preconception Care

Preconception vaccination reduces maternal morbidity and mortality, minimizes the risk of transplacental disease transmission, and enables passive antibody transfer to the fetus and neonate. Recommended vaccines include[46]:

- **Varicella:** 2 doses spaced 4-12 weeks apart (if no prior varicella infection and no illness history)
- **MMR:** If not taken earlier, 4 doses spaced 4 weeks apart
- **HPV:** 2 doses (0, 6 months) of the quadrivalent or nonavalent HPV vaccine for children aged 9-15 years; 3 doses (0, 2, 6 months) for adults aged 15-26 years; HPV vaccination is licensed for upto 45 years
- **Hepatitis B:** 3-dose schedule at 0, 2, 6 months (if not taken earlier)
- **Japanese encephalitis vaccines:** 2 doses given in an endemic zone separated by a month

- **According to Indian Consensus guideline on adult immunization and CDC-ACIP:**
  - All women from age ≥19 up to 49 years with chronic medical condition* are recommended to get one dose of PCV13 followed by one dose of PPSV23 after 1 year.
  - In immunocompromised condition**, CSF leak and Cochlear implant cases: PCV13 followed by PPSV23 after 8 weeks is recommended.
  - One dose of PCV 20 only for all females from ≥19 up to 49 years with chronic medical condition* and immunocompromising conditions** is recommended.[47]

* Alcoholism, chronic heart disease, including congestive heart failure and cardiomyopathies, chronic liver disease, chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma, cigarette smoking, diabetes mellitus
** Chronic renal failure, congenital or acquired asplenia, congenital or acquired immunodeficiency, generalized malignancy, HIV infection, Hodgkin disease, iatrogenic immunosuppression, leukemia, lymphoma, multiple myeloma, nephrotic syndrome, sickle cell disease/other hemoglobinopathies, solid organ transplant.

Preconception counseling and hormonal contraception[48]

The mother should be counseled regarding avoiding future pregnancies until she optimizes her health. The Counseling sessions should include a discussion of all available contraceptive options. The options should be based on medical eligibility criteria of the patient.

Inter-conceptional period[49]

The mother should be advised to an avoid interpregnancy interval of lesser than 6 months. She should be Counseling on the risks and benefits of inter-pregnancy interval of 18 months.

If there is a history of prior preterm birth, short inter-pregnancy intervals should be avoided. Even if there is history of infertility, the same recommendation is given.

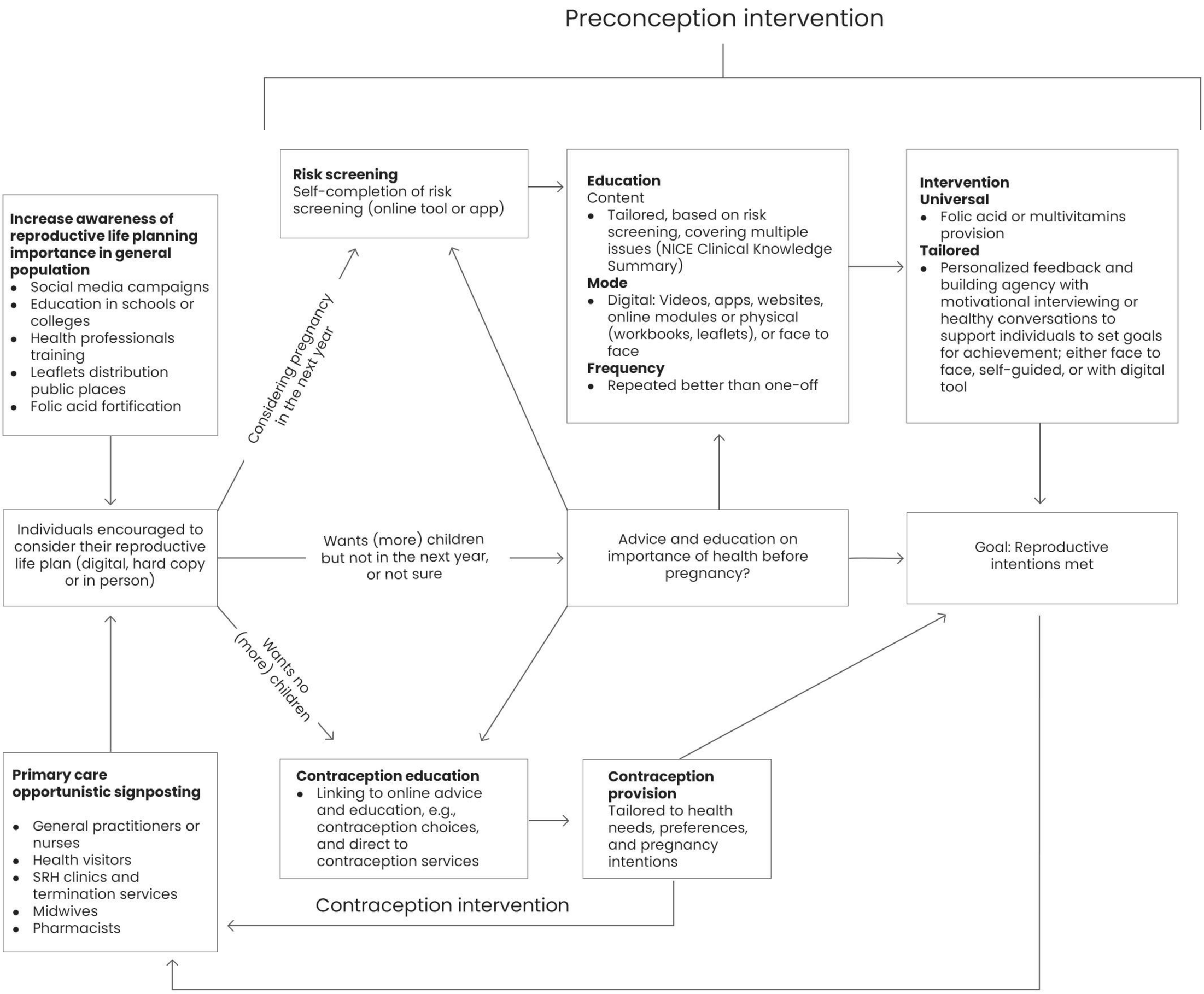
In a history of prior cesarean delivery, trial of labour in subsequent delivery with a short interpregnancy interval is associated with a higher risk of uterine rupture.

Community-Based Interventions in Preconception Care

India has a high incidence of low birth weight (LBW) neonates, often linked to maternal undernutrition. Factors such as ID, low maternal weight, and short stature can hinder fetal development and raise the likelihood of LBW. Enhancing women's health before conception through Preconception Care (PCC) has shown positive effects on birth outcome. However, India has yet to integrate PCC into its healthcare programs.[50]

Postponing childbirth, particularly, during adolescence, has been associated with improved maternal and infant health. Effective interventions may include access to contraception, health education, and personalized Counseling or sex education. These initiatives can be implemented in various setting such as schools, community programs, healthcare facilities, and broader population-based approaches.[51]

Proposed integrated, community-based model merging contraception and preconception care for managing reproductive health needs[52]



Conclusion

Health optimization before conception is important for enhancing pregnancy outcomes, as recommended by the ACOG and WHO. An organized and healthy lifestyle, including routine exercise, appropriate nutrition, and multivitamin supplementation, plays a pivotal role. Along with managing pre-existing diseases such as hypertension, diabetes, and thyroid disorders, addressing essential micronutrient deficiencies like folic acid, iron, iodine, and vitamin D is critical. Evidences recommend screening for STIs, immunizations, and genetic risks for enhancing reproductive health. Folic acid supplementation is required to prevent neural tube defects, while iron and vitamin B12 supplementation can help address anaemia, a prevalent issue among Indian women. Obesity and elevated homocysteine levels demand targeted nutritional interventions, including vitamin B6, B12, and folic acid. Community-based interventions, specifically in India, focus on addressing maternal undernutrition to decrease low birth weight rates, while access to contraception and preconception Counseling assists in reproductive health planning. Delaying childbirth and educating women on hormonal contraception further contribute to better maternal and fetal health.

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Chapter 3

Pregnancy
Navigating the Challenges of Motherhood

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Introduction to **Pregnancy Care**

Pregnancy is a journey full of profound physical, social, and emotional changes. It is a wonderful transition encompassing the various facets of life, both physiologically and psychologically. In spite of global efforts to improve maternal health, many countries face substantial challenges. Around 2,95,000 women die every year due to complications of pregnancy and childbirth, with the maximum of these deaths seen in low and middle-income countries.[1, 2] Globally, maternal mortality rate (MMR) is considered to be a critical healthcare issue which reflects upon inequalities in access to quality healthcare services. Hence, there is a compelling need to place maternal health high on global health and development agenda.[3] As per several studies, low knowledge about danger signs during pregnancy and delivery contributes to high maternal mortality ratios globally.[4] Hence, it is important to address the less discussed aspects like the multi-dimensional challenges faced in pregnancy and an obstetrician's role to show a way to address and effectively mitigate them through early detection and identification, supportive care and evidence-based intervention. In an effort to address these challenges, the United Nations, through Sustainable Development Goal 3, urged its member countries to work to reduce the maternal mortality rate (MMR) to less than 70 per 1,00,000 live births by 2030.[5]

Antenatal care (ANC) is care provided by skilled healthcare professionals to adolescent girls and pregnant women to safeguard the best health conditions for both the mother and the baby. It has components like risk identification, prevention and management of diseases, health promotion and health education.[6] Faulty care during this time breaks a critical link in the continuum of care, affecting both women and children.[7] An important aspect in addressing the gaps in providing adequate antenatal care is the role of a healthcare worker, who is necessary to provide knowledge to make pregnancy and childbirth a positive experience.

Respectful maternity care (RMC) is care provided to women during labor and childbirth ensuring their privacy, dignity, confidentiality and freedom from mistreatment/harm, and empowering them to take an informed choice.[8]

Multidimensional Challenges in Pregnancy and Their Management

Challenges faced in pregnancy

Barriers	Details
Physical	Nausea, fatigue, back pain, Heartburn, GERD, Increased urinary frequency, constipation and more severe- anemia, GDM, HDP.

Barriers	Details
Operational	Women hailing from low-resource areas and low-income countries face problems of lack of awareness and understanding of the need for early ANC, lack of access to effective ANC, long distances to healthcare facilities and poor roads, lack of means of transportation, lack of proper nutrition and diet.
Socio-cultural	Lack of knowledge about the need for ANC, health checkups, and pregnancy complications, differing perceptions of ill health, religious beliefs and role of family members in decision making affect healthcare-seeking behavior, gender-based discrimination and partner support. Women often experience mistreatment in the form of neglect, abuse, violence when trying to seek care, there is often a need to attend to domestic chores and care for children at home preventing them from seeking medical care.
Financial	Inequality and poverty play a role in seeking care; pregnancy can have a profound economic impact, especially for those from developing countries.
Psychological	• Anxiety, stress, sleep deprivation, and depression may be prevalent. • Due to hormonal fluctuations, a woman may experience bursts of emotions like mood swings & depressive episodes. • Impact on self-esteem and self-doubt due to inability to produce enough milk, fear of being incapable of meeting demands of motherhood.
Organization of health services and resource allocation	• Shortage and poor allocation of healthcare resources like essential drugs, equipment, and staff leading to an overworked, fatigued workforce, contributing to poor ANC.[9] • Mismanagement of resources by the local governments and authorities. • Lack of proper training of healthcare staff, along with disrespectful care towards expectant mothers in some places, also leads to poor ANC.

Navigating through the challenges and optimizing them

1. **Clinical Care –** Treatment of nausea, vomiting, GERD, heartburn, anaemia, GDM, HDP, liver disorders

Minor ailments in pregnancy along with interventions[6]

Nausea and vomiting	Ginger, vitamin B6, chamomile and/or acupuncture

Constipation	Wheat bran or other fibre supplements
Heartburn and epigastric pain	Diet and lifestyle modification, antacid preparations like combinations of magnesium hydroxide, aluminium hydroxide or calcium carbonate by neutralizing gastric acid, local anesthetic like oxetacaine[10, 11] and reducing acid delivery to duodenum, sucralfate, histamine-2-receptor blockers like ranitidine, proton pump inhibitors like pantoprazole
Leg cramps	Magnesium, calcium or non-pharmacological treatment options
Low back and pelvic pain	Regular exercise, support belts, acupuncture and physiotherapy
Varicose veins and edema	Compression stockings, water immersion and leg elevation

2. **Increased staffing –** Providing ANC clinics with midwives to improve ANC educational services and increasing clinical staff. A classical Cochrane study in consistency with WHO found that pregnant women who received care from a midwife had lower chances of delivering prematurely, needed fewer medical interventions like fewer epidurals and fewer episiotomies and more chances of spontaneous vaginal birth when compared to women who were cared for by obstetricians and family physicians.

3. **Quality of health services –** Improvement in health services by ensuring equitable access to medicines and medical products of assured quality, efficacy, and safety, is the need of the hour. Support and love from family and peers, self-help groups, interacting with other pregnant women, and sharing experiences. Access to mental health care needs improvisation, and it must be integrated into the ANC. Facilities for meditation, yoga, chanting and reading need to be provided. Also, ensuring adequate access to family planning services and contraception for women is critical, women having unplanned pregnancies are less likely to obtain ANC.[12] Provision of lactation specialists and sessions on breastfeeding techniques would help, along with provision of telephone service for pregnant women for their queries.

4. **Investing in Healthcare –** This must be increased to help improve data collection and to increase utilization of digital health and its tools like using social media as a means of awareness about ANC and services, which will further tackle the challenge of shortage of human resources and widen its reach to rural inaccessible areas.
   - The creation of innovative financial programs aiming at mitigating the financial barriers to ANC and increasing the coverage of such care is a must and should be central in the government's policy plans.
   - Enhance access to insurance policies considering the high cost of private maternity services.

5. **Capacity building –** It is a strategy linking the gaps between healthcare workers and their supervisors, crucial for improving healthcare outcomes. Health workers must possess appropriate knowledge and skills to identify and treat high-risk cases. It administers classroom training, mentorship, resource allocation, and on-field support. Their knowledge must be routinely monitored. Capacity-building programs like Basic and Comprehensive Emergency Obstetric and New-born Care, must be organized for various health workers, such as skilled birth attendants (SBA).
   - It enhances technical skills via means of skill labs, obstetric drills, continuing education, updates on new research and best practices, pairing them with experienced practitioners help them by acquiring adequate training.
   - Improves communication skills via counseling and education and a patient-centred approach, which involves understanding patient's needs and preferences.
   - Addresses system-level factors like resource allocation, policy, and guidelines, and coordination between different healthcare and social workers.
   - Focuses on areas to manage high-risk pregnancies, complications, postpartum-care.

Infrastructure

- Delivery points- there is a minimum benchmark of performance that needs to be maintained at delivery points, they should be strengthened via the provision of trained staff and equipment, drugs, and transport systems.
- Obstetric HDU/ ICU - they are being operated across the country for complicated pregnancies.
- MCH wings- Maternal and Child Health Wings have been sanctioned at District Hospitals and other high-load facilities to provide quality obstetric and neonatal care.

6. **Policy making and audit**

- Maximal implementation of guidelines and strategies must be ensured.
- Programs must be organized at various levels to promote health education among women and families with low levels of education to raise awareness about ANC.
- The government must ensure that all young girls and boys have access to education, which may lead to greater utilization of ANC care in the future.[13]
- Community-based interventions, facilitated by community health workers (CHW) and women's groups, can effectively strengthen ANC. These groups aim to empower and support their members.
- Specialists must be posted in rural areas to ensure the provision of adequate care.
- Provision of maternity leave.
- To improve maternity and child health services (MCH), India is promoting government programs like the Janani Suraksha Yojana (JSY) scheme, which was brought out by the National Rural Health Mission (NRHM) in 2005 to give cash support to underprivileged pregnant women.[14]
- To improve ANC care among women, the government has recently announced MCH schemes - Pradhan Mantri Matru Vandana, Pradhan Mantri Surakshit Matritva Abhiyan, and LaQshya programs.[15]
- While these initiatives are applicable and required, assessing how these programs may perform must be documented in the scientific literature to guide future MCH programs in India.

Clinical Evaluation and Screening Protocols in Antenatal Care

History taking in pregnancy

Identification & demographic data

- Name
- Age
- Address
- Contact number
- Registration number
- Religion
- Occupation
- Husband's name and occupation
- Date of first examination

Menstrual history

- Previous cycles
- Regularity
- Reliability
- Decidual bleeding
- LMP
- EDD
- POG

Obstetric history

- Gravida/parity
- Duration of married life
- Whether consanguineous
- Details of past pregnancies, parturition, puerperium, living children and delivery outcomes
- History of any infertility treatment taken

Chief complaints and history of presenting illness

- Amenorrhea
- Confirmation of pregnancy
- Nausea, vomiting
- Heart burn
- Fever with rash
- Drug intake,
- Radiation exposure
- Episode of BPV
- Urinary or bowel complaints
- Headache, epigastric pain, blurring of vision
- Swelling
- Itching, jaundice
- Leaking PV, pain abdomen, decreased fetal movements

History of present pregnancy

- Whether spontaneous conception
- Trimester wise history to be elicited
- Iron and folic acid intake
- Tetanus and influenza immunization

Past medical history

- History of DM, HTN, TB, Asthma, cancer, thyroid disorder, epilepsy, STDs, heart disease, thalassemia

Past surgical history

- History of any surgical procedure
- History of blood transfusion

Family history

- History of DM, HTN, TB, Asthma, cancer in family
- History of any congenital/genetic disorders in family
- History of any mental disorders, blood dyscrasias, multiple pregnancy

Dietary history

- Details of diet consumed

Personal and drug history

- Sleep, Appetite, Bowel, Bladder
- H/o any chronic drug intake
- H/o any habits-smoking, alcohol

Physical examination

- General appearance, Build
- Nutritional status, hydration
- Height: Short stature
- Weight, BMI
- Gait
- Pallor, icterus, cyanosis, clubbing, edema
- Oral cavity: Tongue, teeth, gums, tonsils
- Neck: JVP, thyroid, lymphadenopathy
- Breasts
- Pulse rate
- Blood pressure
- Respiratory rate
- Temperature
- Per abdomen, liver, spleen
- Vulva
- Varicosities
- Hernial sites
- Local examination-bleeding/leaking/discharge

Initial evaluation to be done at the first visit

Standard panel of investigations

- CBC with hematocrit, MCV
- ABO and Rh type and antibody screen
- Urine routine and microscopy and culture and sensitivity
- Documentation of rubella and varicella immunity
- Cervical cancer screening
- Viral markers- HIV/HbSAg/Anti-HCV/VDRL

Selective Screening

- Type 2 diabetes
- Thyroid function test
- Tests for Infection- Gonorrhea, Hepatitis A, Tuberculosis, Measles, Toxoplasmosis, Bacterial vaginosis, *Trichomonas vaginalis,* COVID-19, Herpes simplex virus, *Cytomegalovirus,* Zika virus

Trimester	Duration	Details
First	From 1-12th week of gestation	• Booking visit is the first visit a woman makes to the healthcare facility; it should be as early as possible, preferably in the first trimester. • Detailed history is taken to detect high-risk cases, to offer tailored ANC accordingly, to offer counseling in cases of unplanned pregnancy, to estimate gestational age and to perform baseline investigations.
Second	From 13-28th week of gestation	• At each visit, the patient is evaluated for signs and symptoms of pre-eclampsia, gestational diabetes. • Assess Fundal height on abdominal palpation after 24 weeks. • Auscultate fetal heart rate using a stethoscope or Doppler. • Check blood pressure, weight, hemoglobin, and urine for albumin at each visit. • Check OGTT 2 hours after 75 gm glucose between 24-28 weeks if the previous report was normal. • Second dose of inj Td to be given. • Serial monitoring of fetal growth and liquor via ultrasound and Doppler according to risk status of mother and fetus.

Trimester	Duration	Details
Third	From 29-40th week of gestation	• At each visit, the patient is evaluated for signs and symptoms of pre-eclampsia, gestational diabetes, pain abdomen, bleeding or leaking PV, perception of fetal movements • Assess Fundal height, presentation on abdominal palpation • Auscultate fetal heart rate using a stethoscope or Doppler • Check blood pressure, weight, hemoglobin, and urine for albumin at each visit • Offer Inj TdaP after 28 weeks • Serial monitoring of fetal growth and liquor via ultrasound (USG) and Doppler according to risk status of mother and fetus

Frequency of ANC visits

MoHFW 2010

- Atleast 4 visits including the first visit/registration
- 1st visit- within 12 weeks- preferably as soon as pregnancy is suspected
- 2nd visit- Between 14 and 26 weeks
- 3rd visit- Between 28 and 34 weeks
- 4th visit- Between 36 weeks and term

WHO guidelines 2016

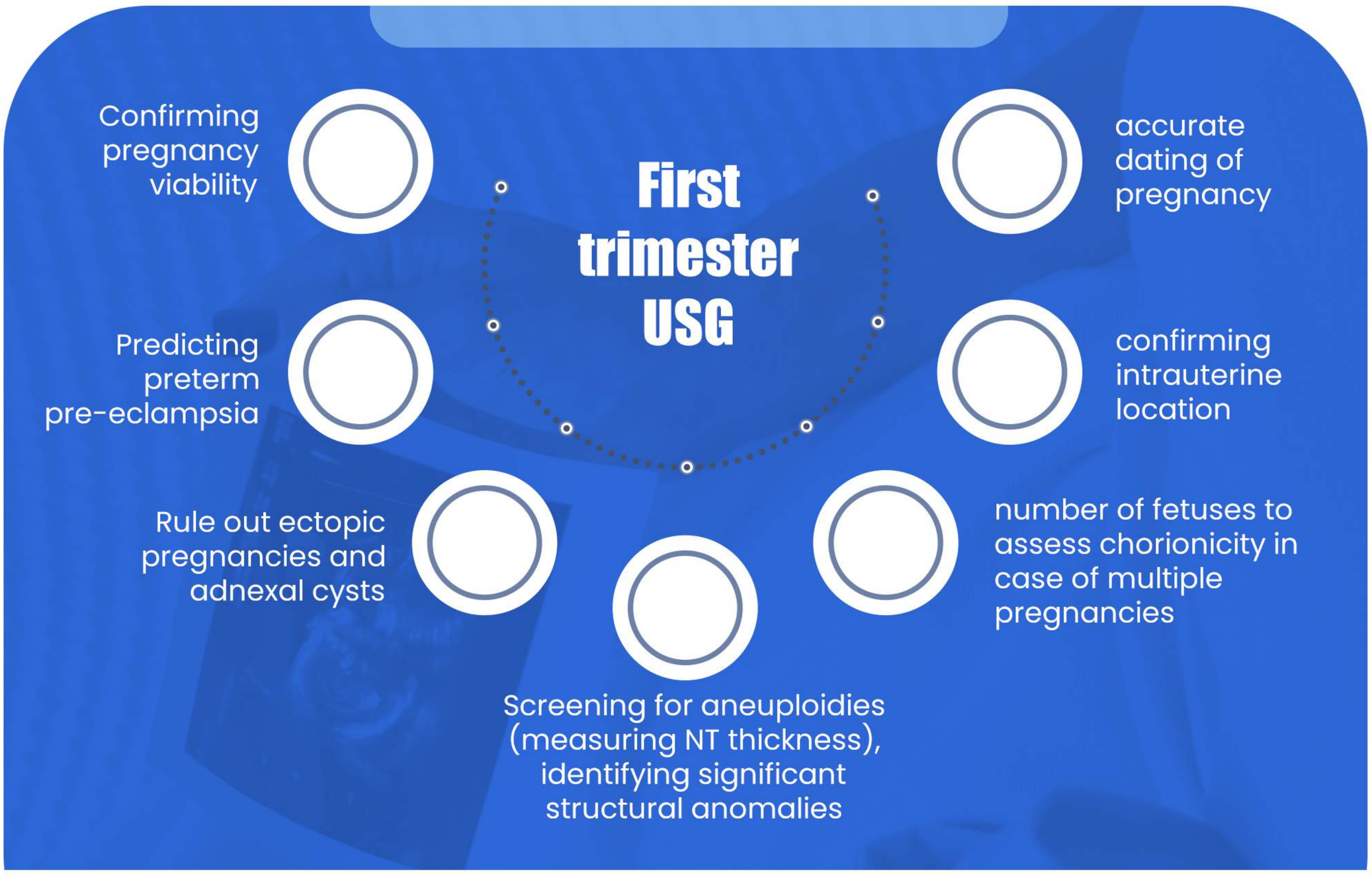
- Minimum of 8 antenatal visits for all women, regardless of parity
- One visit in the first trimester
- Two in the second trimester
- Five in the third trimester
- High risk pregnancies need additional care

ACOG recommendations 2017

- Nulliparous women with uncomplicated pregnancies (16 VISITS):
  - Every 4 weeks till 28 weeks
  - Every 2 weeks from 28 -36 weeks
  - Weekly until delivery
- Parous women with uncomplicated medical and obstetrical histories=less frequently
- Women with problems are seen more frequently, depending on the nature of the problems

NICE guidelines 2021

- 10 appointments for nulliparous women
- 7 appointments for parous women
- Each visit should have a specific purpose/goal



Timing – Best done between **11-14 weeks** of gestation if an earlier scan has not been done
Time taken during scanning should be limited, and the lowest possible power output must be used so as to obtain diagnostic information according to the ALARA (As Low As Reasonably Achievable) principle.

Danger signs in pregnancy
When a woman experiences any one of these in pregnancy, she immediately needs to be taken to the hospital.

- Fits or convulsions
- Vaginal bleeding
- Severe headache with blurring of vision
- Fast or labored breathing
- Fever
- Severe abdominal pain
- Leaking per vaginum

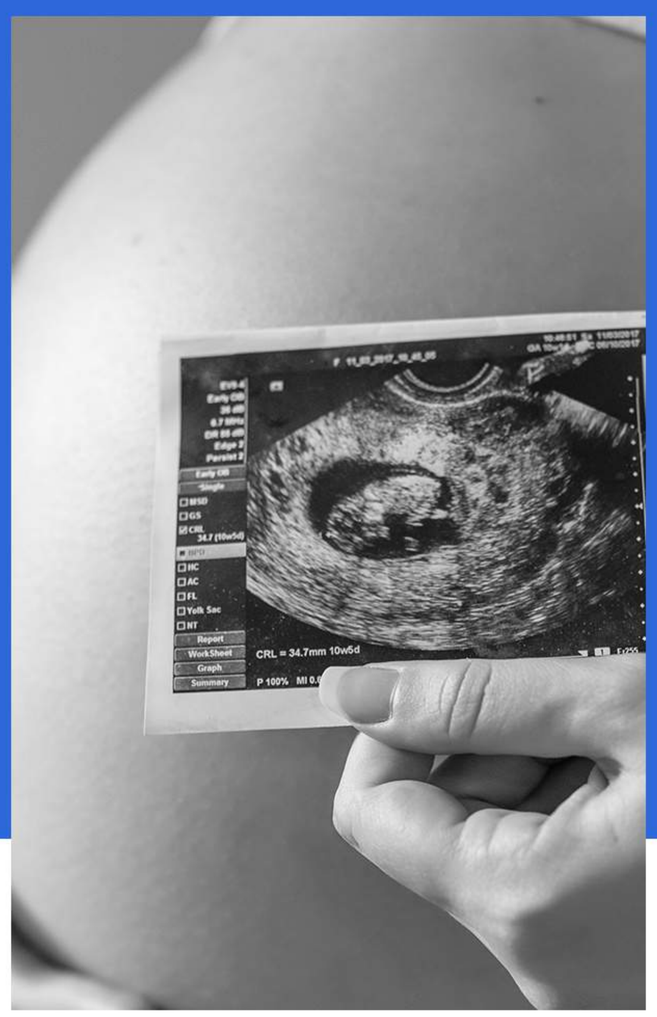
Minimum requirements for scan at 11-14 weeks' period of gestation[16]

Anatomical Region	Minimum Requirements
General	Confirm singleton pregnancy
Head and Brain	Axial view of head: - Cranial calcification - Shape/contour of cranium - Two halves of brain separated by interhemispheric falx - Butterfly sign- choroid plexuses almost filling lateral ventricles in posterior 2/3rd
Neck	Sagittal view of head and neck: confirm whether NT thickness <95th percentile
Heart	Axial view of heart at four chamber level Heart with regular rhythm

Abdomen	Axial view: Stomach visible Intact abdominal wall Axial or sagittal view: Bladder visible and not dilated
Extremities	Visualize 4 limbs, each with 3 segments
Placenta	Ascertain normal appearance without cystic structures
Biometry	Sagittal view: CRL and NT thickness Axial view: BPD

Second and third trimester USG

- Anomaly scan is done between 18 to 22 weeks of gestation to look for various structural anomalies.
- Assessment of fetal size using head circumference (HC), biparietal diameter (BPD), femur length (FL) and abdominal circumference (AC).
- Determine gestational age, if not done previously. HC or HC+FL is the most reliable to estimate gestational age after 14 weeks.
- Estimate the fetal weight, amniotic fluid index (AFI), presentation, and placental position.
- This can be supplemented with Doppler examination of vessels like uterine artery, umbilical artery, ductus venosus and middle cerebral artery.



First trimester aneuploidy screening

It mainly consists of 2 tests.

Combined first-trimester screening

- Tests for common trisomies like 21, 18, and 13, comprise around 50% of all genetic aberrations, identifiable prenatally by array-based genomic assessment. This test is also practical for Turner's syndrome. Most clinicians use a risk algorithm freely available from The Fetal Medicine Foundation to calculate the risk.[17]
- The basic algorithm involves calculating a-priori risk based on the mother's age, gestational age and maternal history of previous pregnancy affected with trisomy 21, 18 or 13 as well as NT thickness and assessment of free β-hCG and PAPP-A in maternal serum. The a-priori risk is altered by multiplying it by a likelihood ratio derived for each factor.[18, 19]
- Recent data have established that low maternal serum concentrations of PlGF at 11 + 0 to 14 + 0 weeks gestation are linked with common trisomies, proposing that PlGF can be incorporated within the risk calculation, mainly when it is used to screen for preterm pre-eclampsia.

cfDNA testing

Non-invasive prenatal testing (NIPT)
or non-invasive prenatal screening (NIPS)

- This test may be extended to include other aneuploidies, including microdeletions and microduplications.
- For trisomy 21, the cfDNA test can detect 99.7% of cases at a 0.04% false-positive rate; for trisomy 18, it can detect 97.9% of cases at a 0.04% false-positive rate; and for trisomy 13, it can detect 99.0% of cases at a 0.04% false-positive rate.[20]
- Currently, the cfDNA test is used as second-tier screening, following first-trimester combined screening.
- It is not recommended as a standalone test without performance of the 11 + 0 to 14 + 0-week scan.

Nuchal translucency (NT) thickness

NT describes the echolucent region seen at the back of the fetal neck during the sonographic assessment. NT should be measured in the midsagittal section using an image that:

- has been magnified to include only the head and thorax of the fetus
- is magnified such that callipers measure 0.1-mm increments
- allows estimation of the entire length of the nuchal region and measurement at its maximum thickness
- demonstrates the fetus separate from the amnion to ensure the appropriate space is measured
- demonstrates the fetus in a neutral position (extension or flexion of the neck affects measurement)

Three measurements will be made (on separate images), and the largest one is used for risk assessment.

Additional USG markers

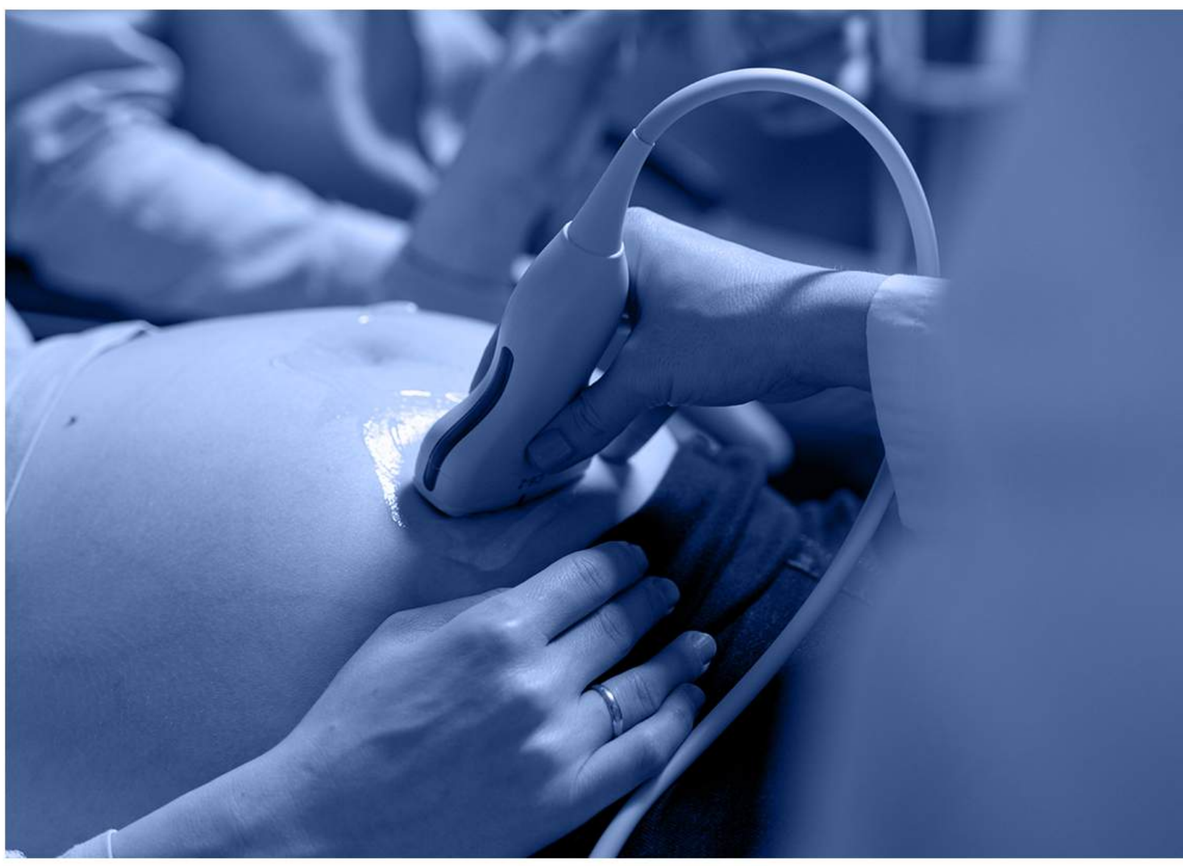
Nasal bone – The nasal bone is seen in the same midsagittal section as NT, with a magnified image that incorporates the echogenic tip of the nose and the rectangular shape of the palate anteriorly. The translucent diencephalon and the nuchal membrane are posterior to it and centrally in the brain. The nasal bone is seen beneath the echogenic skin line of the face. It is usually more echogenic than the skin at the tip and the bridge of the nose, which lies above the bone itself.[21] If the nasal bone cannot be visualized to be more echogenic than the skin above, then it is considered 'hypoplastic or absent', which is referred to when there is delayed ossification of the nasal bone at 11-14 weeks/gestation. It is a powerful marker to screen for trisomy 21. In euploid fetuses, the nasal bone is rarely hypoplastic or absent.[22]

Ductus venosus flow – Fetuses affected by aneuploidy are more likely to have structural or functional cardiac defects at 11 + 0 to 14 + 0 weeks' gestation. Functional anomalies include abnormal flow in the ductus venosus and tricuspid regurgitation. An association has been seen between reversal of the ductus venosus A-wave and aneuploidy.[23] However, more recent studies showed that increased ductus venosus pulsatility index for veins (PIV) was associated with an increased risk for common trisomies.

Tricuspid flow – Tricuspid regurgitation is defined as flow >60 cm/s for >50% of the cardiac cycle.[24] This variable is rarely abnormal in euploid foetuses. While including the additional USG markers helps improve the efficacy and specificity of screening, their application requires additional skills for reliable diagnosis. It leads to a reduction in efficacy if done poorly. Hence, most examiners continue to use a combination of NT thickness, free beta-hCG and PAPP-A.

Screening for pre-eclampsia at 11-14 weeks' scan

The most established approach to screening, namely, the first-trimester combined test for pre-eclampsia, combines the a-priori risk from maternal characteristics and medical history with measurement of UtA-PI, serum PlGF and mean arterial pressure (MAP)[25] with a risk cut-off of ≥1 in 100 to define screen positivity.[26] Women identified as being at high risk should receive aspirin prophylaxis commencing between 11 and 15 + 6 weeks gestation at a dose of 150 mg to be taken at night daily until either 36 weeks gestation, when delivery occurs or when pre-eclampsia is diagnosed In women with low calcium intake (<800 mg/day), either calcium replacement (≥1 g elemental calcium/day) or calcium supplementation (1.5-2 g elemental calcium/day) may reduce the rates of both preterm and term pre-eclampsia.[27]



Maternal Counseling for Nutrition, Physical Activity, and Risk Mitigation in Pregnancy

Counseling

1. **Diet and nutrition in pregnancy**

   It is a key modifiable factor affecting the birth outcomes and long-term effects on both the mother and the neonate.
   Balanced Diet (ICMR) comprises of:
   - Carbohydrate – 50-70%
   - Protein – 15 – 20%
   - Fat – 20 – 30% (essential fatty acid – 50%)
   - Micronutrients

Do's and Don'ts in Pregnancy

Do's	Don'ts
Increase intake of green leafy vegetable (high fiber) such as fenugreek, spinach	Avoid foods containing hydrogenated fat
Include Vit. C rich fruits like guava, orange, amla to improve iron absorption	Avoid carbonated beverages and caffeinated drinks
Include good sources of Folic Acid - legumes, nuts & green leafy vegetables	Avoid smoking, chewing tobacco or consuming alcohol
Include foods that increase daily requirement of all micro nutrients	Do not sleep immediately after having a meal
	Do not lift heavy objects or do strenuous physical activity

a. **Vitamin D supplementation in pregnancy –** Oral vitamin D supplementation is not recommended for all pregnant women. Sunlight is the most important source of Vitamin D. The Amount of time needed to be spent in the sun is not known and depends upon the time of day, amount of skin exposed, season, sunscreen use, and skin pigmentation; darker skin pigments synthesizing less Vitamin D. Vitamin D supplements may be given to women with suspected deficiency at the current recommended nutrient intake of 200 IU (5 mcg) daily. Another advice is to increase exposure to direct sunlight for at least 15 minutes for sufficient Vitamin D.[28]

b. **Iron and folic acid supplementation –** Folate deficiency may lead to some pregnancy complications, such as neural tube defects (NTD), including spina bifida and anencephaly. A daily dose of 5 mg is recommended for women with pregestational diabetes. Vitamin B9 demand for pregnant women is 400 µg/day and it is recommended to be taken for at least 3 months before pregnancy. RDA of Iron in pregnancy is 27 mg/day.

   Daily oral iron supplementation with 30 to 60 mg of elemental iron is recommended for pregnant women to prevent maternal anemia, low birth weight, puerperal sepsis and premature deliveries. **Intermittent** oral iron and folic acid supplementation with 120 mg of elemental iron and 2800 µg of folic acid once a week is recommended for women if daily iron intake is not well tolerated due to side effects.[6]

c. **Calcium –** The skeleton of a full-term baby contains around 30 g of calcium, and most of this is deposited during the last trimester of pregnancy, increasing the need for maternal calcium notably from the third trimester (calcium need ranging from 1000 to 1200 mg/day).[6] The WHO only recommends Calcium supplementation for pregnant women with low calcium intake to cut down the risk of pre-eclampsia. As per WHO, calcium can relieve pregnant women's leg cramps.
d. **Magnesium –** Requirements in pregnant women are around 350 mg/day; 80% of women have an intake of less than 300 mg/day, resulting in neuromuscular consequences like cramps. Hence, supplementation with 200 mg/day is then effective. Magnesium deficiency is associated with the occurrence of hypertensive disorders, gestational diabetes mellitus, intrauterine growth restriction, and preterm labor.[29]
e. **Iodine –** Thyroid homeostasis is essential for the development of brain tissue. Iodine requirements are increased by approximately 50% during pregnancy due to maternal thyroid stimulation by hCG, an increase in renal iodine clearance and its transfer to the fetus to synthesize fetal thyroid hormones from the second trimester. The WHO recommends iodine intake during pregnancy at 220–250 µg/day.[29]
f. **Zinc –** It is essential for many biological processes like cell division, protein synthesis and growth, and nucleic acid metabolism. Zinc deficiencies in pregnancy may lead to congenital malformations, intrauterine growth retardation, low birth weight and preterm delivery. The demand for zinc in pregnant women has slightly increased (11 mg/day); however, zinc is mainly present in meat, fish, and seafood. Zinc supplementation in pregnant women is only recommended as part of rigorous research.[30]
g. **Vitamin A –** There is a role of retinoic acid in regulating gene expression and cell differentiation. Retinol is also essential for vision and the functionality of the immune system. Vitamin A is teratogenic. The RDA in pregnancy is around 770 mcg/day. The risk of deficiency is low. There is a risk of hypervitaminosis A. Vitamin A supplementation is only recommended in pregnancy in areas where vitamin A deficiency is a serious public health concern to prevent night blindness.[30]
h. **Other B group vitamins –** RDA of Vitamin B1 & B2 is 1.4 mg/day, Vitamin B3 is 18 mg/day, Vitamin B6 is 1.9 mg/day & Vitamin B12 is 2.6 mg/day. The recommended intake of most B-group vitamins is increased during pregnancy.[30]
i. **Vitamins E and C –** WHO does not recommend their pregnancy supplementation to improve maternal and perinatal outcomes.
j. **Phosphorous –** RDA in pregnancy is 700 mg/day.
k. **Selenium –** RDA in pregnancy is 60 mcg/day.[30]
l. **Omega-3 fatty acids –** Polyunsaturated fatty acids (PUFAs) are essential for optimal brain functioning. Low intake of Omega-3 or docosahexaenoic acid (DHA) is associated with behavioural and cognitive disorders. Their dietary intake is important for brain development. The incorporation of DHA in the brain is approximately 3 mg/day during the third trimester. There is not enough data to recommend supplementation with Omega-3 fatty acids to reduce the risk of preterm labor or to prevent perinatal depression.

Recommendations for total and rate of weight gain for singleton pregnancies

Pre-pregnancy BMI	Total weight gain		Rate of weight gain, 2nd and 3rd trimester	
	Range in kg	Range in lbs	Mean (Range) kg/week	Mean (Range) lbs/week
Underweight (<18.5 kg/m²)	125-18	28-40	0.51 (0.44-0.58)	1 (1-1.3)
Normal weight (18.5-24.9 kg/m²)	11.5-16	25-35	0.42 (0.35-0.50)	1 (0.8-1)
Overweight (25.0-29.9 kg/m²)	7-115	15-25	0.28 (0.23-0.33)	0.6 (0.5-0.7)
Obese (≥30.0 kg/m²)	5-9	11-20	0.22 (0.17-0.27)	0.5 (0.4-0.6)

Source: Institute of Medicine and National Research Council of the National Academies.[5]

2. Exercise during pregnancy

- Regular physical activity throughout pregnancy has minimal risks and is known to promote many health benefits and avoid adverse outcomes. A woman practicing a form of exercise before conception can continue with it after conceiving, with some modifications due to regular physiologic changes.
- Women with uncomplicated pregnancies- encouraged to engage in strength conditioning and aerobic exercises before, during and after pregnancy.
- Activity restriction is not to be advised routinely as a treatment for preterm labor.
- At least 150 minutes of moderate-intensity aerobic activity per week is recommended during pregnancy and the postpartum period as per the 2018 update to the U.S. Department of Health and Human Services Physical Activity Guidelines.
- Duration of a session should be around 30-60 minutes, at least 3-4 (up to daily) times/ week.
- Adverse outcomes related to physical inactivity and excessive weight gain -maternal obesity, its associated complications and gestational diabetes.

Activities to be avoided

- Scuba diving
- Sky diving
- Contact sports like ice hockey, soccer, boxing, basketball
- Activities with a high risk of falling or hitting the abdomen like gymnastics, horse riding

ACOG 2015[31]

Absolute contraindications to aerobic exercise during pregnancy	Relative contraindications to aerobic exercise during pregnancy
Severe anemia	Heavy smoker
Hemodynamically significant heart disease	Anemia
Pre-eclampsia or Gestational hypertension	Extreme morbid obesity and extreme underweight
Restrictive lung disease	Poorly controlled hypertension
Multiple pregnancy	Chronic bronchitis
Cervical insufficiency or cerclage	Unevaluated maternal cardiac arrhythmia
Preterm labor in current pregnancy	Orthopedic limitations
Ruptured membranes	Fetal growth restriction in current pregnancy
Placenta previa after 26 weeks	Poorly controlled diabetes
Persistent bleeding per vaginum	Poorly controlled seizure disorder

Excercises found to be safe and beneficial

- Aerobic excercises
- Walking
- Some forms of yoga
- Dancing
- Stationary cycling
- Resistance and stretching excercies (using elastic bands)
- Water aerobics

Benefits

- Higher chances of vaginal delivery
- Lower chances of:
  - GDM
  - Hypertensive disorders
  - Excessive gestational weight gain
  - Low birth weight
  - Preterm birth
  - Cesarean section
  - Reduces risk of postpartum depression
  - Helps in weight loss post delivery, if combined with caloric restriction

When to discontinue

- Abdominal pain
- Vaginal bleeding
- Regular uterine contractions
- Rupture of membranes
- Headache
- Dizziness
- Chest pain
- Dyspnea
- Muscle weakness affecting stability
- Pain or swelling in calf

3. Travel

Car travel: Travelling during pregnancy is safe for most women.
Pregnant women should continue wearing three-point seat belts during pregnancy. The correct use of seatbelts in pregnancy:

- Above and below the bump, not over it.
- Use 3-point seatbelts with the lap strap placed comfortably low beneath the 'bump', lying across the thighs with the diagonal shoulder strap lying between the breasts.
- Adjust the fit to be as snug as comfortably possible

Tips for safe travel

- Always buckle up, try to remain seated in a moving bus, use rails for navigating till restroom, while trains comparatively have more room to walk
- Avoid long distances to avoid increased risk of venous thromboembolism
- Take repeated stops and do stretches and take short walks
- Dress comfortably in loose clothes and comfortable footwear
- Carry healthy snacks

Air travel

- In the absence of any obstetric or medical complications, occasional air travel is generally safe during uncomplicated pregnancy.
- Fetal heart rate is not affected during flight if the mother and fetus are healthy.
- Most airlines allow women to fly up to 36 weeks of gestation, avoid air travel from 37 weeks of gestation in an uncomplicated singleton pregnancy.
- Precautions same as general population need to be observed.
- Seats belts should be worn continuously while seated in case of any unexpected turbulence.
- Women with complicated pregnancies that may be exacerbated by flight conditions or require emergency care should avoid air travel.
- Supplemental oxygen should be administered to pregnant women (e.g., women with sickle cell disease, severe anemia [Hb <8 g/dL], or cyanotic heart disease) who must travel and may not tolerate the relatively hypoxic environment of high altitude flying, even in pressurized aircraft.
- Air travel is prohibited for people having certain communicable disease or have been exposed to them since that would be a threat to others, e.g., lower case active tuberculosis, COVID-19 infection.
- Fetal risks from cosmic radiation is negligible, although frequent flyers may exceed these limits.

Preventive measures against lower limb edema and thrombotic events:

- Occasional mobilization
- Periodic movement of lower limbs
- Adequate hydration
- Support stockings
- Avoid restrictive clothing

4. Sexual intercourse in pregnancy

- Generally considered safe in pregnancy.
- No increased risk of preterm labor or infectious complications has been associated with sexual activity unless a sexually transmitted infection is acquired.
- In the absence of pregnancy complications like vaginal bleeding, ruptured membranes, and preterm cervical dilatation, there is insufficient evidence to recommend against sexual intercourse during pregnancy.
- Some obstetricians advise abstinence in the last 4 weeks of pregnancy for fear of ascending infection.

5. Hair dyes and other cosmetic products

- Exposure to hair dyes or hair grooming/styling products results in minimal systemic absorption unless the skin over the scalp is compromised by disease. Therefore, these chemicals are unlikely to cause adverse fetal effects in women with a normal scalp.
- Plant-based hair dyes are probably safe and usage of ammonia- and peroxide-based products can be avoided owing to the wide availability of non-ammonia-based products.
- One should avoid using new products during pregnancy since skin sensitivity is more common.

6. Employment

- Physically exhausting work may increase the risk of preterm labor, growth restriction and hypertensive disorders during pregnancy.
- Any occupation that increases physical strain on the body must be avoided.
- Adequate periods of rest are advised between work hours.
- Avoid continuing work until undue fatigue develops
- Women with high-risk factors in pregnancy, like the history of preterm labour, must minimize physically demanding work.
  Those women with uncomplicated pregnancies can continue working till labor onset.

7.Bathing

- Early pregnancy- exposure to hot water at 100 degrees F or higher in a tub may increase the chance of miscarriages and neural tube defects.
- Late pregnancy- pregnant women may have difficulty in balancing due to weight gain, leading to an increased risk of falling/ slipping while bathing.

8. Clothing and footwear

- Pregnant women should avoid tight-fitting garments; loose, airy cotton clothes should be worn.
- Footwear should be comfortable with good arch support, and high heels should be avoided since they increase lumbar lordosis, leading to strain on the back and an increased risk of falling.
- Proper breast support must be ensured to avoid pendulous and painful breasts.

9. Alcohol intake

- Alcohol consumption leads to adverse effects throughout pregnancy.
- There is no exact dose-response relationship between the amount of alcohol consumed and the extent of damage caused by alcohol in the infant.
- Abstinence from alcohol is advised from conception and throughout pregnancy.
- Identification and Counseling of women taking alcohol can decrease intake during pregnancy.
- For pregnant women consuming alcohol who are not heavy drinkers, a brief intervention like motivational counseling or educational sessions is advisable.
- Heavy drinkers, on the other hand, should be referred for professional advice and treatment.

10. Cigarette smoking

- It is to be avoided entirely during pregnancy.
- Risks due to first/second-hand smoke: spontaneous pregnancy losses, preterm delivery, growth restriction, low birth weight, preterm rupture of membranes, placenta previa and abruption, and stillbirth.
- The five A's (ask, advise, assess, assist, and arrange) provide a general approach to helping patients stop smoking.
- For women who are heavy smokers and are unable to quit on their own, drug therapy is suggested. Both nicotine replacement therapy and bupropion are reasonable drug options.

11. Immunization in pregnancy

- Tetanus schedule- Tetanus and diphtheria (Td, adsorbed) is advisable
  – 0.5 ml deep IM in the upper arm
  – Early in pregnancy- first dose

- 4 weeks after 1st dose- 2nd dose
- Pregnancy conceived within 3 years of last pregnancy with completed two doses of tetanus vaccine- Booster dose
- TdaP - can be given as a second dose instead of TT or Td between 28-36 weeks since maternal anti-pertussis antibodies are short-lived, to maximize fetal transfer

- Inactivated influenza vaccine (quadrivalent)
  - Dose- 0.5 ml IM, given any time in pregnancy, important to give between Oct and Jan.
- COVID 19 vaccine
  - Pregnant women can choose to take the vaccine or not

Vaccination befor pregnancy	Vaccination during Pregnancy	Vaccination contraindicated in pregnancy	Vaccination under special circumstances
• MMR • Varicella • Sickle cell disease/ splenectomy- pneumococcal, meningococcal, *H.influenza*	• Td • TdaP ((tetanus, diphtheria and pertussis) • Influenza	• Herpes zoster • Varicella • BCG • MMR • HPV	• Hepatitis A, B • Meningococcal • Pneumococcal • Yellow fever • Rabies • Typhoid

Global regulatory authorities such as US FDA and EMA have approved RSV prefusion F protein vaccine for providing passive protection against lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus in infants from birth through 6 months of age following maternal immunization during pregnancy.[32]

Future Direction: RSV is one of the commonest respiratory viral etiologies across the age groups contributing to 29% of total respiratory related infections in India. Having an RSV vaccine in our armamentarium will be helpful in reducing the burden of RSV-related hospitalizations and mortality in infants and adults.

Recent Advances in **Antenatal and Intrapartum Care**

Intrapartum monitoring

This is an eminent part of the process of labor to ensure a good perinatal and maternal outcome. When the process of labor begins with the onset of strong and repetitive uterine contractions, this compromises the blood supply to the fetus due to the collapse of spiral arterioles and repetitive squeezing of blood vessels within the umbilical cord, posing a threat to fetal oxygenation. This puts the fetus under stress, making it prone to fetal acidosis. Hence, intrapartum fetal monitoring aims to timely identify when the fetus is at risk based on prompt recognition of features signaling the onset of fetal decompensation on cardiotocograph (CTG), to ensure timely obstetric intervention, to help avoid hypoxic ischemic encephalopathy (HIE) or perinatal deaths.

The methods of fetal monitoring are as follows

1. Intermittent auscultation

- Offer women with a low risk of complications when in the established first stage of labor using either a stethoscope or Doppler ultrasound (USG).
- Perform immediately after a palpated contraction for at least 1 minute, repeated at least once every 15 minutes.
- Once the woman has signs of or is in the confirmed second stage of labor, perform intermittent auscultation for at least 1 minute, repeated at least once every 5 minutes.

2. Cardiotocography (CTG)

- Advise continuous CTG monitoring if:
  i. there are continuing fetal heart rate concerns with intermittent auscultation, or
  ii. intrapartum maternal or fetal risk factors develop.
- Continuous CTG monitoring is used to monitor the fetal heart rate and labor contractions.
- A normal CTG trace implies that the baby is coping well with labor.
- Changes to the baby's heart rate pattern during labor are common and do not usually cause concern.

But they may represent developing fetal hypoxia, so continuous CTG monitoring is advised if these occur. The 4 features of the cardiotocography trace are classified as white, amber or red indicating increasing levels of concern and use alongside consideration of the presence of accelerations and classify the overall CTG trace.

Categorization of CTG traces (all stages of labor)

Features of Intrapartum CTG	White	Amber	Red
Contractions (Use a tocodynamometer to record contraction frequency and length).	<5 contractions in 10 minutes	>/=5 contractions in 10 minutes or Hypertonus	
Baseline fetal heart Rate (Determined by looking at the mean fetal heart rate, excluding accelerations and decelerations over 10 minutes when the fetal heart rate is stable. To decide whether there is any change in the baseline, compare it with earlier CTG traces.	Stable baseline of 110 -160	Increase in baseline FHR of >/= 20 beat/minute from the start of labour or since the last review an hour ago, or • 100-109 beats/minute), or • unable to determine baseline	• <100 beats/minute, or • >160 beats/minute
Variability (It is determined by noticing the minor oscillations in the fetal heart rate, which generally occur at 3 to 5 cycles a minute. It is measured by estimating the difference in beats per minute between the highest and the lowest heart rate in a 1-minute segment of the trace between contractions, excluding accelerations and decelerations.	5 - 25 beats/minute	• < 5 beats/minute for between 30 and 50 minutes, or • > 25 beats/minute for up to 10 minutes	• <5 beats/minute for more than 50 minutes, or • > 25 beats/minute for more than 10 minutes, or • sinusoidal

Decelerations (Defined as transient episodes when the fetal heart rate slows below the baseline level by more than 15 beats a minute, each lasting 15 seconds or more. An exception is in a trace with reduced variability, where decelerations may be shallow. Described as early, variable or late.	No decelerations, or early decelerations, or variable decelerations that are not evolving to have concerning characteristics	• repetitive variable decelerations with any concerning characteristics for <30 minutes, or • variable decelerations with any concerning characteristics for >30 minutes, or • repetitive late decelerations for <30 minutes	• repetitive variable decelerations with any concerning characteristics for > 30 minutes, or • repetitive late decelerations for > 30 minutes, or • acute bradycardia, or a single prolonged deceleration lasting >/= 3 minutes

When determining the importance of decelerations in fetal heart rate, consider

- Their timing (early, variable or late) associated with the peaks and duration of the contractions
- The period of the single deceleration
- Whether the fetal heart rate returns to the baseline heart rate or not
- Whether they occur with >50% of contractions (called as repetitive)
- Whether shouldering is seen
- The variability within the deceleration

The following are the concerning characteristics of variable decelerations:

- Lasting >60 seconds
- Reduced variability within the deceleration
- Failure or slow return to baseline fetal heart rate

They are transient increases in fetal heart rate of 15 beats/minute or more, lasting 15 seconds or more.
Consider the following when evaluating accelerations:
o the presence of accelerations, even with decreased variability, is usually, a sign that the baby is healthy
o the absence of accelerations on an otherwise typical CTG trace does not indicate fetal acidosis.

Categories of CTG traces based on each of the above 4 features and on their scoring as white, amber or red, as follows[33]:

Normal	No amber or red features (all 4 features are white)
Suspicious	Any 1 feature is amber
Pathological	Any 1 feature is red, or 2 or more features are amber

CTG based management- NICE guidelines 2022

Normal

Continue CTG and hourly assessment

Suspicious

If no concerning risk factors

- Full risk assessment
- Acidosis is unlikely if accelerations are present
- Compare with prior CTG trace
- Conservative measures

Conerning intrapartum risk factors present

- Full risk assessment
- Determine underlying cause, conservative measures
- Fetal Scalp Stimulation- if accelerations+ and improving CTG- monitor, if no acceleration- expedite delivery

Pathological

- Exclude acute events like cord prolapse, abruption, uterine rupture
- Assessment of risk factors
- Determine possible underlying cause, conservative measures

In acute bradycardia/single prolonged deceleration for >/= 3 minutes

- Prepare for urgent delivery
- Establish cause- conservative measures
- If persists-expedite delivery

3. Fetal scalp blood sampling (FBS)

- There is an apparent lack of appreciation that the skin of the fetal scalp is a non-essential peripheral tissue that undergoes catecholamine induced vasoconstriction in the early stages of the fetal stress response, and therefore, fetal scalp blood sampling (FBS) does not reflect the oxygenation of fetal central organs.
- Recent Cochrane Systematic reviews have highlighted a lack of evidence of any improvement in long-term outcomes or reduction in operative deliveries associated with FBS use.

4. Fetal pulse oximetry

A Cochrane Systematic Review has concluded that fetal pulse oximetry does not reduce operative interventions, and this is likely because, similar to FBS, it attempts to determine the oxygenation of fetal skin, which is a peripheral non-essential tissue and has no correlation with oxygenation of fetal central organs.

5. Fetal scalp stimulation (FSS)

- If the CTG trace is suspicious, risk factors for fetal compromise are present, consider digital fetal scalp stimulation. If this leads to an acceleration in fetal heart rate and an improvement in the CTG trace, monitor the fetal heart rate and clinical picture.
- The absence of an acceleration in response to fetal scalp stimulation is a concerning sign that fetal compromise may be present, and that birth must be expedited.

6. Fetal electrocardiograph (ECG) using ST-Analyser (STAN)

STAN is the only adjunctive test that assesses the oxygenation of a fetal central organ (i.e., myocardium). It is based on the computer- sized analysis of the biochemical changes during anaerobic metabolism within the myocardium, using the fetal ECG as a surrogate marker of hyperkalemia due to cardiac glycogenolysis.

Fetal growth restriction

- All women must be assessed for SGA and FGR risk factors at their booking visit, and their surveillance frequency must be determined.
- Women at risk of pre-eclampsia to start aspirin 150 mg at night from 12-36 weeks of gestation to help prevent SGA and FGR.
- USG fetal biometry is advised every 2 weeks in SGA fetuses and umbilical artery doppler is also to be done two weekly.
- In fetuses with EFW lying between the 3rd and 10th percentile, the presence of other high-risk features are necessary to recommend birth earlier than 39 weeks of gestation.
- In pregnancies complicated by late-onset FGR, birth should be started by 37 weeks and completed by 37+6 weeks of gestation.

Based on **risk of FGR**

Low risk	Moderate risk	High risk
Serial assessment of symphysio-fundal height (SFH) needs to be carried out every 2 weeks from 24 weeks of gestation.	Serial assessment of fetal growth via ultrasound every 4 weeks is to be done from 32 weeks of gestation until birth.	Uterine artery dopplers should be done from 18-23+6 weeks of gestation. If doppler and biometry is normal at midtrimester scan- do serial scans for biometry from 32 weeks and if it is abnormal, start scans from 24-28+6 weeks of gestation.

Postpartum hemorrhage (PPH)

According to ACOG, it is defined as a blood loss of more than or equal to 1000 ml, accompanied by features of hypovolemia within 24 hours of delivery.

Carbetocin

It is a newer synthetic analog of natural oxytocin

With some structural modifications, stable at room temperature

Increasing its half life to 40 minutes, compared to oxytocin i.e. 4-10 minutes, increasing duration of action from 1.5 hours of oxytocin to 5 hours

Advantages
- Simpler to use
- Avoids multiple injections
- Significantly reduces PPH
- Decreases need for uterotonics and other hemostatic measures

Dose
100 mcg IV/IM
Adverse effects
- Generally well tolerated, vomiting, abdominal pain, headache

Contraindications
- Hepatic or renal disorders
- Epilepsy
- Severe cardiovascular disorders
- Hypersensitivity
- Not used in labor induction

WHO recommended the use of room-temperature stable carbetocin for PPH prevention, where its cost is similar to other uterotonics.[34]

Telemedicine

This innovative approach incorporates technology with medicine, being a development in the field of obstetrics and gynecology, revolutionizing prenatal care with various benefits like:

- **Increased access** to remote and inaccessible areas.
- **Decreased cost** of transportation, and **increased convenience** and comfort for pregnant women.
- Remote monitoring of pregnancies and fetal growth to identify concerning signs and symptoms timely.
- Promotion of **educational opportunities** virtually like seminars, workshops, patient awareness sessions.
- **Continuous care** for patients, reduction in loss of follow-up.

Various challenges

- Privacy concerns- protecting patient data and ensuring encryption methods are important.
- Diagnostic limitations due to lack of examination and diagnostic tests requiring the patient's presence.
- Technological aspects due to limited and poor access to the internet in some areas.
- Doctor-patient relationship is compromised due to no face-to-face interactions.
- Problems in medicolegal aspects like liability in case of adverse reactions and reimbursement policies.

Artificial intelligence (AI) in pregnancy

The healthcare sector is dynamic and has welcomed growth in care related to artificial intelligence. It aims to interpret patient data effectively, enhance diagnosis, reduce human involvement and costs, and improve patient outcomes.

Various examples include:

1. Predictive analytics: By processing patient data, AI can help in assessing risks of various conditions like pre-eclampsia, aneuploidies, and FGR by incorporating patient data, medical history, genetic and lifestyle factors.
2. Diagnostics: AI-powered tools help in the analysis of medical images, particularly in obstetric ultrasound and MRI scans, biometric measurements, and anomaly detection, improving diagnostic accuracy, reducing workload for ultrasonologists, and reducing the time taken per scan.
3. Workflow automation: AI helps automate tasks and patient records, thus allowing the staff to focus more on patient care instead.
4. Personalized medicine- AI can help in tailoring treatment plans according to different individuals like diet plans, medicine regimens, exercise plans.
5. Decision making- AI can help clinicians in decision-making by providing real-time insights and can guide medical professionals through complex procedures.
6. Psychological support- AI-powered virtual support groups and chatbots help reduce feelings of isolation and help new mothers.
7. Postoperative rehabilitation- AI-powered tools can help in monitoring recovery, detecting postoperative complications, and provide rehabilitation programs leading to faster recovery.

Applications of AI in obstetrics

- AI in CTG monitoring- AI has been incorporated to interpret the results of CTG via Computerized CTG to ensure consistency among interpretations. Also, since conventional CTG requires regular observation periods to detect suspicious patterns, AI systems overcome human limitations of bias, fatigue, distraction, poor communication, or fear of harm. More advanced computer systems will come into play that automatically analyse CTG in the future.
- AI in USG- AI-based tools have higher performance in measuring dimensions, identifying the placental appearance of women with the risk of developing HDP.
- AI in fetal ECHO- Fetal cardiac function monitoring with USG is challenging due to involuntary fetal movements, the small size of the heart, the fast heart rate and lack of expertise. Hence, AI is beneficial here in automatically calculating the fetal heartbeat.
- AI in MRI- majorly used in the detection of placenta accreta spectrum and fetal brain conditions.
- AI in maternal health monitoring- AI assesses maternal health by analysing vital signs like heart rate and blood pressure, biomarkers like cytokines, and diagnostic tests like blood glucose levels. AI-powered remote monitoring devices are available, too.By embracing AI, prenatal care becomes less burdensome for practitioners and more beneficial for patients.

Conclusion

Having realized that maternal morbidity and deaths have been attributed to complications that are preventable and could be reduced if women have access to relatively basic maternal health education and services that will help them to increase their awareness and recognize signs of danger and act accordingly. Efforts should be made to strengthen ANC quality and services for better maternal and fetal outcomes. Emphasis must be to concentrate on various domains that lead to poor ANC and ensuring respect which will be the beginning of the continuum of care for mother and child.

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Chapter 4

Post-Pregnancy
Restoring and Maintaining Health

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Introduction to **Common Postpartum Concerns**

Post-delivery days are regarded as a crucial timeframe for both a mother and her child, as this period significantly influences their immediate and long-term health and well-being. The puerperium (also referred to as the postpartum period) begins with the expulsion of the placenta and continues until the complete physiological recovery of various organ systems is achieved. Notably, the fourth stage of labor is traditionally defined as the immediate postpartum period following the delivery of the placenta, typically extending up to the first 24 hours. This period is critical for monitoring the mother for early postpartum complications, such as hemorrhage or hemodynamic instability, and is clinically considered to conclude at 24 hours post-placental delivery.

Throughout the postpartum period, women experience a range of social, physical, and psychological changes. Emotional struggles are common as a new mother adapts to the physical and emotional demands of caring for a newborn. Often referred to as baby blues, symptoms of postpartum depression (PPD) and postpartum anxiety (PPA) can range from profound sadness and irritability to feelings of hopelessness and detachment from the child. These emotional changes are largely influenced by hormonal fluctuations.[1-4]

Common **postpartum concerns**[5]

Category	Conditions/Diseases
Potentially non-life-threatening conditions	- Urinary tract infection (UTI) - Mastitis - Wound infections - Breastfeeding disorders - Incontinence - Pelvic floor dysfunction - Postpartum thyroiditis
Potentially life-threatening conditions	- Severe hemorrhage (immediate postnatal period) - Hypertensive complications (early postnatal period) - Infections (early postnatal period) - Thrombosis/embolism (throughout puerperium) - Complications from preexisting diseases (e.g., cardiac disease)

Postpartum Recovery: **Physiological, Psychological, and Nutritional Dimensions**

Anticipatory guidance must start during pregnancy by creating a postpartum care plan that supports both the transition to parenthood and ongoing well-woman care. The timing of a thorough postpartum visit should be personalized and centered around the mother's needs. Recognizing and addressing the hormonal and emotional aspects of the postpartum period is crucial for a smooth and successful transition into motherhood.

Physiological recovery

Hormonal fluctuations: Estrogen (estriol) and progesterone are most well-studied hormones. Physiologic shifts of key hormones estrogen, progesterone, oxytocin, prolactin, and thyroid hormones occur after childbirth. During pregnancy, hormones rise steadily, whereas after delivery, levels drop swiftly. This sudden decline is undeniably obligatory but may cause different symptoms, such as mood swings, irritability, hot flashes, vaginal dryness, sleep disturbances, loss of libido, breast pain, extreme fatigue, postpartum depression and brain fog.

Studies on women with a history of PPD but no other affective disorders found that prophylactic oral heterogenous estrogen, given immediately after delivery to prevent estrogen withdrawal, helped most women remain well throughout the postpartum period and the first year after birth.[6]

Vital role of oxytocin and prolactin

Oxytocin	Prolactin
Uterine contractions, essential uterus shrinkage to pre-pregnancy size	Levels rise after childbirth
Postpartum bleeding reductions	Stimulates milk production
Release of milk from the breasts	Contribute to mood swings (however, balanced by Oxytocin)
Counteracts emotional challenges	Linked to mild rises in serotonin and dopamine

By recognizing the functions and interplay of these hormones throughout pregnancy and postpartum, healthcare providers can more effectively support maternal physiology during the recovery period.[2]

Uterine involution: Monitoring for incomplete involution and abnormal bleeding[7, 8]

Bleeding and disturbances of uterine involution are the prevalent and severe complications in the post-placental phase.

Uterine involution, or uterine contraction, is the process by which the **uterus returns to its pre-pregnancy state**, ultimately weighing approximately 60 grams.

Recent advances in monitoring

The postpartum uterine ultrasonographic scale (PUUS) is a novel tool for assessing uterine involution in all patients, irrespective of mode of delivery.

Oxytocin role

As uterine contractions influence uterine involution and a hormone important for strengthening and regulating uterine contractions is Oxytocin. Oxytocin can be provided either through oral, intra-nasal, intramuscular, or by massage that stimulates the hormone oxytocin release.

Discomfort management: **Lochia, perineal tears, and pelvic floor rehabilitation**[2, 3, 9-11]

Postpartum challenges can impact the overall childbirth experience. Perineal trauma is a common occurrence following vaginal birth, affecting nearly 90% of women. Additionally, lochia, a vaginal discharge originating from the uterus, cervix, and vagina, may persist for up to 5 weeks postpartum.

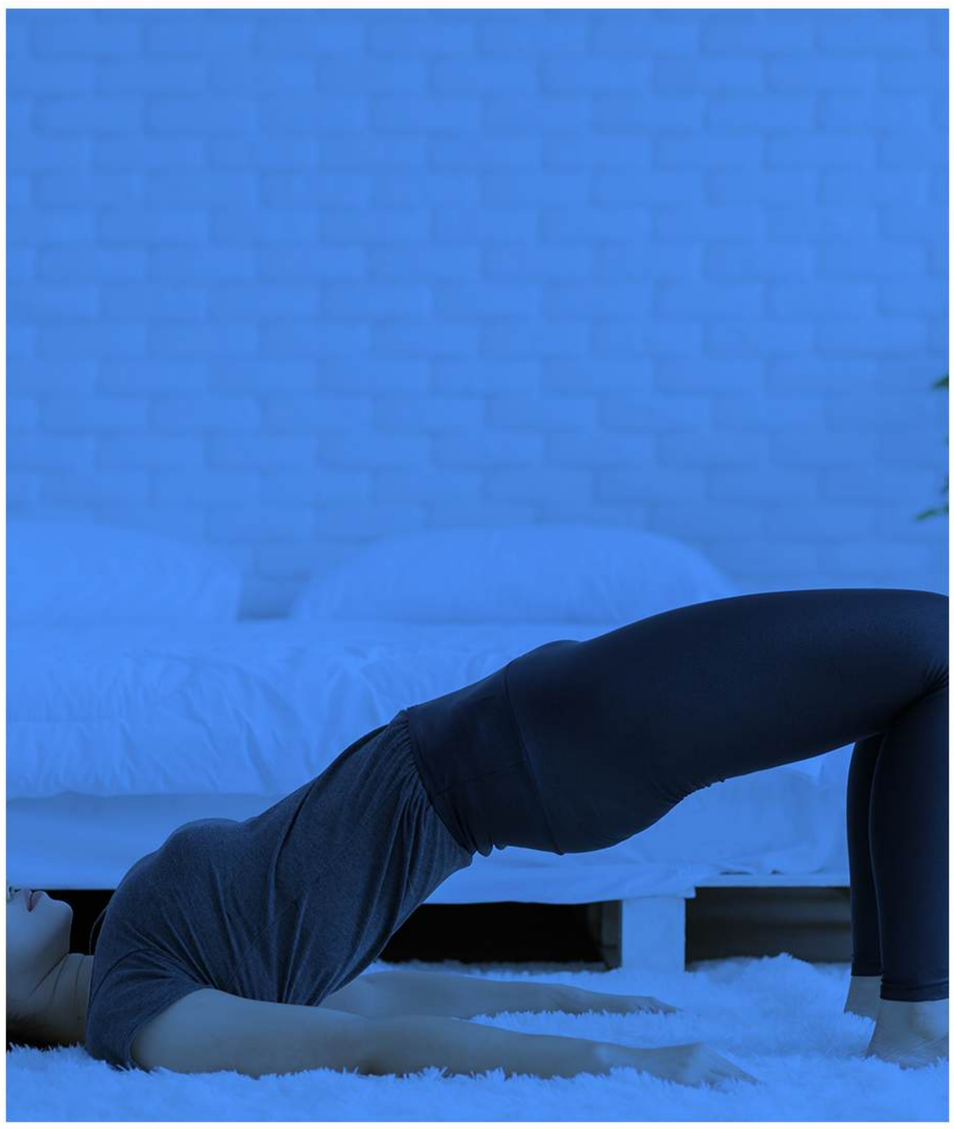
Tear management

- Best treatment includes continuous locking sutures using chromic catgut or polyglactin, with the cervix stabilized by atraumatic forceps.
- Fragile vaginal mucosa that cannot be sutured must be tightly packed for 12 to 24 hours.

Pelvic floor rehabilitation

Vaginal birth results in pelvic floor trauma, causing significant damage to both muscle and nerve tissues. Postpartum pelvic floor recovery is crucial.

- Gentle exercises, such as the Kegel exercise, can help restore pelvic strength and function.
- Other professional interventions include pelvic physical therapy or chair treatments.



Weight management and nutritional recovery

Reversal of gestational weight gain[11, 12]

The childbearing years are a crucial phase in a woman's life, often leading to significant weight gain. Weight gain before, during, and after pregnancy is a key factor in the later development of obesity, which can elevate the risk of heart disease, diabetes, and hypertension in midlife and beyond.

Weight management program for whom?

BMI of all postpartum women must be assessed at 6 weeks.

- Postpartum women with BMI >23 kg/m^2 at 6 weeks must undergo a weigh management program.
- Women with normal BMI (18.5-22.9 kg/m^2) can adopt lifestyle measures
  if they have:
  - Retained >4-5 kg as compared to pre-pregnancy weight
  - Waist circumference >80 cm
  - Waist-to-hip ratio >0.81
  - Body fat composition >30%.

Weight management advice

- Moderate-intensity aerobics for at least 150 min per week, excluding the warm-up and cool-down time and minimum of 10-min bouts per session, can be followed.
- Exercise prescription (4 weeks after normal delivery and 6 weeks after a C-section):
  Includes walking, deep breathing with abdominal contraction, Kegel exercises, and more extensive program (6-8 weeks later).
- Breastfeeding women need about 500 calories more than a non-pregnant woman.
- Iron and vitamin D supplementation should be ensured and caffeine consumption must be limited.
- Dietary calcium is important for offspring for bone/teeth formation, breast milk secretion and osteoporosis prevention.
- Galactagogues must be high in green leafy vegetables and whole grains. For calorie restriction, fat and sugar must be lowered.

Postpartum mental health management strategies[13]

Most pregnant women are excited about their pregnancy and start weaving dreams, even before a child is born, of motherhood in eagerness and anticipation; however, some mothers, during pregnancy or after childbirth, develop a certain kind of unhappiness or dissatisfaction about their motherhood journey.

Postpartum mood disorder classification

Baby blues	Short-lived mood fluctuations
Postpartum anxiety disorder	Generalized anxiety disorder (GAD), panic disorder, and OCD
Postpartum depression (PPD)	Sadness, hopelessness, and losing interest in previously enjoyed activities
Postpartum psychosis	Hallucinations, delusions, and disorganized thoughts

Screening and assessment tools

Edinburgh postnatal depression scale (EPDS)

- Reliable self-report questionnaire for identifying mothers at risk of PPD
- Explore mood dimensions and emotional symptoms (sadness, anxiety, and irritability)
- Quantifies symptoms severity
- Simple interpretation

Postpartum depression screening scale (PDSS)

- Incorporates various emotional, cognitive, and physical symptoms
- Formulated questions aid in understanding emotional state complexity of mother
- Multidimensional approach improves assessment accuracy, and provide detailed information of mother's mental well-being

Treatment

Preventive measures	Psychotherapy options (Fundamental cornerstone)	Pharmacological interventions
• Prenatal education and preparation • Lifestyle modifications regular physical activity during both pregnancy and postpartum; certain nutrients (omega-3 fatty acids and B vitamins) alleviate mood regulation and mental clarity	• Cognitive-behavioral therapy (CBT) • Interpersonal therapy (IPT)	• Antidepressants and anti-anxiety medications • Selective serotonin reuptake inhibitors (SSRIs) (forefront medicine)

Early Warning Systems for **Detecting Severe Maternal Complications**[14, 15]

- Infections and sepsis are major contributors to illness and death among women during pregnancy and after childbirth.
- The Maternal Early Warning Score (MEWS) is a widely used bedside screening tool that monitors vital physiological signs. When certain thresholds are exceeded, it prompts immediate evaluation by a healthcare provider.

Physiological parameters	Normal values	Yellow alert	Red alert
Respiratory rate	10-20 breaths per minute	21-30 breaths per minute	<10 or >30 breaths per minute
Oxygen saturation	96-100%	–	< 95%
Temperature	36.0-37.4°C	35-36°C or 37.5-38°C	<35°C or >38°C
Systolic blood pressure	100-139 mmHg	150-180 mmHg or 90-100 mmHg	>180 mmHg or <90 mmHg
Diastolic blood pressure	50-89 mmHg	90-100 mmHg	>100 mmHg
Heart rate	50-99 bpm	100-120 or 40-50 bpm	>120 or <40 bpm
Neurological response	Alert	Voice	Unresponsive, pain

Triggers in the MEWS system are designed to facilitate earlier detection of conditions that may increase the risk of maternal complications and death, such as cardiovascular disorders, infections like sepsis, blood clots, excessive bleeding, and pre-eclampsia. MEWS serves as a support tool for clinical decision-making but is not a substitute for professional medical judgement.

Management of Postpartum Hemorrhage (PPH), **Lactation Support, and Contraceptive Counseling**

PPH: An overview of management

Definition

- A cumulative blood loss of ≥1000 mL or blood loss along with signs or symptoms of hypovolemia within 24 hours after childbirth.

- **Following are the causes**[16]

Placental complications	Placenta previa and placenta accreta
Uterine atony	Due to uterine overdistension (multiple pregnancies, polyhydramnios, or a large fetus), prolonged labor, induction of labor, oxytocin use, and anesthesia

Genital tract trauma	Ruptured uterus; cervical, vaginal, or perineal lacerations; episiotomy; forceps delivery
Coagulation disorders	Inherited bleeding dysfunction, such as von Willebrand disease; anticoagulant therapy; thrombocytopenia; liver dysfunctions; disseminated intravascular coagulopathy

Management

The primary focus is on resuscitation and determining the underlying cause of hemorrhage. Further management is guided by the working diagnosis, the patient's condition, and their response to initial resuscitation. A concurrent approach involving both resuscitation and treatment, whether medical or surgical, is essential.

Drug therapy for PPH[11]

Oxytocin	• 10 units IM • 5 units IV bolus • 20 units/l IV infusion
Misoprostol	600 micrograms orally or rectally
Carboprost tromethamine	0.25 mg IM, can be repeated every 15 min to a maximum of 8 doses
Methylergonovine maleate	0.25 mg IM, can be repeated every 15 min to a maximum of 5 doses

Management of massive PPH

Getting help Senior obstetrician, anesthetist and OT staff	**Local control** Bimanual compression, intrauterine tamponade, uterine packing, embolization (if available)	**Coagulation and BP** Resuscitation with crystalloids
Surgery		
Repair of genital tract trauma	**Vessel ligation** Uterine artery-ovarian vessel Internal iliac artery	**B-Lynch brace suturing** **Obstetric hysterectomy**
Post hysterectomy bleeding		
Surgical re-exploration	Abdominal packing	Embolization

Prevention: Third stage of labor active management

- Active and expectant management are used to manage the third stage of labor to prevent PPH.
- Active management: Early cord clamping, a prophylactic uterotonic, and controlled cord traction to promote the placenta delivery; Oxytocin use reduces the PPH risk in both cesarean and vaginal births.
- Expectant or physiologic management: Placenta delivered spontaneously or with maternal pushing efforts only (hands-off).

Monitoring for hemorrhagic shock and transfusion protocols

- Hemorrhagic shock is the most common type of shock in obstetrics patients, and once it occurs in PPH, mortality risk increases significantly.[17]

FIGO recognizes the shock index as an important marker of PPH severity, with values exceeding 0.9 signaling hemodynamic instability.

Metabolic complications management

- **Hypotensive fluid resuscitation:** Involves restrictive crystalloid resuscitation during hemorrhagic shock early stage to maintain lower than normal systolic or mean BP, supporting organ perfusion until control of the bleeding occurs.
- **Transfusion protocols:** Trauma-based massive transfusion protocols with high ratios may be beneficial for PPH. The ACOG recommends blood product administration in a 1:1:1 ratio to mimic whole blood replacement. Massive transfusion is defined as:
  - ≥4 units of PRBCs (some sources define it as ≥10 PRBCs within 24 hours)
  - Replacement of total blood volume within 24 hours
  - Replacement of 50% of blood volume within 3 hours.

Massive transfusion protocol in obstetrics

	PRBCs	FFP	Platelets	Cryoprecipitate
Round 1	6 U	6 U	6 U	10 U
Round 2	6 U	6 U	6 U	10 U
Round 3	Tranexamic acid 1 g intravenously over 10 min			
Round 4	6 U	6 U	6 U	

Postpartum health considerations

Effect of lactation on the woman health care[11, 18-20]

Breast milk is widely regarded as the gold standard for infant nutrition. Successful lactation requires preparation that begins not only during pregnancy but well in advance. A well-planned approach should empower every woman to make an informed breastfeeding decision.

WHO and UNICEF recommendations

1. Exclusive breastfeeding for the first 6 months (no water or other foods)
2. Introducing complementary foods alongside breastfeeding up to 2 years or beyond
3. Initiating breastfeeding within one hour after birth
4. Feeding on demand, responding to the child's hunger cues

Advantages of breastfeeding

- Maternal health: Low risk of cardiovascular morbidity and breast and ovarian cancers.
- Child health: Low risk of infection, obesity, and asthma.

Breastfeeding challenges

- Intense feelings of inadequacy, failure, and powerlessness and high PPD risk
- Ineffective latch, nipple pain, low milk production

Lactation and nutritional supplementation: Studies have found that

- Vitamin A supplementation significantly increases retinol and β-carotene levels in human milk.
- Supplementing mothers with vitamin D prevent deficiencies in both mother and infant. Studies show vitamin D supplementation during lactation raises 25-hydroxy-vitamin D in human milk.
- B-vitamin supplementation (B1, B2, B6, B12) is linked to high levels of these vitamins in human milk.
- Folic acid intake during lactation correlates with higher RBC folate and serum folate levels.
- Vitamin C supplementation (1000 mg/10 days) in lactating mothers significantly raised its concentration in human milk.
- Zinc sulfate supplementation (10 mg/day) in lactating women resulted in higher zinc levels in human milk, hair, and nails.
- Increased calcium intake during early lactation may reduce bone loss in mothers with low dietary calcium intake.
- DHA supplementation boosted DHA levels in maternal plasma, human milk, and children's blood plasma. Children of supplemented mothers performed better on psychomotor development tests.

Preventive postpartum care

The postpartum period, spanning 12 weeks after childbirth, is a crucial phase for the mother and her family, often referred to as the fourth trimester. Postpartum care should begin within 3 weeks after delivery, either through in-person visits or phone consultations, with multiple follow-ups as needed to address concerns. A comprehensive evaluation is advised within 12 weeks.

Some postpartum health challenges and treatment options are discussed below[21]

Condition/Concern	Diagnosis	Treatment options
Hypertensive disorders	Highest risk: <48 hours after delivery Office visit recommended to check BP within 7 days of delivery	• Lifestyle modifications • Treating if BP ≥150/100 mm Hg (oral Nifedipine or Labetalol) • Signs of end organ damage or BP ≥160/110 mm Hg: Hospitalization
Gestational diabetes mellitus	75-g, 2-hour fasting oral glucose tolerance test 4-12 weeks postpartum to detect type 2 diabetes, then screening every 1-3 years	• Lifestyle modifications and annual follow-up
Thyroid disorders	• Hyperthyroidism or hypothyroidism symptoms • Tests: TSH and free thyroxine • Positive TSH receptor antibodies distinguish Graves' disease from postpartum thyroiditis	• Hyperthyroidism: Transient and usually not treated • Beta-blockers used for symptoms • Hypothyroidism: Thyroid hormone therapy

Contraception counseling[22]

95% of women postpartum wish to avoid pregnancy within 2 years. Pregnancies within a year increase risks like low birth weight, preterm birth, and child mortality. Effective postpartum family planning and contraception can prevent over 30% of maternal deaths and 10% of child mortality by spacing pregnancy over 2 years.

Timing

- Progestin-only methods: Offered immediately (Etonogestrel implant, Levonorgestrel-releasing intrauterine system, Medroxyprogesterone)
- Estrogen: Not recommended until 3 weeks postpartum (regardless of lactation)
- COCs: After 6 months of delivery, after ruling out pregnancy (fully breast feeding); after 6 weeks of delivery, after ruling out pregnancy (Partially/non-breastfeeding)

Types of contraceptives

Injectable contraceptives	Progestogen-only injectables (POI)	• Medroxyprogesterone acetate (3 monthly) • Norethisterone Enanthate (2 monthly)
	Combined injectables contraceptive (CIC)	• Estrogen (usually Ethinyl-estradiol) and Progesterone (1 monthly)
Oral contraceptives	Progestin only pills (POPs)	• Norethindrone (0.35 mg taken daily at same time each day) • Norgestrel (0.075 mg taken daily at same time each day) • Drospirenone (4 mg 24/4 regimen: 24 days active pill, 4 days placebo) • Desogestrel (0.075 mg taken daily at same time each day)
	Combined oral contraceptives	• Consist of hormonal tablets, and non-hormonal (iron) tablet • Each hormonal tablet contains Levonorgestrel (0.15 mg) and Ethinyl estradiol (30 µg). • Effective if taken correctly • Protection against ovarian and endometrial cancer • Decrease the risk of ectopic pregnancy

Long-term health implications of pregnancy and childbirth[23]

There is growing awareness of the link between pregnancy complications and the risk of chronic diseases later in life.

- Gestational diabetes is related to postnatal depression, risk of thyroid and stomach cancers.
- Gestational diabetes, pre-eclampsia, early miscarriage and recurrent miscarriage are associated with high risk of diabetes mellitus.
- Stillbirth, miscarriage and recurrent miscarriage are linked with high risk of mental health issues.
- Pre-eclampsia, stillbirth and recurrent miscarriage are related to VTE development risk.

Collaboration between maternity and primary care ensures better follow-up for high-risk women. Lifestyle changes like weight control, smoking cessation, healthy diet, and exercise reduce disease risk and improve mental health.

Evidence-Based Practices for the Prevention and **Treatment of Maternal Peripartum Infections**[24,25]

Postpartum infections, as defined by the World Health Organization (WHO), are infections affecting the genital tract and surrounding tissues occurring from the onset of labor or rupture of membranes up to 42 days after delivery. These infections pose a considerable healthcare burden, which is often preventable.
However, treating postpartum infections has become increasingly challenging due to the growing misuse and overuse of antibiotics, leading to a rise in antibiotic-resistant pathogens that are commonly responsible for these infections.

Pregnancy	Routine antibiotics for women with PPROM
Labor	• Digital exam every four hours for assessment of labor progress in active first stage • Intrapartum antibiotics for women with GBS colonization to prevent newborn infection • Ampicillin and Gentamycin as first-line treatment for chorioamnionitis
Childbirth	• Vaginal cleansing with Povidone-iodine immediately before cesarean section • Routine antibiotics for women with the following conditions: - Manual removal of placenta - Third- or fourth-degree perineal tear - Prophylactically, before incision, for any cesarean section (single dose of first-generation Cephalosporin or Penicillin) • Ampicillin and Gentamycin as first-line treatment for chorioamnionitis
Postnatal period	Combination of Clindamycin and Gentamicin as first-line treatment for postpartum endometritis

Conclusion

The postpartum phase is a transformative period in a woman's life, which is characterized by psychological, physiological, and emotional challenges. To ensure the health and well-being of both child and mother, comprehensive care is crucial during this time. A multidisciplinary approach, including hormonal shift and involution management, lactation promotion, and control of emotional vulnerabilities, is often preferred. Preventive options, such as early screening for postpartum depression, timely management of complications like PPH, and individualized weight and nutrition counseling, aid in long-term maternal health management. Additionally, contraception counseling during postpartum empowers women with choices that support both recovery and family planning goals. Adoption of evidence-based methods allows for early identification of risk, enhancing maternal outcomes. Conclusively, an individualized and organized postpartum care model prevents chronic disease development, improves quality of life, and fosters recovery, underscoring the importance of recognizing the fourth trimester as a crucial element of women's reproductive life.

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Chapter 5

Menopause
Transition and Beyond

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Introduction to Menopause: **Hormonal Shifts and Managing Symptoms**

Menopause is a noteworthy physiological milestone in a woman's life, marking the ovarian function cessation and the reproductive phase conclusion. The average age is ~51years, though around 4% of women reach menopause before 40years of age.
Multiple factors influence the menopause timing, including obesity, alcohol consumption, genetic predisposition, ethnicity, education, diet, pesticide exposure and reproductive history. Recently, increasing attention has been given to the age at which menopause occurs due to its potential impact on long-term health.

- Early Menopause (menopause occurring between 40-45 years of age) is associated with an elevated risk of cardiovascular (CV) disease, atherosclerosis, stroke, osteoporosis, and Alzheimer's disease.
- Delayed Menopause (menopause occurring after the age of 55) is linked to an increased likelihood of breast, ovarian, and endometrial cancers.

Women experiencing POI, early menopause, or surgically induced menopause require ongoing medical, psychological, and endocrinological support. Their healthcare needs evolve over time, necessitating continuous monitoring, periodic adjustments in hormone therapy, and regular assessments for long-term health risks. Early identification and specialized care are essential to improving their quality of life and overall well-being.[1-3]

Decline in estrogen and multi-organ impact[4-6]

The menopausal transition proceeds gradually, and the menstrual cycle exhibits a change in patterns. The alteration in hormones affects emotional stability, physical function and mental well-being. This transition also influences the body composition and cardiovascular risk. Further, disease activity is primarily dependent on exposure to estrogen, and during post-reproductive life, cardiovascular and musculoskeletal disorders occur more commonly. Due to hormonal deprivation in the menopausal transition, a decline in cognitive function is observed in menopausal women.

Bone health

- Estrogen deficiency: Decrease in bone mineral density (BMD) and alterations in bone microarchitecture.
- Women with moderate/severe VMS have lower BMD (at the femoral neck and lumbar spine) and increased hip fractures rates.

Cognitive decline

- Estradiol fluctuating level: Causes the transient cognitive deficits, especially when VMS present.
- Induce a hypometabolic state related to neurological dysfunction due to fatty acid catabolism and β-amyloid deposition (a hallmark of Alzheimer's disease pathology).
- Influence microglial function and clearance mechanisms, aggravating neuroinflammation and neurodegeneration.

Urogenital system

- Estrogen loss: Major cause of urogenital atrophy in menopausal women; vagina shortens and narrows and vaginal surface becomes friable with ulcerations, petechiae, and bleeding on minimal trauma.
- Low estrogen levels sign: Vaginal dryness in the postmenopausal years and colonization of the vagina by fecal flora.

CVD risk

- CVD prevalent in women after age 75.
- Women with early menopause history have worse CHD and impaired stroke-free survival.
- Low estradiol levels: Cause increase in visceral fat deposition, dyslipidemia, hypertension, and insulin resistance, leading to high CVD risk later in life.
- **Menopausal transition and cardiovascular risk**[7]: Menopausal women have an increased risk of CVD, and the menopause transition is recognized as a significant contributing factor to the development of coronary heart disease.

Cardiometabolic health changes **SWAN and ARI studies findings**[7, 8]

- Different lipid parameters, such as total cholesterol, apolipoprotein B levels, and LDL-C increase exponentially within a short duration (from the year before to the year after the final menstrual period [FMP]). These changes are independent of the natural aging process.
- HDL-C levels have an intricate association with menopause, with the functional capacity of HDL undergoing modifications. HDL-C levels and HDL function may increase premenopause but deteriorate postmenopause.
- Higher HDL-C levels are related to less carotid atherosclerosis before menopause and greater carotid atherosclerosis following menopause.
- Additionally, the crucial antiatherogenic function (which is the promotion of the first step in reverse cholesterol transport) of HDL particles may weaken during the menopause transition.
- The incidence of metabolic syndrome increases with menopause, surpassing the impact of chronological aging alone, though menopause is not independently related to an increase in BP, insulin, or glucose.
- Atherosclerosis Risk in Communities report: Furthermore, it has been observed that metabolic syndrome progression and severity were maximum during the late premenopausal and perimenopausal years compared to the postmenopausal period.

Recommended Annual Screening Tests **During Perimenopause and Postmenopause**[9]

History and examination	• Gynecological history: Current menstrual status, age at menarche/menopause, last menstrual period, flow pattern before menopause, and contraception • Obstetric history: Number of pregnancies, abortions, living children, lactation, postpartum depression, history of gestational diabetes and hypertension • Surgical history: Any surgery in the past gynecological or non-gynecological • Family history: Chronic disorders such as diabetes mellitus, hypertension, CVD, stroke, cancers, early menopause, osteoporosis, Alzheimer's disease, and rheumatoid arthritis • Personal history: Diet, physical activity, mental attitude, social relationship, habits, stress, mood changes, memory and concentration, caffeine use, and tobacco and alcohol consumption; details of bowel and urinary dysfunction • Skeletomuscular: Body and joint pains, unintentional weight loss, loss of height, low physical activity, weakness, and exhaustion • Medication history: Current medication, use of prescription and non-prescription drugs, allergies to any medication, and use of therapy to treat menopause symptoms and contraceptive methods • Sexual history: History of difficulty in having sexual relations and lack of sexual desire • Weight history: Changes in total body weight and the waist • Immunization history
Clinical examination	• General examination: Height, weight, BMI, waist circumference, pulse and BP
Skeletomuscular health	• Spine curvature, gait, knee flexion, and extension
Breast examination	• Self-examination of breast on the same day of every month
Abdominal examination	• Any organomegaly, free fluid, hernial sites, and abnormal veins
Pelvic examination	• Done to assess for complications of menopause, such as urogenital atrophy, a litmus test, pap smear/liquid-based cytology
Eye checkup	• Intraocular pressures, refractive index, and retinal examination
Laboratory tests (ideal)	• CBC • Fasting blood glucose or Hb1Ac, or 75 g oral glucose tolerance test • Lipid profile • Serum TSH • Urine routine examination • Stool for occult blood

Tests performed solely on indication

Test	Indication
FSH	• POI, contraceptive pill users, post-hysterectomy women, secondary amenorrhea or hot flushes, fertility assessment
Estradiol	• Same indications as FSH
Tests for risk of thrombosis	• Relevant personal/family history, thromboembolic episodes; estimation of antithrombin III, tissue factor pathway inhibitor activity, protein C/S, lupus anticoagulant, anticardiolipin antibodies
Endometrial biopsy	• Postmenopausal bleeding, irregular bleeding, previous unopposed estrogen uses with intact uterus
Bone mass measurement	• Specific indications only
LFT	• Relevant with suspected liver disease or recent liver disease history
Urodynamic study	• Diagnose and differentiate types of incontinence before surgery planning
ECG, 2D Echo	• CVD assessment
Vaginal pH, VMI	• Vaginal atrophy assessment
25(OH) Vitamin D	• Rule out secondary causes of osteoporosis

Scores to be accessed[10-14]

OSTA	Screening for osteoporosis in women
SARC-F	Individuals with suggestive signs of sarcopenia
Gail model	Breast cancer risk prediction model
FRAX (computer-based algorithm)	Calculates the 10-year probability of a major osteoporotic fracture and a hip fracture
WHO /ISH SCORES	Total 10-year risk of developing fatal and non-fatal major CVDs (heart attack or stroke)

Use of Combined Oral Contraceptives (COCs) in Perimenopausal Women[15]

In perimenopausal women, COCs, besides serving as contraception, aid in improving heavy menstrual bleeding, vasomotor symptoms, irregular periods, and menstrual pain. Furthermore, it lowers the risk of colorectal, ovarian, and endometrial cancer while supporting BMD.

Circumstances for COC use in perimenopausal women

Many perimenopausal women assume they can no longer conceive, but fertility, though reduced, still exists. According to CDC, women over 44 must continue contraception if they wish to avoid pregnancy. ASRM and NAMS recommend using contraception for 12 months after the last menstrual period.

COCs effectively regulate menstrual cycles in 80% of cases. For this purpose, COCs with 30-35 µg of ethinyl estradiol are recommended.

COCs can help alleviate menstrual pain, with extended or continuous dosing being particularly beneficial.

Around 70–80% of perimenopausal women experience vasomotor symptoms, which COCs can help manage.

BMD declines by about 1% per year after age 40, but COC use in this age group can help preserve bone mineral density.

HMB is common in the late 40s, and COCs can reduce blood loss by approximately 40%. The FDA has approved Estradiol valerate/Dienogest combination COCs for HMB treatment.

Monophasic COCs with Ethinyl estradiol can also be used for HMB. Extended dosing regimens, such as a pill-free interval every 3 months or continuous use for 6-12 months, may be more effective.

IMS governing principles on MHT[16]

- MHT is the most effective therapy for VMS and urogenital atrophy.
- Individualized MHT may improve both sexuality, menopause-related complaints and QoL.
- The consideration of MHT must be part of an overall strategy including lifestyle recommendations for maintaining the health of peri- and postmenopausal women.
- MHT must be individualized as per the symptoms and the need for prevention, as well as medical history, investigation results and the woman's preferences and expectations.
- The risks and benefits of MHT differ for women during the menopause transition compared to those for older women.
- Women experiencing spontaneous or iatrogenic menopause before the age of 45 years and specifically before 40 years are at higher risk for CVD and osteoporosis and may be at high risk of affective disorders and dementia. MHT may reduce or preserve bone density and is advised at least until the average age of menopause. Women with POI should also continue MHT until average menopause age.
- Counseling should convey the benefits and risks of MHT.
- MHT is not recommended without a clear indication of its use.
- Women taking MHT should have at least an annual evaluation and a discussion on strategies to prevent or reduce chronic disease. There is currently no indication for increased mammographic or cervical smear screening.
- Data from the WHI trial and other studies support safe use for at least 5 years in healthy women initiating treatment before age 60.
- Whether or not to continue therapy should be decided at the discretion of the well-informed woman and her health professional dependent.
- The dosage should be titrated to the lowest effective dose.
- Lower doses of MHT than previously used may reduce symptoms sufficiently and maintain quality of life for many women.

Evidence-Based Approaches to Managing Menopausal Symptoms

Genitourinary syndrome of menopause (GSM)[17, 18]

The North American Menopause Society (NAMS) coined the term genitourinary syndrome of menopause to indicate the clinical features related to the deficiency of estrogen influencing the genitourinary tract of females during menopause.Most women have reported a negative impact on their quality of life and their sexual health due to vaginal symptoms.

- As per the NAMS 2020 position statement, GSM symptoms—such as vaginal dryness, urinary incontinence, and sexual dysfunction impact between 27% and 84% of postmenopausal women.

Estrogen low levels during menopause causes issues like

- Vaginal pain
- Vaginal dryness
- Urinary incontinence
- Overactive bladder
- Dysuria
- Urinary tract infections
- Dyspareunia and other related issues

Vaginal microbiota after menopause

- Anaerobic and aerobic bacteria population increase and *Lactobacillus* spp. are less likely to dominate.
- Postmenopausal women with microbiota categorized as CST-IV-B (high *G vaginalis* and low *Lactobacillus* relative abundance) have the maximum covariate-adjusted odds of vaginal atrophy, low libido, and vaginal dryness.

Management

- Non-hormonal moisturizers and isomolar lubricants: First-line therapy for vulvovaginal symptoms.
- Second-line treatment: Hormonal therapy for moderate-severe symptoms. Low-dose vaginal estrogen (cream, tablet, ring); systemic estrogen + progestogen in women with a uterus.
- Oral Ospemifene or laser therapy: For patients not responding to vaginal therapy or cannot use hormone therapy.

Estrogens and Progestins for GSM

Conjugated equine estrogen (CEE), synthetic conjugated estrogens, micronized 17b-estradiol and ethinyl estradiol are commonly prescribed estrogens.

- Estrogen alleviates genitourinary symptoms, (dyspareunia and vaginal dryness), with no substantial dissimilarities among estrogen formulations.
- Combining progestin with estrogen is recommended for women with an intact uterus. Common progestogens used are Medroxyprogesterone acetate, Norethindrone acetate and natural progesterone. The combination therapy alleviates vasomotor symptoms and vaginal dryness.

Non-hormonal therapies[19-21]

Before the final menstrual period, women may experience aggravating symptoms that can affect their quality of life. Apart from hormonal therapy, treatment approaches for menopausal manifestations include non-hormonal medications and non-pharmacologic treatments.

FDA-approved non-hormonal options

Drug/Drug class	Application
Selective serotonin reuptake inhibitor (SSRI)	Paroxetine 7.5 mg daily: Only non-hormonal therapy approved for hot flashes; Escitalopram may be used for patients with a concurrent mood disorder or poor sleep
DHEA	GSM treatment; limited evidence
Ospemifene (selective estrogen receptor modulator)	Considered for dyspareunia and GSM, vaginal dryness
Serotonin-norepinephrine reuptake inhibitors (Venlafaxine and Desvenlafaxine)	Alleviates VMS
Gabapentin	Improves VMS
Clonidine	Considered for patients with hypertension

Cognitive behavior therapy (CBT): An effective non-pharmacologic approach for managing menopausal symptoms

- CBT is relatively risk-free and is an effective non-pharmacological option for improving VMS.
- CBT for insomnia must be a front-line therapy for women with midlife insomnia.
- Studies have established that women who undergo CBT experience improvement in their VMS manifestations compared to no intervention.
- CBT reduces the severity of the VMS, and internet-delivered CBT has been demonstrated to have high compliance rates, making it a reasonable option for management.

Phytoestrogens: A potential solution for menopause-related mood disorder

- Mood disturbances are common in menopausal women, and growing evidence indicates that low serotonin levels due to estrogen fluctuation during menopause contribute to this condition. Estrogen use can aid in addressing menopause-related depression, while phytoestrogen, plant-derived compounds (primarily isoflavones), offer a potential alternative.
- Research indicates a significant decrease in symptoms of depression and possible relief from night sweats and hot flashes. However, further research is needed to confirm their effectiveness.

Menopausal Hormone Therapy (MHT)

Current indications for MHT, its risks and benefits[22, 23]

MHT involves the use of progestogen and estrogen in peri- and postmenopausal women to treat genitourinary and climacteric symptoms. Furthermore, MHT is also employed for addressing or preventing diseases impacted by estrogen deficiency, including diabetes, osteoporosis, colon cancer, and metabolic syndrome.

Curative indications

- Menopausal symptoms (moderate-to-severe VMS, GSM)
- Urological symptoms
- Urogenital atrophy

Preventive indications

- Postmenopausal osteoporosis
- Premature ovarian insufficiency (premature menopause, oophorectomy)
- Urogenital atrophy
- Colorectal cancer
- Type 2 diabetes

Presumed preventive indications

- Coronary heart disease
- Metabolic syndrome
- Different atrophic-degenerative diseases
- Rheumatic diseases
- Mental health conditions
- Alzheimer's disease

Advantages of MHT

Reduced risk of vaginal atrophy and osteoporotic fractures, better glycemic control, and improved vasomotor and urogenital symptoms.

Risk management

- **Endometrial hyperplasi**
  - Adequate addition of progestogen
  - Regular monitoring to minimize risk
- **Breast cancer**
  - Using micronized Progesterone or Dydrogesterone to lower risk
  - Early detection through screening methods (baseline mammography)
- **Coronary heart disease and stroke**
  - Early initiation of MHT before age 60 or within 10 years of FMP (low-dose, transdermal or vaginal administration preferred)[24]

Role in managing vasomotor symptoms, vaginal atrophy, and osteoporosis[25, 26]

Vasomotor symptoms

- Low-dose MHT effective for treating VMS
- Progestogen (Medroxyprogesterone acetate [MPA] 10 mg/day, oral Megestrol acetate 20 mg/day, and MP 300 mg/day) improves VMS with minimal risk; highly effective for severe VMS
- MHT improves HRQoL and menopause-specific QoL

Vaginal atrophy

- Cornerstone therapy: Maintenance therapy with estrogens
- Very low dose, low potency estrogens like estriol (with or without probiotic) safe and efficient treatments for VVA, even for patients with breast cancer

Osteoporosis

- MHT standard dose improves bone density and reduces bone remodeling process
- MHT prevents menopause-related bone loss and decreases the fracture risk
- MHT needed for premature ovarian insufficiency cases or osteopenia to prevent bone loss

Types of MHT[27, 28]

Different formulations, doses, and routes of delivery for MHT are available. The treatment must be tailored depending on the patient's attributes and personal choices.

Estrogen	• Available in transdermal (patch, gel, or spray), oral, and vaginal formulations • Available formulations: micronized 17β-estradiol, CEE, conjugated estrogens (CE), and ethinyl estradiol • Estrogen alone can be used in women without a uterus • Lowest effective dose be used first
Systemic vaginal estrogens	• Available as vaginal Estradiol acetate (12.4 mg or 24.8 mg) • Progestogen also used to protect against endometrial cancer in women with a uterus
Local low-dose vaginal estrogens	• Used for genitourinary symptoms • Applied as a cream, tablet, insert, or ring • Does not need a progestogen as there is less systemic absorption
Progestogens	• Progestins (synthetic progestogens)- Each drug specified by their grouping: - Pregnanes: Nomegestrol acetate, Medroxyprogesterone acetate (MPA) - Estranes: Norethindrone, Ethynodiol diacetate, Norethynodrel, Norethindrone acetate - Gonanes: Levonorgestrel, Norgestimate, Desogestrel, Gestodene • Available formulations include micronized Progesterone, Levonorgestrel, Norethindrone acetate, and MPA
Estrogen–progestogen combination	• Available in oral and transdermal formulations • Combination therapy can be taken continuously, i.e., estrogen and progestogen taken every day, or cyclically (where the estrogen taken every day while the progestogen taken only for 12-14 days of the month) • Women with a uterus taking systemic estrogen, a progestogen must be added to estrogen therapy

Holistic Postmenopausal Care: **From Cardiovascular Care to Bone Health and Preventive Immunization**

Cardiovascular Health in Postmenopausal Women

Estrogen exerts a protective role against cardiac disorders in women and the risk increases once they enter menopause. The most common contributing factors for CVD in menopausal women are glucose intolerance, central obesity, atherogenic dyslipidemia, and hypertension.[29]

CVD screening in women[30, 31]

- Cardiovascular risk screening must be executed at all routine visits for women aged 40-75 years.
- Coronary artery calcium screening is recommended for intermediate risk cases, individuals with family history of early heart attacks and strokes.
- Periodic screening is suggested for various risk factors: BP, lipids/cholesterol, diabetes for all women starting at 18-21 years, with calculated ASCVD risk score use among women 40 years or older.
- The North American Menopause Society has included the ACR/AHA atherosclerotic CVD risk score into an app-based clinical decision support tool for assessing CV risk before employing postmenopausal hormone therapy.

Evidence-based lifestyle modifications for preventing CVD: NICE guideline recommendations[32]

- Adopting a diet in which total fat intake 30% or less of total energy intake, saturated fats are 7% or less of total energy intake.
- Replacing saturated fats with mono-unsaturated and polyunsaturated fats.
- Performing aerobic, resistance, and muscle-strengthening activities.
- Encouraging people who cannot do moderate-intensity physical activity to exercise at their maximum safe capacity.
- Offering weight management interventions to people who are overweight or obese.
- Advising on managing health risks from drinking alcohol to a low level.
- Advising and supporting all people who smoke to stop.

Protective role of estrogens

The risk of CVD significantly increases after menopause due to declining estrogen levels.

- Estrogen (E2) plays a cardioprotective role by enhancing angiogenesis and vasodilation and reducing ROS, oxidative stress, and fibrosis. Even low-dose oral estrogen yields benefits, and it also slows atherosclerosis progression.[33]

Clinical findings

- A dose of 0.3 mg/day of oral conjugated equine estrogen provides similar benefits to a standard 0.625 mg/day dose.[34]
- Studies suggest a cardioprotective effect even with low doses of oral hormone therapy.
- HT may slow the progression of carotid artery intima-media thickness, reducing atherosclerosis and coronary calcification.[35]

Exploration of hormone therapy's effects on CV outcomes and its continued use beyond the age of 65 years[36]

Earlier, it was assumed that MHT after the age of 65 years was unwarranted, as manifestations due to estrogen withdrawal rarely persisted beyond that age. However, reports suggest the persistence of VMS in many elderly women. The Menopause Society modified their position regarding the usage of HT in women aged ≥65 years, recommending to begin or continue HT beyond age 65 years.

- **Use of estrogen therapy beyond age 65 is associated with reduced risks of:**
  - CV conditions (congestive heart failure, VTE, AF, and AMI)
  - Osteoporosis
  - Breast, lung, and colorectal cancer
  - Dementia

- **Studies have proved that risk reduction is greater for estradiol (vs CEE), low or medium (vs high dose), and vaginal and transdermal (vs oral).**

- **Remarks: Research suggests that MHT beyond the age of 65 may offer significant health benefits.**

Vaccination of elderly women

Immunosenescence refers to the age-related decline in systemic immunity, affecting both innate and adaptive immune responses. As a result, older adults are generally more vulnerable to vaccine-preventable diseases, which often present with greater severity compared to younger population.[37]

According to Indian consensus guideline on adult immunization and CDC-ACIP

- All menopausal women below 50 years of age with chronic medical condition* are recommended to get one dose of PCV13 followed by one dose of PPSV23 after 1 year. In immunocompromised condition**, CSF leak and Cochlear implant cases: PCV13 followed by PPSV23 after 8 weeks is recommended.
- All women above 50 years of age are recommended to get 1 dose of PCV13 followed by 1 dose of PPSV23 after 1 year and another dose of PPSV23 after 5 years.
- One dose of PCV20 to women ≤49 years with chronic medical condition* and immunocompromising conditions** and one dose to all women ≥50 years of age is recommended.[38]

* Alcoholism, chronic heart disease, including congestive heart failure and cardiomyopathies, chronic liver disease, chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma, cigarette smoking, diabetes mellitus

**Chronic renal failure, congenital or acquired asplenia, congenital or acquired immunodeficiency, generalized malignancy, HIV infection, Hodgkin disease, iatrogenic immunosuppression, leukemia, lymphoma, multiple myeloma, nephrotic syndrome, sickle cell disease/other hemoglobinopathies, solid organ transplant.

Bone density screening and recommendations for calcium, vitamin D, and weight-bearing exercises

Vitamin D and calcium role

- Important for bone health maintenance
- Their deficiency: Notable risk factor for osteoporosis development

The determination of normal and insufficient levels for serum vitamin D is a disputed topic. Although it is widely accepted that 25(OH)D levels <10 ng/mL (25 nmol/L) indicate severe deficiency, there is no clear consensus on the threshold for what constitutes a "normal" value.

Osteoporosis diagnosis

- An investigation of BMD and independent risk factors is suggested to identify patients at high risk of fractures.
- DXA is a commonly used bone densitometry technique and considered the gold standard reference. Women over 65, or younger with risk factors, should undergo routine DEXA scans, with treatment based on T-score and fracture risk. The AACE/ACE guidelines regard a very low T-score of < -3.0 as suggestive of a very high risk of fracture.

Further, CT and peripheral quantitative CT (pQCT) are 3D techniques that can construct bone images, using X-ray attenuation.

Calcium and vitamin D supplementation

Recommended for the prevention of osteoporosis and subsequent fractures in osteoporotic cases:

- For postmenopausal women with osteoporosis: Daily calcium intake of 800-1200 mg from diet and/or supplements
- Postmenopausal women at high risk of fracture and vitamin D insufficiency: Daily dose of ≥800 IU vitamin D

An overview of treatment guideline based on fracture risk

Low fracture risk

- Optimization of calcium and vitamin D status
- Bone-friendly lifestyle

High fracture risk

- Optimization of calcium and vitamin D status
- Bone-friendly lifestyle
- Antiresorptive therapy
- Falls prevention

Very high fracture risk

- Optimization of calcium and vitamin D status
- Bone-friendly lifestyle
- Anabolic therapy for 12-18 months followed by antiresorptive therapy
- Falls prevention

Bone health and exercise

- Research on osteoporosis cases has demonstrated the positive effect of exercise programs on BMD and bone metabolic biomarkers.
- To maintain bone health, the American College of Sports Medicine (ACSM) has recommended jumping exercise, weight-bearing aerobic exercises (3 days/wk), and resistance exercise (moderate-high intensity for 30-60 min/day for 2-3 days/wk).
- Weight-bearing aerobic exercise include jogging, stair climbing, volleyball, tennis, dancing, Tai Chi, and walking.
- Studies have shown that weight-bearing exercise with weighted vests, even for just six weeks, is effective in improving bone metabolic markers.

Pharmacological Interventions

Bisphosphonates

- Commonly prescribed antiresorptive therapy.
- Available options: Oral Alendronate, Risedronate and Ibandronate, intravenous (IV) Ibandronate and Zoledronic acid.
- Overall favorable benefit/risk ratio despite concerns regarding jaw osteonecrosis and atypical femur fractures.
- Recommendation: Continuation of therapy be reconsidered after 5 years of oral Alendronate or 3 years of IV therapy based on therapy response.

Menopausal hormone therapy

- MHT considered in women at risk of fracture before 60 years or within 10 years after menopause.
- Study findings: HRT increases BMD in the forearm, lumbar spine, and femoral neck in postmenopausal women.
- Progesterone used in conjunction with estrogen in women who still have their uteruses.
- Women's Health Initiative (WHI) shown that 0.625 mg/day of conjugated equine estrogen alone or with 5 mg/day Methoxyprogesterone reduces fractures risk in osteoporotic and non-osteoporotic women.

Selective estrogen receptor modulators

- Raloxifene and Bazedoxifene advised in women at risk of vertebral fracture and breast cancer.
- Clinical trials demonstrated that daily dose of Raloxifene 60 mg effective for prevention and treatment of postmenopausal osteoporosis and vertebral fractures.

Denosumab: An alternative to the bisphosphonates

- Bisphosphonates increase BMD, but this effect limited to the first 3 years of therapy; Denosumab can enhance BMD beyond the initial 3 years.
- Denosumab administered as a 60 mg subcutaneous injection every 6 months.
- 10-year follow-up study shown its protective effect against fractures persists over time.
- Suitable option for impaired renal function cases as Denosumab not excreted by the kidneys.

Conclusion

Menopause typically occurring around 51 years, is characterized by the end of ovarian function and reproductive years. The timing of the menopause is affected by the lifestyle, genetics, and environmental factors. Medical care is crucial for women experiencing premature, early, or induced menopause. The decline the level of estrogen impacts various organs, and increases the risk of CVD, osteoporosis, and cognitive decline. Menopausal manifestations, such as vasomotor symptoms and genitourinary syndrome, can be managed with non-hormonal (cognitive behavioral therapy) and hormonal options. Menopausal hormone therapy (MHT) aids in improving symptoms and addresses and prevents diseases like osteoporosis and metabolic syndrome. Perimenopausal contraception is important until 12 months post-menopause. Long-term wellness strategies include CVD risk assessment, lifestyle modifications, bone health preservation, and tailored pharmacological interventions.

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