

A review of RLS -- symptoms, frequency, and treatment

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Uncomfortable Sensations

- Creepy, crawly - crawling or creeping
- Worms crawling in veins
- Pepsi-Cola in the veins
- Nervous feet
- Itchy bones
- Crazy Legs or heebie-jeebies
- Tooth ache feeling -Can't leave it alone
- Excited nerves, Electric-like shocks
- JUST NEED TO MOVE
- Pain about 35% of cases

4 Criteria Boiled Down to Basics

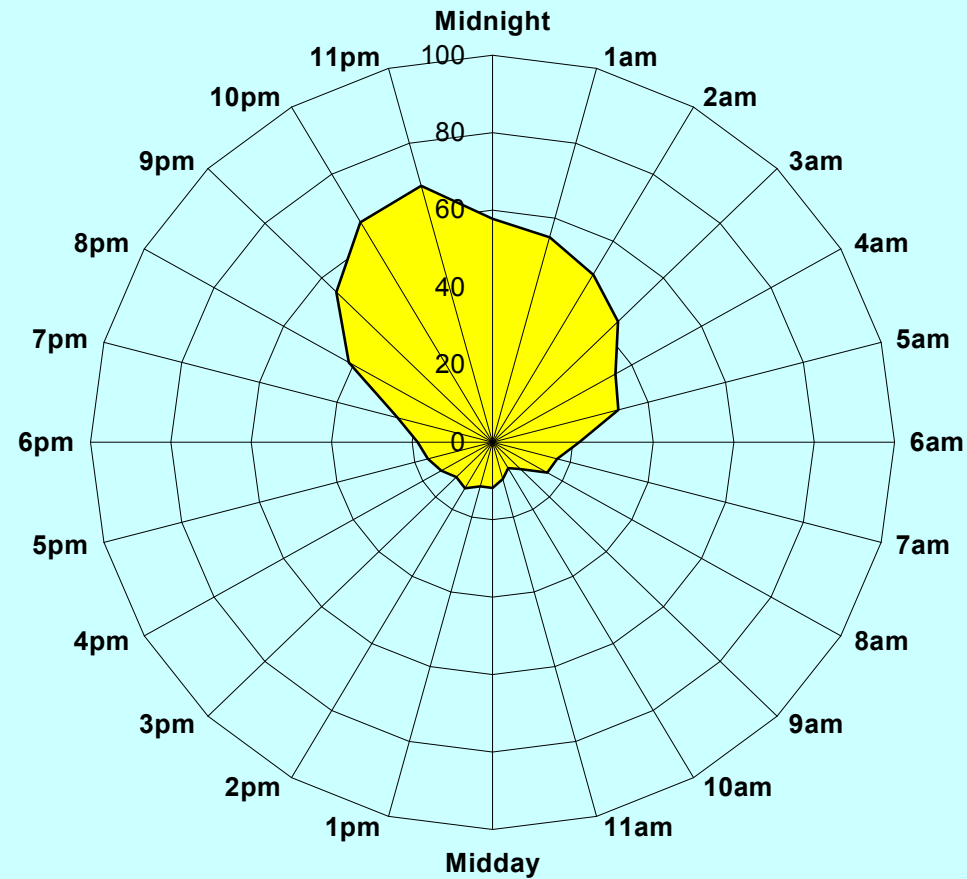
The urge to move the legs which usually comes with some funny, hard to describe feelings

The urge comes on at rest

Goes away with activity

And is worse in the evening and at night

Q20 Times of the day or night when these feelings and the need to move are experienced



N=102 (remaining 4 stated Don't know/Ccan't say)

NL-DCQ

Supportive Clinical Features for Diagnosis

1. Response to dopaminergic therapy
2. Periodic Leg Movements (during wake or sleep)
3. Family history of RLS

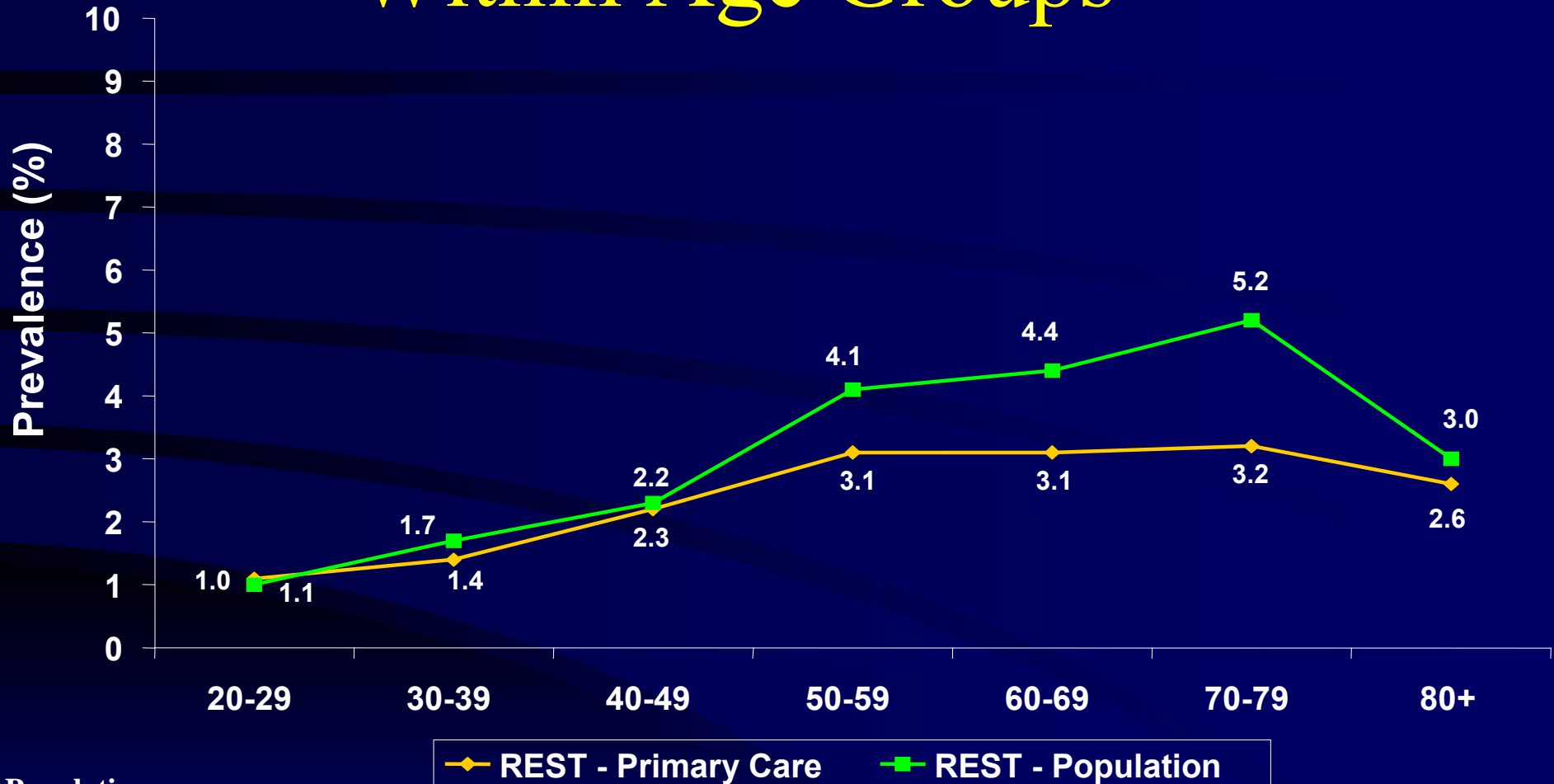
Significance and Value of these supportive features remain to be determined.

Associated clinical features

1. Progressive clinical course
2. Physical examination normal in absence of underlying cause or comorbidity
3. Sleep disturbance most significant clinical complaint --

May mediate many of daytime difficulties of energy, cognitive function, mood -- Kushida et al, 2004

The Prevalence of RLS Symptoms Within Age Groups



Target Populations

Prevalence

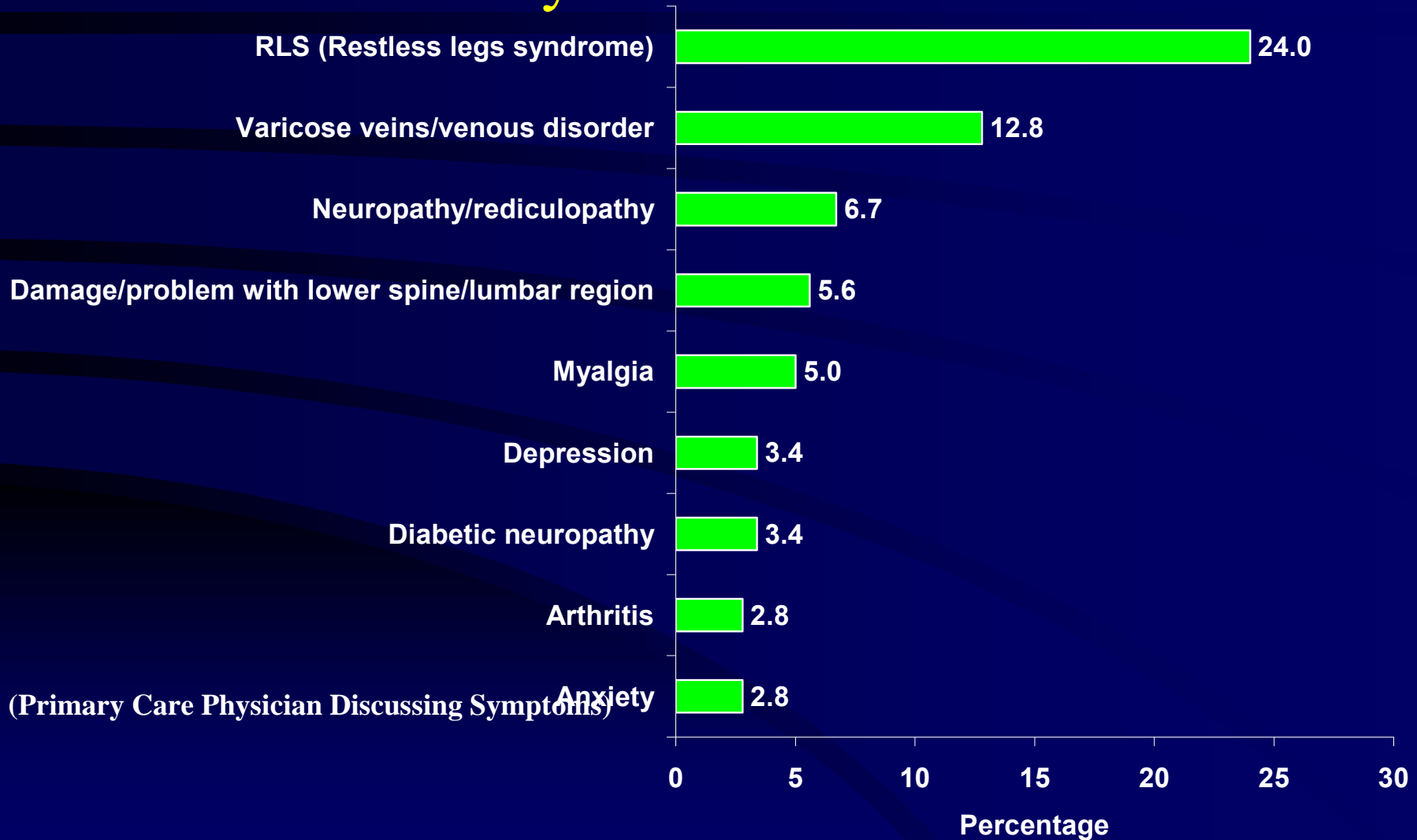
**Yes' to all questions, symptoms at least twice a week and moderate or severe distress
+ Positive RLS diagnosis on interview**

App. 6%

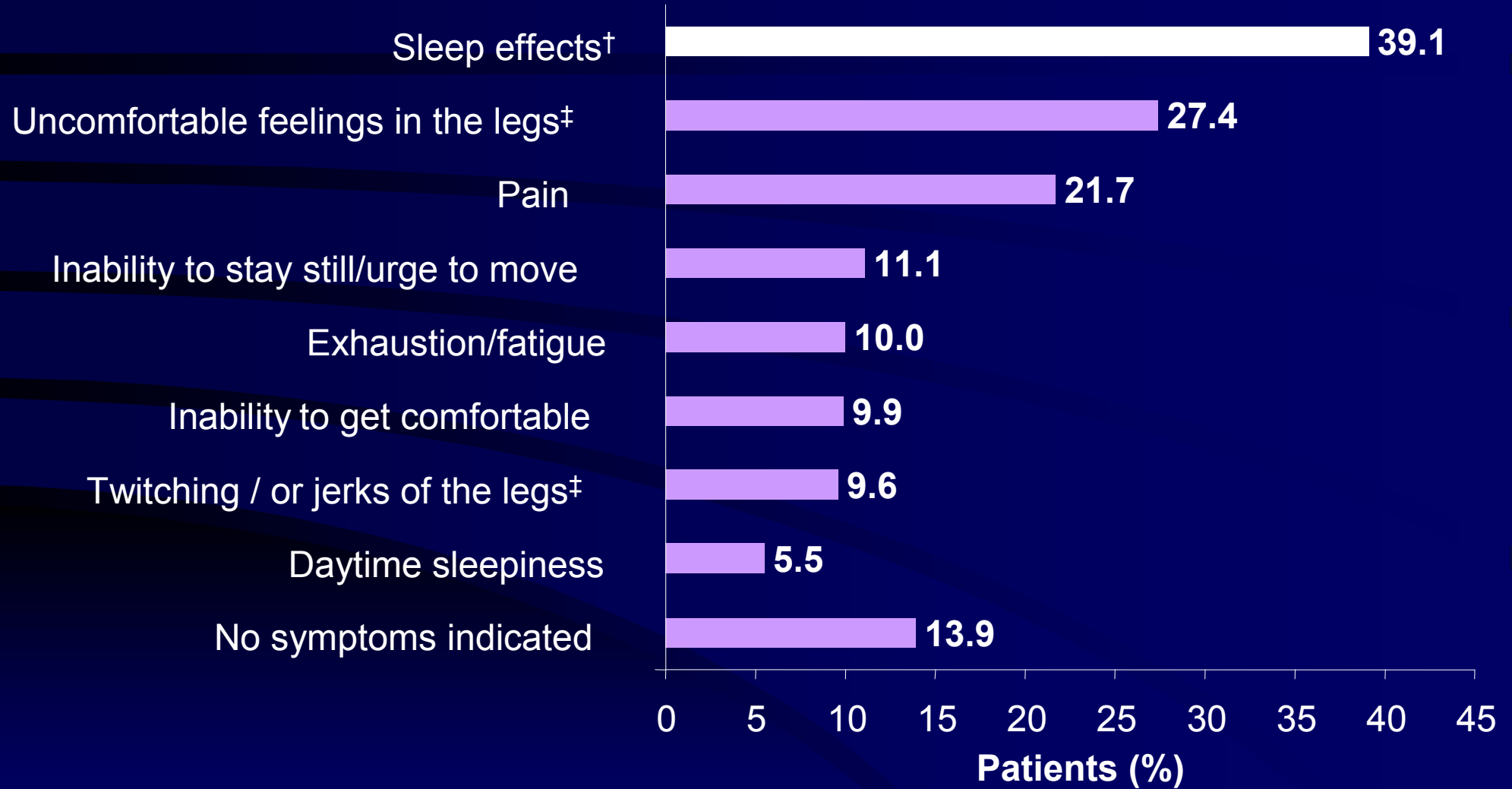
0.5-1% needs therapy

Diagnosis Made for the Symptoms of RLS Physician Records

(n=43)

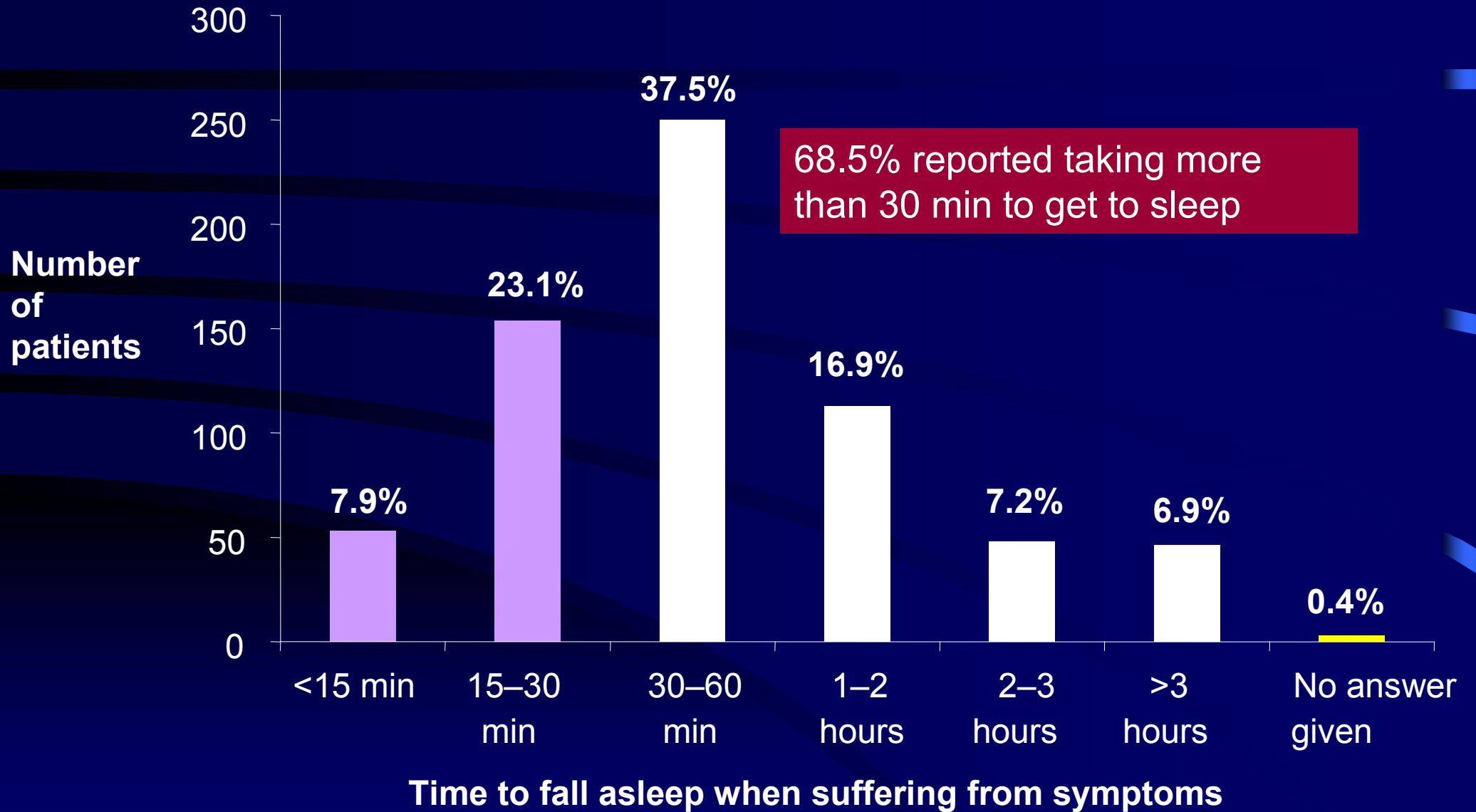


Most troublesome symptoms*

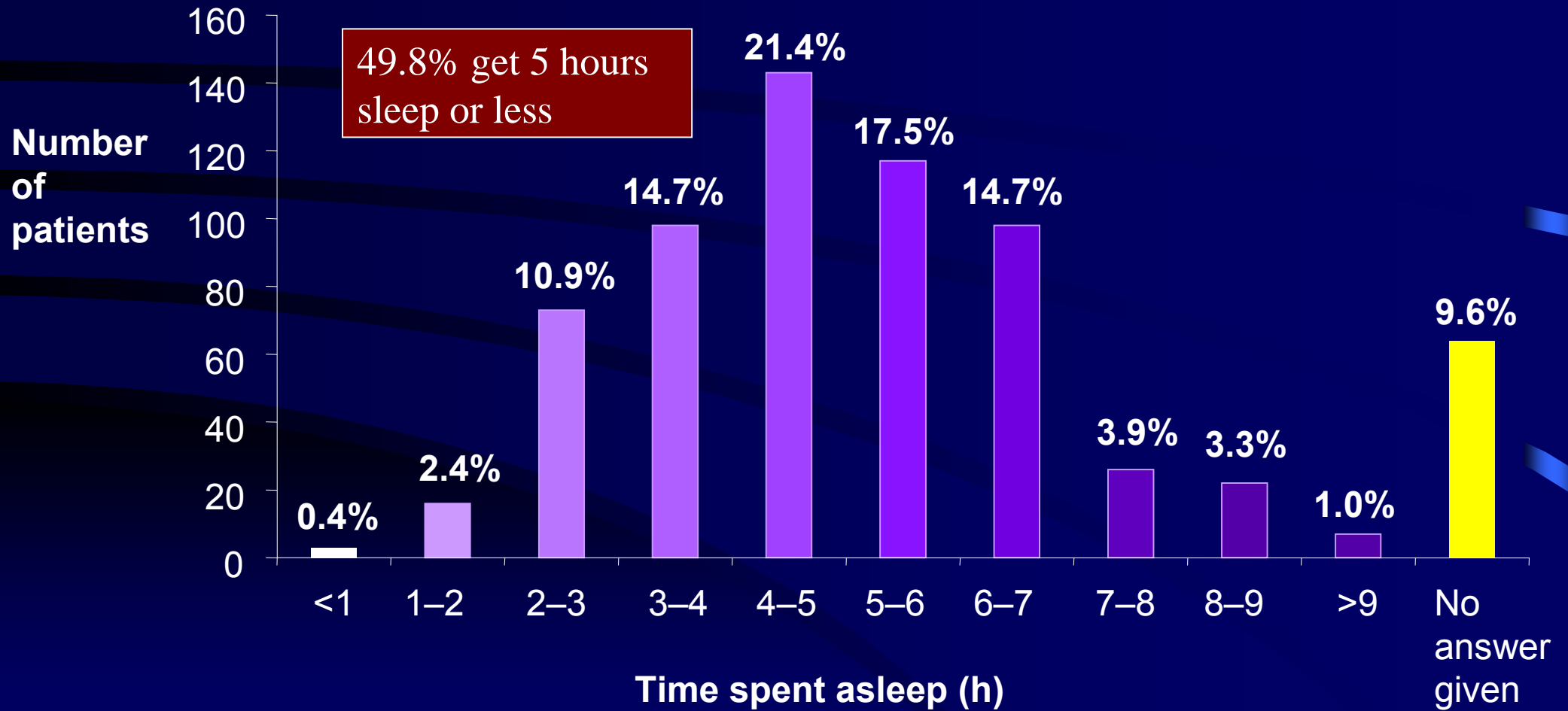


*Multiple answers were given in some cases; [†]includes inability to fall/stay asleep and disturbed sleep; [‡]or other parts of the body

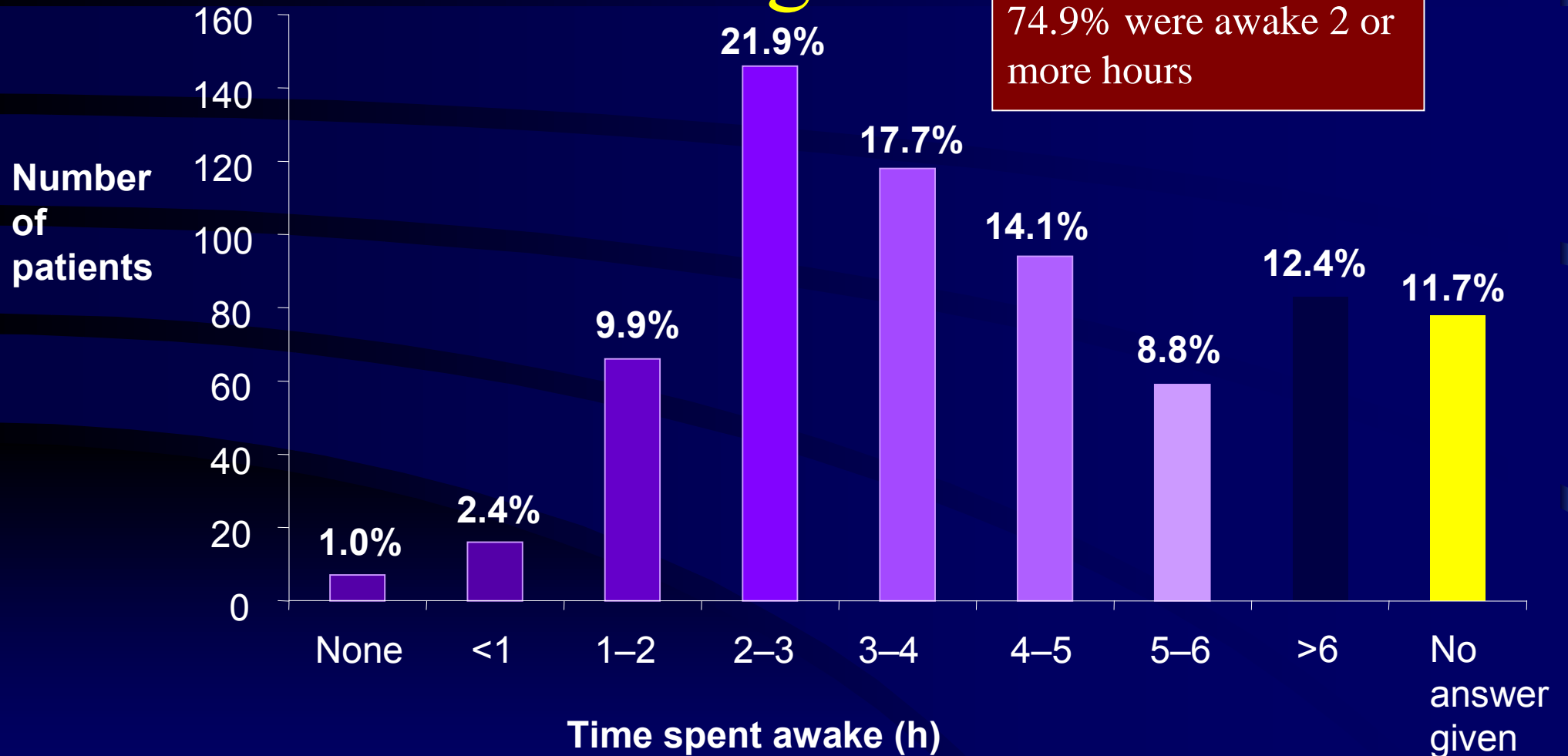
Sleep latency



Number of hours of *sleep* on a poor night



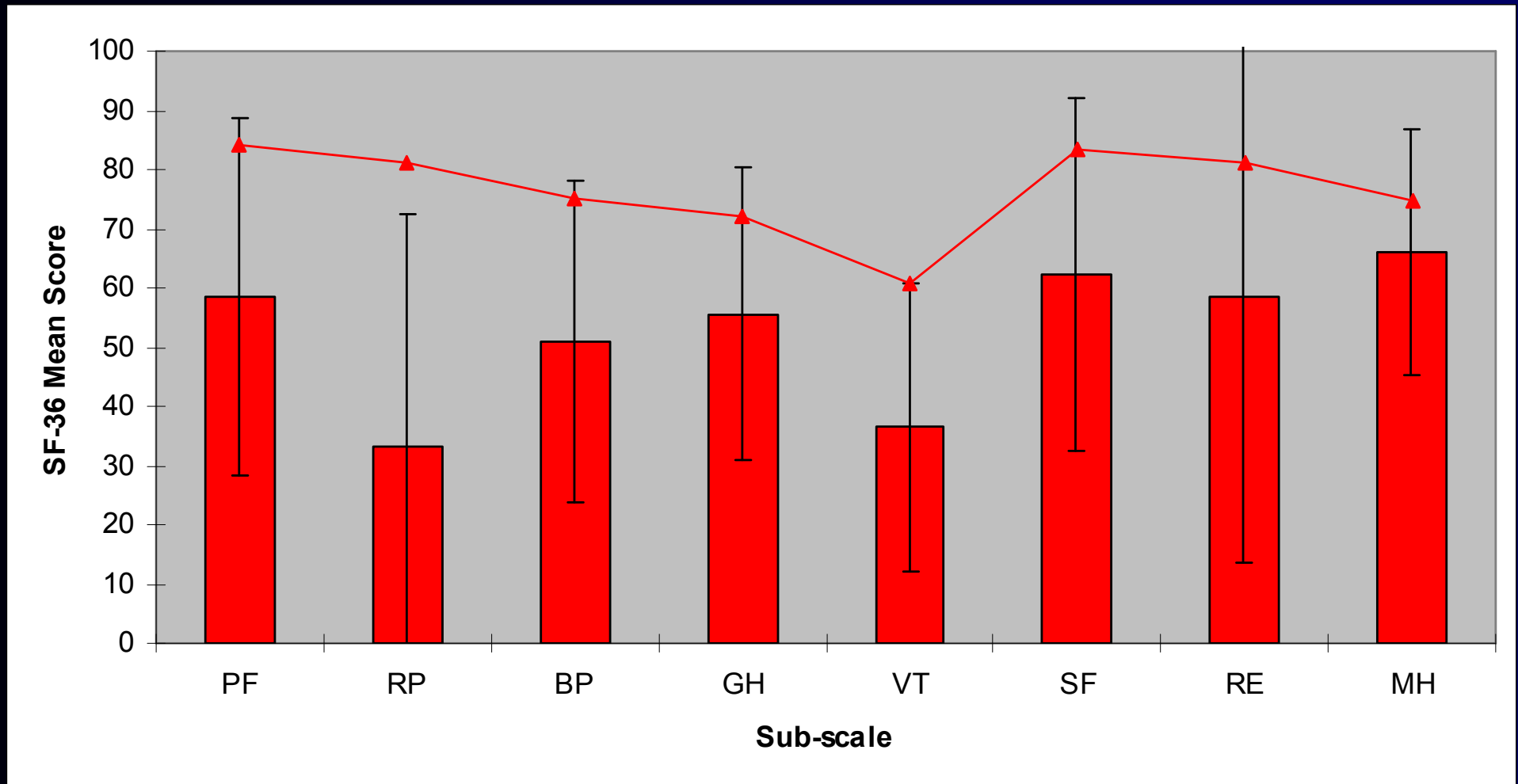
Number of hours *awake* on a poor night



Daytime effect of RLS symptoms

- Daytime Symptoms effects reported by individuals in the study population:
 - 59.7% ‘lack energy’
 - 57.7% ‘find it difficult to sit still or relax’
 - 54.4% report that ‘daily activities are disturbed’
 - 54.3% ‘have a tendency to become depressed/ low’
 - 49.6% ‘find it hard to concentrate the next day’

Total SF-36 Sub-scale Scores Compared to Normative Population



US General Population Norms n = 2474

Secondary RLS

- Iron deficiency/anemia
- Uremia
- Pregnancy
- Rheumatoid Arthritis
- Medication (see later on)
- ??Parkinson's disease, diabetes, neuropathy
- Secondary RLS may be present at high frequency even in populations with a low frequency of idiopathic RLS

RLS and Dopamine

- Studies have inconsistently found that dopamine markers for post>pre synaptic dopamine are mildly reduced in RLS (10-15%)
- RLS patients as a group respond to all dopaminergic agents

Treatment of RLS

- Non-pharmacologic -- sleep hygiene, moderate exercise, hot baths or massage at bedtime
- Pharmacologic --
 - Dopaminergic agents
 - Levodopa for occasional low-dose use
 - Dopamine agonists for daily treatment
 - Pramipexole, ropinirole, rotigotine, apomorphine, pergolide, cabergoline
 - Ropinirol and Pramipexol approved
 - Rotigotine in phase 3 studies
 - Other agents for daily therapy -- opioids, anticonvulsants: gabapentin, clonazepam
 - Adjuvants -- sedative/hypnotics: clonazepam

Prohibited Medications

- Antidepressants (including SSRIs*)
- Lithium
- Dopamine antagonists, (including domperidone)
- Neuroleptics/Antipsychotics
- Clonidine

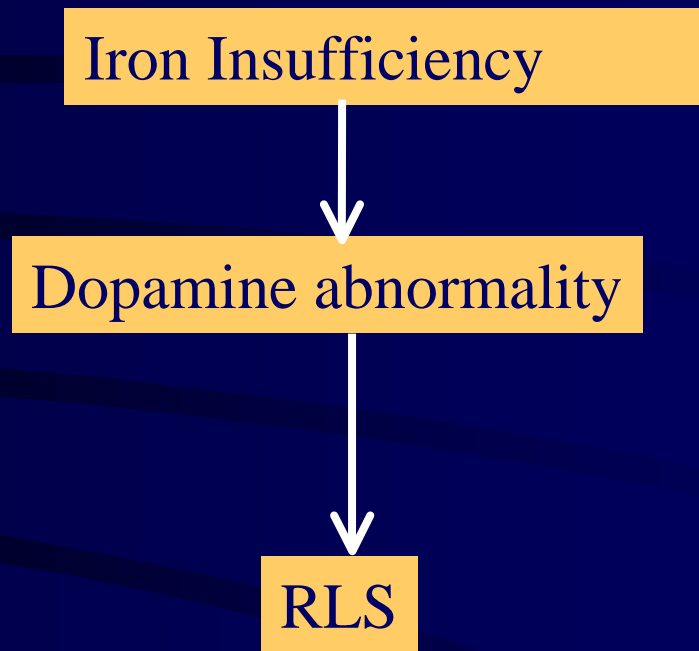
Algorithm

- All RLS -- Nonpharmacological measures
 - Behavioral, including sleep hygiene
 - Seek secondary causes and potential aggravators
- Intermittent RLS -- prn meds (ldopa, opioids, sedative-hypnotics, dopamine agonists?)
- Daily RLS -- dopamine agonist, clonazepam, opioid, gabapentin
- Refractory RLS -- try another agonist, switch to stronger opioid or gabapentin, combination therapy, rotating therapy
- Augmentation– as in refractory RLS

Problems with Dopaminergics

- Side effects -- nausea and vomiting, hypotension, headache, nasal stuffiness
 - Low dose treatment does not bring late PD problems
 - Start slowly
- Augmentation -- iatrogenic worsening -- earlier onset, more severe, spread
 - Most with L-dopa, 1/3 with agonists, ??little if any with other drugs

IRON model of RLS



Treatment: Dopamine YES
 IRON if low ferritin

Summary

- 1. RLS is a common sleep/wake sensorimotor disorder whose diagnosis remains primarily clinical**
- 2. Treatment is now available using Dopaminergics and several other effective medication classes**
- 3. A key pathophysiologic element in RLS may be deficiencies in brain storage of iron which may influence the circadian pattern of dopamine activity**