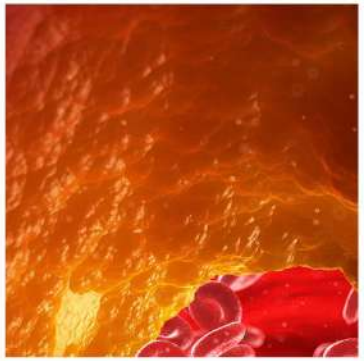
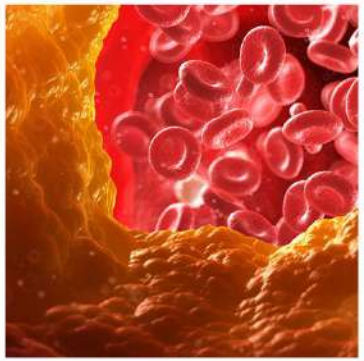
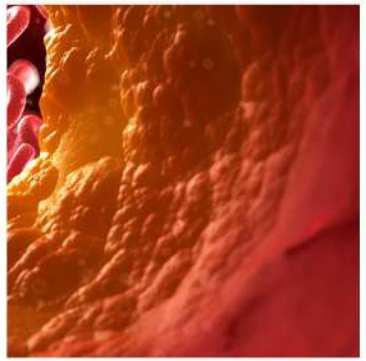
# The 2019 EMEA Cardiometabolic Workshop







Saturday,
16 November 2019

Baku, Azerbaijan

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# Hypothyroidism and pregnancy

Bernadette Biondi

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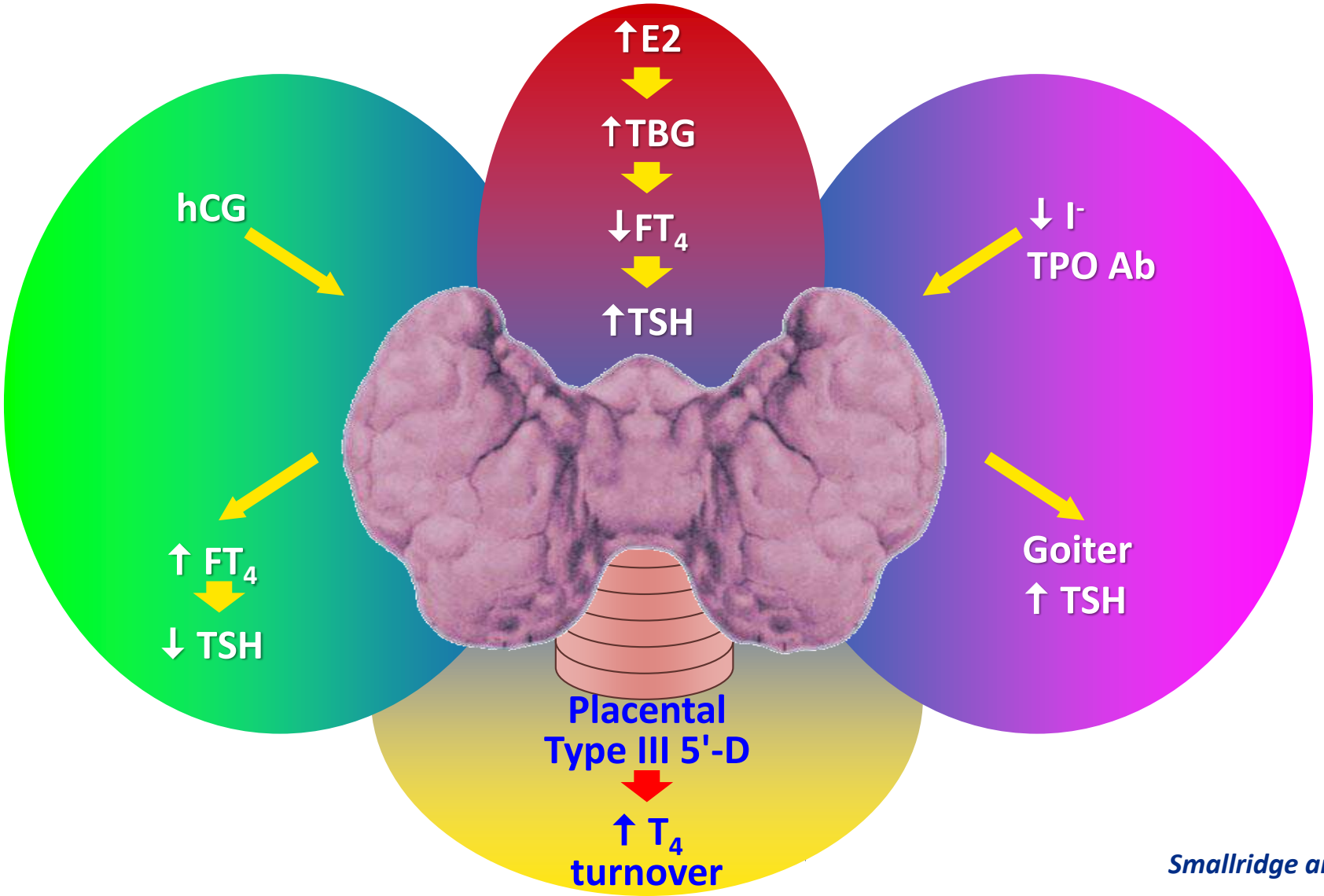
# Disclosures

## Declared no potential conflict of interests

# Learning objectives

- ✓ Assess the recommendations for the diagnosis of thyroid hormone deficiency in pregnancy
- ✓ Summarize the clinical consequences of hypothyroidism
- ✓ Discuss how to treat subclinical and overt hypothyroidism in pregnant women, according to the available guidelines
- ✓ Understand the current areas of controversy regarding L-T4 therapy in pregnant women

# The regulation of thyroid Function in normal pregnancy




*Smallridge and Ladenson, JCEM 2001*

# Thyroid function during pregnancy

**During pregnancy:**

- ✓ **The thyroid gland increases in size by about 10% in iodine-repleted countries and by 20%-40% in presence of iodine deficiency**
- ✓ **The production of T4 and T3 increases by 50%**
- ✓ **The daily iodine requirement increases by 50%**

Guidelines

European
Thyroid Journal

Eur Thyroid J 2014;3:76–94
DOI: 10.1159/000362597

Received: February 13, 2014
Accepted after revision: April 1, 2014
Published online: June 7, 2014

# 2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children

John Lazarus[a] Rosalind S. Brown[c] Chantal Daumerie[d]
Alicja Hubalewska-Dydejczyk[e] Roberto Negro[f] Bijay Vaidya[b]

Clinical Practice Guideline

# Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline

Leslie De Groot, Marcos Abalovich, Erik K. Alexander, Nobuyuki Amino, Linda Barbour, Rhoda H. Cobin, Creswell J. Eastman, John H. Lazarus, Dominique Luton, Susan J. Mandel, Jorge Mestman, Joanne Rovet, and Scott Sullivan

THYROID
Volume 27, Number 3, 2017

DOI: 10.1089/thy.2016.0457

SPECIAL ARTICLE

# 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum

Erik K. Alexander,[1,*] Elizabeth N. Pearce,[2,*] Gregory A. Brent,[3] Rosalind S. Brown,[4] Herbert Chen,[5] Chrysoula Dosiou,[6] William A. Grobman,[7] Peter Laurberg,[8,†] John H. Lazarus,[9] Susan J. Mandel,[10] Robin P. Peeters,[11] and Scott Sullivan[12]

# Learning objectives

- ✓ **Assess the recommendations for the diagnosis of thyroid hormone deficiency in pregnancy**
- ✓ Summarize the clinical consequences of hypothyroidism
- ✓ Discuss how to treat subclinical and overt hypothyroidism in pregnant women according to the available guidelines
- ✓ Understand the current areas of controversy regarding L-T4 therapy in pregnant women

THYROID
Volume 21, Number 10, 2011
© Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2011.0087

# Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum

The American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum

Alex Stagnaro-Green (Chair),[1] Marcos Abalovich,[2] Erik Alexander,[3] Fereidoun Azizi,[4] Jorge Mestman,[5] Roberto Negro,[6] Angelita Nixon,[7] Elizabeth N. Pearce,[8] Offie P. Soldin,[9] Scott Sullivan,[10] and Wilmar Wiersinga[11]

**RECOMMENDATION 1**

- ✓ **Trimester-specific reference ranges for TSH, as defined in populations with optimal iodine intake, should be applied. Level B-USPSTF**

**RECOMMENDATION 2**

- ✓ **If trimester-specific reference ranges for TSH are not available in the laboratory, the following reference ranges are recommended:**
- ✓ **first trimester 0.1–2.5 mIU/L**
- ✓ **second trimester 0.2–3.0 mIU/L**
- ✓ **third trimester 0.3–3.0 mIU/L**
- ✓ **Level I-USPSTF**

Lancet Diabetes Endocrinol
2013; 1: 228–37

# Hypothyroidism in pregnancy

Weiping Teng, Zhongyan Shan, Komal Patil-Sisodia, David S Cooper

| | Country, study type | Number enrolled | Weeks of pregnancy | TSH assay method | TSH (mIU/L) reference range | Raised TSH (%) | Overt hypothyroidism (%) | Subclinical hypothyroidism (%) |
|---|---|---|---|---|---|---|---|---|
| Casey et al (2005)[1] | USA (Texas), retrospective | 17 298 | <20 weeks | Chemiluminescent immunoassays (Immulite 2000 Analyzer) | >97·5th for TSH corrected for gestational age varied between 2·74 and 5·09 | 2·5% | 0·2% | 2·3% |
| Casey et al (2007)[4] | USA (Texas), retrospective | 17 298 | <20 weeks | Chemiluminescent immunoassays (Immulite 2000 Analyzer) | 2·5th–97·5th 0·08–3·0 | – | – | 3·4% |
| Cleary-Goldman et al (2008)[5] | USA, prospective multicentre | 10 990 | Trimester 1 and trimester 2 | Chemiluminescent immunoassays (Immulite 2000 Analyzer) | 2·5th–97·5th 0·036–4·28 in trimester 1, 0·213–3·93 in trimester 2 | – | – | 2·2% in trimester 1, 2·2% in trimester 2 |
| Lazarus et al (2012)[6] | UK and Italy, prospective | 21 846, 10 924 in SG, 10 922 in CG | <15 weeks and 6 days | Immunochemiluminescence (ADVIA Centaur) in UK, Immunofluorescence method (AutoDELFIA) in Italy | 2·5th–97·5th 0·15–3·65 in UK 0·11–3·5 in Italy | – | 0·25%, 0·23% in SG, 0·27% in CG | 2·27%, 2·12% in SG, 2·42% in SG |
| Potlukova et al (2012)[7] | Czech Republic, retrospective | 5223 | 9–12 weeks | Chemiluminescent assay (ADVIA Centaur Analyzer) | 2·5th–97·5th 0·06–3·67 | 5·63% | 0·4% | 3·89% |
| Blatt et al (2012)[8] | USA, retrospective | 117 892 | Trimester 1, trimester 2, and trimester 3 | – | 0·10–2·50 in trimester 1 0·55–2·75 in trimester 2 0·43–2·91 in trimester 3 | 15·5% | 0·37% (2·4% of 15·5%) | 15·13% (97·6% of 15·5%) |
| Shan et al (2009)[9] | China (Shenyang), prospective, iodine sufficient | 4800 | <20 weeks | Chemiluminescent assay (Immulite 2000 Analyzer) | 2·5th–97·5th, 0·59–4·38 in G4, 0·21–3·80 in G8, 0·09–2·96 in G12, 0·05–3·29 in G16, 0·35–3·88 in G20 | – | 1·01% in G4, 0·37% in G8, 0% in G12, 0·32% in G16, 0% in G20 | 4·59% in G4, 6·15% in G8, 4·68% in G12, 4·53% in G16, 5·96% in G20 |

TSH=thyroid-stimulating hormone. SG=screening group. CG=control group. G=gestational week.

Table 1: Reported p ice of hypothyroidism in pregnancy

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The pregnancy-specific TSH reference range should be defined as follows:

- When available, population and trimester-specific reference ranges for serum TSH during pregnancy should be defined by a provider's institute / laboratory, and should represent the typical population for whom care is provided. Reference ranges should be defined in healthy, TPOAb-negative pregnant women with optimal iodine intake and without thyroid illness. ***(Strong recommendation, High quality evidence)***
- When this is not feasible, pregnancy-specific TSH reference ranges obtained from similar patient populations, and performed using similar TSH assays should be substituted. **(Table 4)**. ***(Strong recommendation, High quality evidence)***
- If internal or transferable pregnancy-specific TSH reference ranges are not available, an upper reference limit of ~ 4.0mU/l may be used. For most assays, this represents a reduction in the non-pregnant TSH upper reference limit of ~0.5 mU/L. ***(Strong recommendation, Moderate quality evidence)***

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## RECOMMENDATION 25

In the setting of pregnancy, maternal hypothyroidism is defined as a TSH concentration elevated beyond the upper limit of the pregnancy-specific reference range.

## RECOMMENDATION 33

Women with overt and subclinical hypothyroidism (treated or untreated) or those at risk for hypothyroidism (e.g., patients who are euthyroid but TPOAb or TgAb positive, post-hemithyroidectomy, or treated with radioactive iodine) should be monitored with a serum TSH measurement approximately every 4 weeks until midgestation and at least once near 30 weeks gestation.

**Strong recommendation, high-quality evidence.**

# Learning objectives

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- ✓ **Summarize the clinical consequences of hypothyroidism**
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# Hypothyroidism and early and late obstetric complications

- ✓ Placental abruption
- ✓ Miscarriage
- ✓ Prematurity
- ✓ Anemia
- ✓ Gestational hypertension
- ✓ Gestational diabetes
- ✓ Low birth weight
- ✓ Breech presentation
- ✓ Neuropsychological and cognitive impairment

THYROID
Volume 29, Number 1, 2019

DOI: 10.1089/thy.2018.0311

# Pregnancy and Perinatal Outcome Among Hypothyroid Mothers: A Population-Based Cohort Study

Suvi Turunen,[1] Marja Vääräsmäki,[1] Tuija Männistö,[2] Anna-Liisa Hartikainen,[1] Anna-Maria Lahesmaa-Korpinen,[3] Mika Gissler,[3,4] and Eila Suvanto[1]

***Background:*** Maternal hypothyroidism has been associated with adverse pregnancy outcomes. A large nationwide register-based cohort with data on medication purchases was established to study the associations between maternal hypothyroidism, levothyroxine (LT4) use, and pregnancy and perinatal complications.
***Methods:*** The data included all singleton births between 2004 and 2013 ($N=571,785$) in Finland. Hypothyroid mothers ($n=16,364$) were identified in the Finnish Medical Birth Register. Of these women, 95.8% used LT4 medication, and 37.5% had consistent LT4 use during pregnancy. Hypothyroid mothers were compared to mothers without thyroid disease ($N=550,860$) using logistic regression. The main outcome measures were pregnancy and perinatal complications.
***Results:*** Maternal hypothyroidism was associated with several pregnancy and perinatal complications, including gestational diabetes mellitus (odds ratio [OR] = 1.19 [confidence interval (CI) 1.13–1.25]), gestational hypertension (OR = 1.20 [CI 1.10–1.30]), severe preeclampsia (OR = 1.38 [CI 1.15–1.65]), cesarean section (OR = 1.22 [CI 1.17–1.27]), preterm births (OR = 1.25 [CI 1.16–1.34]), large-for-gestational age newborns (OR = 1.30 [CI 1.19–1.42]), major congenital anomalies (OR = 1.14 [CI 1.06–1.22]), and neonatal intensive care unit admission (OR = 1.23 [CI 1.17–1.29]). However, among mothers with consistent LT4 purchases, only the associations between gestational diabetes mellitus (OR = 1.12 [CI 1.03–1.22]), cesarean section (OR = 1.13 [CI 1.06–1.21]), neonatal intensive care unit admission (OR = 1.09 [CI 1.01–1.29]), and large-for-gestational age newborns (OR = 1.26 [CI 1.10–1.45]) and maternal hypothyroidism remained.
***Conclusions:*** Maternal hypothyroidism is associated with several pregnancy and perinatal complications, but consistent LT4 use may reduce many of the risks.

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Volume 27, Number 3, 2017

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- ✓**There is an association between overt thyroid dysfunction and an increased risk of infertility. Treatment with L-T4 is safe and may exert a positive effect on fertility. Therefore, it is reasonable to treat overt thyroid dysfunction in infertile women with the goal of normalizing thyroid function**
- ✓**Limited evidence suggests that women with female-factor infertility are more likely to be TPOAb positive than age matched women who are not infertile, even if euthyroid**

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- **RECOMMENDATION 16**
  Evaluation of serum TSH concentration is recommended for all women seeking care for infertility.

  **Weak recommendation, moderate-quality evidence.**

- **RECOMMENDATION 17**
  LT4 treatment is recommended for infertile women with overt hypothyroidism who desire pregnancy.

  **Strong recommendation, moderate-quality evidence.**

- **RECOMMENDATION 18**
  Insufficient evidence exist to determine if LT4 therapy improves fertility in subclinically hypothyroid, thyroid autoantibody–negative women who are attempting natural conception (not undergoing ART). However, administration of LT4 may be considered in this setting given its ability to prevent progression to more significant hypothyroidism once pregnancy is achieved. Furthermore, low dose LT4 therapy (25–50 $\mu$g/d) carries minimal risk.

  **Weak recommendation, low-quality evidence.**

- **RECOMMENDATION 21**
  Insufficient evidence exists to determine whether LT4 therapy improves the success of pregnancy following ART in TPOAb-positive euthyroid women. However, administration of LT4 to TPOAb-positive euthyroid women undergoing ART may be considered given its potential benefits in comparison to its minimal risk. In such cases, 25–50 $\mu$g of LT4 is a typical starting dose.

  **Weak recommendation, low-quality evidence.**

| Study Author (Year) | Country or Countries | Participant Characteristics | No. (%) of TPOAb-Positive Subjects | TFT Cutoff | L-$T_4$ Treatment (No. Treated) | Comparison | Clinical Outcomes |
|---|---|---|---|---|---|---|---|
| Wang et al. (2017)[9] | China | Euthyroid, TPOAb-positive women undergoing IVF | 100%<br>TPOAb titer ≥60 IU/L | TSH, 0.5–4.78 mIU/L | (n = 300)<br>Started 2-4 wk before IVF treatment at 25 µg/day if TSH <2.5 or 50 µg if TSH >2.5 mIU/L<br>Starting dose reduced by 50% if body weight <50 kg<br>Dose titrated to achieve TSH goal of 0.1 to 2.5 mIU/L during 1st trimester or 0.2 to 3.0 mIU/L during 3rd trimester | No treatment (n = 300) | Treatment did not significantly alter miscarriage (10.3%, vs. 10.6%), pregnancy, or birth rates as compared with no treatment. |
| Dhill-on-Smith et al. (2019)[16] | UK | TPOAb-positive euthyroid women with history of miscarriage or infertility | 100%;<br>TPOAb positivity based on hospital lab thresholds | TSH, 0.44–3.63 mIU/L and $FT_4$, 10.0–21 pmol/L | (n = 470)<br>50 µg/d; initiated before conception | Placebo (n = 470) | Treatment in TPOAb-positive euthyroid women did not result in a higher rate of live births (37.4%, vs. 37.9% TPOAb-positive with placebo). There was **no** significant effect on miscarriage, preterm birth, or neonatal outcomes. |

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Authors: Erik K. Alexander MD[1] (co-chairperson), Elizabeth N. Pearce MD,MSc[2] (co-chairperson and corresponding author), Gregory A. Brent MD[3], Rosalind S. Brown MD[4], Herbert Chen MD[5], Chrysoula Dosiou MD, MS[6], William A. Grobman MD[7], Peter Laurberg MD[8], John H. Lazarus MD[9], Susan J. Mandel MD[10], Robin P. Peeters MD, PhD[11], and Scott Sullivan MD[12]

- **RECOMMENDATION 14**

  Insufficient evidence exists to conclusively determine whether LT4 therapy decreases pregnancy loss risk in TPOAb-positive euthyroid women who are newly pregnant. However, administration of LT4 to TPOAb-positive euthyroid pregnant women with a prior history of loss may be considered given its potential benefits in comparison with its minimal risk. In such cases, 25–50 $\mu$g of LT4 is a typical starting dose.

  **Weak recommendation, low-quality evidence.**

- **RECOMMENDATION 15**

  Insufficient evidence exists to recommend for or against treating euthyroid pregnant women who are thyroid autoantibody positive with LT4 to prevent preterm delivery.

  **No recommendation, insufficient evidence.**

JAMA | Original Investigation

# Association of Thyroid Function Test Abnormalities and Thyroid Autoimmunity With Preterm Birth

## A Systematic Review and Meta-analysis

The Consortium on Thyroid and Pregnancy—Study Group on Preterm Birth

**IMPORTANCE** Maternal hypothyroidism and hyperthyroidism are risk factors for preterm birth. Milder thyroid function test abnormalities and thyroid autoimmunity are more prevalent, but it remains controversial if these are associated with preterm birth.

**OBJECTIVE** To study if maternal thyroid function test abnormalities and thyroid autoimmunity are risk factors for preterm birth.

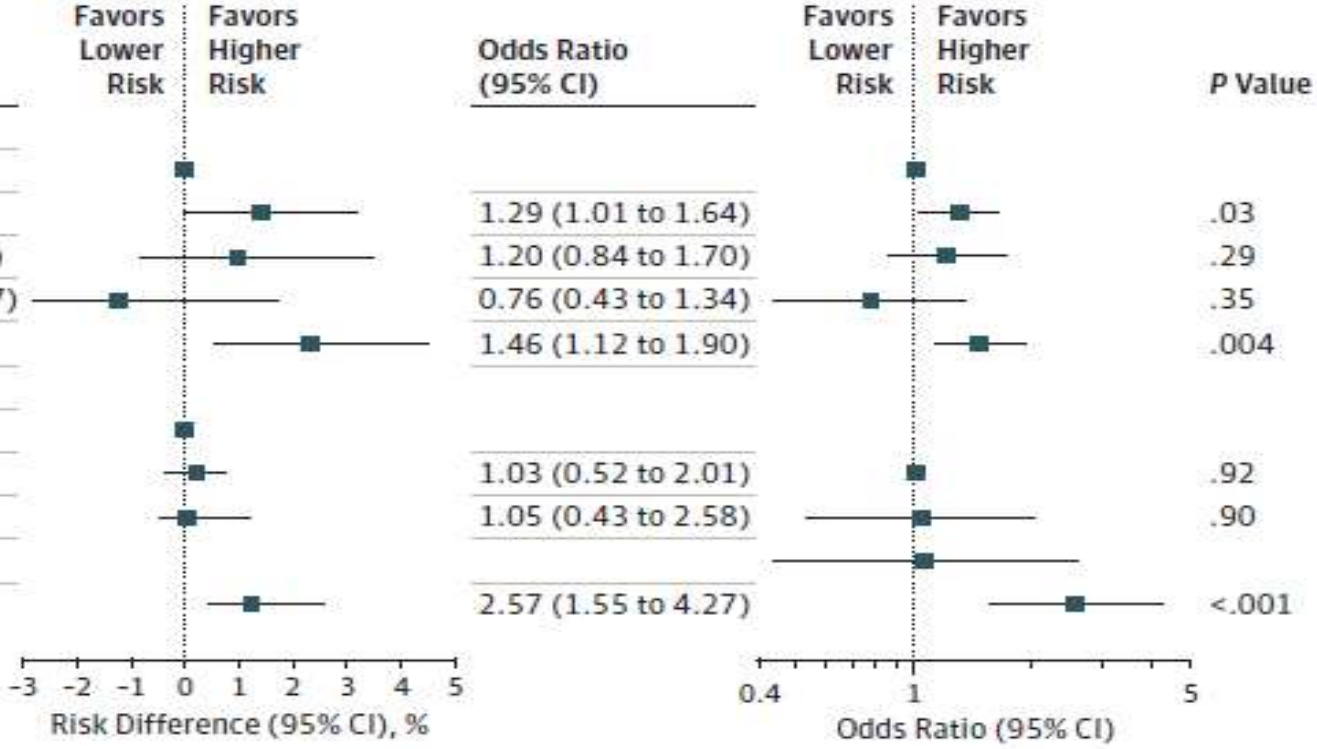
**DATA SOURCES AND STUDY SELECTION** Studies were identified through a search of the Ovid MEDLINE, EMBASE, Web of Science, the Cochrane Central Register of Controlled Trials, and Google Scholar databases from inception to March 18, 2018, and by publishing open invitations in relevant journals. Data sets from published and unpublished prospective cohort studies with data on thyroid function tests (thyrotropin [often referred to as thyroid-stimulating hormone or TSH] and free thyroxine [$FT_4$] concentrations) or thyroid peroxidase (TPO) antibody measurements and gestational age at birth were screened for eligibility by 2 independent reviewers. Studies in which participants received treatment based on abnormal thyroid function tests were excluded.

**DATA EXTRACTION AND SYNTHESIS** The primary authors provided individual participant data that were analyzed using mixed-effects models.

**MAIN OUTCOMES AND MEASURES** The primary outcome was preterm birth (<37 weeks' gestational age).

## Association of Thyroid Function Test Abnormalities With Preterm Birth

| | No. of Events/ Total No. (%) | Risk Difference (95% CI), % | Odds Ratio (95% CI) | *P* Value |
|---|---|---|---|---|
| Preterm birth (gestational age <37 wk) | | | | |
| Euthyroid (reference group) | 1859/37 202 (5.0) | | | |
| Subclinical hypothyroidism | 75/1234 (6.1) | 1.4 (0 to 3.2) | 1.29 (1.01 to 1.64) | .03 |
| Subclinical hyperthyroidism | 35/594 (5.9) | 1.0 (-0.8 to 3.5) | 1.20 (0.84 to 1.70) | .29 |
| Overt hyperthyroidism | 13/328 (4.0) | -1.2 (-2.8 to 1.7) | 0.76 (0.43 to 1.34) | .35 |
| Isolated hypothyroxinemia | 64/904 (7.1) | 2.3 (0.6 to 4.5) | 1.46 (1.12 to 1.90) | .004 |
| Very preterm birth (gestational age <32 wk) | | | | |
| Euthyroid (reference group) | 289/37 202 (0.8) | | | |
| Subclinical hypothyroidism | 9/1234 (0.7) | 0 (-0.3 to 0.8) | 1.03 (0.52 to 2.01) | .92 |
| Subclinical hyperthyroidism | 5/594 (0.8) | 0 (-0.4 to 1.2) | 1.05 (0.43 to 2.58) | .90 |
| Overt hyperthyroidism | 1/328 (0.3)[a] | | | |
| Isolated hypothyroxinemia | 17/904 (1.9) | 1.2 (0.4 to 2.5) | 2.57 (1.55 to 4.27) | <.001 |




All analyses were adjusted for maternal age, body mass index, ethnicity, smoking, parity, gestational age at blood sampling, and fetal sex. Euthyroid was defined as the 2.5th-97.5th cohort-specific percentile for thyrotropin (often referred to as thyroid-stimulating hormone or TSH) and free thyroxine ($FT_4$) concentrations; subclinical hypothyroidism, increased thyrotropin concentration with a normal $FT_4$ concentration; subclinical hyperthyroidism, decreased thyrotropin concentration with a normal $FT_4$ concentration; overt hyperthyroidism, decreased thyrotropin concentration with an increased $FT_4$ concentration; and isolated hypothyroxinemia, a normal thyrotropin concentration with a decreased $FT_4$ concentration. These clinical entities were calculated for cohorts that had thyrotropin concentration, $FT_4$ concentration, and thyroid peroxidase antibody data available. Absolute differences and corresponding 95% CIs were back-calculated from the results of multivariable models and adjusted for baseline risk imprecision.

[a] There were too few samples to conduct a reliable analysis.

**RESULTS** From 2526 published reports, 35 cohorts were invited to participate. After the addition of 5 unpublished data sets, a total of 19 cohorts were included. The study population included 47 045 pregnant women (mean age, 29 years; median gestational age at blood sampling, 12.9 weeks), of whom 1234 (3.1%) had subclinical hypothyroidism (increased thyrotropin concentration with normal $FT_4$ concentration), 904 (2.2%) had isolated hypothyroxinemia (decreased $FT_4$ concentration with normal thyrotropin concentration), and 3043 (7.5%) were TPO antibody positive; 2357 (5.0%) had a preterm birth. The risk of preterm birth was higher for women with subclinical hypothyroidism than euthyroid women (6.1% vs 5.0%, respectively; absolute risk difference, 1.4% [95% CI, 0%-3.2%]; odds ratio [OR], 1.29 [95% CI, 1.01-1.64]). Among women with isolated hypothyroxinemia, the risk of preterm birth was 7.1% vs 5.0% in euthyroid women (absolute risk difference, 2.3% [95% CI, 0.6%-4.5%]; OR, 1.46 [95% CI, 1.12-1.90]). In continuous analyses, each 1-SD higher maternal thyrotropin concentration was associated with a higher risk of preterm birth (absolute risk difference, 0.2% [95% CI, 0%-0.4%] per 1 SD; OR, 1.04 [95% CI, 1.00-1.09] per 1 SD). Thyroid peroxidase antibody–positive women had a higher risk of preterm birth vs TPO antibody–negative women (6.6% vs 4.9%, respectively; absolute risk difference, 1.6% [95% CI, 0.7%-2.8%]; OR, 1.33 [95% CI, 1.15-1.56]).

**CONCLUSIONS AND RELEVANCE** Among pregnant women without overt thyroid disease, subclinical hypothyroidism, isolated hypothyroxinemia, and TPO antibody positivity were significantly associated with higher risk of preterm birth. These results provide insights toward optimizing clinical decision-making strategies that should consider the potential harms and benefits of screening programs and levothyroxine treatment during pregnancy.

*JAMA*. 2019;322(7):632-641. doi:10.1001/jama.2019.10931

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- **Recommendation 29**

Subclinical hypothyroidism in pregnancy should be approached as follows:

a) Levothyroxine therapy is recommended for:

- TPO antibody positive women with a TSH greater than the pregnancy specific reference range (see Recommendation 1)

***(Strong recommendation, Moderate quality evidence)***

- TPO antibody negative women with a TSH greater than 10.0 mU/L.

***(Strong recommendation, Low quality evidence)***

b) Levothyroxine therapy may be considered for:

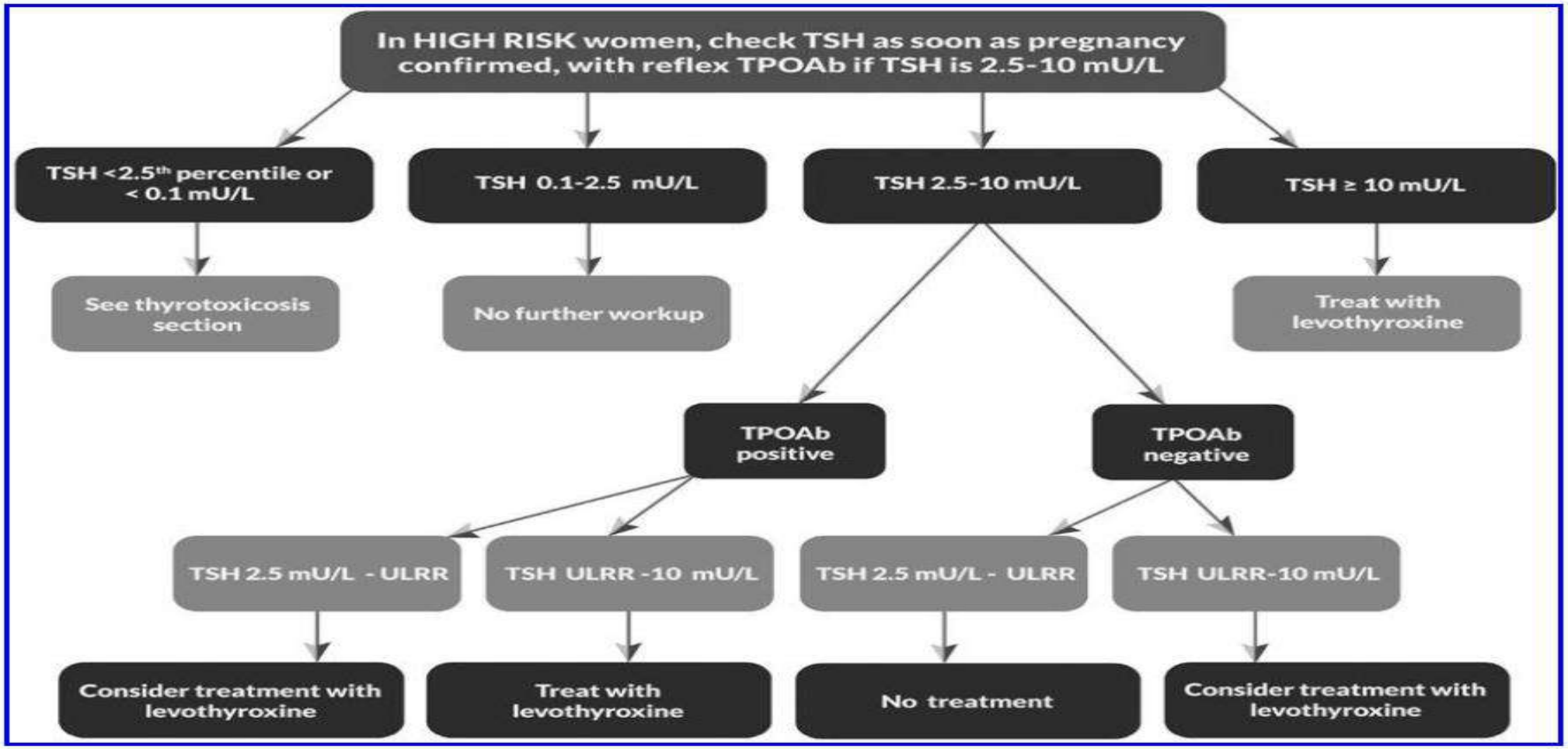
- TPO antibody positive women with TSH concentrations > 2.5 mU/L and below the upper limit of the pregnancy specific reference range.

***(Weak recommendation, Moderate quality evidence)***

- TPO antibody negative women TPO antibody negative women with TSH concentrations greater than the pregnancy specific reference range and below 10.0 mU/L.

# Testing for thyroid Dysfunction in pregnancy






Testing for thyroid dysfunction in pregnancy. ULRR, upper limit of the reference range.

# Learning objectives

- ✓ Assess the recommendations for the diagnosis of thyroid hormone deficiency in pregnancy
- ✓ Summarize the clinical consequences of hypothyroidism
- ✓ **Discuss how to treat subclinical and overt hypothyroidism in pregnant women according to the available guidelines**
- ✓ Understand the current areas of controversy regarding L-T4 therapy in pregnant women

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- **Recommendation 31**

The recommended treatment of maternal hypothyroidism is administration of oral levothyroxine. Other thyroid preparations such as triiodothyronine (T3) or desiccated thyroid should not be used in pregnancy. ***(Strong recommendation, Low quality evidence)***

J Endocrinol Invest
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CONSENSUS STATEMENT

# Recommendations for treatment of hypothyroidism with levothyroxine and levotriiodothyronine: a 2016 position statement of the Italian Society of Endocrinology and the Italian Thyroid Association

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## Recommendation 3 on thyroid extracts, iodine-containing preparations, dietary supplementations and nutraceuticals (1/+++)

- The routine use of thyroid extracts, iodine-containing preparations, dietary supplementations and nutraceuticals is not recommended in hypothyroid patients,
- The use of L-T3 as monotherapy is not recommended because of its pharmacokinetic profile which results in a relatively short half-life and in wide non-physiological fluctuations in serum TSH and TT3 or FT3 levels;
- Treatment with L-T4 + L-T3 is not recommended in pregnant women and children.

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# 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum

Authors: Erik K. Alexander MD[1] (co-chairperson), Elizabeth N. Pearce MD,MSc[2] (co-chairperson and corresponding author), Gregory A. Brent MD[3], Rosalind S. Brown MD[4], Herbert Chen MD[5], Chrysoula Dosiou MD, MS[6], William A. Grobman MD[7], Peter Laurberg MD[8], John H. Lazarus MD[9], Susan J. Mandel MD[10], Robin P. Peeters MD, PhD[11], and Scott Sullivan MD[12]

- **RECOMMENDATION 35**

  In hypothyroid women treated with LT4 who are planning pregnancy, serum TSH should be evaluated preconception, and LT4 dose adjusted to achieve a TSH value between the lower reference limit and 2.5 mU/L.

  **Strong recommendation, moderate-quality evidence.**

- **RECOMMENDATION 36**

  Hypothyroid patients receiving LT4 treatment with a suspected or confirmed pregnancy (e.g., positive home pregnancy test) should independently increase their dose of LT4 by ~20%–30% and urgently notify their caregiver for prompt testing and further evaluation. One means of accomplishing this is to administer two additional tablets weekly of the patient's current daily LT4 dosage.

  **Strong recommendation, high-quality evidence.**

# Learning objectives

- ✓ Assess the recommendations for the diagnosis of thyroid hormone deficiency in pregnancy
- ✓ Summarize the clinical consequences of hypothyroidism
- ✓ Discuss how to treat subclinical and overt hypothyroidism in pregnant women according to the available guidelines
- ✓ **Understand the current areas of controversy regarding L-T4 therapy in pregnant women**

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European Thyroid Journal

Guidelines

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# 2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children

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11 To date, no study of intervention is available to demonstrate a benefit from treating hypothyroxinaemic women in terms of obstetric complications. (1S)

12 However, levothyroxine therapy may be considered in isolated hypothyroxinaemia detected in the first trimester because of its association with neuropsychological impairment in children. (3W)

13 Levothyroxine therapy is not recommended in isolated hypothyroxinaemia detected in the second to third trimester. (3S)

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SPECIAL ARTICLE

# 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum

Erik K. Alexander,[1,*] Elizabeth N. Pearce,[2,*] Gregory A. Brent,[3] Rosalind S. Brown,[4] Herbert Chen,[5] Chrysoula Dosiou,[6] William A. Grobman,[7] Peter Laurberg,[8,†] John H. Lazarus,[9] Susan J. Mandel,[10] Robin P. Peeters,[11] and Scott Sullivan[12]

**Recommendation 30**

Isolated hypothyroxinemia should not be routinely treated in pregnancy. ***(Weak recommendation, Low quality evidence)***

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# 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum

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- **Recommendation 5**

  All pregnant women should ingest approximately 250 µg iodine daily. To achieve a total of 250 µg iodine ingestion daily, strategies may need to be varied based on country of origin. ***(Strong recommendation, High-quality evidence)***

- **Recommendation 6**

  In most regions, including the United States, women who are planning pregnancy or currently pregnant, should supplement their diet with a daily oral supplement that contains 150 µg of iodine in the form of potassium iodide. This is optimally started 3 months in advance of planned pregnancy. ***(Strong recommendation, Moderate-quality evidence)***

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SPECIAL ARTICLE

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## RECOMMENDATION 93

There is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations in early pregnancy.

**No recommendation, insufficient evidence.**

## RECOMMENDATION 94

There is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations preconception, with the exception of women planning assisted reproduction or those known to have TPOAb positivity.

**No recommendation, insufficient evidence.**

## RECOMMENDATION 95

Universal screening to detect low FT4 concentrations in pregnant women is not recommended.

**Weak recommendation, moderate-quality evidence.**

## RECOMMENDATION 96

All pregnant women should be verbally screened at the initial prenatal visit for any history of thyroid dysfunction, and prior or current use of either thyroid hormone (LT4) or antithyroid medications (MMI, CM, or PTU).

**Strong recommendation, high-quality evidence.**

## RECOMMENDATION 97

All patients seeking pregnancy, or newly pregnant, should undergo clinical evaluation. If any of the following risk factors are identified, testing for serum TSH is recommended:

1. A history of hypothyroidism/hyperthyroidism or current symptoms/signs of thyroid dysfunction
2. Known thyroid antibody positivity or presence of a goiter
3. History of head or neck radiation or prior thyroid surgery
4. Age >30 years
5. Type 1 diabetes or other autoimmune disorders
6. History of pregnancy loss, preterm delivery, or infertility
7. Multiple prior pregnancies (≥2)
8. Family history of autoimmune thyroid disease or thyroid dysfunction
9. Morbid obesity (BMI ≥40 kg/m$^2$)
10. Use of amiodarone or lithium, or recent administration of iodinated radiologic contrast
11. Residing in an area of known moderate to severe iodine insufficiency

**Strong recommendation, moderate-quality evidence.**

# Conclusions

- Women with reduced thyroid reserve can develop overt hypothyroidism during pregnancy. Maternal hypothyroidism is associated with adverse obstetric and neonatal outcomes.
- Women with a diagnosis of pre-conceptional or gestational hypothyroidism have a higher risk for gestational diabetes, severe preeclampsia, and preterm birth. These risks are considerably lower or even absent among women are treated with levothyroxine throughout pregnancy.
- Oral L-T4 should be used for treatment of overt and subclinical hypothyroidism. The goal of L-T4 treatment is to normalize maternal serum values within the trimester specific pregnancy reference range.
- In patients with isolated hypothyroxinemia, the initiation of L-T4 treatment falls under the judgment of the clinician until new data might clarify the consequences of isolated hypothyroxinemia.
- Treatment of euthyroid TPO posive women can be considered in patients with recurrent miscarriage and in those submitted to ART.

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# *THANK YOU*