Before I kick the bucket, I want to say thank you

John D Townsend

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Patients don't always get a chance to tell people when and how care is superb. John D Townsend explains why he needs to say it now. For more information about the series, contact Rosamund Snow, patient editor, rsnow@bmj.com.

My GP is absolutely fantastic. Three years ago I sat in front of her describing my symptoms. She listened carefully, examined me, and then she asked:

"What do you think it is?"

I knew I'd lost a lot of weight, lost my appetite, and had even been passing blood. I'd had to put extra holes in my belt to keep my trousers up. There wasn't any point in beating about the bush, so I told her: "I think it's bowel cancer."

She looked taken aback. I don't think she had expected me to be quite that blunt, or quite that cheerful. But I'd already decided that if this was what nature was going to throw at me I'd just deal with it. As she referred me for further investigations, she said she'd never seen anyone face the idea of an operation for cancer with such a positive attitude.

The local hospital sent me a thick booklet with information, laxatives, the lot, all within two days. This is in a system that politicians and the press tell us, every day, isn't working; a system that is supposed to be slow. I don't understand why people moan about the NHS—I have never had a problem with it.

When they did the investigations for bowel cancer they found that I also had cancer of the oesophagus. They asked me if I had pain or difficulty swallowing, but I told them I had no symptoms for that cancer at all. Because the bowel cancer was growing more slowly, they decided to remove the oesophageal cancer first, and 13 months later when my body had recovered I went back in for the bowel operation.

How long have I got?

My oncologist is also wonderful. We understand each other, and we know how to talk to each other. On one visit to her clinic I arrived feeling awful. Bear in mind that I never used to go to the doctor and I was never unwell. In fact, until I had to retire because of the cancer I had worked for 27 years without a single day off sick. It was not typical for me to feel this bad. I told my oncologist that I was feeling rough; I wanted it all to be over. She listened to me describing how I felt and picked up the phone immediately: "I want a bed now. And I want a wheelchair here now." It was meant to be an outpatient appointment, but I was taken to hospital to be treated for double pneumonia. I didn't know I had pneumonia—I'd never had it before so how would I know? But she knew right away, she took me seriously, and she acted fast. Again, people talk about the amount of time it takes to get anything done in the NHS, but that's not my experience.

In the middle of February this year my oncologist sent for me.

"The cancer we took out of your oesophagus has come back," she told me. "We can't do any more for you because your body's not strong enough for chemo."

"Right," I said. "How long have I got, weeks or months?"

> All this bullshit about the NHS being rubbish is not true

"Months."

(Look, I'm practical, I need to know where I'm going with this.)

"So this time next year I won't be here?"

"Yes. That's right."

Sometimes it's worth being direct. There's no sitting on the fence, she calls a spade a spade. She wrote a letter to my GP, perhaps she rang her too, I don't know. I know she sent the letter because she sent me a copy so I could see that she had written: "John isn't afraid of dying."

Treated wonderfully

Everybody's an individual. You have to talk to patients to understand their attitude. Ask questions and see what the replies are—that way you can see whether the person is the kind to get upset. Share that information, so others know how to communicate in the way the patient likes best.

I'm not going to fight it. I've already said to my wife that when I'm gone I don't want her putting in the paper that I lost a battle with cancer. I didn't lose any battle, because I'm not fighting this cancer. If I get worried about it, is that going to get rid of it? No. If I get stressed what good will that do? None.

Before I go I'm going to write to my member of parliament, to the prime minister, and to the management at my local hospital that all this bullshit about the NHS being rubbish is not true, not where I live. I've been treated so wonderfully that you wouldn't believe it.

THE BOTTOM LINE

- Don't have fixed ideas about how people will respond to being on a cancer ward. Some of us like you to be very direct; everyone's different
- You can help each other. If you have learnt the best way to talk to an individual patient take a moment to put it in the referral letter or a phone call. Pass that information on to other staff who are dealing with that person
- People don't thank healthcare staff enough. I want to say to all of you—GPs, surgeons, nurses of all kinds, right through to those who do the seemingly menial tasks (the people who got me fresh water or clean the wards)—thank you. I can't fault you

For more on the series contact our patient editor, Rosamund Snow rsnow@bmj.com

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UNCERTAINTIES

Are we overtreating subclinical hypothyroidism in pregnancy?

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This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. The series adviser is David Tovey, editor in chief, the *Cochrane Library*. To suggest a topic for this series, please email us at uncertainties@bmj.com

Overt hypothyroidism is diagnosed with a high serum thyroid stimulating hormone (TSH) concentration in conjunction with a low serum thyroxine concentration or an isolated TSH concentration above 10 mU/L. Subclinical hypothyroidism is a biochemical diagnosis based on a high TSH concentration with normal thyroxine.

The benefits of treating overt hypothyroidism during pregnancy include improved obstetric and neonatal outcomes. However, evidence for the management of subclinical hypothyroidism and appropriate treatment targets in pregnancy are lacking. Despite this, international guidelines have set a low TSH threshold for the diagnosis and treatment of both new and pre-existing hypothyroidism in pregnancy.[1 2] This threshold potentially increases the prevalence of subclinical hypothyroidism in pregnancy and may "medicalise" women despite a lack of clear evidence that treatment improves outcome.

What is the evidence of the uncertainty?

We reviewed the evidence used to produce international guidelines on hypothyroidism and pregnancy.[1 2] In addition, we searched PubMed, Web of Science, and Google Scholar by using the terms subclinical hypothyroid*, thyroxine, thyroid, and thyrotropin in combination with pregnan* and miscarriage to find additional data from randomised trials, cohort studies, systematic reviews, and meta-analyses published between 1990 and 2014.

What is a "normal" TSH in pregnancy?

The upper limit for TSH outside of pregnancy is 4.12 mU/L.[3] However, guidelines recommend a TSH concentration of less than 2.5 mU/L in the first trimester,[1] despite the fact that observational studies give a much broader normative range for TSH, especially when ethnicity is considered. First trimester TSH data from cohorts of pregnant women without pre-existing thyroid disease include concentrations as high as 4.87 mU/L in China,[4] 5.09 mU/L in the United States,[5] and 5.5 mU/L in the United Kingdom.[6]

In 2007 a cohort study of more than 17 000 pregnant women found that 3.4% had subclinical hypothyroidism when the diagnosis was based on TSH above the 97.5th centile, corrected for gestational age (TSH 2.74-5.09 mU/L).[5] However, a threshold of 2.5 mU/L may be associated with a higher prevalence of gestational hypothyroidism: more than 15% of pregnant women in the United States and the Netherlands and 28% of Chinese women.[4 7]

Thus we recommend basing TSH thresholds on the local gestation specific reference range, rather than a universal threshold of 2.5 mU/L.

Should thyroxine dose be increased empirically in pregnancy?

To achieve a target TSH below 2.5 mU/L, guidelines recommend that women with known hypothyroidism empirically increase their dose of thyroxine during pregnancy.[1] The presumption that most women need to increase their dose is based on data from small cohort studies. The most commonly cited of these included only 19 women, of whom six had a diagnosis of thyroid cancer, in which treatment aims to suppress TSH rather than keep it within a normal reference range.[8] Observational data suggest that most women with a preconception TSH below 1.2 mU/L will maintain a normal concentration in pregnancy without an increase in thyroxine dose.[9]

Retrospective observational data have examined thyroxine requirements in pregnancy in relation to aetiology. Patients with primary hypothyroidism and a pre-pregnancy TSH concentration below 3.4 mU/L did not need a significant increase in thyroxine dose in the first trimester, and an increased dose later in pregnancy reduced a mean TSH concentration that was already within the specified reference range (<4.1 mU/L). By contrast, athyreotic patients needed larger cumulative increases in thyroxine dose to maintain TSH below 4.1 mU/L.[10]

An empirical increase in thyroxine treatment carries theoretical risk.[11] Women with genetic resistance to thyroid hormone provide a model of increased prevalence of miscarriage in association with excess circulating thyroxine in the absence of autoimmunity.[12] However, no evidence of iatrogenic maternal hyperthyroidism or adverse fetal outcome exists.

THE BOTTOM LINE

- Base the diagnosis of subclinical hypothyroidism in pregnancy on a normal thyroxine concentration and thyroid stimulating hormone above the local gestation specific reference range, rather than a universal threshold of 2.5 mU/L
- Base any change in thyroxine dose in pregnancy on thyroid function tests interpreted according to gestation specific normal ranges
- No consistent evidence shows that subclinical hypothyroidism in pregnancy causes adverse outcomes or that empirical treatment has clear benefit or harm

HOW WERE PATIENTS INVOLVED IN THE CREATION OF THIS ARTICLE?

One of the authors has experience of being diagnosed as having subclinical hypothyroidism in pregnancy

Thus thyroid function test results should determine the need for an increase in thyroxine dose in pregnancy. Insufficient data are available on the benefit and harm of empirical treatment.

Does subclinical hypothyroidism adversely affect pregnancy?

Concern about hypothyroidism in pregnancy stems from data linking maternal hypothyroidism to impaired neuropsychological development in the infant.[13] These data come from an overtly hypothyroid population with a mean TSH of 13.2 mU/L. This does not allow advocacy of TSH concentrations below 2.5 mU/L. Case-control data from a Chinese population show no difference in mental and psychomotor development when the maternal TSH is within the pregnancy specific reference range, even if it is above 2.5 mU/L.[4]

Part of the rationale for a low target TSH concentration stems from the suggestion of a continuous, rather than threshold, pathological effect derived from retrospective, observational data including small samples and subgroup analysis without correction for confounding factors.[7] By contrast, a more recent, larger prospective cohort study found no association between TSH concentrations above 2.15 mU/L in the first trimester and adverse pregnancy outcome after 20 weeks.[14] Thus a complex clinical model may have been forced to over-fit the available TSH data.

A systematic review of thyroid autoimmunity and disease in pregnancy included four cohort studies of pregnancy outcome specifically in subclinical hypothyroidism (1028 women with TSH >3.0 mU/L) compared with euthyroid controls (35 222 women). This review found no association between isolated subclinical hypothyroidism and miscarriage, gestational diabetes, placenta praevia, placental abruption, preterm labour, preterm delivery, or caesarean delivery.[15] Although subclinical hypothyroidism was linked to an increased risk of perinatal mortality and pre-eclampsia in the meta-analysis, this was limited by the inclusion of overtly hypothyroid women in the cohorts and non-matched controls. A more detailed review of the data shows that subclinical hypothyroidism is not associated with either pre-eclampsia or perinatal mortality in any of the included studies.[5 16 17]

Overall, data examining the relation between subclinical hypothyroidism and obstetric outcomes are conflicting, with retrospective and prospective cohort study data both showing and refuting associations between subclinical hypothyroidism and adverse pregnancy outcomes including miscarriage, preterm delivery, hypertensive complications, and fetal death.[7] This is likely to reflect inconsistency in risk reporting, failure to correct for covariates of pregnancy risk, under-powered studies, and limited interpretation due to the use of dependent obstetric outcomes.

Thus data fail to show a consistent association between any adverse pregnancy outcome and subclinical hypothyroidism in pregnancy.

Does treating subclinical hypothyroidism improve pregnancy outcome?

A 2013 Cochrane review assessed interventions for thyroid dysfunction in pregnancy. Four randomised controlled trials were included, none of which included intervention in a cohort with isolated subclinical hypothyroidism. Insufficient data meant that no recommendations for clinical practice could be made.[18]

A single randomised controlled trial, not included in the Cochrane review, assessed the effect of thyroxine replacement on the IQ of children born to women with thyroid dysfunction in pregnancy. The study included 390 women with abnormal thyroid function (232 women with raised TSH and normal thyroxine) treated with thyroxine replacement in pregnancy, compared with 404 untreated women (264 with raised TSH and normal hyroxine).[19] No significant differences in pregnancy outcomes were seen between the thyroxine and placebo groups, including preterm delivery, birth weight, or offspring's IQ at 3 years of age. This was a well conducted trial with a moderate risk of bias. The median TSH concentration for which thyroxine treatment conferred no measurable difference in outcome was 3.8 mU/L.

Thus insufficient evidence exists that thyroxine replacement in subclinical hypothyroidism alters pregnancy outcome.

What should we do in the light of the uncertainty?

We recommend diagnosis and treatment of subclinical hypothyroidism in pregnancy based on TSH above the upper limit of a local gestation specific reference range (rather than a universal 2.5 mU/L). Where this reference range is not available, attempts should be made to establish an appropriate reference range.

Pregnant women with normal thyroxine and TSH within the local gestation specific reference range—Those with well controlled primary hypothyroidism may not need to increase their thyroxine dose in pregnancy to maintain a TSH within the gestation specific reference range. Athyreotic women are, however, more likely to need an increase in thyroxine dose, which can be titrated according to TSH concentration. No published data on the iatrogenic effects of an empirical increase in thyroxine dose for pregnancy exist.

Pregnant women with normal thyroxine and TSH above the local gestation specific reference range (not just >2.5 mU/L)—These women have subclinical hypothyroidism. Evidence that this will cause adverse pregnancy outcome is inconsistent and conflicting. Equally, treatment with thyroxine has not been shown to be beneficial. While results of ongoing trials are awaited, thyroxine treatment is recommended in the absence of evidence of harm. However, the possibility of overtreatment in pregnancy should be considered. Monitor for iatrogenic hyperthyroidism with a repeat TSH four to six weeks after any change in thyroxine dose and be aware that most of these women will not need ongoing thyroid replacement after pregnancy.[7]