PES Endocrine Monthly Round-Up

July 2026

Editor's Perspective

July's selection converges on a single theme: proportionate rather than reflexive intensification of testing and treatment. A joint European consensus statement sets out a stepped-care model for patients receiving incretin-based therapies. The largest longitudinal analysis to date of cortisol trajectories in adrenal incidentaloma finds repeated dexamethasone suppression testing adds little beyond conventional cardiovascular risk assessment. Forty-four years of Danish follow-up offer reassurance on cancer risk in acromegaly while localising concern to the colorectum. The month's Review Article challenges BMD targets in osteoporosis.

Research Highlights

1. Nutritional, Functional, and Psychological Considerations for Incretin-Based Therapies in Adults — an EASO, EFAD, and ECPO Consensus Statement

Guideline Focus: Joint European consensus (EASO, EFAD, ECPO) addressing the nutritional, functional, and psychological consequences of GLP-1 and dual GLP-1/GIP receptor agonist therapy — domains largely unreported in the pivotal efficacy trials. Framed as “considerations” rather than mandatory recommendations; excludes pregnancy and preconception.

Key Messages:

- Proportionate, stepped care is the governing principle. Basic monitoring suffices for most, with escalation reserved for baseline vulnerability, rapid weight loss, poor intake, persistent GI intolerance, or functional decline. Universal specialist referral and routine DXA are explicitly rejected.
- Protein 1.0–1.5 g/kg adjusted bodyweight daily during active weight loss (minimum 60 g), reducing to 0.8–1.0 g/kg in maintenance; lower disease-specific targets in CKD.
- Energy thresholds guide escalation: below 1500 kcal/day signals deficiency risk, below 1200 kcal/day warrants multivitamin–mineral plus additional protein, and sustained intake below 800 kcal/day should prompt down-titration, pause, or discontinuation.
- Two symptom-based red flags: protracted vomiting beyond a week risks thiamine depletion, with Wernicke encephalopathy reported in case reports — consider empirical supplementation. Hair loss should be read as a nutritional sign prompting review of weight-loss rate, protein, iron, and zinc.
- Lean mass accounts for approximately 24–30% of total weight loss, with concern concentrated in older adults, low baseline muscle mass, and frailty. A minimum monitoring set is proposed: bodyweight, waist circumference, handgrip strength or sit-to-stand, and one patient-reported question on new weakness.

Clinical Takeaway: The first European document treating these domains as a coherent clinical field. Its value lies in the stepped-care architecture — a defined minimum monitoring set for all, with explicit escalation triggers. Most specific thresholds are consensus-derived and flagged as such by the authors.

2. Temporal Changes in Cortisol Secretion and Long-Term Outcomes in Benign Adrenal Incidentalomas — an ENSAT Retrospective Cohort Study

Study Design: International retrospective cohort across 25 ENSAT centres in 14 countries. 2525 adults with benign adrenal incidentalomas, two or more 1-mg dexamethasone suppression tests, and at least 36 months of follow-up (median 80 months), classified into five cortisol secretion trajectory groups using the ESE–ENSAT 50 nmol/L threshold.

Key Findings:

- Cortisol suppression status changed in 563 patients (22.3%), most within 3 years of baseline.
- Persistent MACS carried the greatest cardiometabolic burden and was independently associated with worsening hypertension (adjusted HR 1.34, 95% CI 1.03–1.73); restricted mean hypertension-free time at 10 years was 60.4 versus 86.1 months against persistently normal patients.
- Crude associations with mortality and cardiovascular events were substantial (MACS-to-MACS mortality HR 2.47) but lost significance after adjustment. Independent predictors were smoking, chronic kidney disease, prior cardiovascular events, older age, and baseline post-DST cortisol.
- Most patients crossing categories had cortisol values close to 50 nmol/L, attributed to biological and analytical variability rather than true change in autonomy. Repeat testing may still inform borderline cases when adrenalectomy is being considered.

Limitations: Retrospective design, non-standardised testing intervals, and no centralised biochemistry, with cortisol assays changing at seven centres during the study. The 36-month minimum follow-up introduced immortal time bias, and the cohort was 96% White, restricting generalisability.

Clinical Takeaway: The key message is a negative one: cortisol trajectory did not independently predict mortality or cardiovascular events once conventional risk factors were accounted for. Persistently abnormal 1-mg DST identifies a high-risk group, but the actionable response is aggressive cardiovascular risk factor management rather than surveillance biochemistry. This does not overturn the 2023 ESE–ENSAT position against routine repeat testing.

3. Long-Term Cancer Risk in Acromegaly: A Population-Based Cohort Study with 44 Years of Follow-Up

Study Design: Nationwide Danish cohort of 809 biochemically validated acromegaly patients diagnosed 1977–2021, matched by sex and birth year to 80,900 controls. Median follow-up 12.2 years (IQR 5.6–21.7), extending to 44 years.

Key Findings:

- Overall cancer risk was not clearly increased (IRR 1.10, 95% CI 0.93–1.30, p=0.27).
- Colorectal cancer risk was elevated (IRR 1.78, 1.22–2.60), as was thyroid cancer (IRR 3.68, 1.16–11.66), though the wide confidence interval on the latter reflects small numbers. Benign colorectal lesions were more than twice as common (IRR 2.32, 1.96–2.76), predominantly tubular adenomas and hyperplastic polyps.
- Endoscopic colorectal procedures were used nearly three times as often (IRR 2.85, 2.54–3.19), and colorectal cancers were more often localised at diagnosis (IRR 2.00, 1.21–3.30).
- All-cause mortality was modestly elevated (IRR 1.18, 1.02–1.36), but cancer-specific mortality was not (IRR 0.95, 0.72–1.25).

Clinical Takeaway: The longest follow-up available on this question, and largely reassuring: acromegaly does not confer a broad excess cancer risk, and patients do not die of cancer more often than matched controls. The colorectal signal warrants continued vigilance, though the near-tripled colonoscopy rate and excess of localised tumours suggest detection intensity contributes to the observed incidence.

Review Article of the Month

Goal-Directed Osteoporosis Treatment: Are Bone Mineral Density Targets Valid?

Focus: A critical appraisal of the treat-to-BMD-target framework, challenging the 2024 ASBMR working group recommendation that osteoporosis management should incorporate specific on-treatment BMD targets.

Key Insights:

- The ASBMR position rests on two observations: higher on-treatment BMD correlates with lower fracture risk, and meta-regression shows agents producing larger BMD gains also produce greater fracture reduction.
- The first is challenged on the grounds that on-treatment BMD is simply baseline BMD plus treatment-induced change. Where trials have modelled both, the apparent effect largely reflects the prognostic weight of baseline BMD, not the change achieved on therapy.
- The second is argued to depend on including less effective agents. Among the more potent antiresorptives the relationship disappears — denosumab produces larger BMD gains than zoledronate, yet anti-fracture efficacy in trials is comparable.
- The conclusion is that the framework's practical corollary — that many patients need denosumab to reach target — lacks trial support, and that mandated frequent BMD monitoring adds cost without demonstrable benefit.

Clinical Takeaway: A well-argued dissent rather than a new evidence base. It does not tell clinicians to stop measuring BMD, but questions whether chasing a numerical target should drive agent selection or monitoring frequency. Readers should note this is a single-author critique of a working group consensus; the debate remains live.

For Further Reading

EASO–EFAD–ECPO Incretin Consensus Statement: https://doi.org/10.1016/S2213-8587(26)00122-1

ENSAT Cortisol Trajectory Cohort: https://doi.org/10.1016/S2213-8587(26)00098-7

Acromegaly Cancer Risk (Danish Cohort): https://doi.org/10.1093/ejendo/lvag121

BMD Targets in Osteoporosis: https://doi.org/10.1016/S2213-8587(26)00123-3

Closing Note

The through-line this month is the difference between doing more and doing better. Each paper asks whether an additional test, a tighter target, or a more intensive pathway actually changes what happens to the patient. The answers are consistent: escalation should be triggered by identifiable clinical vulnerability rather than applied uniformly, and the modifiable determinants of long-term outcome remain the familiar ones.

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