

# Meet the Professor:

## Controversies and Uncertainties - Thyroid Cancer During Pregnancy

---

**Erik K. Alexander, MD**

Division of Endocrinology  
Brigham & Women's Hospital  
Associate Professor of Medicine,  
Harvard Medical School



**Sanziana Roman, MD FACS**

Division of Endocrine Surgery  
Duke University Hospital  
Professor of Surgery  
Duke University School of Medicine



# Disclosures:

Dr. Alexander – research support (paid to institution) from Asuragen, Inc. & Veracyte, Inc. Consultant to Genzyme, Asuragen (SAB), & Veracyte, with stock options.

Dr. Roman - none

# Goals:

---

- To review the epidemiology, risk and recommended approach to thyroid nodular disease during pregnancy
- To understand the benefits (utility) and risks of thyroid surgery during pregnancy.
- To provide clinical guidance for the care of patients you will likely see in the days ahead.

# Outline:

---

1. **Thyroid Nodules** - background epidemiology, risk assessment & evaluative strategy:
2. **Review** available evidence-based literature specific to pregnancy.
3. **Clinical cases & discussion** → the ‘grey’ areas



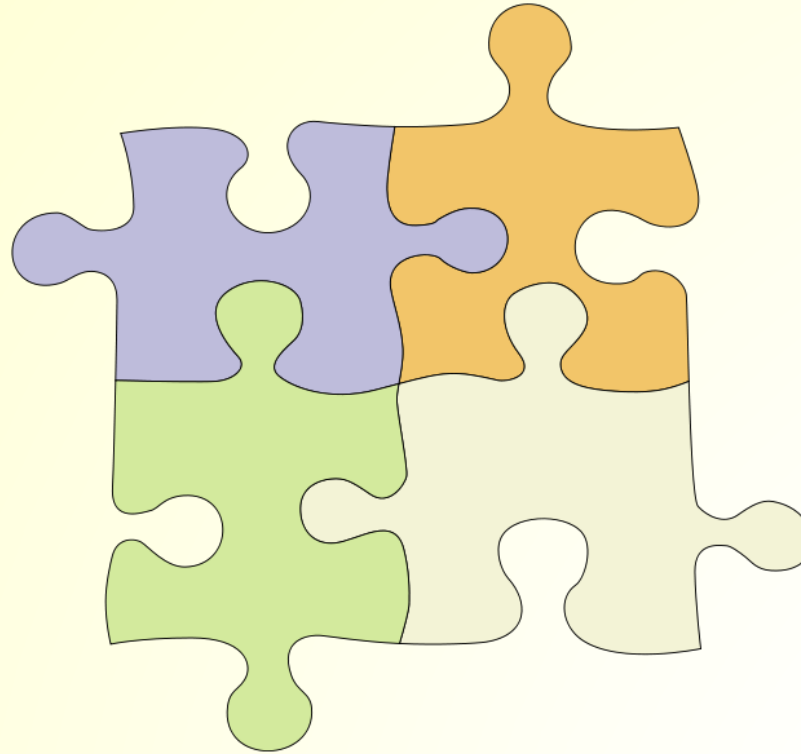
# Thyroid Nodules & Pregnancy ?

## *... a Heterogeneous Disorder*

---

Who are we  
evaluating?

What are our  
priorities?



When are we  
assessing?

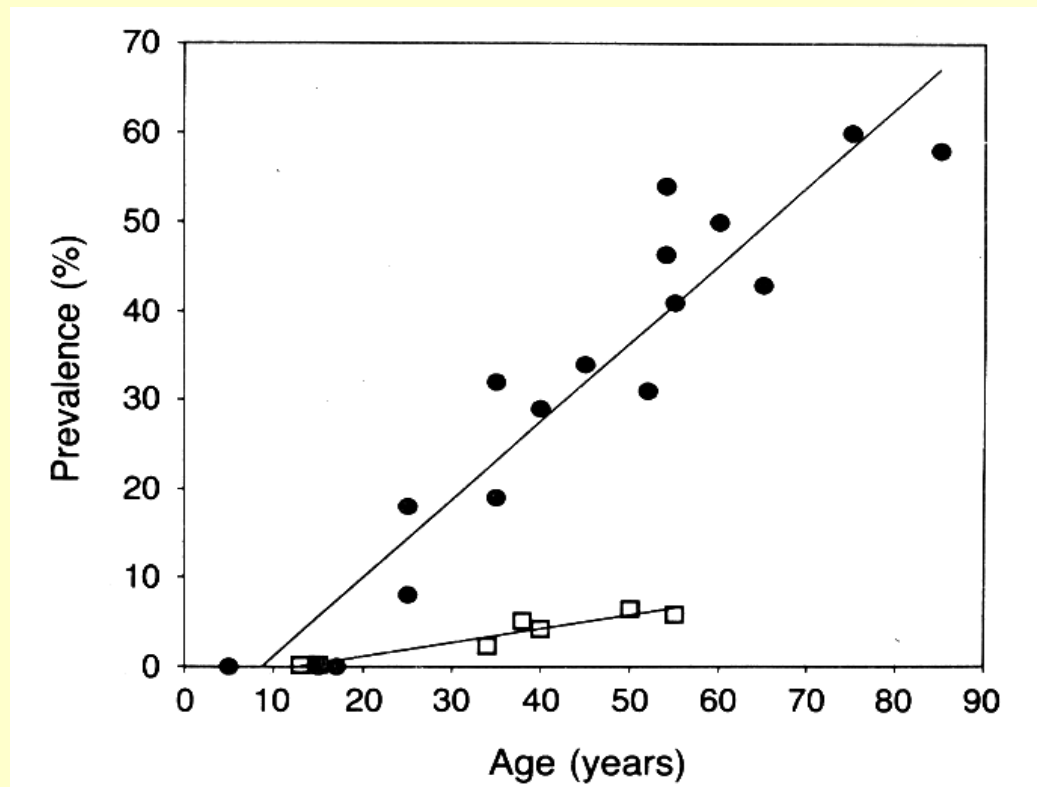
How are we  
testing?

Difficulty: Lack of prospective data

# Background:

## Thyroid Nodule *Epidemiology*

- I. Thyroid nodules are **common**. Most are **asymptomatic**
- II. Pregnancy is often when patients seek initial medical care.  
**Incidental detection** of thyroid nodules common.

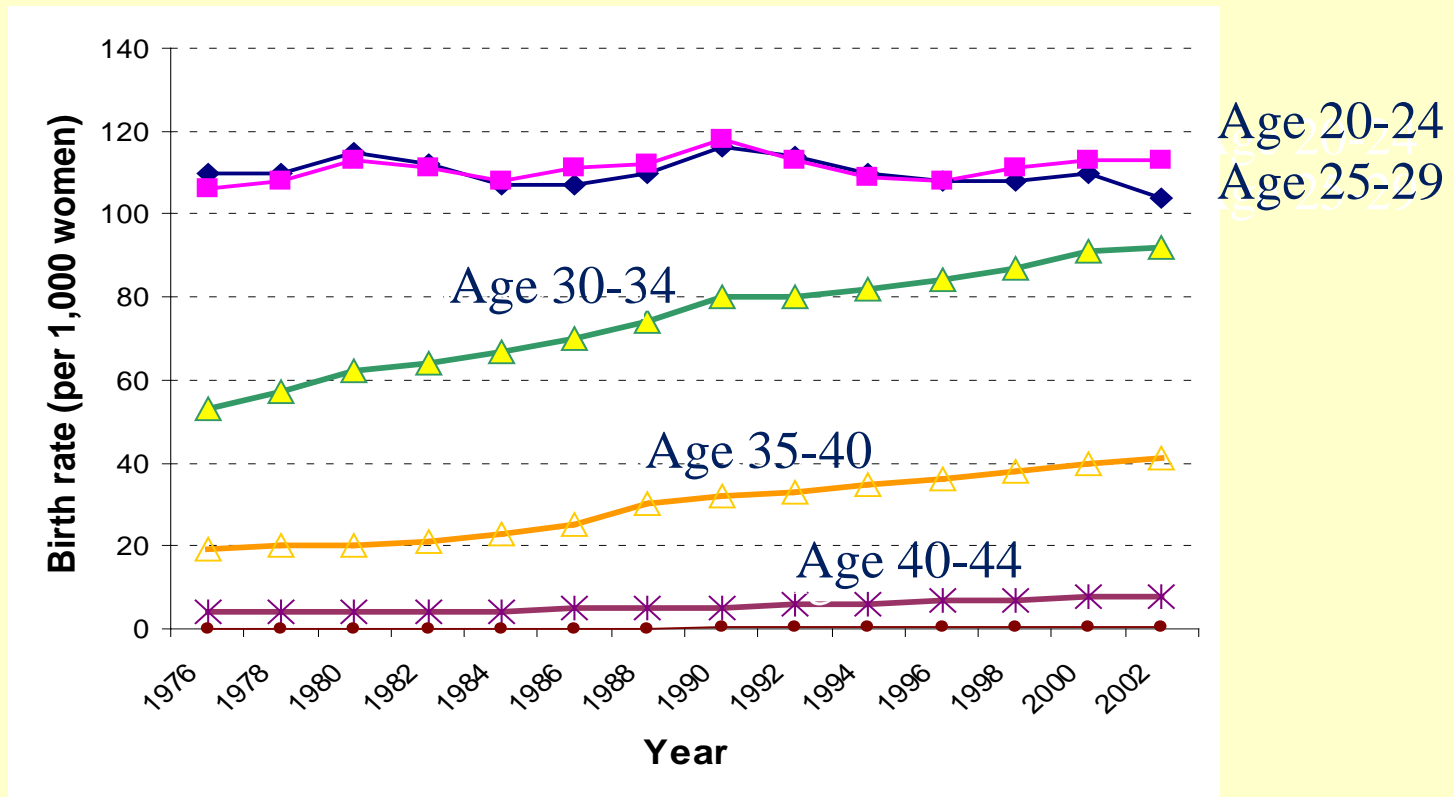


# Age of Pregnancy – *Increasing*

1970

2007

Average birthage: 21.4 yr → 25.1 yr (all time high)

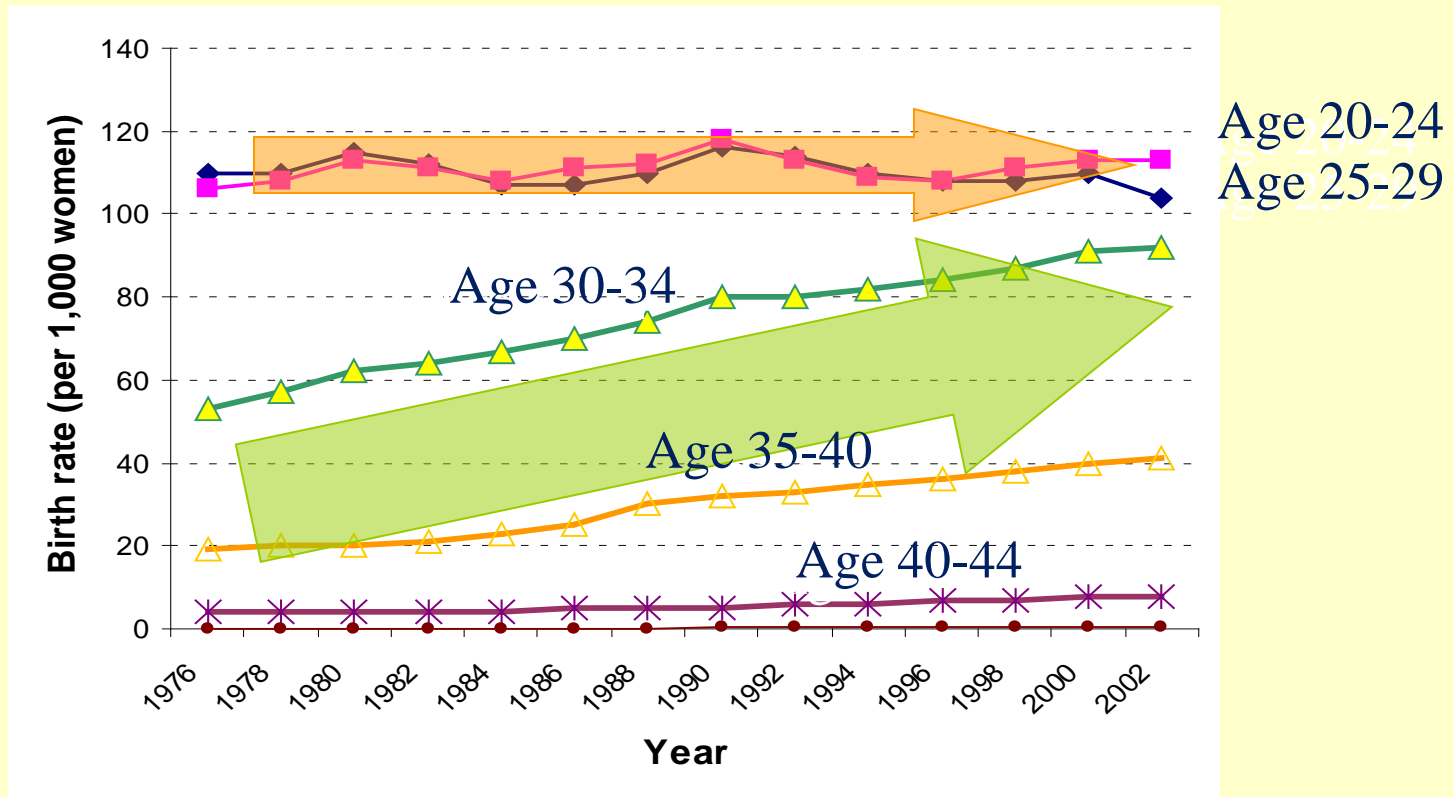


# Age of Pregnancy – *Increasing*

1970

2007

Average birthage: 21.4 yr → 25.1 yr (all time high)

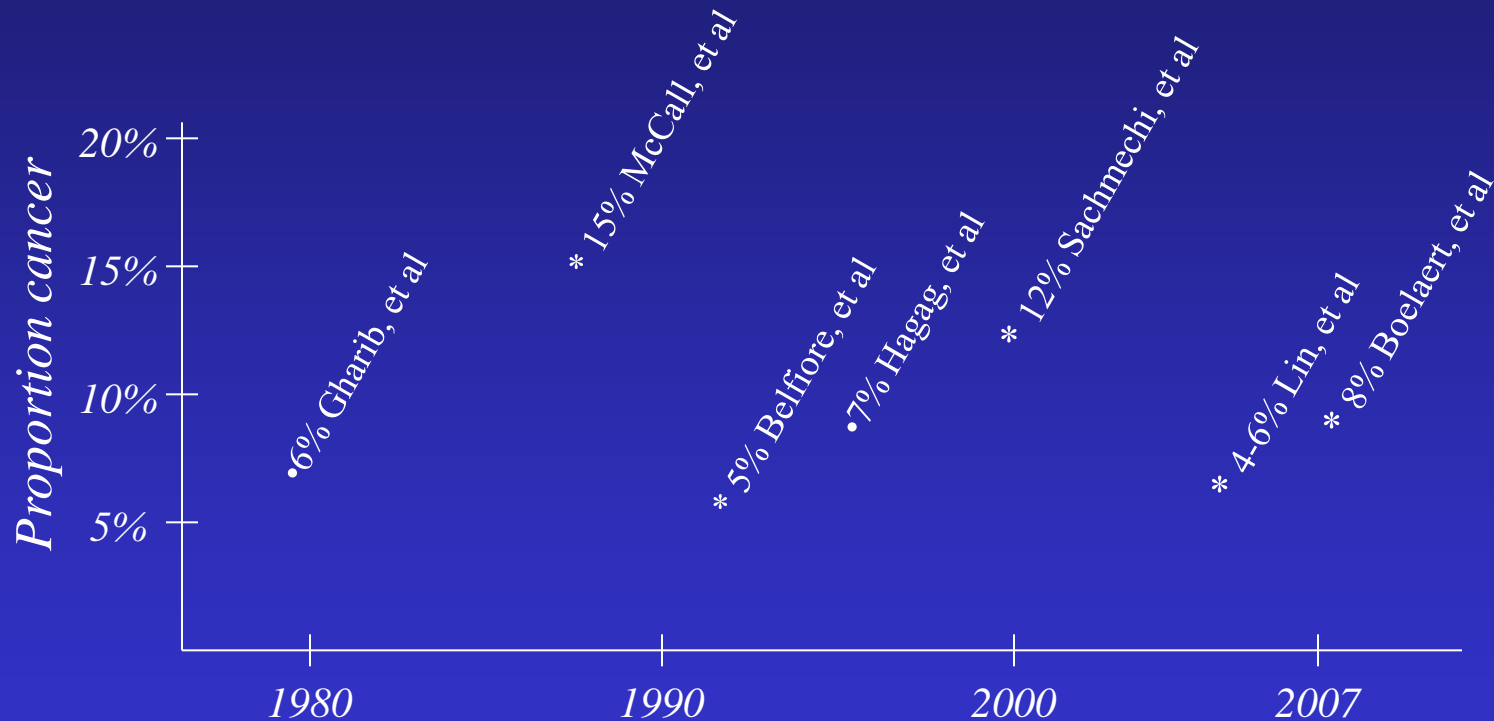




# Background:

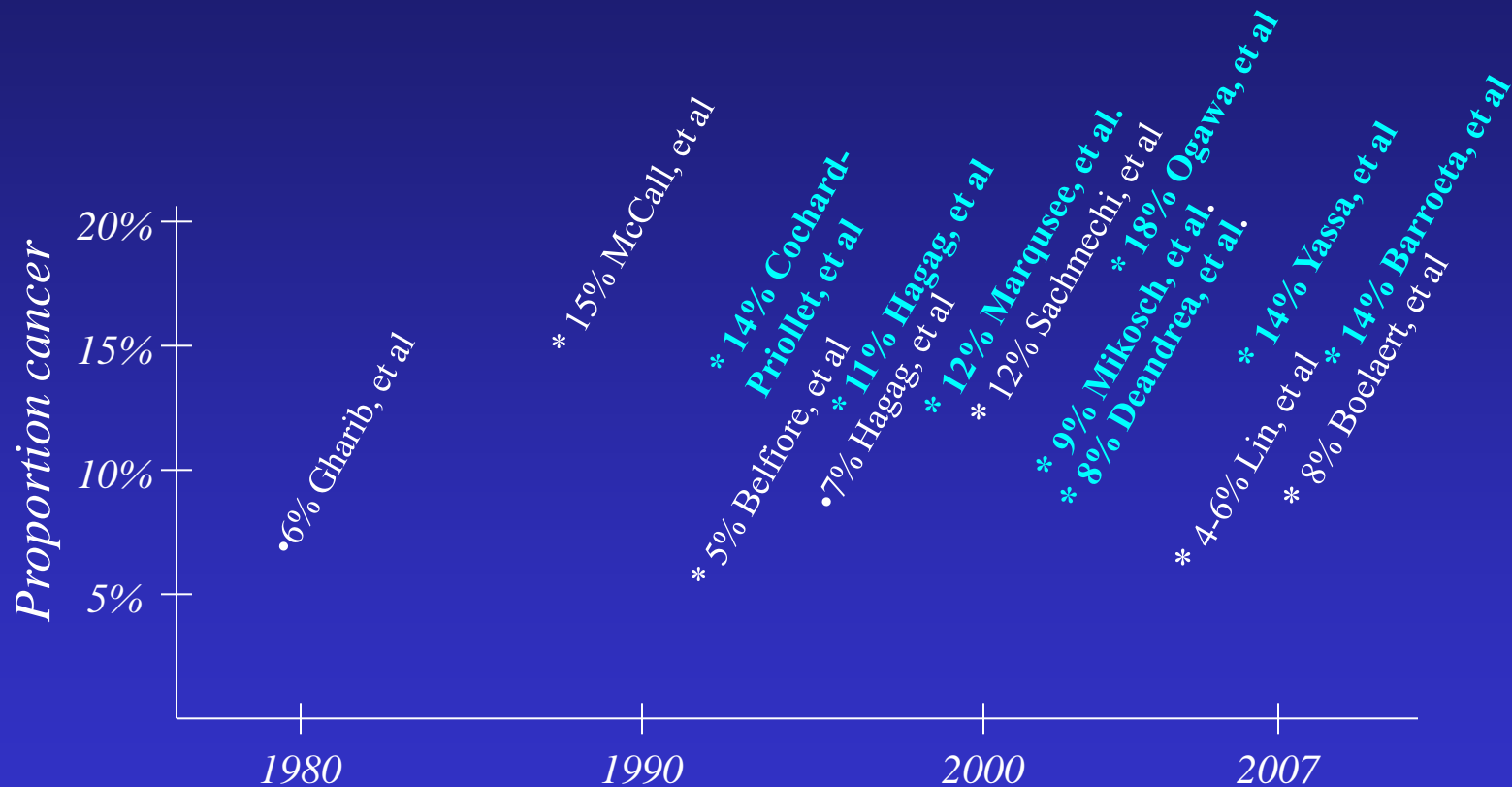
## *Risk* of a Thyroid Nodule >1cm

---



# Background:

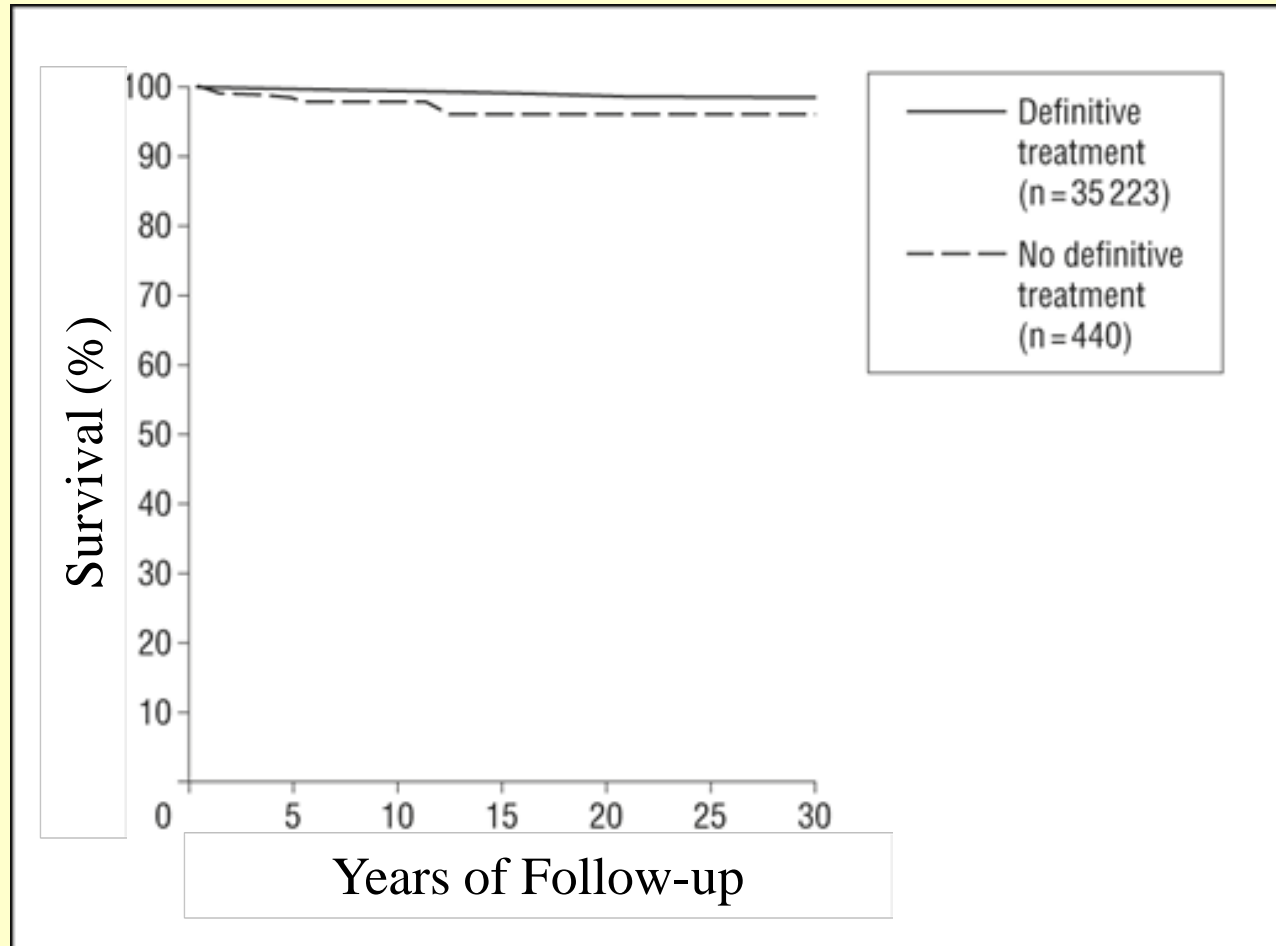
## *Risk* of a Thyroid Nodule >1cm



There exists a low but not inconsequential  
(~8-15%) risk of cancer

# Survival in patients with ‘Localized’ Papillary Thyroid Carcinoma

---



# But not all Carcinoma is 'localized'

*Distant Metastasis in 3 Retrospective analyses of  
745 thyroid cancers <1.5cm*

## *Finding:*

*Pellegriti et al <sup>1</sup>:*

299 patients; PTC  $\leq 1.5\text{cm}$

*Distant Mets (%)*

8 (2.7%)

*Other Finding:*

*Cancers >1cm had more LN  
involvement, bilaterality,  
and vascular invasion*

*Roti et al <sup>2</sup>:*

243 patients; PTC  $\leq 1.0\text{cm}$

4 (1.6%)

*All Distant Mets in  
cancers >8mm*

*Chow et al <sup>3</sup>:*

203 patients; PTC  $\leq 1.0\text{cm}$

5 (2.5%)

*1% disease related  
mortality*

*There exists a small, but consistent rate of distant  
metastasis among cancers ~9-10mm in diameter.*



AMERICAN COLLEGE OF  
OBSTETRICIANS AND  
GYNECOLOGISTS



AMERICAN  
THYROID  
ASSOCIATION  
FOUNDED 1923



## Recent Guidelines!

- ***NEW!***...ATA Thyroid & Pregnancy Guidelines – 2011
- ***REVISED!***...Endocrine Society Thyroid & Pregnancy Guidelines – 2012
- ***EXPECTED!***...ATA Thyroid Nodule & Cancer Guidelines

Most recommendations based upon expert opinion (Level I), or low quality evidence.

# Common Clinical Cases & Questions...

THE ROANOKE TIMES  
Monday, September 20, 2004



STEPHANIE KLEIN-DAVIS | The Roanoke Times

Mellisa Williamson, 35, a Bullitt Avenue resident, worries about the effect on her unborn child from the sound of jackhammers.

## Case #1a

32yo healthy female presents for care and is found to be **newly pregnant** (estimated 11 weeks gestation). She is known to have a **2cm thyroid nodule** confirmed with ultrasound 6 months ago. An UG-FNA revealed 'benign' cytology. She asks if pregnancy will cause new nodules to form?

*What do you respond?*



## Case #1b

32yo healthy female presents for care and is found to be **newly pregnant** (estimated 11 weeks gestation). She is known to have a **2cm thyroid nodule** confirmed with ultrasound 6 months ago. An UG-FNA revealed 'benign' cytology. She asks if pregnancy will cause the current nodule to change or grow?

*What do you respond?*





# Does Pregnancy Stimulate Nodule *Formation*?

- **Hong Kong:** *Propsective analysis of 221 newly pregnant patients:*
- *Thyroid US, TFT's measured 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> trimesters & Post-partum*

## I. Nodules (usually very small) appeared during gestation:

<u>Assessment:</u>	<u>Findings:</u>
	<i>Proportion (%)</i>
1 <sup>st</sup> Trimester	n=34 (15%)
2 <sup>nd</sup> Trimester	n=40 (18%)
3 <sup>rd</sup> Trimester	n=50 (23%)
6-wk Postpartum	n=53 (24%)

*TINY (4mm) nodules may form during pregnancy*



# Does Pregnancy Stimulate Nodule *Formation*?

- **Germany:** *Case-control Thyroid Screening Study of 424 women:*
- *Questionnaire & Ultrasound:*

## I. Nodules more common if parous (prior pregnancy):

<u>Parity:</u>	<u>Nodularity:</u>
	$\geq 1$ nodule(s) in gland:
Prior Pregnancy (385 pts)	177 (46%)
Never Pregnant: (39 pts)	15 (38.5%)

*Supportive, though  $p > 0.05$  given small sample size*



# Does Pregnancy Stimulate Nodule *Growth*?

- **Hong Kong:** *Propsective analysis of 221 newly pregnant patients:*
- *Thyroid US, TFT's measured 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> trimesters & Post-partum*

## I. Nodules increased in size throughout pregnancy:

<u>Assessment:</u>	<u>Findings:</u>	
	<i>Proportion (%)</i>	<i>Median Nodule Size (mm<sup>3</sup>)</i>
1 <sup>st</sup> Trimester	n=34 (15%)	60mm <sup>3</sup>
2 <sup>nd</sup> Trimester	n=40 (18%)	65mm <sup>3</sup>
3 <sup>rd</sup> Trimester	n=50 (23%)	65mm <sup>3</sup>
6-wk Postpartum	n=53 (24%)	103mm <sup>3</sup>

*MINOR (1-3mm) growth may occur during pregnancy*

## Case #2

32yo healthy female presents for care and is found to be **newly pregnant** (estimated 11 weeks gestation). She is known to have a **2cm thyroid nodule** confirmed with ultrasound 6 months ago. An UG-FNA revealed 'benign' cytology. She asks if pregnancy will increase the risk this nodule will convert to 'cancer'.

*What do you respond?*

## Case #3a

24yo female is 9wks pregnant and presents for prenatal care. She has noticed mild nausea & fatigue, but is feeling 'well'. She takes no medications. A physical exam reveals a new thyroid nodule.

- Ultrasound confirms a 1.5cm solid thyroid nodule (no micro-calcification, isoechoic – low risk lesion)

*What would you recommend?*

## Case #3b

24yo female is 9wks pregnant and presents for prenatal care. She has noticed mild nausea & fatigue, but is feeling 'well'. She takes no medications. A physical exam reveals a new thyroid nodule.

- Ultrasound confirms a 3.5cm solid thyroid nodule (no microcalcification, isoechoic – low risk lesion)

*What would you recommend?*

## Case #3c

24yo female is 9wks pregnant and presents for prenatal care. She has noticed mild nausea & fatigue, but is feeling 'well'. She takes no medications. A physical exam reveals a new thyroid nodule.

- Ultrasound confirms a **1.5cm** solid thyroid nodule (**microcalcifications, hypoechoic**) – **high risk lesion**. No abnormal LAD.

*What would you recommend?*

# Do you Agree?

## *The 2011 ATA Guidelines:*

---

- Thyroid nodules discovered during pregnancy that have suspicious ultrasound features, as delineated by the 2009 ATA guidelines, should be considered for FNA. In instances in which nodules are likely benign, FNA may be deferred until after delivery based on patients' preference.  
Level I - USPSTF



# Current Approach to Thyroid Nodule >1cm: *Pregnant or not....*

## Initial Assessment:

Check TSH

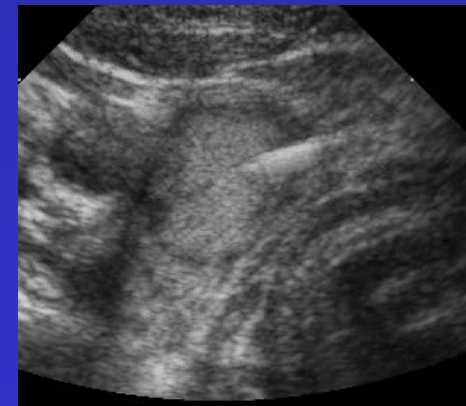
*suppressed*  
( $< 5\%$ )

*normal or elevated*  
( $\sim 95\%$ )

Thyroid Scan

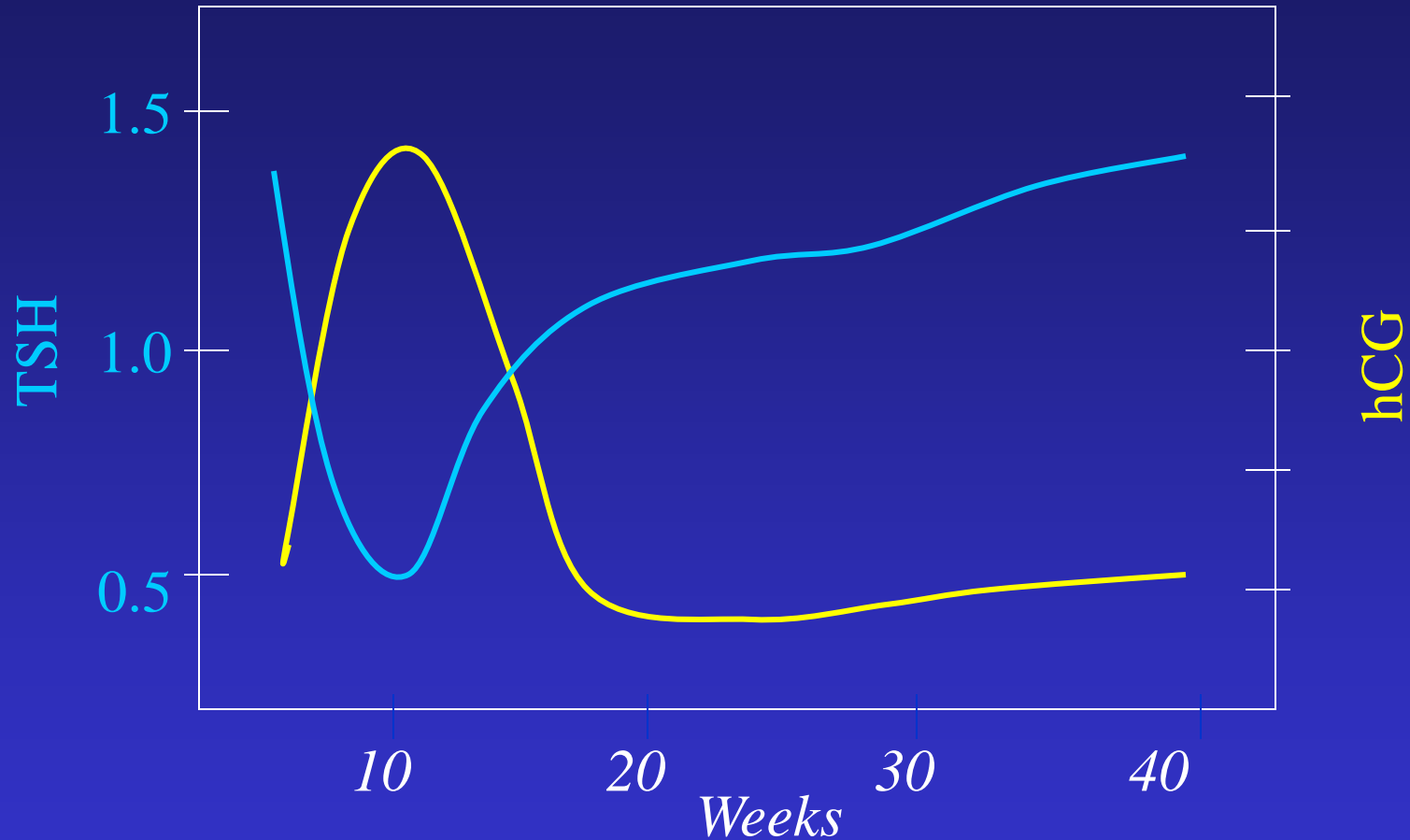


Fine Needle Aspiration





# hCG effect and TSH



*Maternal hCG substantially effects serum Thyroid hormone and TSH concentrations late 1st Trimester*

## Case #4a

32yo healthy female presents for care and is 20 weeks pregnant. Five months ago, a 3cm thyroid nodule was detected on CT scanning, and FNA was performed. Cytology was classified as 'follicular neoplasm', though the patient was lost to follow-up. She now seeks to establish new care with yourself. You confirm a 3cm low-risk nodule on ultrasound

*What would you do?*

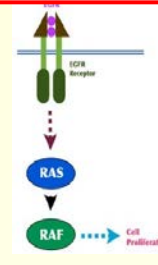
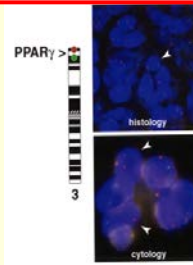
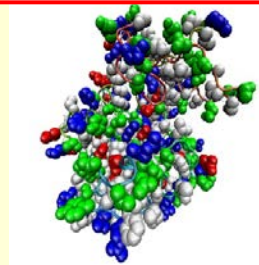
## Case #4b

32yo healthy female presents for care and is 20 weeks pregnant. Five months ago, a 3cm thyroid nodule was detected on CT scanning, and FNA was performed. Cytology was classified as 'follicular neoplasm', though the patient was lost to follow-up. She now seeks to establish new care with yourself. You confirm a 3cm low-risk nodule on ultrasound

*She asks if you can perform 'molecular testing' on the nodule?*

# There exist **NO** data regarding any molecular testing during pregnancy

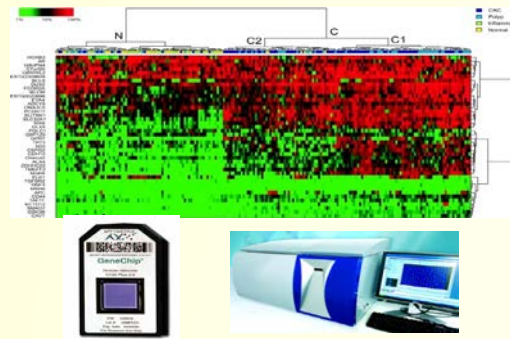
## *Single Gene Mutation Analysis*



Reasonable

(BRAF, RAS, RET/PTC, PAX8:PPAR $\gamma$ )

## *Afirma Gene Expression Classifier*



Avoid

# Do you Agree?

## *The 2011 ATA Guidelines:*

---

- Pregnant patients with an FNA sample that is suspicious (~70% risk) for thyroid cancer do NOT require surgery while pregnant except in cases of rapid nodular growth and/or the appearance of lymph node metastases. Thyroid hormone therapy is NOT recommended. Level I - USPSTF

## Case #5a

24yo healthy female presents for care and is 16 weeks pregnant. A 0.7cm thyroid nodule is detected on exam, and an UG-FNA is performed by another provider. Cytology returns 'Positive for Papillary Carcinoma'. Ultrasound reveals no adenopathy. She has no other thyroid cancer risk factors, and feels well. She inquires about next steps.

*What would you recommend?*

## Case #5b

24yo healthy female presents for care and is 16 weeks pregnant. A 2.3cm thyroid nodule is detected on exam, and an UG-FNA is performed by another provider. Cytology returns 'Positive for Papillary Carcinoma'. Ultrasound reveals no adenopathy. She has no other thyroid cancer risk factors, and feels well. She inquires about next steps.

*What would you recommend?*





# Thyroid Cancer Prognosis

## *Pregnancy does not Influence Outcome*

- New Mexico: *Case-Control study of 505 new diagnosis cancer:*
- *Followup assessment (median 12yrs) and mortality*
- *Limitation: Unclear if treatment delayed to postpartum*

<i>Thyroid Cancer Diagnosis:</i>	<i># Deaths from Thyroid Cancer:</i>	<i>12-Year Survival Rate:</i>
During Pregnancy (22 pts)	0 (0%)	98.2%
Not Pregnant: (483 pts)	1 (0%)	98.4%

*Prognosis unchanged when diagnosis  
made during pregnancy*



# Thyroid Cancer Prognosis

## *Delay in Treatment does not Influence Outcome*

- Ohio St: *Case-Control study of 589 new diagnosis cancer:*
- *Followup assessment (median ~20yrs) – recurrence & mortality*

<i>Thyroid Cancer Diagnosis:</i>	<i>Time to Treatment:</i>	<i>Cancer Recurrence:</i>	<i># Deaths from Thyroid Cancer:</i>
During Pregnancy (61 pts)	16mo.	9 (15%)	0 (0%)
Not Pregnant: (528 pts)	1mo.	107 (23%)	6 (1.2%)

*15 month delay was not harmful*



# Thyroid Cancer Treatment (Surgery)

## *The Influence of Pregnancy*

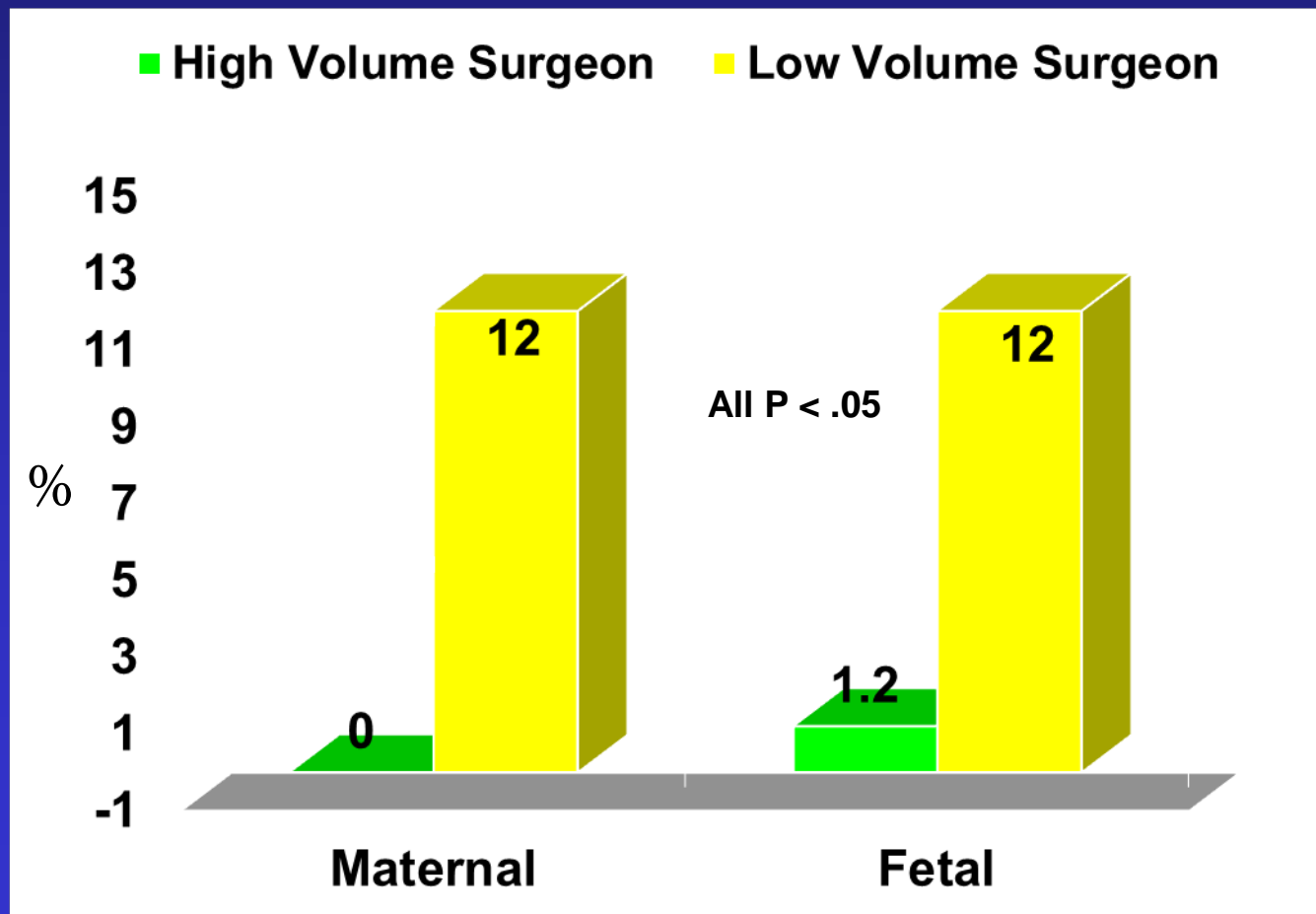
- NCUP-NIS: *Case-Control study of 31,356 women:*
- *All underwent thyroid or parathyroid surgery 1999-2005*
- *Followup assessment for fetal, maternal complications; LOS; cost:*

<i>Neck Surgery:</i>	<i>Complications:</i>	<i>Length of Stay:</i>	<i>Cost:</i>
During Pregnancy (201 pts)	23.9%	2 days	\$6,873
	vs.	vs.	vs.
Not Pregnant: (31,155pts)	10.4%	1 day	\$5,963
	p<0.001		

*Surgery during Pregnancy is higher risk*

# Maternal & Fetal Complications

- Maternal 4.5%
- Fetal 5.5%



# Do you Agree?

## *The 2011 ATA Guidelines:*

---

- When a decision has been made to defer surgery for well-differentiated thyroid carcinoma until after delivery, neck ultrasounds should be performed during each trimester to assess for rapid tumor growth, which may indicate the need for surgery. Level I - USPSTF

# Do you Agree?

## *The 2011 ATA Guidelines:*

---

- Thyroid hormone may be considered in pregnant women who have deferred surgery for well-differentiated thyroid carcinoma until postpartum. The goal of L-T4 therapy is a serum TSH level of 0.1-1.5mIU/L.  
Level I - USPSTF

## Case #5c

24yo healthy female presents for care and is 16 weeks pregnant. A 4.0cm thyroid nodule is detected on exam, and an UG-FNA is performed by another provider. Cytology returns 'Positive for Medullary Carcinoma' (calcitonin +). Ultrasound reveals abnormal neck adenopathy. She inquires about next steps.

*What would you recommend?*



# But some Thyroid Cancers are dangerous? *...surgery is recommended*

---

## Who? When? And What to do?



# Which Cases Require Urgent Treatment?

- Expert *opinion* only:
- *Clinical judgement is paramount*
- *Nonetheless – some general consensus:*

- Evidence or concern for high-risk malignancy
  - medullary CA, anaplastic CA, non-thyroid metastasis
- Findings of Distant Metastatic Disease
- Airway, Throat or Structural (impending) Compromise
- Well-differentiated malignancy (papillary & follicular) with advanced, local disease – Lymph node involvement; Invasion

*When performed, surgery  
recommended before 24wks*



The patient is so (!) worried, and asks:

“Should I terminate my  
pregnancy?”

---

*...how do you respond?*



The patient is so (!) worried, and asks:

“Should I terminate my pregnancy?”

---

*...how do you respond?  
Do I need  $^{131}\text{I}$  therapy soon?*



# Conclusions:

---

- Thyroid nodules are common during pregnancy, though the **influence of gestation** upon formation & growth is **minimal**.
- The evaluation of thyroid nodules during pregnancy similar to that for non-pregnant patients (**NO radioisotopes**).
- Surgical intervention in a pregnant patient is associated with **higher complications, length of stay, and cost**.
- Most patients diagnosed with thyroid cancer during pregnancy can be **safely followed without treatment until after delivery** – no effect on mortality or recurrence risk.
- Rarely, patients with high-risk or advanced disease require surgical intervention during pregnancy. When occurring, this should be performed **prior to 24wks** gestation.

