UNRAVELING THE COMPLEXITY OF CHRONIC PAIN AND FATIGUE

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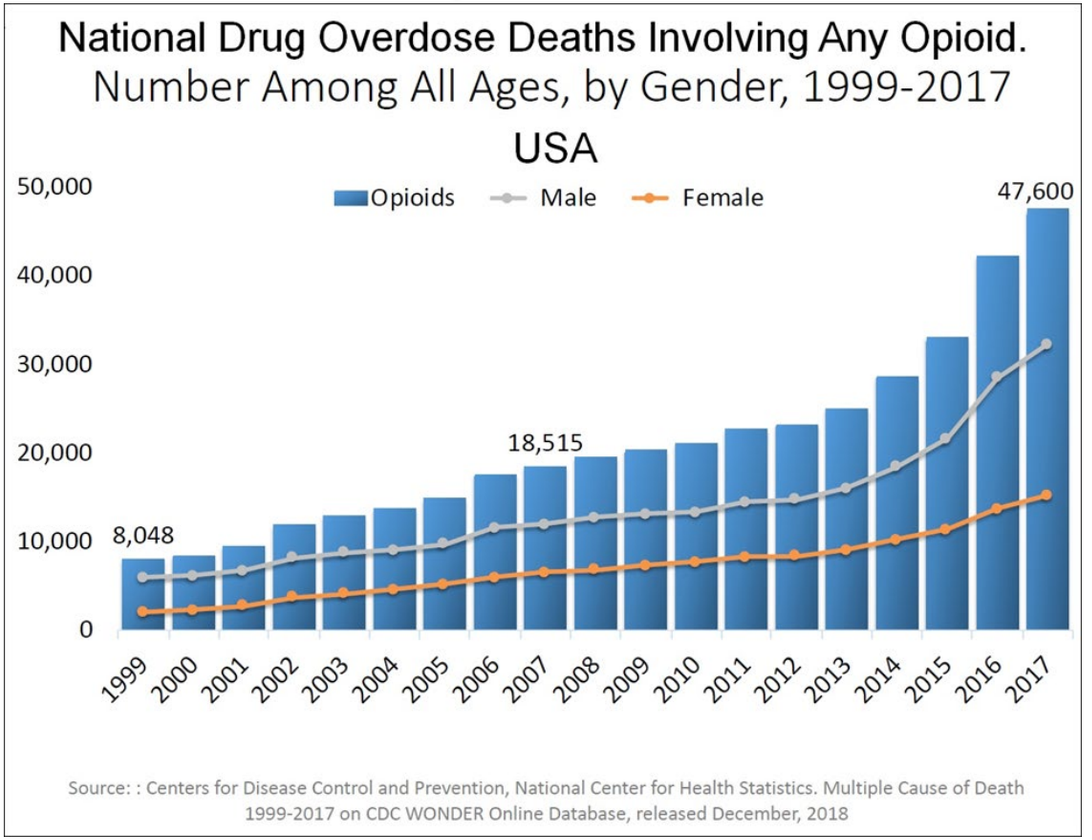
SESSION #1

Strategies for recognizing multisystem illnesses, often presenting as widespread pain and chronic fatigue

"BANDAID" MEDICINE HAS CREATED SIGNIFICANT PUBLIC HEALTH PROBLEMS

CHRONIC FATIGUE

CHRONIC PAIN

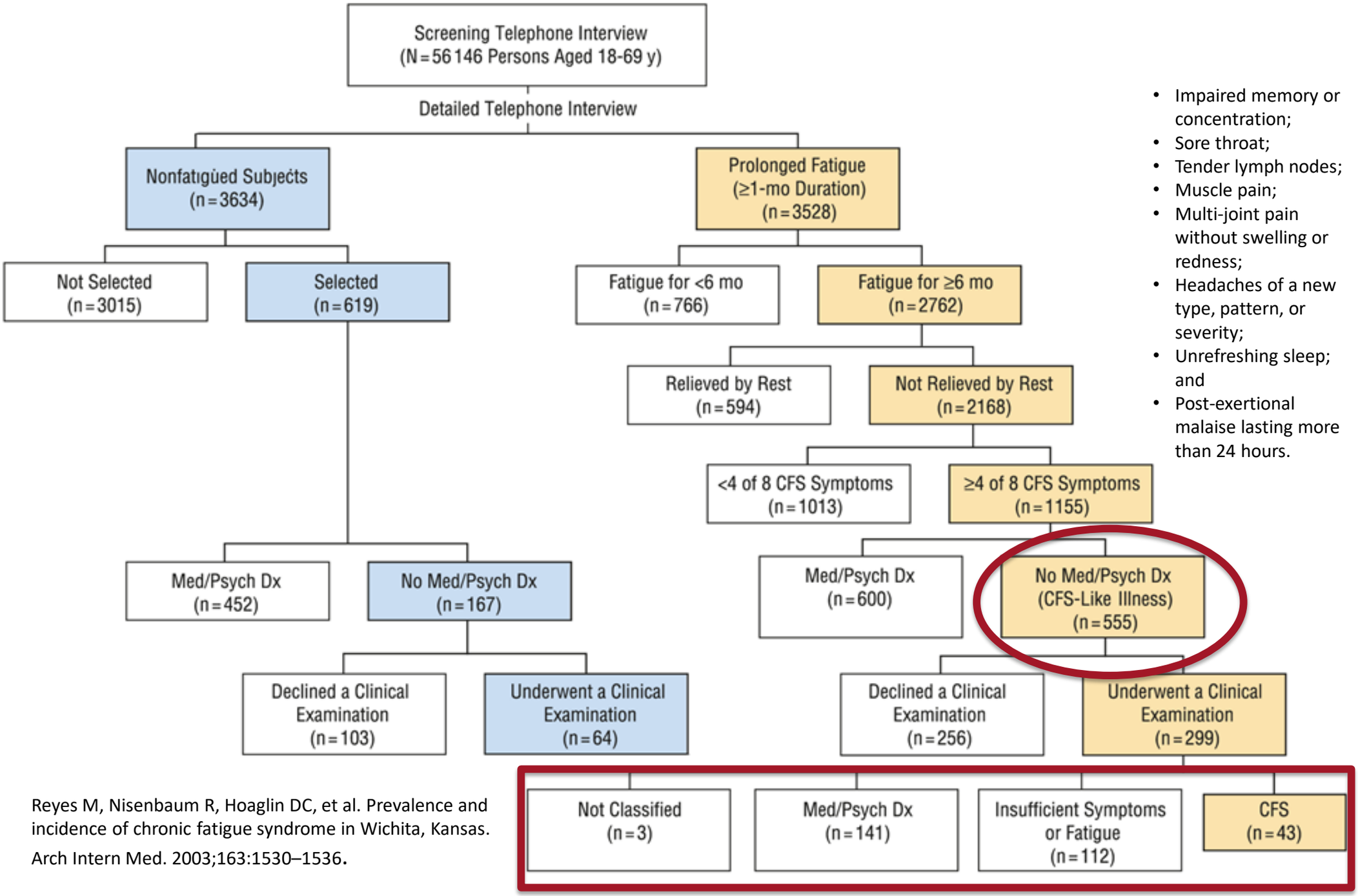


CENTERS FOR DISEASE CONTROL:
1997 CHRONIC FATIGUE SYNDROME PREVALENCE STUDY (USING 1994 FUKUDA CRITERIA FOR CFS)

- Population-based random digit–dialing survey of residents of Sedgwick County, Kansas: demographically similar to that of the whole USA for age, sex, race, ethnicity, and income…

- The study had 3 components:
  - a screening telephone interview
  - a detailed telephone interview,
  - and a clinical examination

Reyes M, Nisenbaum R, Hoaglin DC, et al. Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas. Arch Intern Med. 2003;163:1530–1536.



- Impaired memory or concentration;
- Sore throat;
- Tender lymph nodes;
- Muscle pain;
- Multi-joint pain without swelling or redness;
- Headaches of a new type, pattern, or severity;
- Unrefreshing sleep; and
- Post-exertional malaise lasting more than 24 hours.

Reyes M, Nisenbaum R, Hoaglin DC, et al. Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas. Arch Intern Med. 2003;163:1530–1536.

Table 1. Exclusionary Medical and Psychiatric Illnesses Identified in the Telephone Interview

Illness	Fatigued Subjects (n = 600), %*†	Nonfatigued Subjects (n = 452), %*
Any medical exclusion	80.7	71.2
Rheumatoid arthritis	30.0	24.1
Lupus or Sjögren syndrome	8.7	2.1
Pregnancy	7.0	35.0
Heart failure or fluid in the lungs	6.0	0.7
Hepatitis or cirrhosis	5.5	5.5
Immunodeficiency disease	3.8	1.1
Multiple sclerosis	3.7	1.3
Heart condition limiting walking	3.3	0.4
Myocardial infarction	2.8	0.7
Organ transplantation	1.5	2.0
Stroke	1.2	0
Other exclusions‡	19.3	2.4
Any psychiatric exclusion	30.2	31.4
Alcohol or other drug dependency	18.2	21.2
Manic depressive disorder	13.2	6.2
Anorexia or bulimia	5.2	4.4
Schizophrenia	1.0	0.9

*Subjects could have more than one exclusionary condition.
†Screened to meet the fatigue and symptom criteria for chronic fatigue syndrome.
‡Includes malignancies, Crohn disease, sleep apnea, and Parkinson disease.

EXCLUSIONARY MEDICAL AND PSYCHIATRIC ILLNESSES IDENTIFIED IN THE DETAILED TELEPHONE INTERVIEW

THE CLINIC VISIT

- Medical history
- Physical exam
- Psychological testing
- CBC, CMP, uric acid, LDH, ESR, ANA, RF, urinalysis

Table 2. Comparison of Unweighted and Weighted Sample Sizes for Adult Survey Respondents by Fatigue Group*

Variable	Unweighted Sample	Weighted Sample
Total respondents	7162	272 838
Nonfatigued respondents	3634	243 272
Respondents fatigued for ≥1 mo	3528	29 566
Respondents with a CFS-like illness†	555	4384
Respondents with CFS‡	43	641

CFS-like 13x CFS

Abbreviation: CFS, chronic fatigue syndrome.

*Weights account for the probability of selection and include adjustments that compensate for nonresponse and bring sample totals into agreement with population totals with respect to race.

†Includes patients with CFS.

‡Additional weight adjustments account for the probability of selection and for nonresponse in the clinical examination.

Table 4. Point Prevalence Estimates per 100 000 Persons by Fatigue Group

Characteristic	Persons With a CFS-Like Illness*	Persons With CFS†
Overall	1607	235 (142-327)
Sex		
Female	2211	373 (210-536)
Male	943	83 (15-150)
Race		
White	1661	224 (145-303)
Nonwhite	1280	300 (0-742)
Age, y		
18-29	600	50 (0-120)
30-39	1601	183 (54-311)
40-49	2424	365 (65-666)
50-59	2375	501 (196-806)
60-69	1149	130 (2-258)
Household income (1996), $		
≤20 000	1980	202 (67-336)
20 001-40 000	1793	280 (97-463)
>40 000	1457	233 (69-397)
Race-sex specific		
White		
Females	2230	352 (221-483)
Males	1040	84 (9-158)
Nonwhite		
Females	2097	495 (0-1310)
Males	344	77 (0-228)

Abbreviation: CFS, chronic fatigue syndrome.
*Includes persons with CFS.
†Data in parentheses are 95% confidence intervals.

PREVALENCE ESTIMATES PER 100,000 PERSONS BY FATIGUE GROUP

CFS-LIKE 6.8X CFS

TODAY IN THE US:

5.3 MILLION VS 775,500

Understanding and deconstructing the multisystem presentation of chronic fatigue and chronic widespread pain

CASE #1:
FEMALE AGE 47 AT ILLNESS ONSET

- **Profound exhaustion**, difficulty getting around the house, mostly homebound, **widespread pain, mixed headaches/migraine**, severe cognitive impairment, nausea, poor appetite, constipation, reflux. Blurred vision. Noise sensitivity.
  - BMI 32.
- **Managed primarily by a psychiatrist at time of presentation**.
- **Consultants**: FP, IM, pulmonary, gastroenterology, neurology
- **Tests:** stress echo, polysomnography, EGD, abd US, brain MRI, many lab tests
- **DX:** migraine, sleep apnea (10 years), IBS, asthma, low back pain (10 years), fibromyalgia

CASE #2:
FEMALE AGE 30 AT ILLNESS ONSET

- **Chronic fatigue**, "*barely able to walk from bed to couch," persistent after rest. Low energy for activity. After activity she crashes and sx worsen for days/weeks. Weakness of arms/legs. Dizzy and "bumping into walls*."
  - BMI 18.8
- **Widespread pain** complaints: burning, achy, morning stiffness, muscle pain, joint (knees), atypical CP, tension headaches and migraines. Numbness and tingling in hands and feet. Sweating, cold and heat intolerance, sound and light sensitivity.
- **Depression, anxiety, suicidal thoughts**.
- **Consultants:** GI, endocrine, OB/gyn, MH APRN, needs PCP.
- **Studies:** ECG & Echo, many labs (TSH mildly low, low iron saturation and ferritin, WBC borderline low).
- **DX:** GERD, IBS, headaches/migraine, anxiety, dysmenorrhea since adolescence, hypothyroid and mono in college.

OVERWHELMED ALREADY????

THE BASICS: YOU KNOW THIS ALREADY

1) Screen for common causes of fatigue and widespread pain
   - Complete a history and Review of Systems
   - Complete a thorough physical exam
   - Standard laboratory tests and imaging based on hx and PE

2) Initiate relevant treatments and interventions

3) Refer as needed to complete a differential diagnosis

4) Maintain the overall management and coordination of care. Help with symptom management focusing on underlying mechanisms.

THE BASICS: YOU KNOW THIS ALREADY

1) **Basic labs**: CBCdiff, CMP, UA, ferritin, Vitamin B12, ESR or CRP, TSH & free T4, fasting lipids

Consider: HgA1C, HIV, Hep C, allergy testing, parathyroid hormone, AM cortisol and ACTH, Sjogrens screen…

2) **Basic tests:** Oximetry, Home Sleep Study or PSG, cardiac studies (stress test, echo, Holter), pulmonary function tests,

Consider: brain MRI

3) Be sure all age and gender appropriate **preventive screens** are up to date: pap, mammogram, colorectal cancer screen, etc.

CHRONIC FATIGUE & WIDESPREAD PAIN

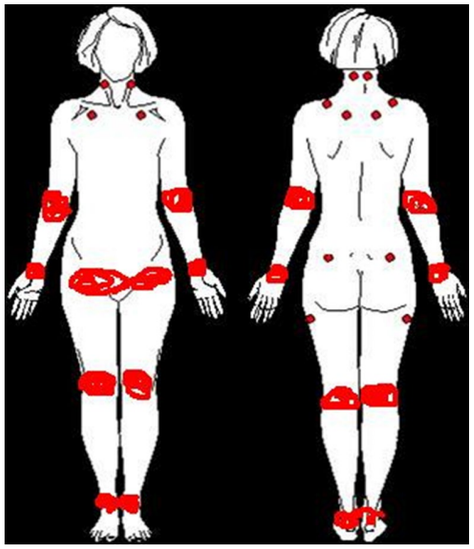
But what if you have done all of the basics and have no clear answers or solutions for your patient?

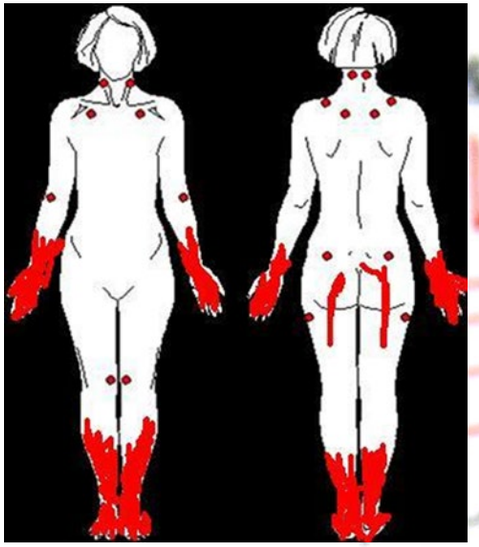
In these 3 sessions on this topic, Dr. Brayden Yellman and I will be sharing some of the insights and strategies we have developed treating hundreds of patients with **chronic fatigue and widespread pain.**

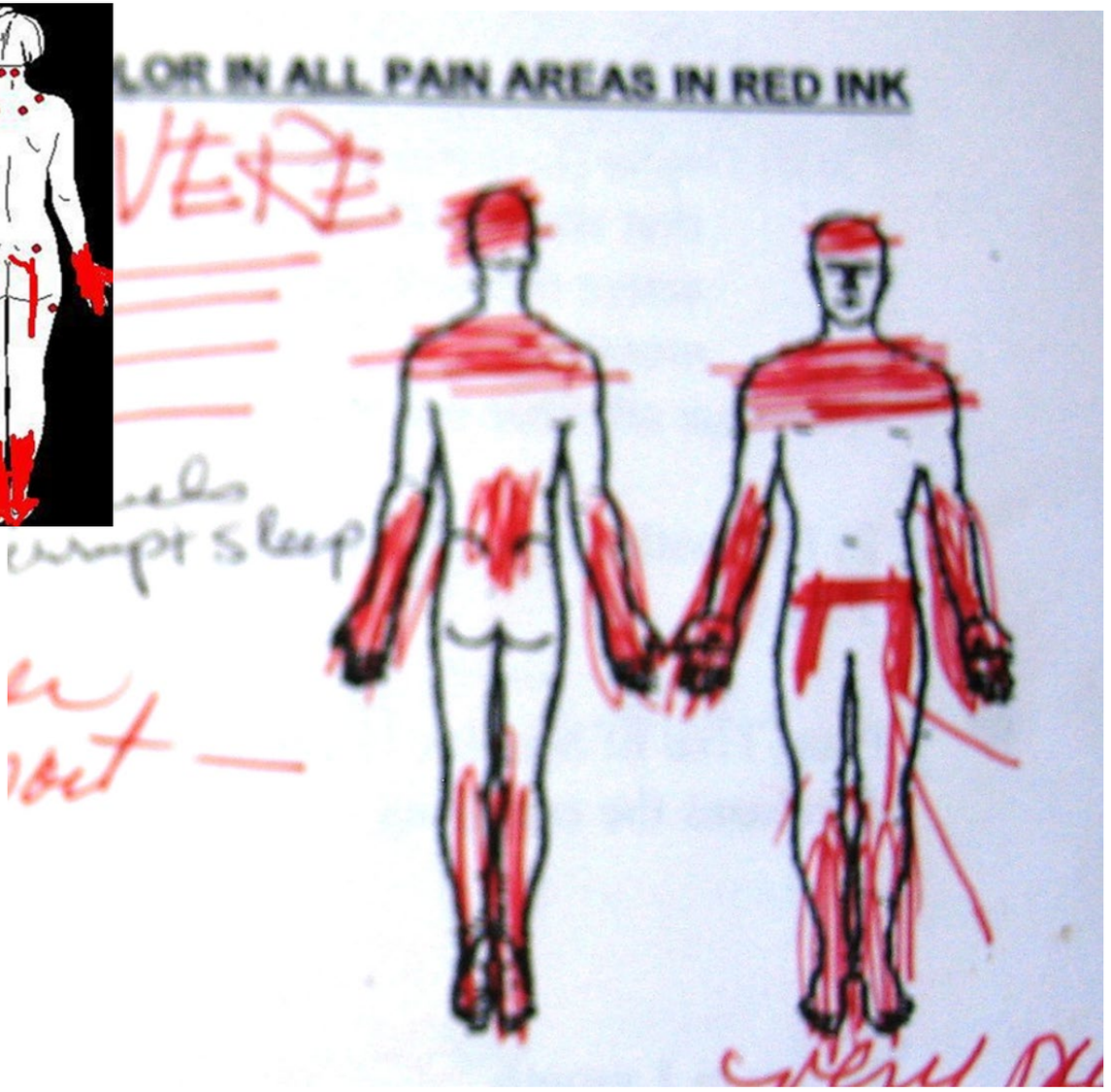
HELPFUL TOOLS FOR ASSESSING **SYMPTOM SEVERITY** AND **ILLNESS IMPACT ON FUNCTION**

- Pain diagrams
- VAS (visual analog scales)
- Expanded ROS with frequency and severity
- FIQ-R(SIQ-R) Fibromyalgia Impact Questionnaire-revised

PAIN DIAGRAMS:
A PICTURE WORTH 1000 WORDS

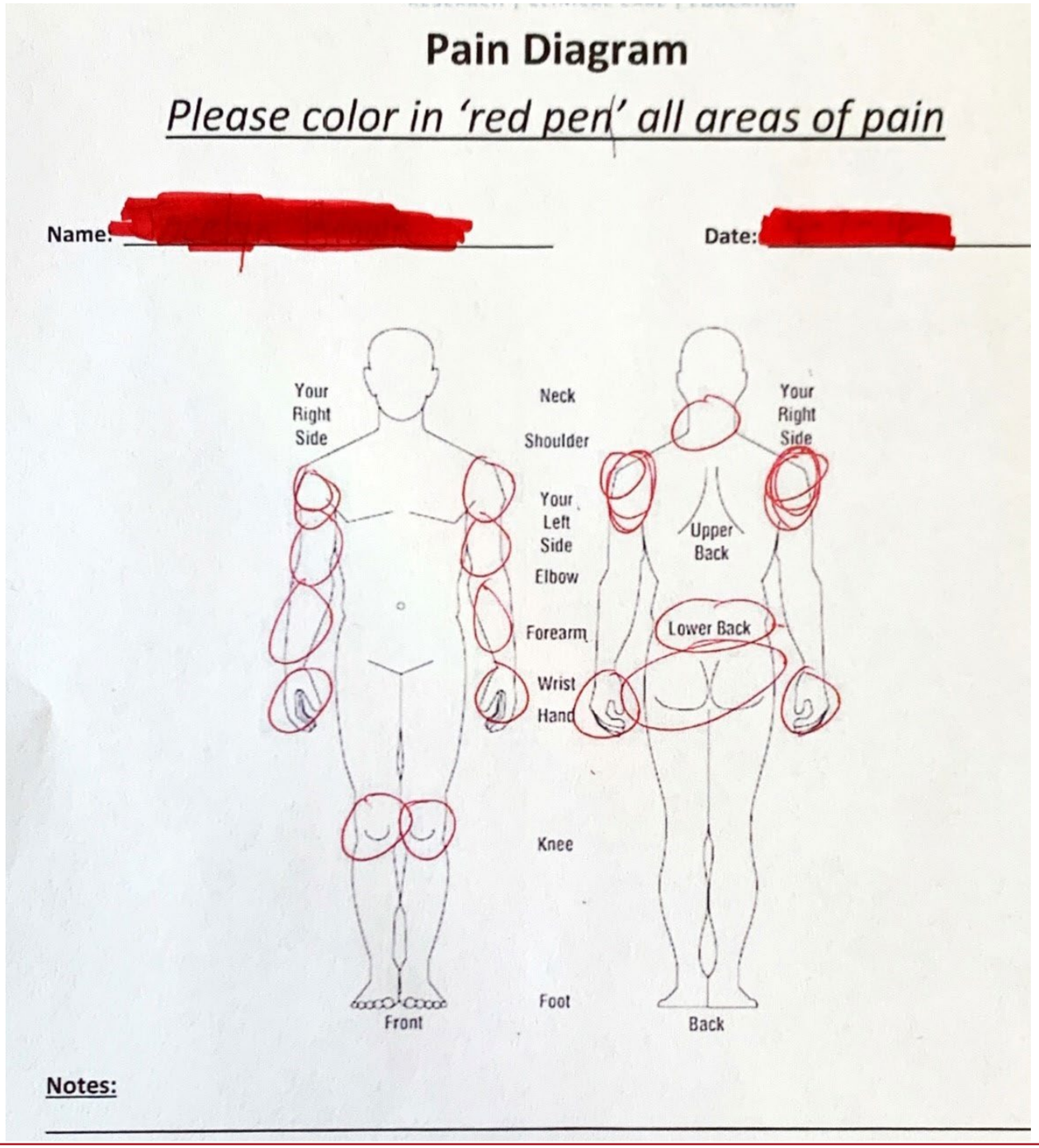






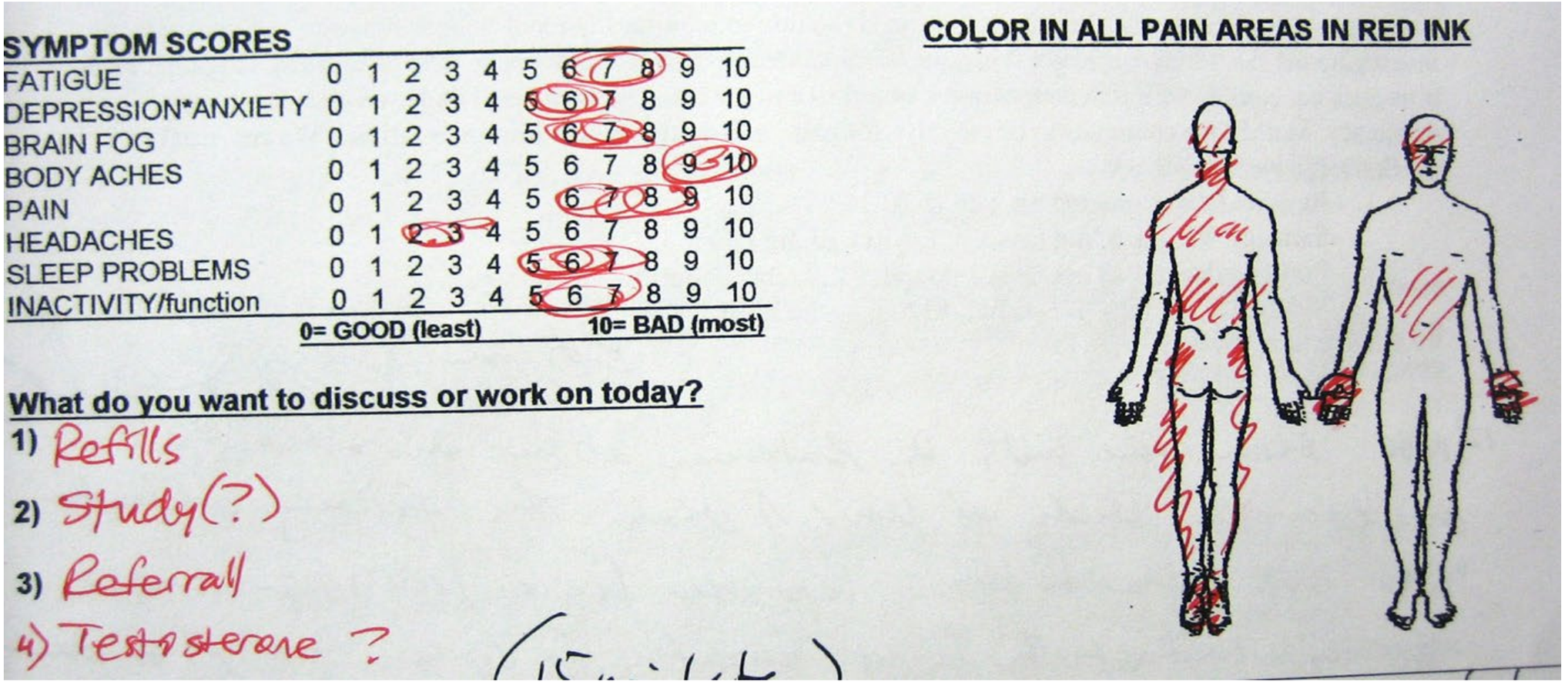
CASE #1:
47 YEAR OLD FEMALE

OA/DJD
SHOULDERS, HANDS, KNEES
C-SPINE &
L-SPINE DJD



VISUAL ANALOG SCALES (VAS)

A quick way to prioritize what is important to the patient.



SYMPTOM SCORES

FATIGUE	0	1	2	3	4	5	6	7	8	9	10
DEPRESSION*ANXIETY	0	1	2	3	4	5	6	7	8	9	10
BRAIN FOG	0	1	2	3	4	5	6	7	8	9	10
BODY ACHES	0	1	2	3	4	5	6	7	8	9	10
PAIN	0	1	2	3	4	5	6	7	8	9	10
HEADACHES	0	1	2	3	4	5	6	7	8	9	10
SLEEP PROBLEMS	0	1	2	3	4	5	6	7	8	9	10
INACTIVITY/function	0	1	2	3	4	5	6	7	8	9	10

0= GOOD (least) 10= BAD (most)

What do you want to discuss or work on today?

1) Refills
2) Study(?)
3) Referral
4) Testosterone ?

COLOR IN ALL PAIN AREAS IN RED INK

VISUAL ANALOG SCALES (VAS)

List all medications and dosage schedule:

1. Probiotic	6.	11.
2. CQ10	7.	12.
3. Multi-vit.	8.	13.
4. Ambien	9.	14.
5.	10.	15.

SYMPTOM SCORES BEST (least) WORST (most)

	0	1	2	3	4	5	6	7	8	9	10
FATIGUE										(9)	
DEPRESSION*ANXIETY								(7)			
BRAIN FOG						(5)					
BODY ACHES							(6)				
PAIN						(5)					
HEADACHES						(5)					
SLEEP PROBLEMS									(8)		

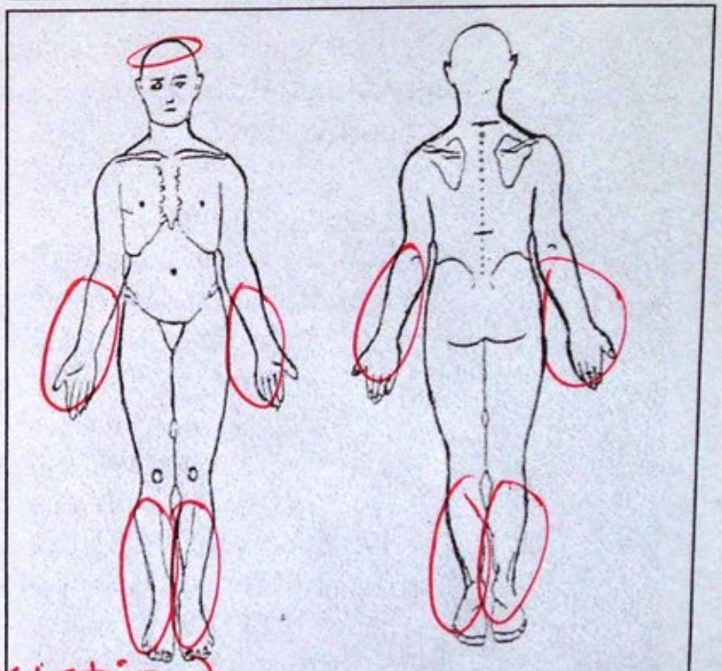
Hours vertical/24 hours 0 1 2 3 (4) 5 6 7 8 9 10 11 12 13 14 15+
(average time with feet on the floor---sitting, standing or walking)

Hours horizontal/24 hours 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 (15+)
(average time with feet up--- resting in recliner, feet up, napping, sleeping in bed)

What do you want to discuss or work on today?

1) Leg/arm Weakness (very heavy @ times)
2) Blood Pressure ↑ w/ activity
3) Not able to engage in life (feel like existing)

COLOR IN ALL PAIN AREAS IN RED INK



EXPANDED ROS WITH FREQUENCY & SEVERITY

KEY: 0 = Never had the symptom or unimportant
1 = Mild or infrequent symptom
2 = Moderate in severity or frequent symptom
3 = Severe or almost constant symptom

SLEEP **Case #2: 30 yo female**

2 Cannot go to sleep
2 Restless sleep
1 Wake up too early
1 Cannot go back to sleep
1 Need to take naps due to daytime sleepiness
2 Need to take naps due to feeling ill
3 Unrefreshing sleep/Wake up feeling unrested
1 Restless legs (or limbs), uncomfortable sensations, or urge to move
2 Leg cramps
1 Myoclonic jerks (involuntary jerking of limbs)
0 Snoring
0 Stop breathing during sleep

EXPANDED ROS WITH FREQUENCY & SEVERITY

PAIN/MUSCULOSKELETAL **Case #2: female age 30**

1 Tender points or trigger points
2 Burning, tingling or numbness burning in arms and legs- tingling in hands and feet
3 Achy all over
2 Tender when touched or squeezed
3 Morning stiffness
3 Joint pain knees
Have you had any evaluations? No
Have you had any joint dislocations? no
3 Muscle pain
1 Neck pain
2 Low back or sciatic pain
0 Abdominal or pelvic pain
2 Chest pain
2 Tension headaches
2 Migraines
I have a low grade headache every day with a few bad migraines a month

FIBROMYALGIA IMPACT QUESTIONNAIRE-REVISED (FIQ-R)

The FIQ-R is a 3-5 min questionnaire that estimates the impact of pain on function

- Functional domain---9 questions
- Overall domain---2 questions
- Symptom severity---9 questions

http://www.fiqr.info/

INTERPRETATION OF FIQ-R SCORE
THE 5 MIN FIBROMYALGIA IMPACT QUESTIONNAIRE

A study of 2228 patients evaluating FM using FIQ suggests the following quartile scores:

- 0 to 42 = mildly affected
- 43 to 59 = moderately affected
- 60 to 74 = severely affected.
- 75 to 100 = extremely affected

The average FIQ-R score in FM studies is 58.2 (± 21.6), with a median value of 58-60.

http://www.fiqr.info/

Bennett RM, et al. Minimal clinically important difference in the fibromyalgia impact questionnaire. J Rheumatol. 2009 Jun;36(6):1304-11. Epub 2009 Apr 15.

FIQ-R SCORES FROM OUR CASES

Case #1: 47 yo

FIQ-R 68

14/18 TP

Case #2: 30 yo

FIQ-R 86

No TP

Score Key: FIQ-R impairment	
0- 42	Mild
43- 59	Moderate
60- 74	Severe
75-100	Extreme

An alternate version is called the SIQ-R or Symptom Impact Questionnaire

http://www.fiqr.info/

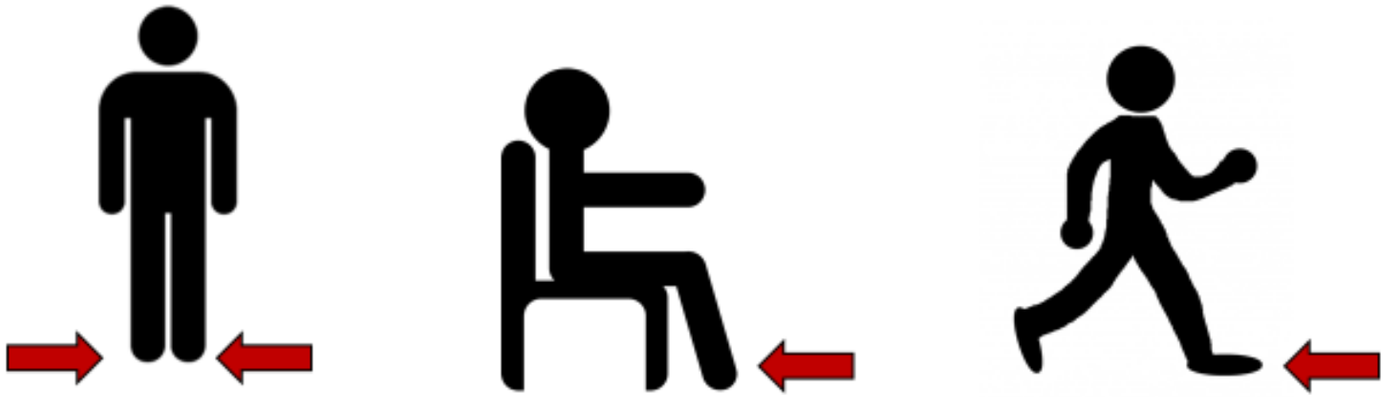
TOOLS TO ASSESS **IMPAIRED FUNCTION**

- Hours of Upright Activity (HUA)
- Good day/Bad day
- RAND-36 (clinical version of research SF-36)
- Orthostatic testing: the 10 minute NASA Lean test

HOURS OF UPRIGHT ACTIVITY (HUA)

An Effective Tool to Estimate Impaired Function:
HOURS OF UPRIGHT ACTIVITY (HUA)

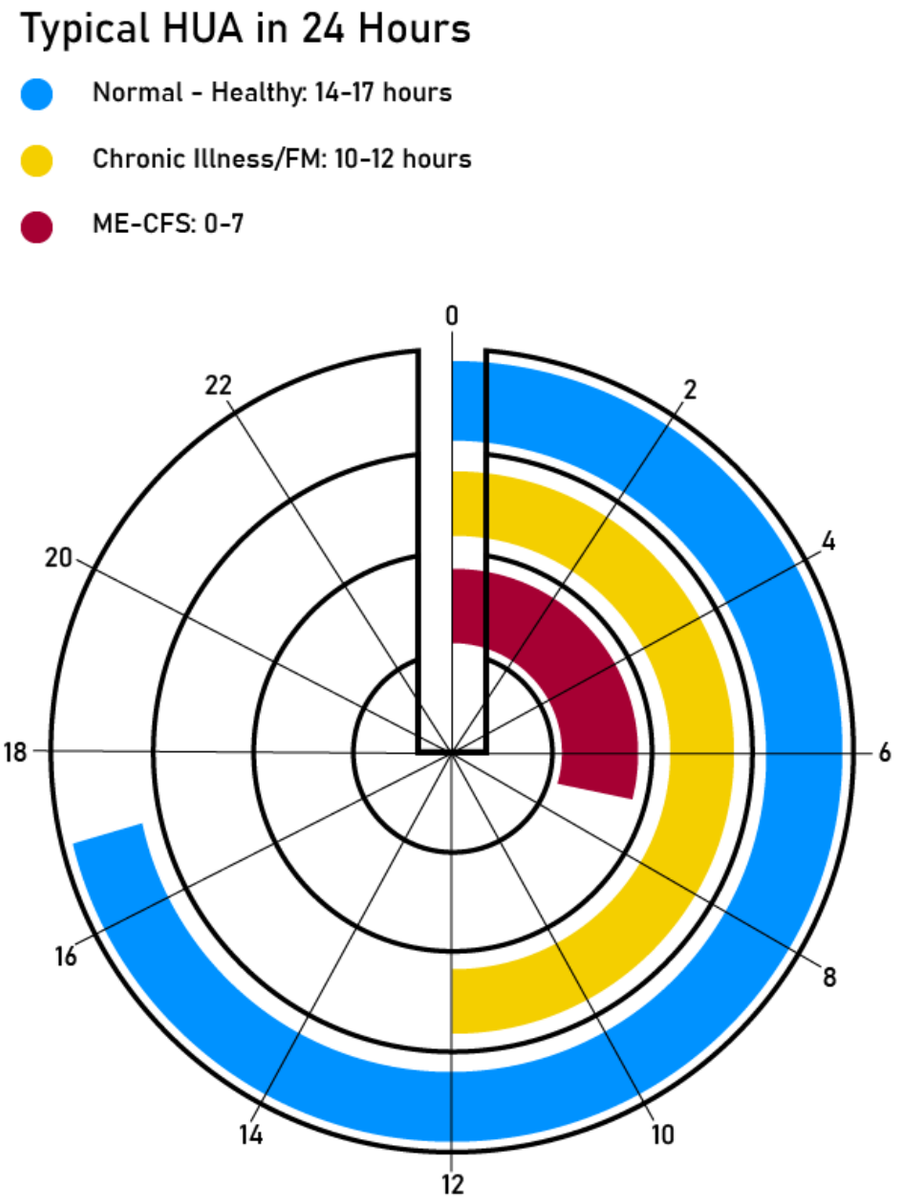
HUA = The number of hours spent with feet-on-floor in 24 hours (sitting, standing, walking)



-Credit to David Bell MD

Must ask the question clearly to be sure time spent sitting is considered in the total.

TYPICAL **H**OURS OF **U**PRIGHT **A**CTIVITY*



HUA 0-7: something is very wrong.

This assumes assessment of mental health has ruled out severe depression

*Based only on BHC clinical research and my clinical experience

ELICIT A RANGE OF SYMPTOM SEVERITY AND REAL EXAMPLES OF FUNCTION

- GOOD DAY vs BAD DAY
- How many of each per month?
- Specific examples of what patient can and cannot do on good or bad days

GOOD DAYS:
CASE #2– FEMALE AGE 30

Average number of GOOD days per MONTH: "5-10 days"

Average Hours of UPRIGHT Activity (HUA) on a GOOD day (sitting, standing, walking --- activities with FEET ON FLOOR): "1-2 hours"

Average hours of non-upright activity on a GOOD day (reclining, elevating feet, laying in bed): "23-24 hours"

Give specific examples of activities/tasks you **CAN do** on a good day: "Drive, go on a short walk, stretch, run an errand with help"

Give specific examples of activities/tasks you **CAN NOT do** even on a good day: "Clean, make my own meals, go to work"

BAD DAYS:
CASE #2– FEMALE AGE 30

Average number of bad days per MONTH: "20-25 days"

Average Hours of UPRIGHT Activity (HUA) on a BAD day (sitting, standing, walking --- activities with FEET ON FLOOR): "30 min- maybe"

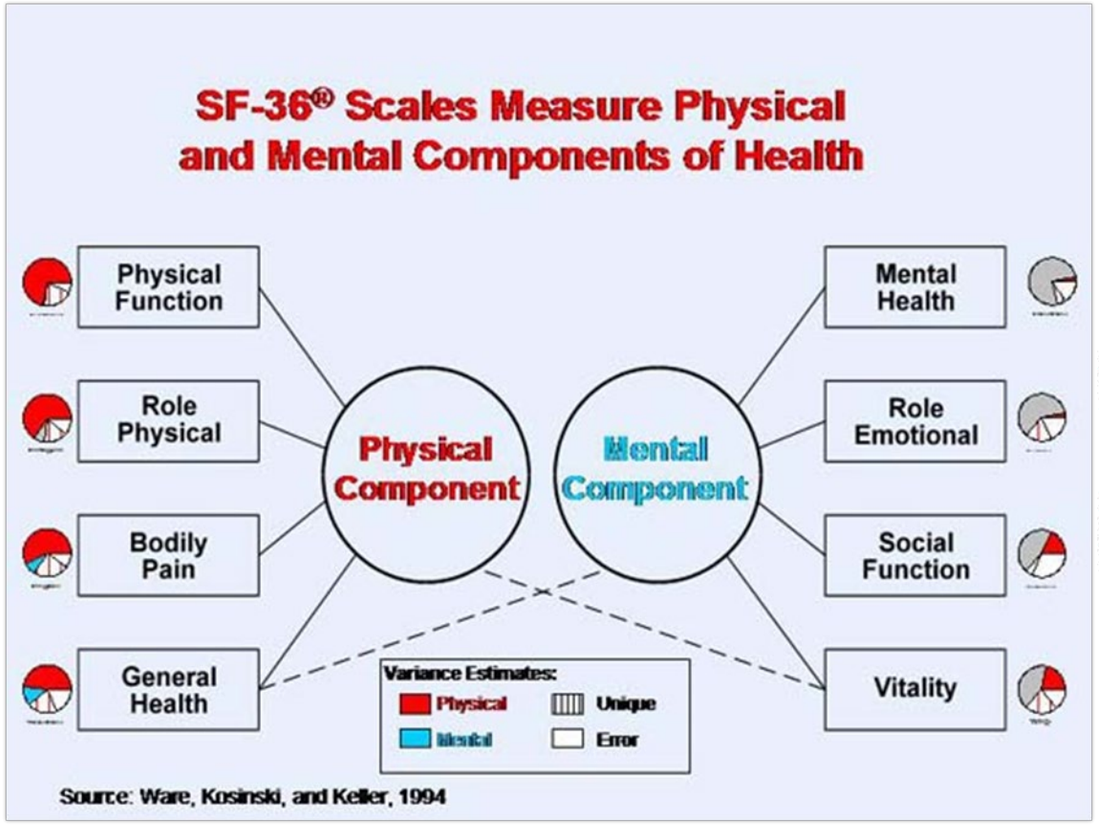
Average hours of non-upright activity on a BAD day (reclining, elevating feet, laying in bed): "All day"

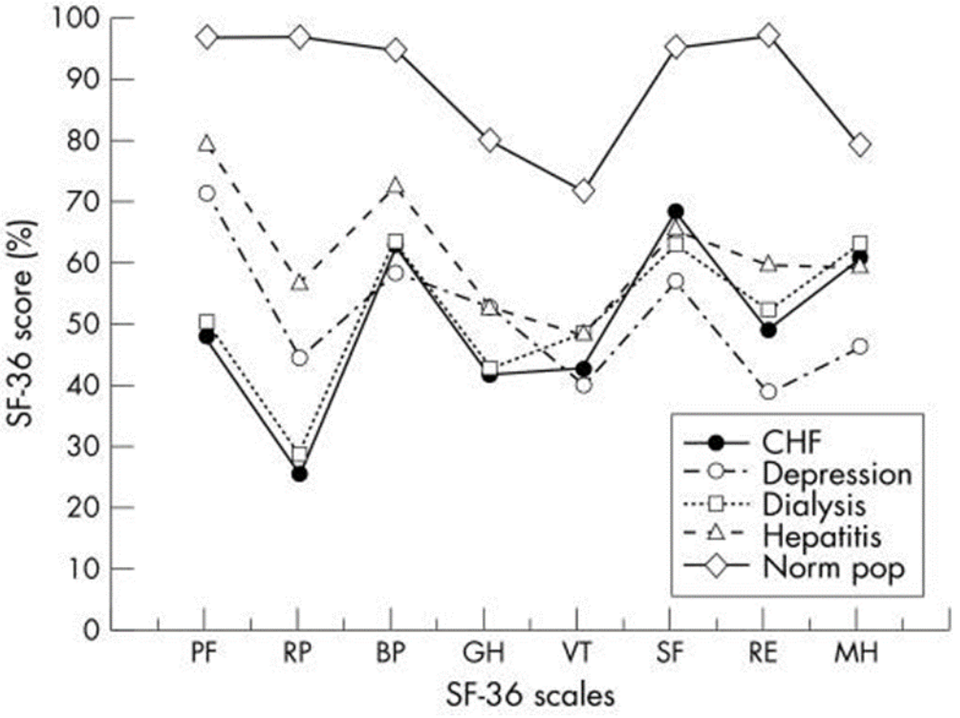
Give specific examples of activities/tasks you **CAN still do** on a BAD day: "Sit up, read, watch tv, eat.."

Give specific examples of activities/tasks you **CAN NOT do** when it's a BAD day: "Walk, have conversations"

RAND-36 (SF-36 IS THE RESEARCH TOOL)

36 questions covering 8 domains of physical and mental wellness





Ware, J.E Jr. and Sherbourne, C.D. The MOS 36-item short-form health survey (SF-36): conceptual framework and item selection. Med Care. 1992; 30: 473–483

Juenger J. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. Heart. 2002 Mar;87(3):235-41

https://www.rand36calculator.com/

RAND-36 SCORES:
CASE #1 FEMALE AGE 47

RAND 36-Item Subscale Scores

Physical Function:	10
Role Physical:	0
Bodily Pain:	32
General Health:	25
Vitality/energy/fatigue:	0
Social functioning:	50
Role Emotional:	100
Mental Health:	72

Score Key: 100/100 possible in each sub-scale. A lower score indicates more severe impairment.

RAND-36 SCORES:
CASE #2 FEMALE AGE 30

RAND 36 Sub-scale Scores [SF-36]

- Physical Function: 0
- Role Physical: 0
- Bodily Pain: 20
- General Health: 25
- Vitality/energy/fatigue: 0
- Social functioning: 0
- Role Emotional: 0
- Mental Health: 16

Score Key: 100/100 possible in each sub-scale. A lower score indicates more severe impairment.

ORTHOSTATIC TESTING: 10 MIN NASA LEAN TEST

BP cuff. Oximeter. Stethoscope. Two operators.

After 10 minutes of quiet supine rest

- Measure supine HR and BP

Move subject to the relaxed stand/lean position

- Measure HR and BP every 1-2 min x 10 min

10 MIN NASA LEAN: CASE #1 FEMALE AGE 47

Orthostatic Vital Signs/The 10 min NASA LEAN Test

Supine 1 minute BP: 124/60 Pulse: 60

Supine 2 minute BP: **118/64** Pulse: **64** **Pulse pressure: 54**

Standing straight, shoulder blades against the wall, feet 6" from the wall:

Standing 0 minute BP: 96/68 Pulse: 87 → Lightheaded and nauseated

Standing 1 minute BP: 100/70 Pulse: 77

Standing 2 minute BP: 90/72 Pulse: 79

Standing 3 minute BP: 96/70 Pulse: 85 → Nauseated, feels faint

Standing 4 minute BP: 93/74 Pulse: 74

Standing 5 minute BP: 94/79 Pulse: 86

Standing 6 minute BP: 90/81 Pulse: 84 → **Pulse pressure: 9-12**

Standing 7 minute BP: **91/79** Pulse: **84** → Fatigued, nauseated, shaky, strong need to lie down, difficulty communicating. Test stopped because of impending-syncope.

Dx: systolic orthostatic hypotension (>20 pt drop in SBP)

10 MIN NASA LEAN: CASE #2–FEMALE AGE 30

Supine measurements: Patient has been resting supine for 10 minutes.

1 min BP: 102/76 PP: 26 HR (bpm): 75 SpO2: 99%

2 min BP: 106/76 PP: 30 HR (bpm): **75** SpO2: 99%

Standing measurements: Shoulder blades against wall, feet 6" from the wall

2 min BP: 102/? PP: ? HR (bpm): 110

4 min BP: ? PP: ? HR (bpm): 108 → Mild mottling of feet and toes cool
"Legs hurt, mild tingling of feet."

6 min BP: 110/94 PP: 16 HR (bpm): 103

8 min BP: 100/92 PP: 8 HR (bpm): **119** → Moderate purple hue of toes.

10 min BP: ? PP: ? HR (bpm): **118** → SpO2: 99%

SUMMARY: HR 75→118 **(+43 bpm).**

Meets criteria for **postural orthostatic tachycardia syndrome (POTS)**

PP/SBP at 6 min 16/110= 14% (normal >25%) **Abnormally narrowed pulse pressure**

"EASY" CLINICAL ASSESSMENT OF CHRONIC ORTHOSTATIC INTOLERANCE

The **Orthostatic Hypotension Questionnaire (OHQ)** was developed with two components: the **6-item symptoms assessment** scale and a **4-item daily activity scale** to assess the burden of symptoms.

The OHQ was validated in 137 Neurogenic Orthostatic Hypotension (NOH) subjects in a phase IV, double blind, randomized, cross over, placebo-controlled trial of the alpha agonist midodrine

Clinical Validity: The floor and ceiling effects were minimal. OHQ scores were highly correlated with other patient reported outcome measures, indicating excellent convergent validity. Test-retest reliability was good

Kaufmann H, et al. The Orthostatic Hypotension Questionnaire (OHQ): validation of a novel symptom assessment scale. Clin Auton Res. 2012 Apr;22(2):79-90. doi: 10.1007/s10286-011-0146-2. Epub 2011 Nov 2.

Clin Auton Res (2012) 22:79–90
DOI 10.1007/s10286-011-0146-2

RESEARCH ARTICLE

The Orthostatic Hypotension Questionnaire (OHQ): validation of a novel symptom assessment scale

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Abstract
Background There is no widely accepted validated scale to assess the comprehensive symptom burden and severity of neurogenic orthostatic hypotension (NOH). The Orthostatic Hypotension Questionnaire (OHQ) was developed, with two components: the six-item symptoms assessment scale and a four-item daily activity scale to assess the burden of symptoms. Validation analyses were then performed on the two scales and a composite score of the OHQ.
Methods The validation analyses of the OHQ were performed using data from patients with NOH participating in a phase IV, double blind, randomized, cross over, placebo-controlled trial of the alpha agonist midodrine. Convergent validity was assessed by correlating OHQ scores with clinician global impression scores of severity as well as with generic health questionnaire scores. Test–retest reliability was evaluated using intraclass correlation coefficients at baseline and crossover in a subgroup of patients who reported no change in symptoms across visits on a patient global impression scores of change. Responsiveness was examined by determining whether worsening or improvement in the patients' underlying disease status produced an appropriate change in OHQ scores.
Results Baseline data were collected in 137 enrolled patients, follow-up data were collected in 104 patients randomized to treatment arm. Analyses were conducted using all available data. The floor and ceiling effects were minimal. OHQ scores were highly correlated with other patient reported outcome measures, indicating excellent convergent validity. Test–retest reliability was good. OHQ scores could distinguish between patients with severe and patients with less severe symptoms and responded appropriately to midodrine, a pressor agent commonly used to treat NOH.
Conclusion These findings provide empirical evidence that the OHQ can accurately evaluate the severity of symptoms and the functional impact of NOH as well as assess the efficacy of treatment.

Keywords Orthostatic hypotension · Autonomic failure · Symptoms · Questionnaire

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Introduction

Neurogenic orthostatic hypotension (NOH) is a disorder of sympathetic vasoconstriction [11]. Upon standing, the release of norepinephrine from sympathetic nerve terminals is decreased or absent, vasoconstriction in the systemic

ORTHOSTATIC ***INTOLERANCE*** QUESTIONNAIRE

OIQ= OISA+OIDAS

Orthostatic Intolerance Symptom Assessment (OISA)

Score: 0=None and 10=Severe

- Dizziness, lightheadedness, feeling faint, or feeling like blackout
- Problems with vision (blurring, seeing spots, tunnel vision, etc.)
- Weakness
- Fatigue
- Trouble concentrating
- Head/neck discomfort

Orthostatic Intolerance Daily Activity Scale (OIDAS)

0=No Interference; 10=Complete Interference

- Standing a short time
- Standing a long time
- Walking a short time
- Walking a long time

OIQ SCORE: CASE #2– FEMALE AGE 30

OIQ: 76/100

- OISA 47/100 (symptoms)
- OIDAS 29/100 (activity)

Orthostatic testing

Seated VS: HR 110 BP 116/84

10 min NASA Lean:

HR 75→118 (+43 bpm= POTS)

PP 30→ 16 or less

PART 1: TOOLS FOR EFFICIENTLY GETTING USEFUL INFORMATION ABOUT SYMPTOM FREQUENCY, SEVERITY, AND IMPAIRMENT OF FUNCTION.

- Pain diagrams
- Visual analog scales (VAS)
- Expanded ROS with frequency and severity
- FIQ-R
- Hours of Upright Activity (HUA)
- Good Day/Bad Day
- RAND-36
- 10 min NASA Lean test

PART 2: NEXT SESSION

- Discussion of conditions that might cause debilitation and a “pan-positive” review of systems despite routine standard labs and tests.