

Wake up!!!

to PEER's Approach to Fatigue

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FMF November 8, 2025

Objectives:

- Utilize an approach to undifferentiated fatigue in family practice
- Assess relevance of commonly ordered tests in fatigued patients
- Discuss the value of supplements, sleep hygiene

Conflict of Interest Disclosure

Presenter / Faculty: Dr. Jennifer Young MD CCFP

- Speakers Bureau/Honoraria: PEER, OCFP
- Consulting Fees: none
- Grants/Research Support: none
- Patents: none
- Other: Part time Physician Advisor CFPC



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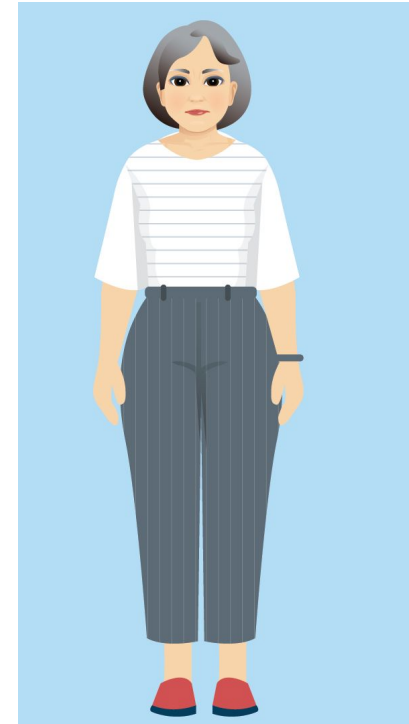
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- Other: Salary University of Manitoba, Faculty of Family Medicine

Leah Sandwich 64

64 year old woman with diabetes, and osteoarthritis of her right hip, chronic insomnia. Medications are metformin 1 g bid and zopiclone 5 mg hs. She takes ibuprofen as needed for her hip pain.

At the end of her diabetes visit, Leah mentioned ongoing symptoms of fatigue and you had her book again to discuss.

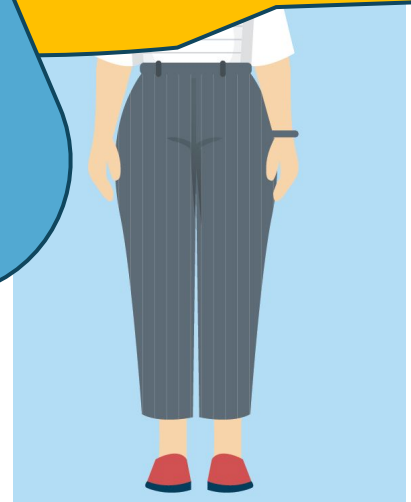


Hi Leah, tell me more about the fatigue you mentioned last time.

Your diabetes is well controlled - HbA1c is 6.5% - but you're still feeling these symptoms.

Chronic Diseases Controlled?

I'm always tired and feel like I'm being bagged. I wake up in the morning feeling tired and feel like I'm being bagged any time I sit down. I'm always tired the day but it is a chronic fatigue log.



AP

...at a busy

Fatigue is 3rd most common symptom presentation for women and 6th most common for men, and ranging from 6-30% of reasons for visits to family physicians.

A review of systems....:

Weight changes, drenching night sweats,
unexplained fever

Headaches, Chest pain, dyspnea, cough,
abdominal pain, change in bowel habits,
MSK pain.

Recent infectious symptoms

Substance use

Explore sleep

Explore stressors

Tell me about your sleep – like when you go to bed, when you get up, how the night goes. You have been taking zopiclone for a quite a while now..

I know I have , and it doesn't seem to work anymore...I usually go to bed at 10:30 p.m. and it takes me a bit to fall asleep with my head going over the stuff I have to do. Then I have to pee at least once in the night and I get up at 7 to get going on my day.

Does your partner think you snore a lot or that your legs are moving around?

No, but sometimes I go to the other room because he is snoring so loud!



Sleep Apnea

If suspect Obstructive sleep apnea: STOP-BANG

- rules out if score <3
- if ≥ 3 consider sleep study

Ask the patient the following:

Do you snore loudly? Louder than talking or loud enough to be heard through closed doors	No 0	Yes +1
Do you often feel tired, fatigued, or sleepy during the daytime?	No 0	Yes +1
Has anyone observed you stop breathing during sleep?	No 0	Yes +1
Do you have (or are you being treated for) high blood pressure?	No 0	Yes +1


Objective measures:

BMI	$\leq 35 \text{ kg/m}^2$ 0	$>35 \text{ kg/m}^2$ +1
Age	≤ 50 years 0	>50 years +1
Neck circumference	$\leq 40 \text{ cm}$ 0	$>40 \text{ cm}$ +1
Gender	Female 0	Male +1

Restless legs:

- “Do you have unpleasant sensations in your legs associated with an urge to move, that occur primarily at rest and in the evening or night?” (sensitivity 80-90%, specificity 90-93%)
- exclude secondary causes (iron deficiency, renal disease, pregnancy, neuropathy, medication effects)

In the past 2 weeks have you felt down depressed or hopeless? Do you still enjoy your hobbies?



I wouldn't say I feel sad, but I am feeling pretty overwhelmed. My mom is on her own and I have to help her with groceries and appointments and she is getting more forgetful.
And my eldest son was just laid off and they are struggling to get a downpayment on a house.

Depression...

AP

Fatigue: 70-90% patients with major depressive disorder are fatigued with 20-50% remaining so even after remission

How many who present with fatigue have a primary diagnosis of fatigue?

Canadian cohort of 259 encounters where the reason for visit was “fatigue” with end of visit codes.

- “weakness tiredness, general” 29.7%
- **Anxiety/Depression 23.9%**
- Anemia 3.1%
- Hypothyroidism 2.3%

Similar findings From a cohort study in the Netherlands of 571 patients, followed for 1 year.

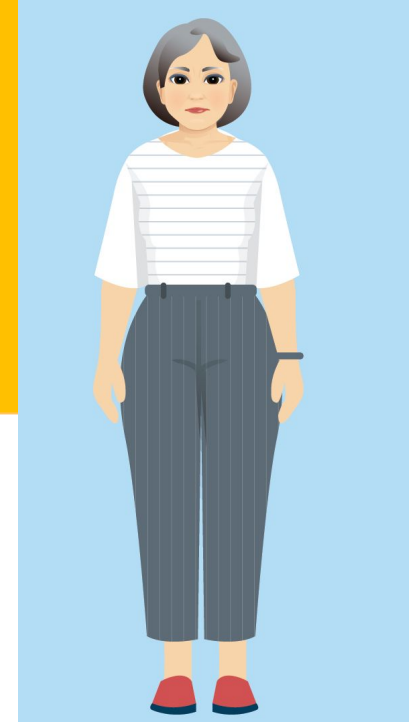
- Unexplained ~50%, **Psychological or social 16.5%**, Anemia 1.6%, Malignancy 0.7%

On examination:

BMI: 29 BP: 138/84 HR: 78 reg no pallor, skin rash, no lymph nodes (neck, supraclavicular, axillary, groin), no pedal edema

Chest clear, Heart sounds normal, abdomen normal to palpation

MSK internal rotation of right hip reduced



And your last blood work for diabetes and kidneys looks pretty good (HbA1C of 7.1%, eGFR 62).

Which of the following would be most appropriate to order for your investigations (you have recently checked her HbA1C and eGFR)? Choose all that apply.

- a. CBC
- b. extended lytes, liver enzymes, ferritin
- c. TSH

Dutch study of 173 patients presenting with fatigue within last 6 months comparing basic (CBC, TSH, glucose, ESR) versus extended testing (basic plus 13 extra). 1 year follow-up.

- no added benefit to extended testing.
- False positives increased from 38/173 (22%) in basic testing to 96/173 (55%) in extended testing.
 - most common false positive result was ESR (and glucose) and in extended set GGT, ferritin, transferrin
 - False negatives: 2 patients with mono, 1 with dust allergy

b. extended lytes, liver enzymes, ferritin

c. **TSH**



ESR?

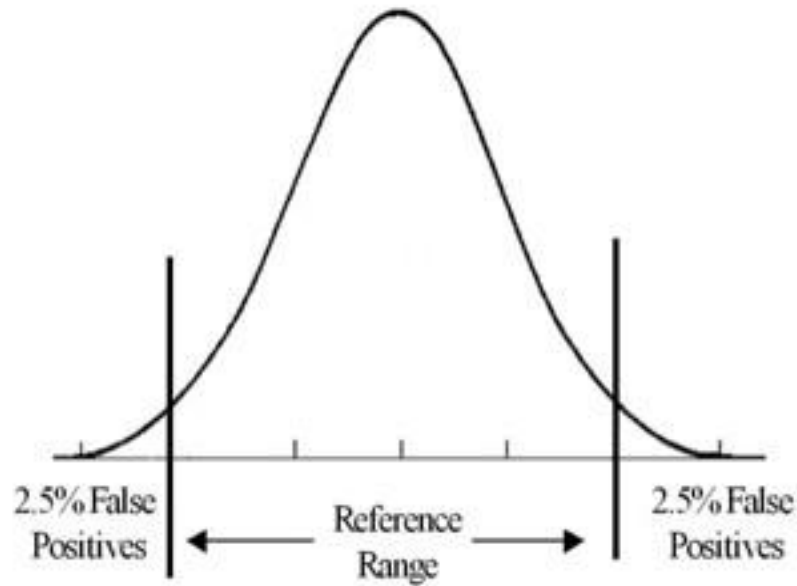
- Elevation of the ESR is non-specific (except where temporal arteritis/polymyalgia rheumatica is considered clinically) and use of it in screening for serious disease is not supported in the literature.
- Choosing Wisely Canada: *“don’t order an ESR as a general test to look for inflammation in patients with undiagnosed conditions.”*
- CRP: slightly more sensitive and specific than ESR

DO NOT ROUTINELY ORDER BOTH

Pitfalls of too many lab tests...

- Pitfalls of ordering lab tests: because reference values are based on 95% confidence intervals, 5% of healthy people will have values outside of this.
- Measurement variation can range from 1-2% to 20-25% for the same test in the same individual.
- Example: TSH may vary up to 50% between tests and daily fluctuations in individuals can be up to 26%.

Most tests are Population-Based Reference Intervals



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Lab results report exact numbers
BUT
Every test result is really only a range that hopefully includes the true result

Measurement variation can be
+/- 1-2% up to +/-20-30% or more

Number of Tests Ordered	Probability of at Least One “Abnormal” Test
1	5%
2	10%
5	23%
10	40%
15	54%
20	64%

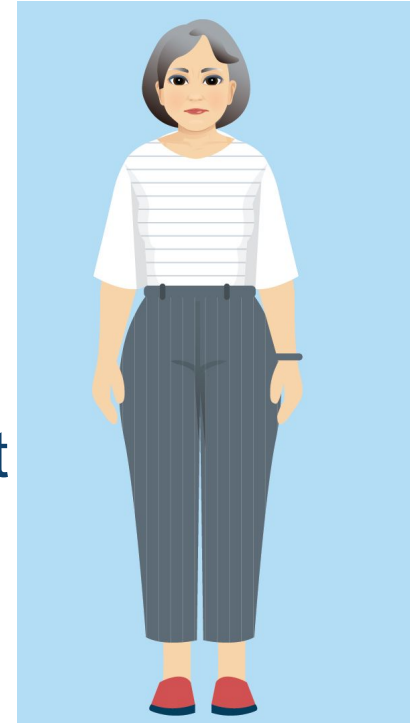
Leah returns 2 weeks later. Her bloodwork results are as follows:

HbA1C: 7.2%

Hb 120 g/L, MCV 90, WBC $4.8 \times 10^9/L$

TSH 6.1 mIU/L (0.34-5.6), free T4 14 pmol/L (10.3 to 24.5)

(When her TSH came back elevated, your office called to get a free T4 before the next appointment.)



T3 not indicated!

In **hypothyroidism**: last test to become abnormal. Patients can be severely hypothyroid with a high TSH and low FT4 but have a normal T3.

In **hyperthyroidism**: useful to diagnose or to determine the severity



Leah returns 2
follows:

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Hb 120 g/L,

TSH 6.1 mIU/L

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to get

Leah's bloodwork is consistent with subclinical hypothyroidism.

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Hb 120 g/L, MCV 90, WBC $4.8 \times 10^9/L$

TSH 6.1 mIU/L (sl inc), free T4 14 pmol/L (N)

Starting levothyroxine will improve Leah's fatigue.

True/False

Leah's bloodwork is consistent with subclinical hypothyroidism.

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Starting levothyroxine will improve Leah's fatigue.

True/**False**

Subclinical Hypothyroidism

- The prevalence of subclinical hypothyroidism (TSH 4-10 mIU/L with normal T4) is 4-10%, increasing with age.
- Only 2-6% of these will develop overt hypothyroidism (low T4).
- Symptoms are poor predictors:
 - ≥ 4 symptoms of hypothyroidism: ~18% of euthyroid, ~22% subclinical hypothyroid, ~26% overt hypothyroid patients reported

Subclinical Hypothyroidism

Treating subclinical hypothyroidism:

- Does not change fatigue, quality of life, depression, weight, cognitive function, cardiovascular disease or mortality.
- Has inconsistent effects on lipids or blood pressure.

Most recent systematic review supports treatment of subclinical hypothyroidism (normal free T4) when TSH >20. Previous practice patterns have been to treat when the TSH >10.

CBC

Screening CBC:

- When CBC is tested routinely without cause, up to 11% are abnormal but <1% require management change. It is unclear which patients benefit and serious disease is virtually never found.

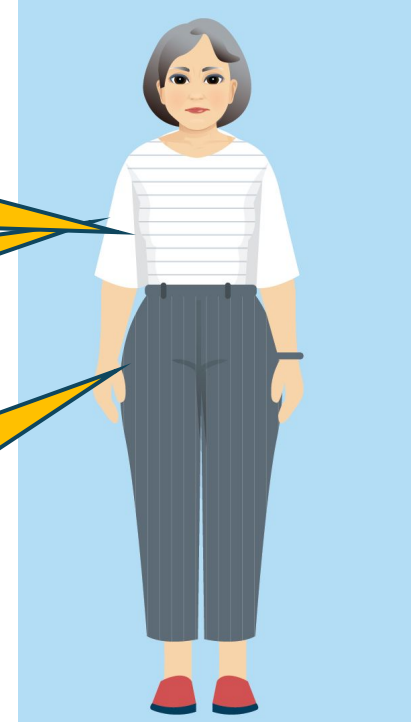
- Does not decrease mortality (cancer/ all-cause)

How are things going with all those responsibilities?

Well, after our appointment last time, I got to thinking that I really need some help.

So, I have hired a personal support worker to visit mom two times a week over lunch and to do her grocery shopping.

I also asked my husband if he could take on at least one meal during the week – He said yes!



In a Canadian primary care database, diagnostic attribution varied by sex.

- Psychosocial problems were similar in women and men (about 24%). But women were more likely to receive a diagnosis of anxiety or depression while men were more likely to receive a diagnosis of “other psychosocial diagnoses.” These “other” diagnoses were not stated but may be related to work or financial stress.
- “Fatigue NYD” remained the diagnosis in 34% of women versus 20% of men.



Last time you mentioned you didn't think the sleeping pill was helping anymore?

Yes, I started it a bunch of years ago when I was going through a stressful time with my dad's death. It helped back then but these days, I don't feel it is doing anything.

Were you interested in trying to stop?

Sure, but I have tried before and I didn't sleep a wink.



Do I really want to tackle the sleeping pill?

CBTi versus sedative hypnotics (network meta-analysis):

- better subjective sleep efficiency, less awake time, lower severity insomnia over long term

RCT 211 patients zopiclone versus behavioural therapy:

- equivalent at 6 weeks, only behavioural therapy had sustained changes at 12 months



CBTi vs. Sleeping Pills for treating Insomnia



CBTi

FIRST-LINE EVIDENCE-BASED
TREATMENT FOR INSOMNIA



Sleeping Pills

ANY MEDICATION USED
TO MAKE YOU SLEEPY

First-line treatment for insomnia.

EXPERT
RECOMMENDATIONS

Second-line treatment for insomnia.

Designed to fix the causes of insomnia,
including what keeps it going.

HOW IT
WORKS

Impact chemical
processes in the
brain.

More effective than sleeping pills overall. Notice
improved sleep within 1-2 weeks of getting
started.

EFFECTIVENESS

A 4-week program can last for
months and years.



and short-term by
recommended for children or
people 65 and older.

short-term plan (1-2 weeks) can evolve into years
of use with no exit strategy.

OTHER
BENEFITS

Early benefits on quality of life can reverse due to
the development of drug dependence and other
side effects.

Available in various formats including self-
guided (books, apps, and online courses) and
therapist-guided (online, in-person) programs.

AVAILABILITY

Widely available.
Require visits to prescribers and pharmacies.

Some health insurance plans pay for some or all
CBTi costs. Cost varies depending on the CBTi
program and format.

COSTS

Most health insurance plans pay for some or all
sleeping pill costs. Personal and health system costs
can be high due to side effects and risks.

Financial contribution:

The views expressed herein do not necessarily
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YAWNS study

The YAWNS trial included 565 Canadians using chronic benzodiazepines for insomnia (average age: 72) . Patients were randomized to a behavioural intervention (either *Sleepwell* or *Empower* booklets) or usual care. The Sleepwell resources, which encourage patient uptake of CBT, were more effective than usual care or Empower booklets in helping patients to stop their sleep meds:

- Discontinuation of benzodiazepines at 6 months: 26.2% with Sleepwell, 20% with Empower and 7.5% usual care.
- Fell asleep 25 minutes faster.
- no difference in falls, driving issues

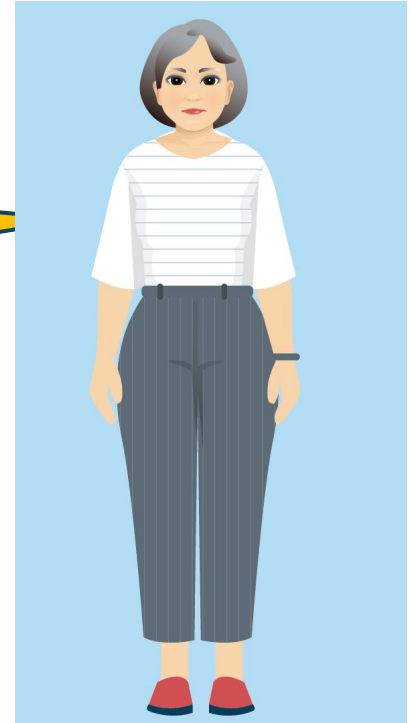
**Booklets
mailed to
patients in the
study (available
now \$5 each on
website)**

**MySleepwell.ca
website**



Oh, I meant to ask you about all those vitamin supplements the TV says I should take

Hard to avoid all those recommendations, isn't it?



Supplements?

Iron: weak evidence to support supplement menstruating women with low ferritin but normal Hb with unexplained fatigue

Multivitamins: prospective study of 1361 people with fatigue without deficiencies

- No difference in fatigue

Large systematic review for US Preventive Task Force, looking at Vitamins A, C, D, beta carotene, calcium, selenium

- No difference in all cause mortality, cardiovascular disease, cancer incidence.

Family Medicine – the secret sauce?

Value of Continuity- follow-up for evolution of this fatigue, and other undifferentiated problems is essential for diagnosis and treatment

Family Medicine – the secret sauce?

In a systematic review of 22 cohort studies, 18 studies found that increased continuity of care in general (mainly provided by family physicians or mixed groups of physicians) was associated with reduced mortality.

An additional 10 family physicians per 100,000 patients is associated with 15 fewer deaths, 40 fewer hospitalizations, and an average increase in life expectancy of 52 days.

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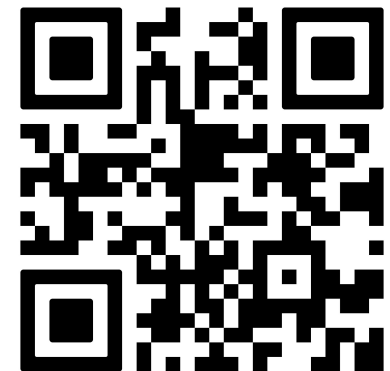
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