



Long-term Management of **Cushing's Disease**

THE IMPACT OF ELEVATED CORTISOL LEVELS

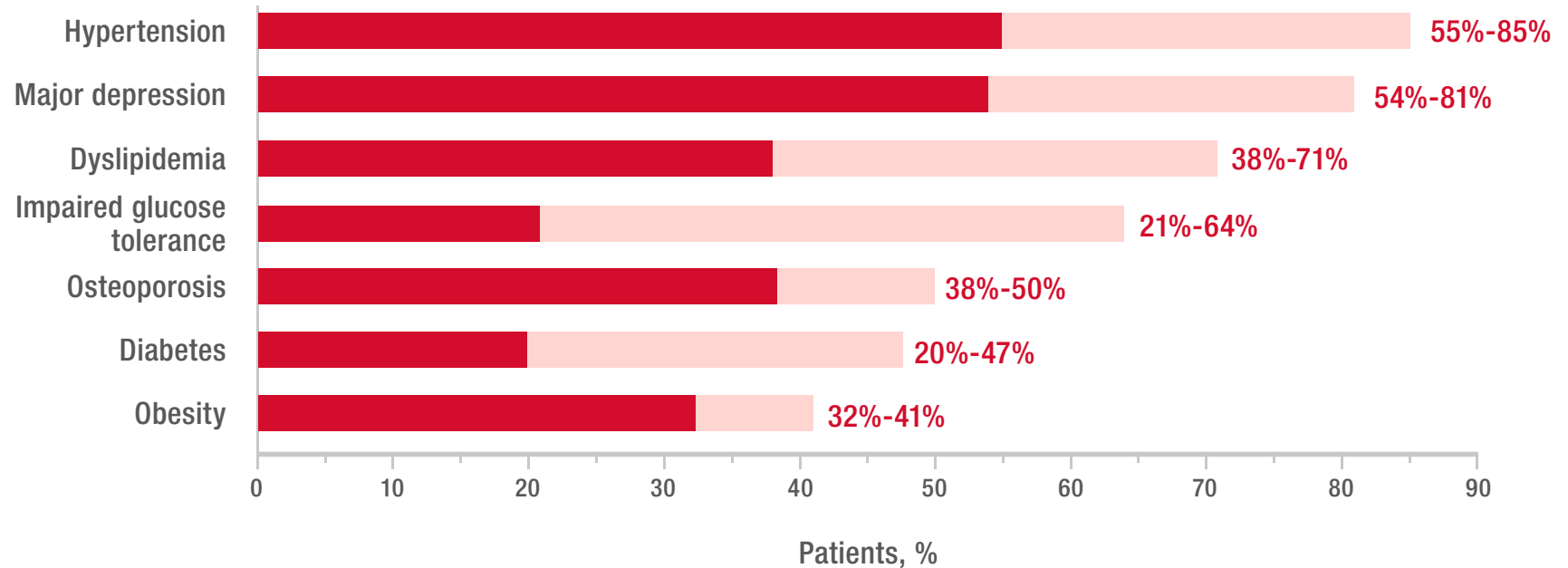


Increased mortality—up to 4 times that of the general population^{1,2}

- Patients with Cushing's disease experience a significant burden due to comorbidities, increased mortality, and impaired health-related quality of life as a result of extended exposure to elevated cortisol levels²



Comorbidities in Cushing's disease²



Treatment options for Cushing's disease³

- Transsphenoidal surgery (TSS) is a first-line option
- There are several available second-line options including repeat TSS, radiotherapy, and medical therapy



After pituitary surgery, persistence or recurrence of hypercortisolism can occur in 40%-50% of cases¹

- Patient recurrence rates after initial successful TSS were up to 25% after 5 years and up to 46% for patients followed for longer than 5 years^{4,5}
- Even after multiple therapies, many patients continue to have active disease, highlighting the need for more effective therapeutic options⁶
 - In a clinical study, despite additional therapies beyond initial TSS, biochemical control was only achieved in about 50% of patients after a median of 2 years of follow-up⁶



Long-term monitoring is crucial

- Biochemical recurrence of Cushing's disease can occur before clinical signs and symptoms appear⁷
- Testing is important in determining both disease remission and recurrence⁸



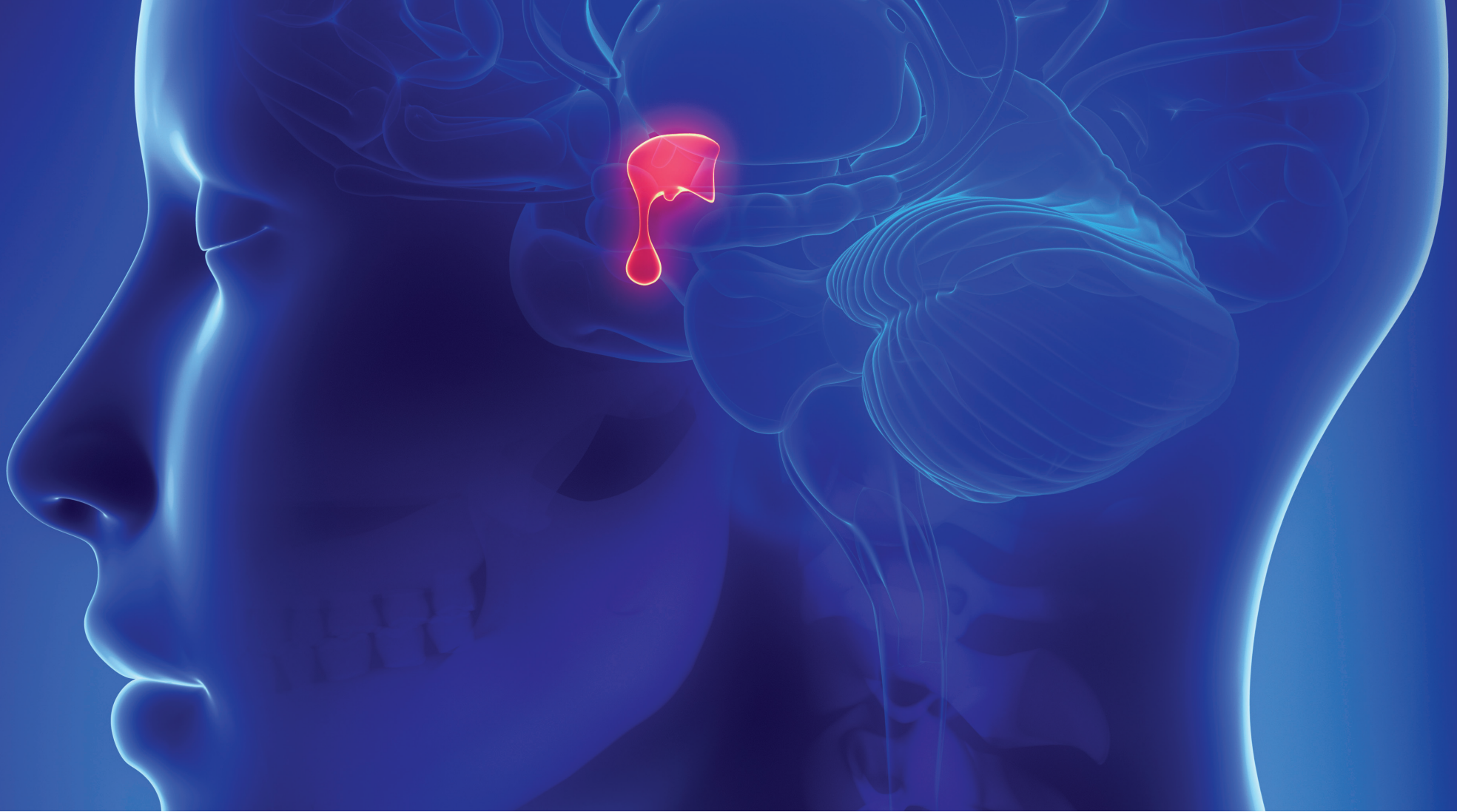
The Endocrine Society Clinical Practice Guidelines recommend³:

- Measuring late-night salivary cortisol (LNSC) or 24-hour urinary free cortisol (UFC) in patients with normalized cortisol levels after TSS
- Using tests to screen for hypercortisolism to assess for recurrence in patients with adrenocorticotrophic hormone (ACTH)-dependent Cushing's syndrome



LNSC measurement is a simple and effective tool to detect recurrence⁸

- LNSC may accurately establish remission after TSS and identify recurrence more accurately than 24-hour UFC during long-term follow-up
- LNSC can be simply collected by patients
 - 24-hour UFC can be inconvenient for patients to perform



References: **1.** Pivonello R, De Martino MC, De Leo M, et al. Cushing's syndrome: aftermath of the cure. *Arq Bras Endocrinol Metabol.* 2007;51(8):1381-1391. **2.** Feelders RA, Pulgar SJ, Kempel A, Pereira AM. The burden of Cushing's disease: clinical and health-related quality of life aspects. *Eur J Endocrinol.* 2012;167(3):311-326. **3.** Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2015;100(8):2807-2831. **4.** Patil CG, Prevedello DM, Lad SP, et al. Late recurrences of Cushing's disease after initial successful transsphenoidal surgery. *J Clin Endocrinol Metab.* 2008;93(2):358-362. **5.** Pivonello R, De Leo M, Cozzolino A, Colao A. The treatment of Cushing's disease. *Endocr Rev.* 2015;36(4):385-486. **6.** Geer EB, Shafiq I, Gordon MB, et al. Biochemical control during long-term follow-up of 230 adult patients with Cushing disease: a multicenter retrospective study. *Endocr Pract.* 2017;23(8):962-970. **7.** Ayala A, Manzano AJ. Detection of recurrent Cushing's disease: proposal for standardized patient monitoring following transsphenoidal surgery. *J Neurooncol.* 2014;119(2):235-242. **8.** Amlashi FG, Swearingen B, Faje AT, et al. Accuracy of late-night salivary cortisol in evaluating postoperative remission and recurrence in Cushing's disease. *J Clin Endocrinol Metab.* 2015;100(10):3770-3777.