CERPO
Centro de Referencia Perinatal Oriente
Facultad de Medicina, Universidad de Chile

Seminario n°135: Consulta Preconcepcional

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MAPA DE LA RUTA:

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CONSULTA PRECONCEPCIONAL

- Introducción
- Objetivos de la consulta preconcepcional
- Áreas de intervención y enfoque de riesgos
- Obesidad
- Desnutrición
- Diabetes mellitus
- Suplemento nutricional: ácido fólico
- Periodo intergenésico
- Edad materna
- Guías internacionales: OMS, Australia-Nueva Zelanda.

Introducción

- **En el marco de los derechos sexuales y reproductivos las parejas deciden el momento del embarazo y el espaciamiento entre estos.**

- **Esto genera la OPORTUNIDAD de realizar un control preconcepcional y a la vez vincular con el control prenatal precoz.**

- **Entender el control preconcepcional como parte de un modelo que abarca los cuidados a lo largo de todo el ciclo vital e incluye a la familia.**

Objetivos CDC

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- 1) Mejorar el conocimiento, actitud y comportamiento de hombres y mujeres en relación a la salud preconcepcional.

- 2) Asegurar que todas las mujeres en edad fértil en EEUU reciban cuidados preconcepcionales (screening de riesgos, promoción de salud e intervenciones basados en evidencia) que permitan que entren al embarazo con una salud óptima.

- 3) Reducir los riesgos indicados por el resultado adverso de un embarazo previo a través de intervenciones durante el periodo intergestacional, las que pueden prevenir o minimizar problemas de salud en la madre o su descendencia futura.

- 4) Reducir la desigualdad en los resultados adversos en el embarazo.

ACOG-AAP

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- 4 categorías de intervención:
  - Evaluación física
  - Detección de riesgos
  - Vacunación
  - Consejería
- 8 áreas de evaluación de riesgos:
  - Conciencia reproductiva
  - Toxinas y teratógenos ambientales
  - Nutrición y ácido fólico
  - Genética
  - Uso de sustancias
  - Condición médica y medicación
  - Enfermedades infecciosas y vacunación
  - Psicosocial

Detección de Factores de Riesgo de resultado adverso perinatal

- Evidencia demostrada de impacto de los cuidados preconcepcionales:

- Uso de Isotretinoína
- Alcohol
- Antiepilépticos
- Diabetes
- Déficit de ácido fólico
- Hepatitis B
- VIH
- PKU
- Rubeola
- Obesidad
- TACO
- ITS
- Tabaco

Recomendaciones a los sistemas de salud

- Responsabilidad individual a lo largo de la vida
- Conciencia del usuario
- Visita preventiva
- Intervenciones para riesgos identificados
- Cuidados intergestacionales
- Revisión pregestacional
- Cobertura de seguros de salud para mujeres de bajos ingresos
- Estrategias y programas de salud pública
- Investigación

Obesidad

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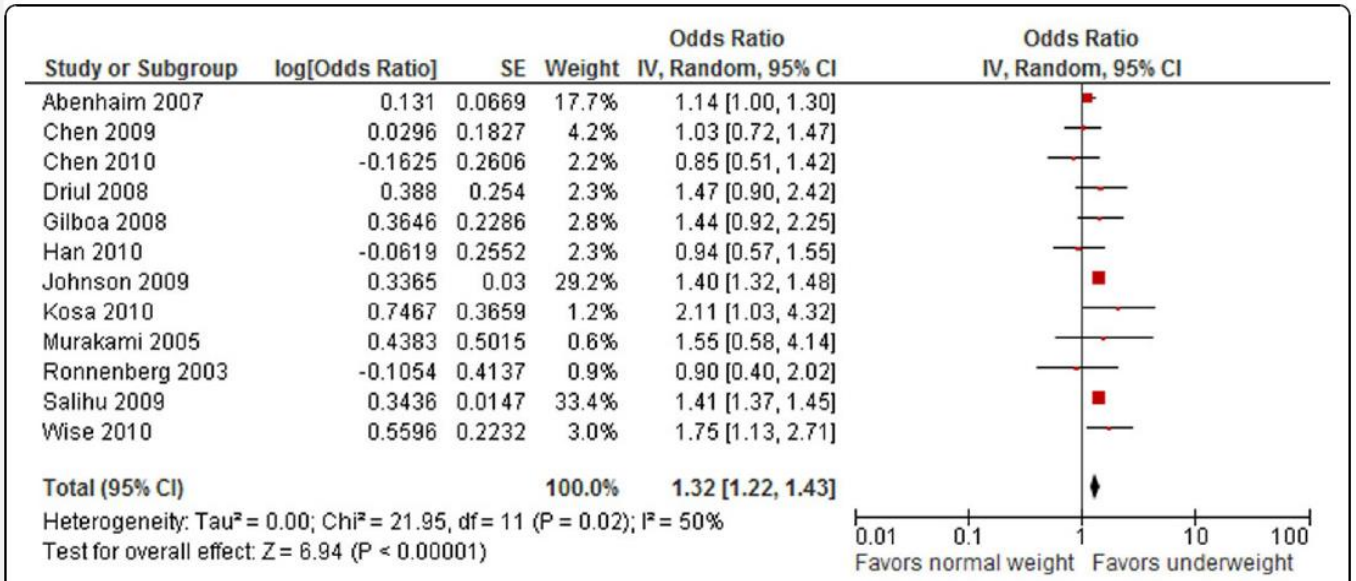
- La reducción del IMC en un 10%, disminuye el riesgo de óbito fetal en un 10%

- Si IMC en sobrepeso, el objetivo es bajar un 5 % del peso
- Si IMC en obesidad, el objetivo es bajar un 10 % del peso

- Riesgos en obesas:
  - PE OR 2,28
  - DG OR 1,21
  - Cesárea OR 1,42
  - Macrosomía
  - GEG OR 1,63
  - Defectos tubo neural
  - Cardiopatía congénita OR 1,15

Desnutrición

- IMC <18,5 kg/m2:
  - PEG RR 1,64



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Abenhaim 2007	0.131	0.0669	17.7%	1.14 [1.00, 1.30]
Chen 2009	0.0296	0.1827	4.2%	1.03 [0.72, 1.47]
Chen 2010	-0.1625	0.2606	2.2%	0.85 [0.51, 1.42]
Driul 2008	0.388	0.254	2.3%	1.47 [0.90, 2.42]
Gilboa 2008	0.3646	0.2286	2.8%	1.44 [0.92, 2.25]
Han 2010	-0.0619	0.2552	2.3%	0.94 [0.57, 1.55]
Johnson 2009	0.3365	0.03	29.2%	1.40 [1.32, 1.48]
Kosa 2010	0.7467	0.3659	1.2%	2.11 [1.03, 4.32]
Murakami 2005	0.4383	0.5015	0.6%	1.55 [0.58, 4.14]
Ronnenberg 2003	-0.1054	0.4137	0.9%	0.90 [0.40, 2.02]
Salihu 2009	0.3436	0.0147	33.4%	1.41 [1.37, 1.45]
Wise 2010	0.5596	0.2232	3.0%	1.75 [1.13, 2.71]
Total (95% CI)			**100.0%**	**1.32 [1.22, 1.43]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 21.95$, df = 11 (P = 0.02); $I^2 = 50\%$

Test for overall effect: Z = 6.94 (P < 0.00001)

Figure 2 Pre pregnancy underweight and risk for preterm birth: evidence from observational studies Citations to the included studies: Abenhaim 2007 [55], Chen 2009 [56], Driul 2008 [57], Johnson 2009 [58], Kosa 2010 [59], Murakami 2005 [60], Ronnenberg 2003 [61], Salihu 2009 [62], Wise 2010[63], Chen 2010 [64], Gilboa 2008 [65], Han 2010 [66].

Diabetes

- El control estricto de niveles de glucosa ha demostrado disminuir la incidencia de malformaciones congénitas, aborto, anormalidades del peso al nacer y parto prematuro.

- 3% de malformaciones congénitas con HbA1C de 6%, que aumenta a 6% con HbA1C de 9%

J. Klein. Preconception care for women with type 2 diabetes mellitus: A mixed-methods study of provider knowledge and practice. Diabetes Research and Clinical Practice 129 (2017) 105 –115.

Suplementación con ácido fólico

Mecanismos que aumentan el riesgo:

- Polimorfismo genético que afecta la eficiencia del metabolismo del folato (anomalías cromosómicas, metilación del DNA, mutaciones)
- Factores ambientales (ingesta, malabsorción, fármacos, metabolismo de la glucosa,OH, tabaco, autoanticuerpos contra receptor de folato)

Table 3. Identified increased risk factors for fetal NTD or low maternal RBC folate status

Personal/family history or ethnic risk[1–5,19–22]	NTD: maternal or paternal affected, previous affected fetus for either parent, child, sibling, or second /third degree relative
	MTHFR genotype 677TT carrier homozygous
	677CST carrier heterozygous
Medical/surgical condition[41,77–79,100–103]	GI: malabsorption/inflammatory bowel, Crohn's, active Celiac disease, gastric bypass surgery, advanced liver disease
	Renal: kidney dialysis
	Pre-gestational diabetes (type I or II)
	Anti-epilepsy or folate-inhibiting medications (see Table 4)
Maternal co-morbidities[81,92–97]	Maternal obesity: BMI > 30 kg/m^2 or 80 kg (pre-pregnancy weight)
Maternal lifestyle factors[82,98,99,190–192]	Smoking
	Alcohol overuse
	Non-prescription drug use/abuse
	Low socio-economic status
	Poor/restricted diet

NTD: neural tube defect; RBC: red blood cell; MTHFR: methylenete trahydrofolate reductase; GI: gastrointestinal

Recommendations

1. Women should be advised to maintain a healthy folate-rich diet; however, folic acid/multivitamin supplementation is needed to achieve the red blood cell folate levels associated with maximal protection against neural tube defect. (III-A)
2. All women in the reproductive age group (12–45 years of age) who have preserved fertility (a pregnancy is possible) should be advised about the benefits of folic acid in a multivitamin supplementation during medical wellness visits (birth control renewal, Pap testing, yearly gynaecological examination) whether or not a pregnancy is contemplated. Because so many pregnancies are unplanned this applies to all women who may become pregnant. (III-A)

Recommendations

3. Folic acid supplementation is unlikely to mask vitamin B12 deficiency (pernicious anemia). Investigations (examination or laboratory) are not required prior to initiating folic acid supplementation for women with a risk for primary or recurrent neural tube or other folic acid-sensitive congenital anomalies who are considering a pregnancy. It is recommended that folic acid be taken in a multivitamin including 2.6 ug/day of vitamin B12 to mitigate even theoretical concerns. (II-2A)

Pre-conception Folic Acid/Multivitamin Supplementation for the Prevention of Neural Tube Defects and Other Congenital Anomalies. SOGC clinical practice guideline. J Obstet Gynaecol Can 2015;37(6):534–549

Suplementación con ácido fólico

- 400-500 mcg de ácido fólico periconcepcional logran reducir 72% el riesgo de defectos del tubo neural
- Reduce 62% el riesgo de recurrencia

- Dosis de 400mcg a 1mg no han demostrado ser dañinas.
- Excreción renal

- Sin evidencia de beneficio en resultado perinatal (pretérmino, bajo peso, óbito, muerte perinatal)

- 1% de recurrencia de defectos del tubo neural incluso con suplementación de 5mg

4. Women at HIGH RISK, for whom a folic acid dose greater than 1 mg is indicated, taking a multivitamin tablet containing folic acid, should be advised to follow the product label and not to take more than 1 daily dose of the multivitamin supplement. Additional tablets containing only folic acid should be taken to achieve the desired dose. (II-2A)

Table 4. Interactions between drugs or medications and folic acid

1. Biology reduced folic acid activity	Interference with erythrocyte maturation	Chloramphenicol
		Methotrexate
	Other	Metformin
2. Reduced folic acid levels	Impaired absorption	Sulfasalazine
	Increased metabolism	Phenobarbital
		Phenytoin
3. Other interactions	Not reported	Primidone
		Triamterene
		Barbiturates

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Suplementación con ácido fólico

- Uso de multivitamínicos:
  - Tumores cerebrales OR 0,73 (0,6-0,8)
  - Neuroblastoma OR 0,53 (0,42-0,68)
  - Leucemia 0,61 (0,5-0,74)
  - Tumor de Wilms
  - Tumor neuroectodérmico primitivo
  - Ependimomas
  - Noruega: menor riesgo de autismo OR 0,61 (0,41-0,9)
  - Altas dosis de ácido fólico podrían asociarse a mayor riesgo de asma y enfermedades respiratorias en la descendencia.

Recommendations

5. Women with a LOW RISK for a neural tube defect or other folic acid-sensitive congenital anomaly and a male partner with low risk require a diet of folate-rich foods and a daily oral multivitamin supplement containing 0.4 mg folic acid for at least 2 to 3 months before conception, throughout the pregnancy, and for 4 to 6 weeks postpartum or as long as breast-feeding continues. (II-2A)
6. Women with a MODERATE RISK for a neural tube defect or other folic acid-sensitive congenital anomaly or a male partner with moderate risk require a diet of folate-rich foods and daily oral supplementation with a multivitamin containing 1.0 mg folic acid, beginning at least 3 months before conception. Women should continue this regime until 12 weeks' gestational age. (1-A) From 12 weeks' gestational age, continuing through the pregnancy, and for 4 to 6 weeks postpartum or as long as breast-feeding continues, continued daily supplementation should consist of a multivitamin with 0.4 to 1.0 mg folic acid. (II-2A)
7. Women with an increased or HIGH RISK for a neural tube defect, a male partner with a personal history of neural tube defect, or history of a previous neural tube defect pregnancy in either partner require a diet of folate-rich foods and a daily oral supplement with 4.0 mg folic acid for at least 3 months before conception and until 12 weeks' gestational age. From 12 weeks' gestational age, continuing throughout the pregnancy, and for 4 to 6 weeks postpartum or as long as breast-feeding continues, continued daily supplementation should consist of a multivitamin with 0.4 to 1.0 mg folic acid. (I-A). The same dietary and supplementation regime should be followed if either partner has had a previous pregnancy with a neural tube defect. (II-2A)

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Table 5. Summary of congenital anomalies (decreased or increased or no effect) following folic acid food fortification

Study reference	Anomaly	Case–Control (95% CI)	Cohort/RCT (95% CI)
	Meta-analysis		
Goh et al. (2006)[15]	Neural tube defect	0.67 (0.58–0.77)	0.52 (0.39–0.69)
	Oral facial cleft	0.63 (0.54–0.73)	0.58 (0.28–1.19)
	Cardiovascular defects	0.78 (0.67–0.92)	0.61 (0.40–0.92)
	Limb reduction defects	0.48 (0.30–0.76)	0.57 (0.38–0.85)
	Cleft palate	0.76 (0.62–0.93)	0.42 (0.06–2.84)
	Urinary tract defects	0.48 (0.30–0.76)	0.68 (0.35–1.31)
	Congenital hydrocephalus	0.37 (0.24–0.56)	1.54 (0.53–4.50)
Johnson and Little (2008)[38]	Cleft lip and palate	0.75 (0.65–0.88)	
	Cleft palate only	0.88 (0.76–1.01)	
	Single Population		
Li et al. (2013)[30]	Heart defects isolated and complex	0.52 (0.34–0.78) 0.27 (0.14–0.55)	
Godwin et al. (2008)[40]	Spina bifida	0.51 (0.36–0.73)	
	OS atrial septal defects	0.80 (0.69–0.93)	
	Ureteric obstruction	1.45 (1.24–1.70)	
	Abdominal wall defect	1.40 (1.04–1.88)	
	Pyloric stenosis	1.49 (1.18–1.89)	
Canfield et al. (2005)[53]	Anencephaly	0.84 (0.76–0.94)	
	Spina bifida	0.66 (0.61–0.71)	
	TGA	0.88 (0.81–0.96)	
	Cleft palate only	0.88 (0.82–0.95)	
	Pyloric stenosis	0.95 (0.90–0.99)	
	Omphalocele	0.79 (0.66–0.95)	
	Upper limb reduction	0.89 (0.80–0.99)	
O'Neill (2007)[37]	Cleft lip ± palate	0.61 (0.39–0.96)	Folic acid 0.4 mg daily
		0.75 (0.50–1.11)	Folate diet only
		0.36 (0.17–0.77)	Supplement + diet
	Cleft palate only	1.07 (0.56–2.03)	
Goh et al (2006)[15]	No effect identified for	Trisomy 21	
		Pyloric stenosis	
		Undescended testis	
		Hypospadias	

RCT: randomized control trial; OS: ostium secunda; TGA: transposition of the great arteries

Periodo intergenésico

- Recomendación OMS: 18-24 meses. Corto <12 meses, largo >60 meses.
- Resultados maternos:
  - PIG corto: Mayor anemia (32%), endometritis puerperal (23%), RPM (42%), rotura uterina (OR 3,04)
  - PIG largo: Más eclampsia (74%), metrorragia tercer trimestre (11%), óbito fetal (18%)

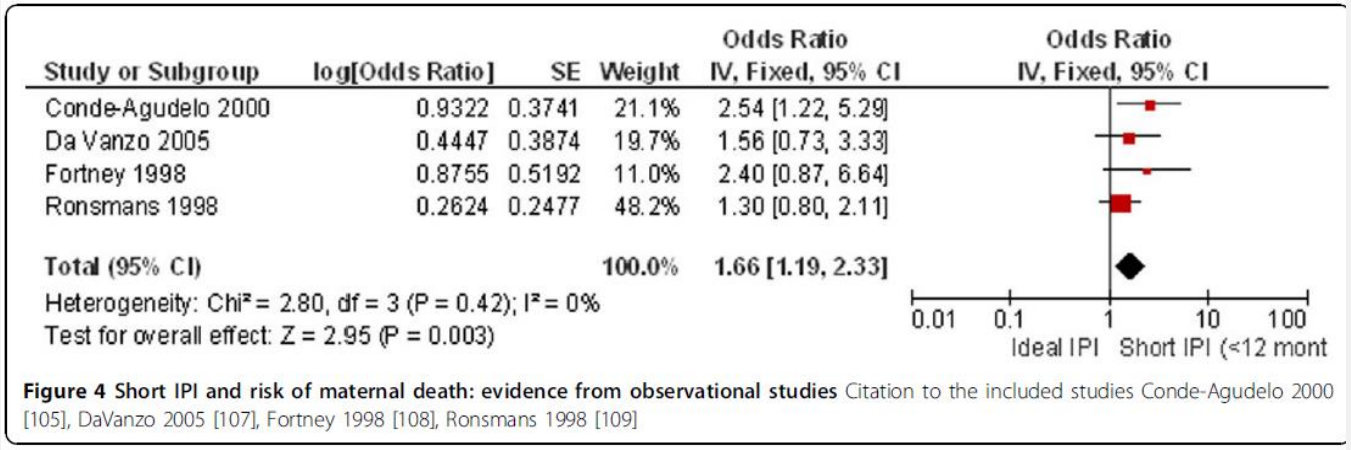

Figure 4 Short IPI and risk of maternal death: evidence from observational studies Citation to the included studies Conde-Agudelo 2000 [105], DaVanzo 2005 [107], Fortney 1998 [108], Ronsmans 1998 [109]

Dean et al.: Preconception care: promoting reproductive planning. Reproductive Health 2014 11(Suppl 3):S2.

Periodo intergenésico

- Resultados perinatales:
  - PIG corto: Mayor parto prematuro (OR 1,45), bajo peso de nacimiento (OR 1,65), defectos congénitos (OR 1,15)
  - PIG largo: Más parto prematuro (OR 1,21), bajo peso de nacimiento (OR 1,37), muerte neonatal (OR 1,15), defectos congénitos (OR 1,15)

Dean et al.: Preconception care: promoting reproductive planning. Reproductive Health 2014 11(Suppl 3):S2.

Edad materna

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- 20 a 35 años, en mayores de 35 años:

- Tasa de cesárea (RR 1.72, 95% CI 1.59-1.85)
- HTA 3 veces
- PE (0R 2.06)
- Hemorragia anteparto 3 veces (placenta previa)
- DG 3 veces
- DPG 6 veces
- Óbito fetal (RR 1,62)
- Muerte perinatal (increased risk by 44%; 95% CI: 1.10-1.89)
- Parto prematuro (increased risk by 29% 95% CI: 1.14-1.46)
- Bajo peso de Nacimiento (increased risk by 61%; 95% CI: 1.16-2.24)

Dean et al.: Preconception care: promoting reproductive planning. Reproductive Health 2014 11(Suppl 3):S2.

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What is the package of preconception care interventions?

Areas addressed by the preconception care package	Examples of evidence-based interventions[1]
Nutritional conditions 	▪ Screening for anaemia and diabetes ▪ Supplementing iron and folic acid ▪ Information, education and counselling ▪ Monitoring nutritional status ▪ Supplementing energy- and nutrient-dense food ▪ Management of diabetes, including counselling people with diabetes mellitus ▪ Promoting exercise ▪ Iodization of salt
Tobacco use 	▪ Screening of women and girls for tobacco use (smoking and smokeless tobacco) at all clinical visits using "5 As" (ask, advise, assess, assist, arrange) ▪ Providing brief tobacco cessation advice, pharmacotherapy (including nicotine replacement therapy, if available) and intensive behavioural counselling services ▪ Screening of all non-smokers (men and women) and advising about harm of second-hand smoke and harmful effects on pregnant women and unborn children

Meeting to develop a global consensus on preconception care to reduce maternal and childhood mortality and morbidity. Geneva, World Health Organization, 2013.

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Genetic conditions

- Taking a thorough family history to identify risk factors for genetic conditions
- Family planning
- Genetic counselling
- Carrier screening and testing
- Appropriate treatment of genetic conditions
- Community-wide or national screening among populations at high risk

Environmental health

- Providing guidance and information on environmental hazards and prevention
- Protecting from unnecessary radiation exposure in occupational, environmental and medical settings
- Avoiding unnecessary pesticide use/providing alternatives to pesticides
- Protecting from lead exposure
- Informing women of childbearing age about levels of methyl mercury in fish
- Promoting use of improved stoves and cleaner liquid/gaseous fuels

Infertility/sub-fertility

- Creating awareness and understanding of fertility and infertility and their preventable and unpreventable causes
- Defusing stigmatization of infertility and assumption of fate
- Screening and diagnosis of couples following 6–12 months of attempting pregnancy, and management of underlying causes of infertility/sub-fertility, including past STIs
- Counselling for individuals/couples diagnosed with unpreventable causes of infertility/sub-fertility

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Interpersonal violence

- Health promotion to prevent dating violence
- Providing age-appropriate comprehensive sexuality education that addresses gender equality, human rights, and sexual relations
- Combining and linking economic empowerment, gender equality and community mobilization activities
- Recognizing signs of violence against women
- Providing health care services (including post-rape care), referral and psychosocial support to victims of violence
- Changing individual and social norms regarding drinking, screening and counselling of people who are problem drinkers, and treating people who have alcohol use disorders

Too-early, unwanted and rapid successive pregnancies

- Keeping girls in school
- Influencing cultural norms that support early marriage and coerced sex
- Providing age-appropriate comprehensive sexuality education
- Providing contraceptives and building community support for preventing early pregnancy and contraceptive provision to adolescents
- Empowering girls to resist coerced sex
- Engaging men and boys to critically assess norms and practices regarding gender-based violence and coerced sex
- Educating women and couples about the dangers to the baby and mother of short birth intervals

Sexually transmitted infections (STIs)

- Providing age-appropriate comprehensive sexuality education and services
- Promoting safe sex practices through individual, group and community-level behavioural interventions
- Promoting condom use for dual protection against STIs and unwanted pregnancies
- Ensuring increased access to condoms
- Screening for STIs
- Increasing access to treatment and other relevant health services

Meeting to develop a global consensus on preconception care to reduce maternal and childhood mortality and morbidity. Geneva, World Health Organization, 2013.

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HIV

- Family planning
- Promoting safe sex practices and dual method for birth control (with condoms) and STI control
- Provider-initiated HIV counselling and testing, including male partner testing
- Providing antiretroviral therapy for prevention and pre-exposure prophylaxis
- Providing male circumcision
- Providing antiretroviral prophylaxis for women not eligible for, or not on, antiretroviral therapy to prevent mother-to-child transmission
- Determining eligibility for lifelong antiretroviral therapy

Mental health

- Assessing psychosocial problems
- Providing educational and psychosocial counselling before and during pregnancy
- Counselling, treating and managing depression in women planning pregnancy and other women of childbearing age
- Strengthening community networks and promoting women's empowerment
- Improving access to education for women of childbearing age
- Reducing economic insecurity of women of childbearing age

Meeting to develop a global consensus on preconception care to reduce maternal and childhood mortality and morbidity. Geneva, World Health Organization, 2013.

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Table 1. Preconception care checklist

Diet
- Nutritional requirements including folic acid supplementation
- Advice on a healthy diet

Weight
- Measurement of body mass index and appropriate advice

Exercise
- Advise 150 minutes of exercise per week or 30 minutes on most days

Pregnancy history
- Screen for any modifiable risk factors

Genetic screening
- If indicated from personal/family history or ethnic background

Smoking/alcohol/illicit drugs
- Assess of intake and provide appropriate advice

Psychosocial aspects
- Screen for domestic violence
- Screen for mental health conditions

Medical conditions
- Review current disease status and medications
- Referral/correspondence with specialist if required

Environmental
- Assess work, home and recreational environments

Contraception/family planning
- Offer appropriate contraception advice for those not desiring pregnancy

Breast examination

Dental health check

Screening for sexually transmissible infections and other infectious diseases
- Measles, mumps, rubella, varicella zoster, hepatitis B
- Human immunodeficiency virus and hepatitis C with appropriate pre-test counselling
- Cervical screening

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Table 2. Periconception nutrition supplementation

SUPPLEMENTATION			
Nutrient	**Target population**	**Recommended dose**	**Evidence**
Folic acid	All women preconception High risk (previous NTD, anticonvulsant medication, GDM, malabsorption, BMI >30 kg/m^2)	400–500 µg daily for at least four weeks prior to pregnancy and for the first 12 weeks of gestation 5 mg daily for at least four weeks prior to pregnancy and for the first 12 weeks of gestation	Prevention of NTD such as spina bifida and anencephaly
Iodine	All women	150 µg daily while pregnant and breastfeeding	Production of maternal thyroid hormone, fetal brain and CNS development
Vitamin D	Women with vitamin D deficiency identified by blood tests	1000 IU/day (vitamin D 30–49 nmol/L) 2000 IU/day (vitamin D <30 nmol/L)	Reduces risk of small-for-gestational-age babies[21] and impaired fetal skeletal development
Iron	Women with iron deficiency identified by blood tests	Oral supplement with at least 60 mg of elemental iron daily	Prevention of anaemia
Vitamin B12	Vegans and vegetarians	2.6 µg/day or intramuscular injection 1000 µg/ampoule	Infant neurological sequelae
Calcium	Women with inadequate dietary intake (<1000 mg daily)	At least 1000 mg daily	Prevention of pre-ecalmpsia

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RESTRICTIONS

Nutrient	Target population	Recommended limitation	Evidence
Vitamin A	All women	Dietary sources do not pose a risk at normal levels Limit vitamin A supplements to 3000 IU per day All synthetic derivatives of retinol should be ceased at least one month prior to conception	Increased risk of miscarriage and CNS malformations
Mercury-containing fish	All women	Limit of one serve per fortnight of fish containing high levels of mercury (shark, billfish) and no other fish to be eaten in that period OR Avoid fish containing high levels of mercury and eat two to three serves of other types of fish per week	Increased risk of negative effects on fetal brain and CNS
Caffeine	All women	Limit to 300 mg or less per day (equivalent to two to three standard cups of coffee)	Increased risk of fetal growth restriction[21]

BMI, body mass index; CNS, central nervous system; GDM, gestational diabetes mellitus; NTD, neural tube defects

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Table 3. Exercise advice for women in the preconception and pregnancy period

Type	Duration/frequency	Intensity	Other information
Aerobic	150–300 minutes of moderate intensity physical activity per week OR 75–150 minutes of vigorous activity per week OR A combination of the two	This is dependent on baseline level of fitness OR Assess via target heart rate: Age <20 years: 140–155 beats per minute Age 20–29 years: 135–150 beats per minute Age 30–39 years: 130–145 beats per minute Age >40 years: 125–140 beats per minute	Women should aim to be active on most days of the week Aim for exercise sessions to be no longer than 60 minutes Ensure adequate nutrition and hydration
Strength	Aim for two strength sessions per week on non-consecutive days	One to two sets of 12–15 repetitions of each muscle group	Can use light weights, resistance bands or body weights
Contact	Avoid contact sports, sports with a risk of falling and scuba diving		

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