emotional lability, termed *pseudobulbar affect*, related to neurologic degeneration of bulbar UMNs.

Amyotrophic lateral sclerosis is diagnosed based on clinical criteria. The key features are muscle weakness with mixed UMN and LMN characteristics that progressively involve other body regions and for which no alternative explanation exists. Laboratory tests, magnetic resonance imaging, electrodiagnostic testing, and other assessments are obtained based on specific symptoms, signs, and risk factors. No currently available biomarker is diagnostic of ALS.

Fifteen percent of patients with ALS have a family history of ALS (ie, fALS), and 85% of patients have sALS. Seventy percent of people with fALS have a single pathogenic genetic variant causing ALS, nearly all of which are autosomal dominant. The Genetic Testing and Counseling Guidelines Expert Panel recommends genetic counseling and gene panel testing for all patients with a diagnosis of ALS. The multiple genetic variants associated with ALS suggest that multiple molecular pathways are involved in the pathophysiology of ALS.

Patients with ALS typically die from hypercapnic respiratory failure due to progressive muscle weakness of the diaphragm and other respiratory muscles. Approximately 10% of patients survive for more than 10 years, and the reasons for this longer survival are unknown. Bulbar symptoms, respiratory compromise, and dementia are associated with poorer survival. Tracheostomy and mechanical ventilation improve survival by supporting respiratory function and prolonging life but do not slow progression or reverse motor deficits associated with ALS.

The correct answer is 3.

Reference: Ravits J, Ferrey D, Gundogdu B, Qayoumi W, Zale C. Amyotrophic Lateral Sclerosis: A Review. *JAMA*. 2026 Jun 9;335(22):1970-1982.
Link: https://jamanetwork.com/journals/jama/fullarticle/2848974
PMID: 42113599

Q21 ARBs vs ACEIs

In individuals with primary hypertension there is no difference between ARBs and ACEIs in all-cause mortality.

- ❍ True
- ❍ False

Educational Point: Inhibitors of the renin-angiotensin-aldosterone system (RAAS) are fundamental therapies in the management of primary hypertension across multiple guidelines. Among these, angiotensin-converting enzyme inhibitors (ACEIs) have traditionally been preferred as first-line agents owing to their well-established efficacy, long history of use, and low cost. In contrast, angiotensin II receptor blockers (ARBs) are often positioned as alternatives, typically reserved for patients who are intolerant to ACEIs. In 2022, approximately 11.3% of Canadians were prescribed an ACEI, compared with only 7.7% prescribed an ARB. This clinical review summarizes the best available evidence comparing ARBs and ACEIs in adults with primary hypertension, with a focus on cardiovascular and renal outcomes. Safety, tolerability, and cost considerations are also discussed to promote evidence-based prescribing decisions.

The MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases were searched for comparative, head-to-head randomized controlled trials (RCTs) and systematic reviews (SRs) evaluating ACEIs versus (vs) ARBs in adults with primary hypertension and common comorbidities.

A 2014 Cochrane review evaluated 9 RCTs directly comparing ARBs and ACEIs in individuals with primary hypertension. The SR showed no difference between ARBs and ACEIs in all-cause mortality (5 RCTs, 10,248 participants; 11.1% vs 11.6%; risk ratio [RR]=0.98; 95% confidence interval [CI] 0.88 to 1.10), cardiovascular mortality (4 RCTs, 9747 participants; 6.9% vs 7.1%; RR=0.98; 95% CI 0.85 to 1.13), and cardiovascular events (3 RCTs, 5499 participants; 19.1% vs 17.9%; RR=1.07; 95% CI 0.96 to 1.19).

A more inclusive SR, primarily of RCTs with at least 12 weeks of follow-up, found no difference in long-term BP control (70 RCTs, 7 non-RCTs; 26,170 participants) or monotherapy success (26 RCTs, 3 non-RCTs; 16,609 participants). Low-quality evidence also suggested similar efficacy for all-cause mortality and cardiovascular events.

In a post hoc analysis of the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET), the largest study included in the Cochrane review, no difference was observed between telmisartan and ramipril among patients with hypertension for the primary renal outcome of dialysis,