# ME/CFS: The Modern Clinical Pathway

A neuroimmune approach to diagnosis, overlap syndromes, and pacing-based management

## Historical Myth

- Dismissively viewed as a psychosomatic illness or "deconditioning"
- Relied on curative psychology and forced exercise
- Resulted in widespread medical trauma, stigma, and severely delayed clinical management

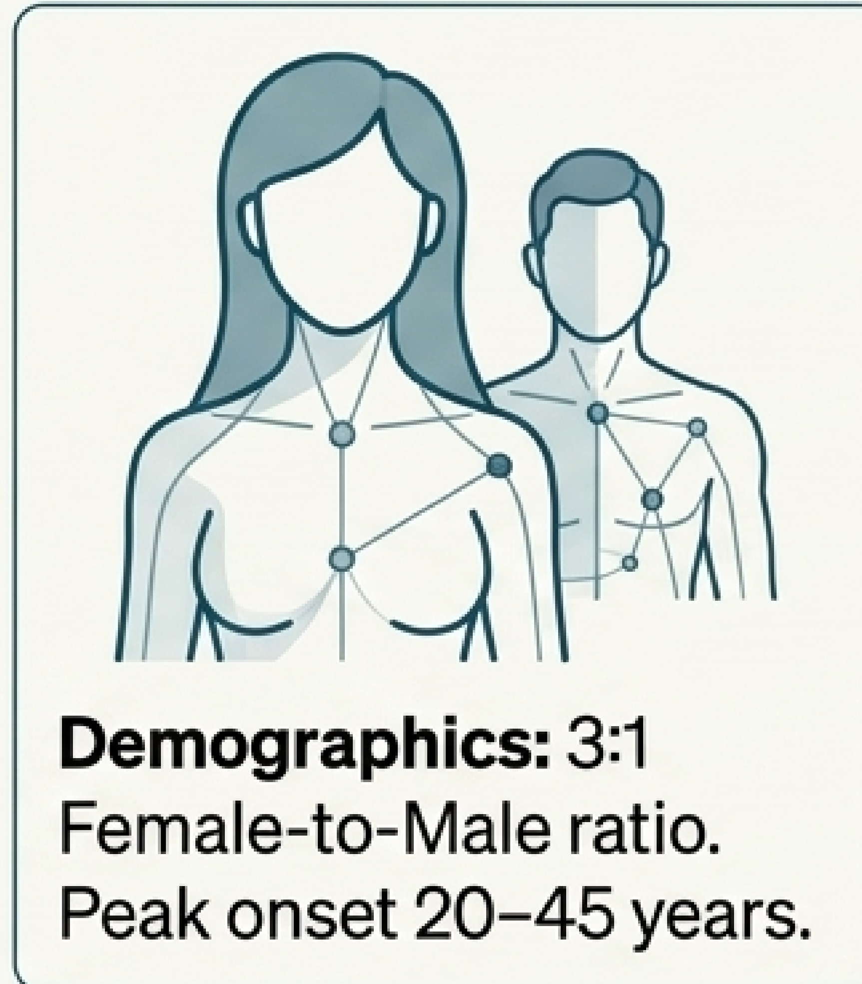
**The Paradigm Shift**

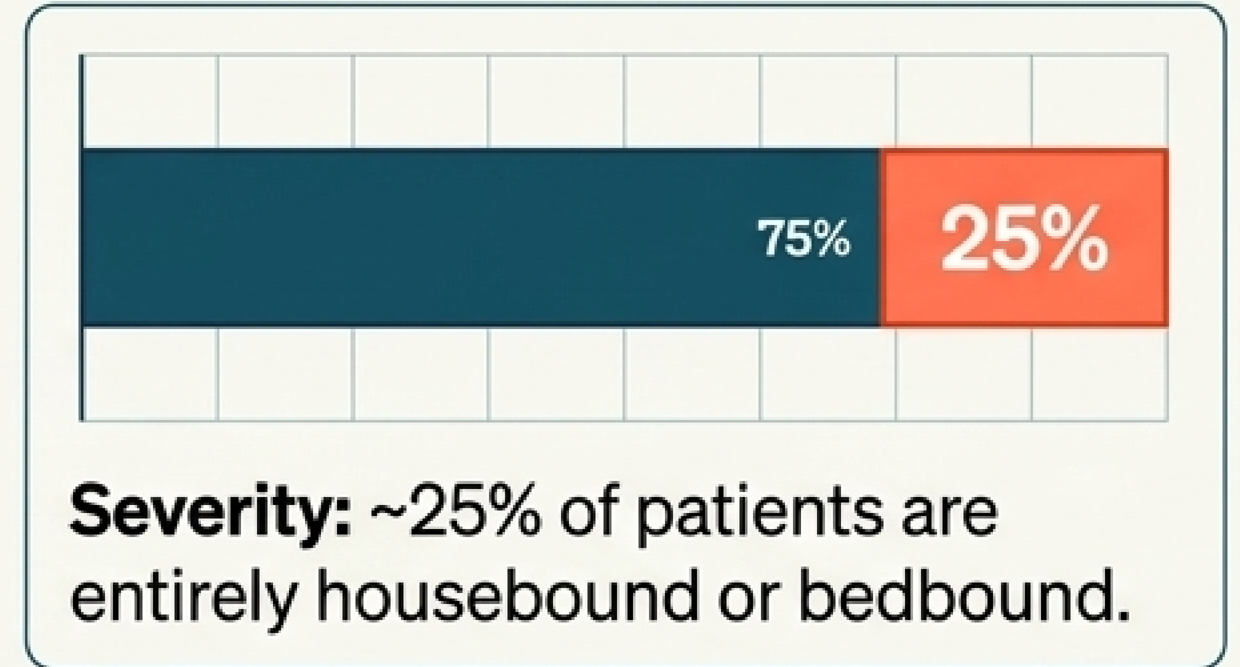
From Misconception to Biological Understanding

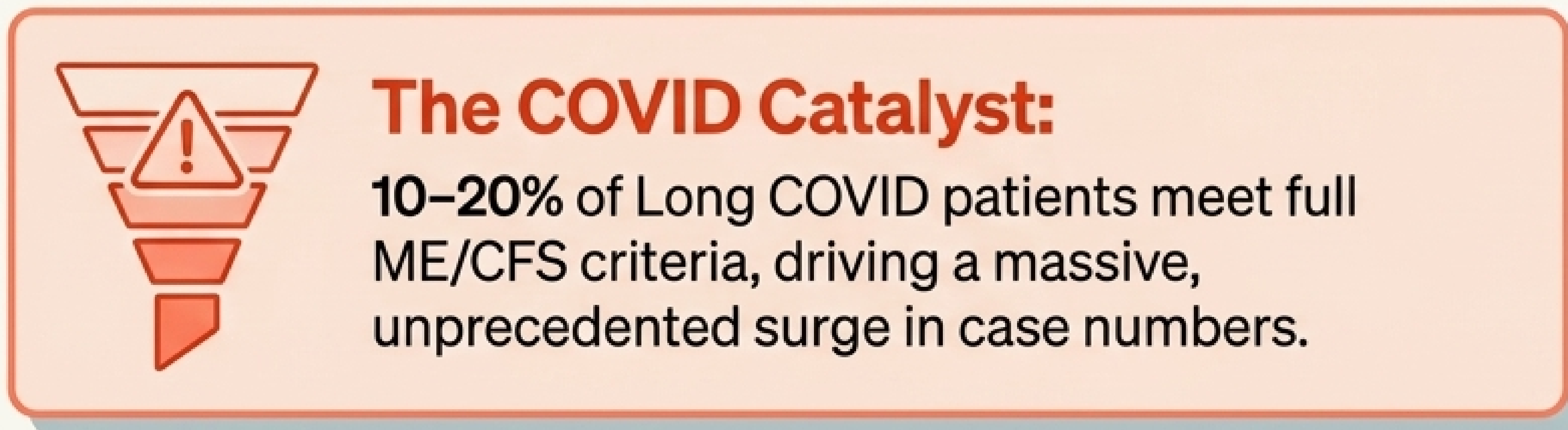
## Current Reality

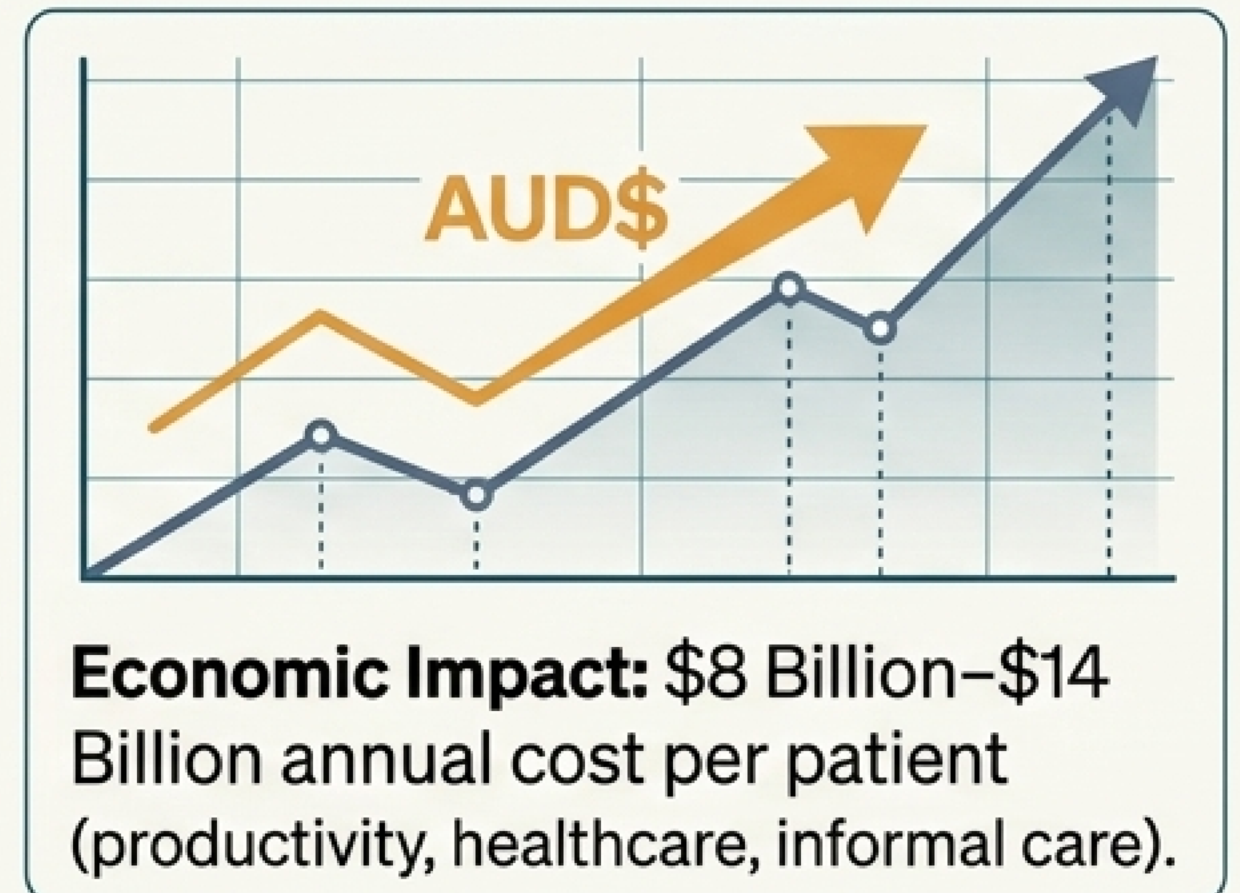
- **Defined as a complex, multi-system neuroimmune condition**
- **Officially classified as a Neurological Disorder (WHO ICD-10 G93.3)**
- **Demands a validated, strictly biomedical, and evidence-based management approach**

# The Australian Burden of Disease



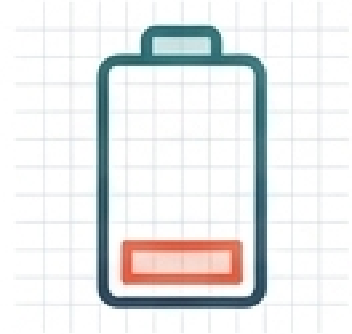



# The Four Pillars of Clinical Presentation

1



### Debilitating Fatigue

Persisting ≥4 weeks (NICE 2021).

Results in a profound impact on baseline functional capacity.

2

### Post-Exertional Malaise (PEM)

The cardinal feature.

Disproportionate symptom exacerbation after physical, cognitive, or emotional effort.

3

### Unrefreshing Sleep

A sleep quality vs. quantity mismatch.

Waking feeling exhausted regardless of total hours slept.

4

### Cognitive Dysfunction

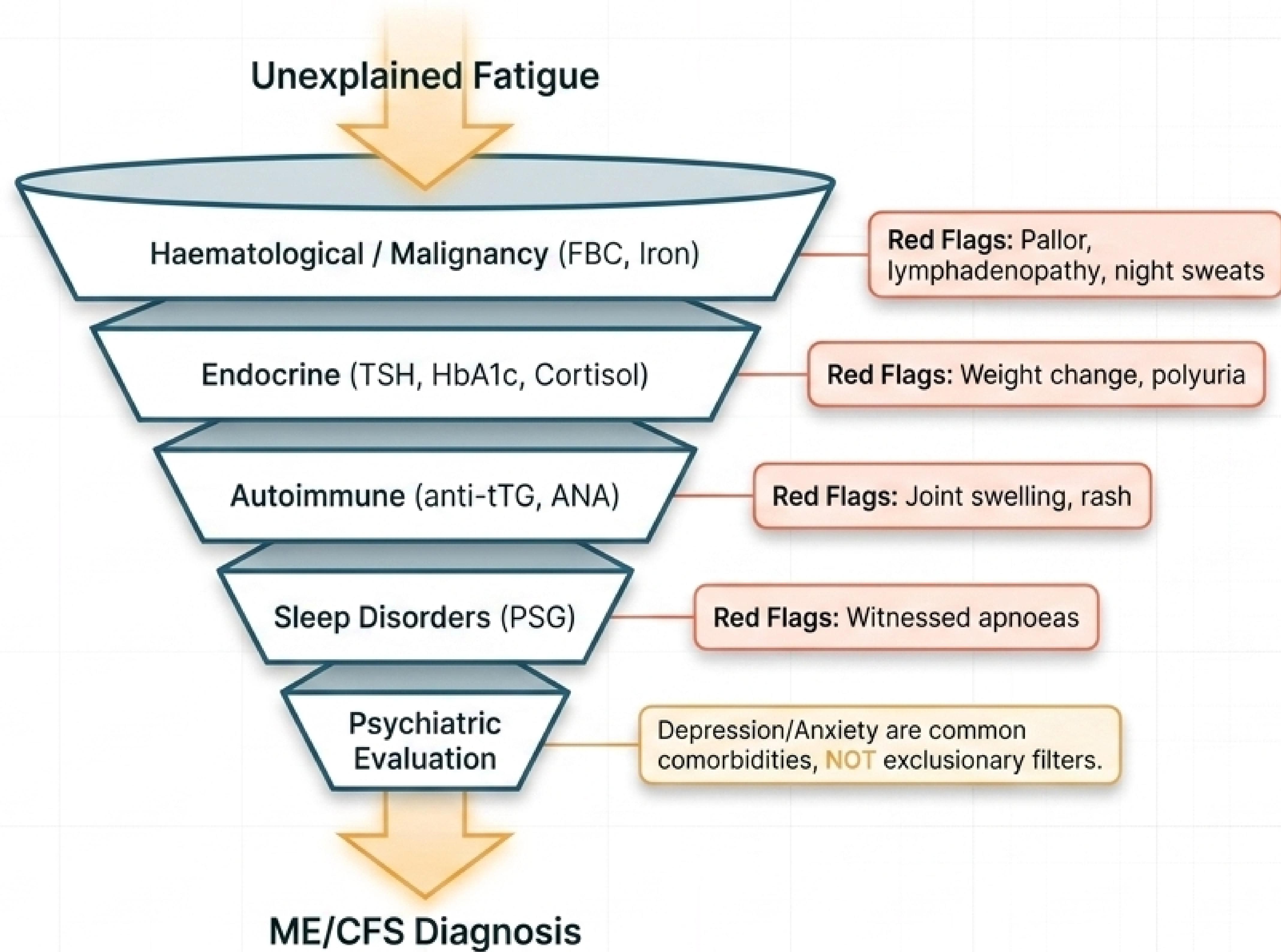
Brain fog, severely slowed processing,

word-finding difficulty, and short-term memory impairment.

# Navigating Diagnostic Frameworks

| NICE 2021 | IOM 2015 | Canadian Consensus 2003 |
| --- | --- | --- |
| Current Global Standard | SEID Framework | Multi-System Approach |
| - Lower threshold for duration (≥4 weeks)<br>- Demands PEM as the absolute cardinal feature<br>- Explicitly opposes and withdraws Graded Exercise Therapy (GET) | - Requires ≥6 months duration<br>- Demands significant activity reduction, PEM, and unrefreshing sleep<br>- Requires either cognitive impairment or orthostatic intolerance | - Requires ≥6 months duration<br>- Demands PEM, sleep dysfunction, and pain<br>- Requires ≥2 manifestations across neurological, autonomic, neuroendocrine, or immune systems |

# The Diagnostic Exclusion Funnel



# First-Line Screening Panel

## Tier 1: The Essential Panel

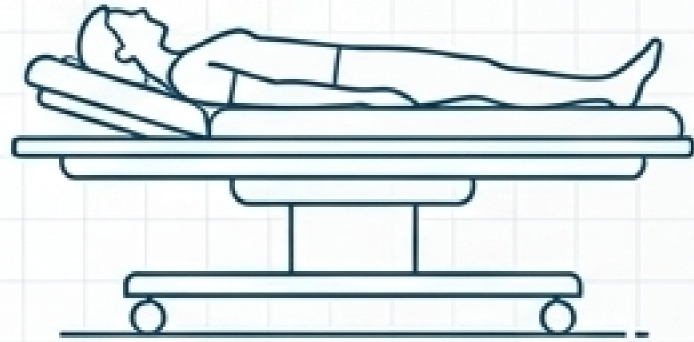
| | | | |
|---|---|---|---|
| Essential | FBC (MBS 66504) | Essential | TSH (most common endocrine cause) |
| Essential | ESR / CRP | Essential | HbA1c / Fasting Glucose |
| Essential | UEC | Essential | Corrected Calcium |
| Essential | LFTs | | |

## Tier 2: Targeted Add-Ons

| | | | |
|---|---|---|---|
| Available / Referral | Ferritin (Fatigue occurs at <30 μg/L without frank anaemia) | Available / Referral | Coeliac Serology (anti-tTG IgA) |
| Available / Referral | Vitamin D | Available / Referral | Morning Cortisol / Synacthen (if adrenal suspected) |
| Available / Referral | B12 / Folate | Available / Referral | Polysomnography (if apnoea suspected) |

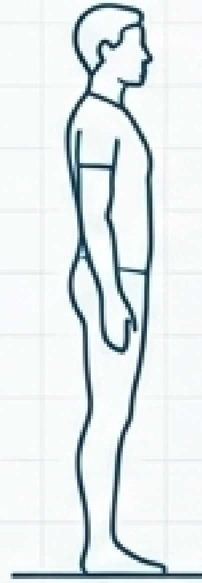
# Autonomic Screening: The Active Stand Test

## Step 1: Supine



Patient lies flat for ≥5 minutes.
Baseline BP and HR recorded.

## Step 2: Stand & Monitor





Patient stands.
Measurements taken at intervals.

**Orthostatic Hypotension** ⚠

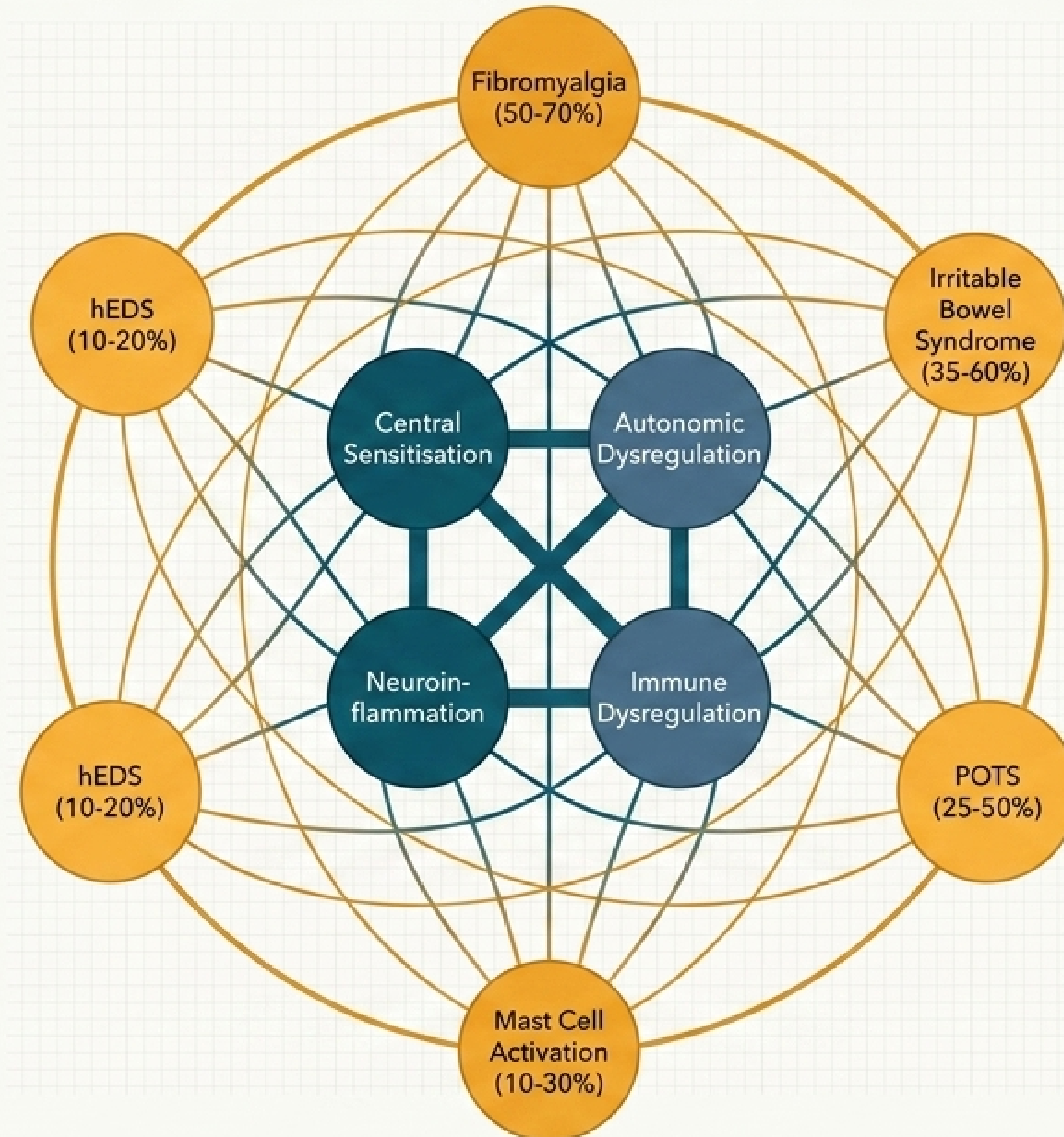
Drop in systolic BP ≥20 mmHg OR diastolic BP ≥10 mmHg within 3 mins.

**POTS** ⚠

Rise in HR ≥30 bpm (≥40 in adolescents) within 10 mins, without a BP drop.

**Context:** Orthostatic Intolerance and POTS co-occur in 25–50% of ME/CFS patients.

# The Pathological Web & Overlap Syndromes

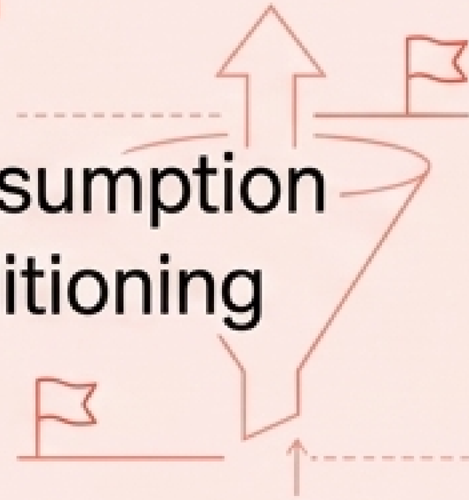



**Key Insight**

*Single-target treatments fail because these overlapping mechanisms must be managed simultaneously.*

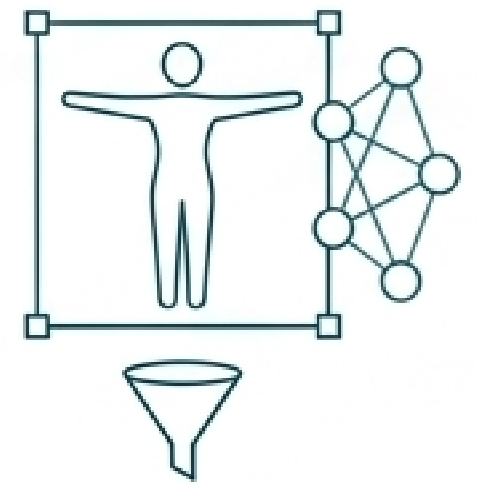
# Management Paradigm Shift: Withdrawing GET

## Graded Exercise Therapy (GET) & Curative CBT



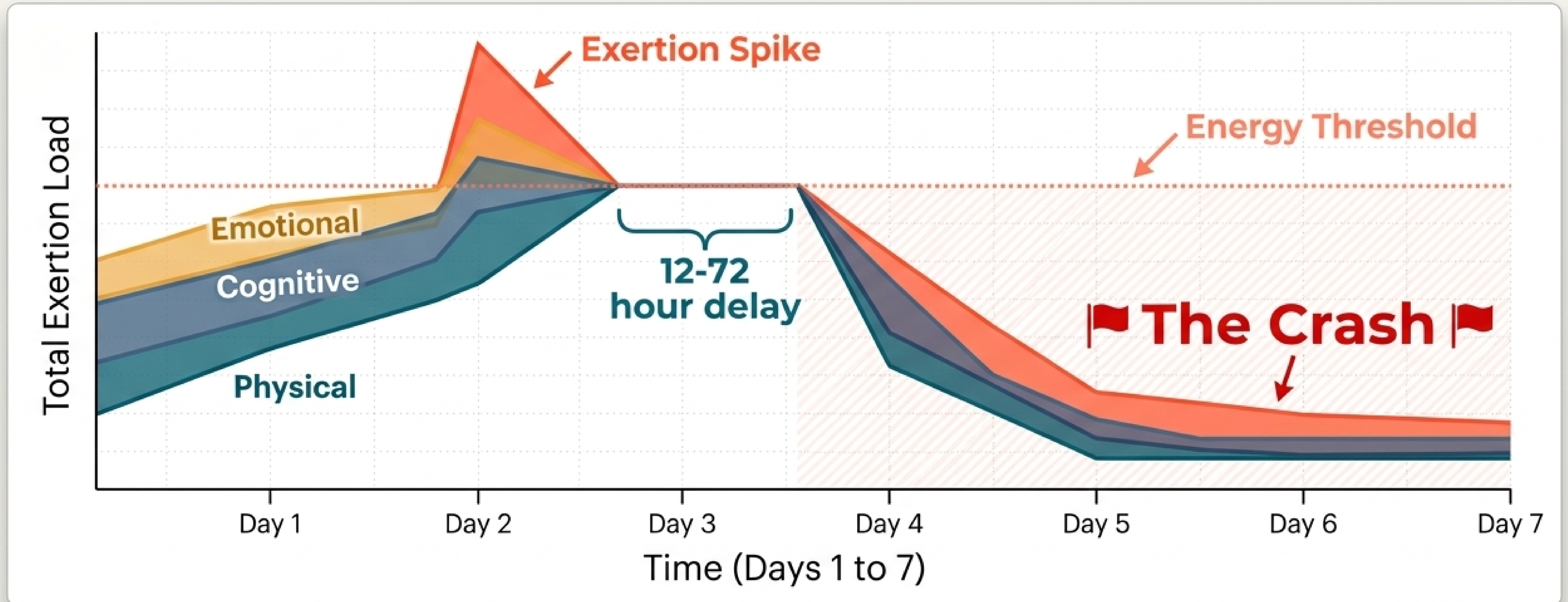
- Based on the outdated assumption that physiological deconditioning drove the illness.
- Explicitly withdrawn by NICE 2021 due to robust clinical evidence of harm.
- Structured, incremental exercise actively triggers Post-Exertional Malaise (PEM).

## Pacing & Supportive Coping



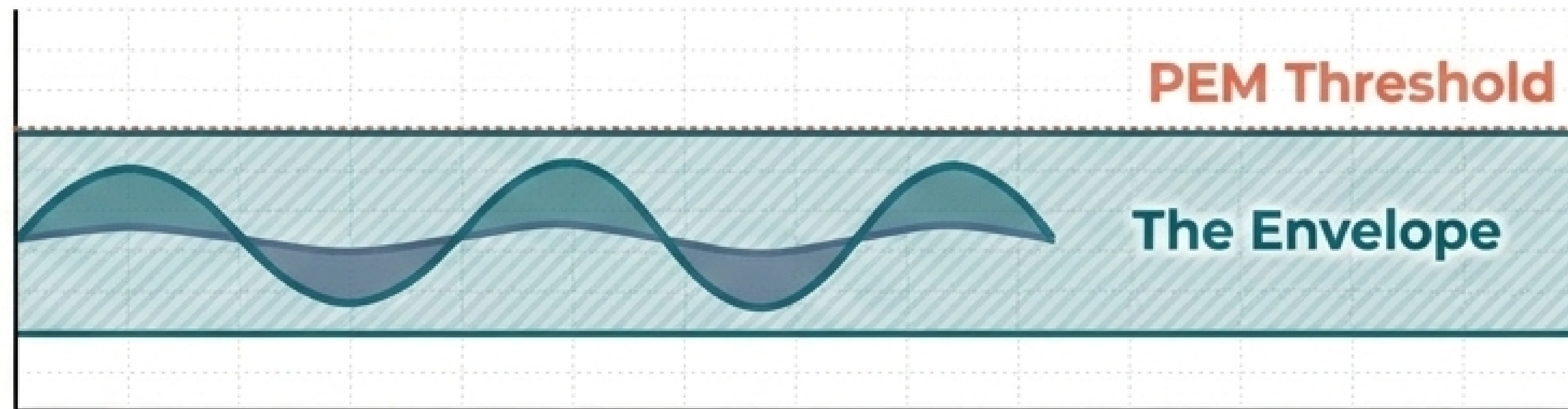
- "Pacing" within the Energy Envelope is now the cornerstone of physical management.
- CBT is repurposed as a psychological tool for adjusting to chronic illness and managing comorbid anxiety/depression, NOT as a cure for "illness beliefs".

# Anatomy of a Crash: Post-Exertional Malaise




PEM is disproportionate, delayed, and compounds across physical, mental, and emotional stressors.

# Pacing Within The Energy Envelope




1. Keep a 2-4 week symptom diary to identify the exact threshold.
2. Distribute activity strictly below that line (alternate physical/cognitive).
3. Mandate proactive rest (not just sleep).
4. Expand capacity by only 5-10% once highly stable.

# The Symptom-Targeted Pharmacopoeia

**Sleep / Brain**

**Melatonin:** 2mg MR (PBS Authority ≥55y).

**Amitriptyline:** Low dose 10-25mg nocte (monitor anticholinergic effects).

**Pain / Musculoskeletal**

**Duloxetine:** 30-60mg (check eGFR >30).

**Low-Dose Naltrexone (LDN):** 1.5-4.5mg nocte (off-label/compounded ~$50-60/mo).

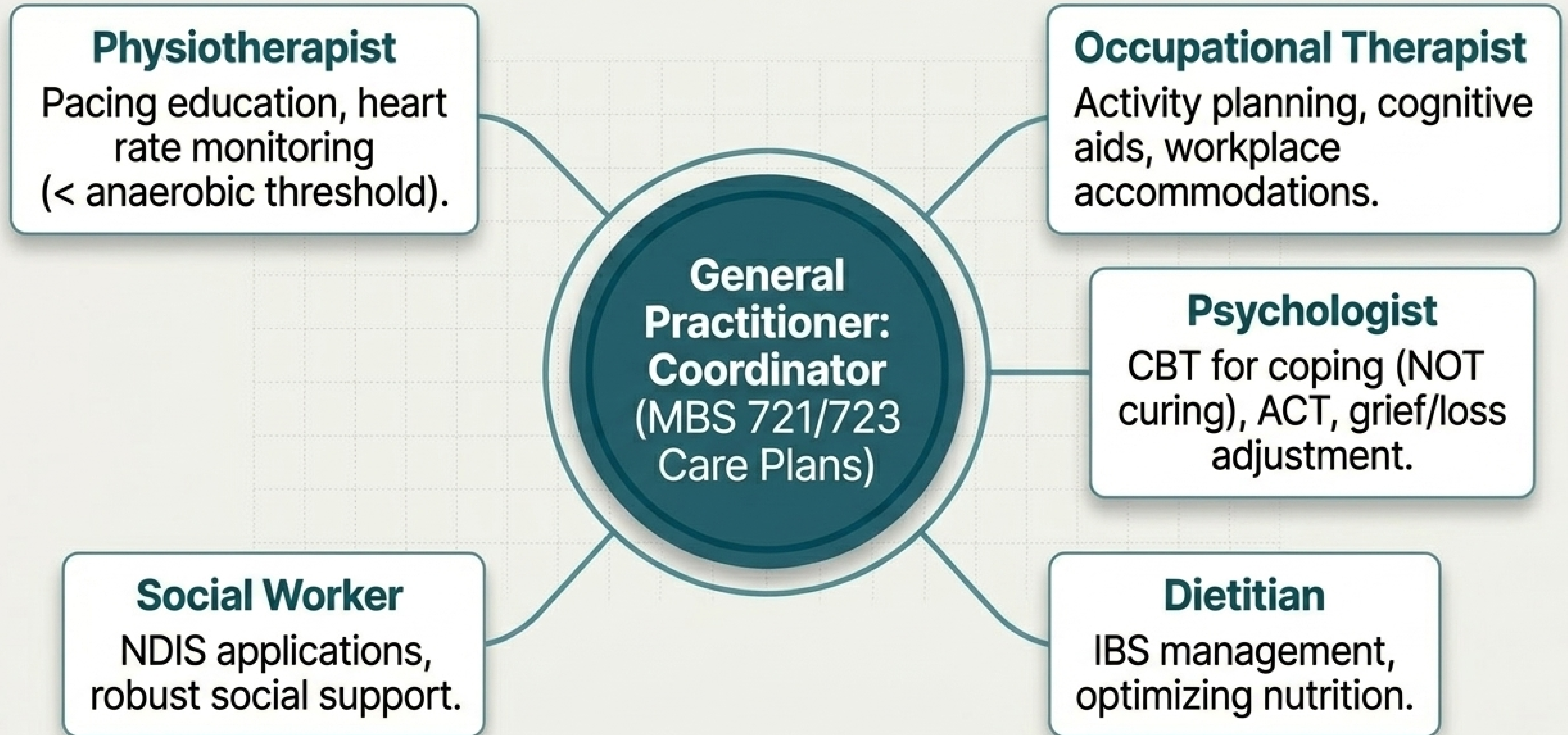
**Autonomic / Heart**

**Fludrocortisone:** 50-200µg mane (monitor $K^+$).

**Midodrine:** 2.5-5mg TDS (watch supine hypertension).

**Note:** No drug cures ME/CFS; pharmacotherapy is strictly utilized for targeted symptom management and quality of life improvement.

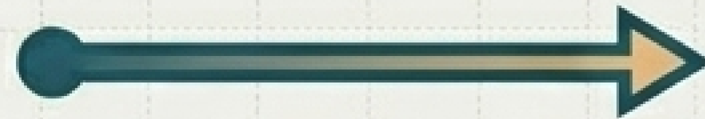
# The Multidisciplinary Care Ecosystem

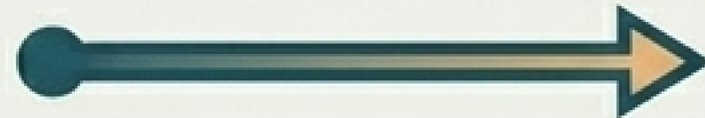


# Equity & Access: Indigenous Health Considerations

## Structural Hurdles

- Diagnostic overshadowing by high comorbidity rates (diabetes, renal).
- Limited remote specialist access.
- Housing and social determinants actively impacting the physical ability to rest and pace.





## Actionable Pathways

- **Telehealth:** Utilize MBS 91790/91800 for remote specialist access.
- **Cultural Safety:** Engage ACCHOs for culturally grounded psychosocial support (e.g., yarning circles).
- **Pharmacotherapy Access:** Apply PBS Closing the Gap (CTG) co-payment measure (max $7.30/script) to directly reduce financial barriers.

# Navigating Special Populations

## Paediatrics

Heavily underdiagnosed. School absence is a key flag. Mandate Individual Learning Plans. NEVER prescribe GET. Melatonin/Amitriptyline strictly off-label.

## Elderly

Exercise extreme diagnostic caution; broadly exclude malignancy and heart failure. Reduce amitriptyline doses (≤10mg) due to severe anticholinergic falls risk.

## Pregnancy

Taper Duloxetine in T3 (neonatal withdrawal). Avoid Amitriptyline in T1. Maintain Fludrocortisone if critically essential for POTS management.

## Renal/Hepatic Impairment

Avoid Duloxetine if eGFR < 30 or if hepatic impairment is present. strictly dose-adjust pregabalin to account for renal clearance.

# The 6-Step Clinical Pathway