0.93–1.1), or risk of type 2 diabetes (2 trials, n=24,407; RR 1.2; 95% CI, 1.0–1.4). All but 1 of the trials had some form of pharmaceutical industry sponsorship.1

A meta-analysis examined 22 RCTs of statin versus placebo (N=134,537, minimum follow-up 4.0 years) for primary and secondary prevention of CVD among patients in 5 CVD risk categories, based on 5-year major vascular event (MVE) risk calculations.2 The stratification by MVE risk calculation (with MVE defined as first nonfatal MI, coronary death, stroke, or coronary revascularization procedure) was established by the researchers.

In 23,798 patients with a 5-year predicted risk of <5% without a known history of vascular disease, a statistically significant reduction in annual risk of major vascular events was noted for every 1.0 mmol/L reduction in low-density lipoprotein (LDL) (22 trials; RR 0.61; 95% CI, 0.45–0.81). For 24,674 patients with 5-year predicted risk of ≥5% to <10% without a known history of vascular disease, there was also a similar statistically significant reduction in annual MVEs per 1.0 mmol/L reduction in LDL (22 trials; RR 0.66; 95% CI, 0.57–0.77) as well as all-cause mortality (RR 0.83; 95% CI, 0.69–0.99). All risk groups of patients without a history of vascular disease had a significant reduction in major coronary events (22 trials, n=69,959, RR 0.71; 95% CI, 0.65–0.77) and all-cause mortality (RR 0.91; 0.85–0.97).2

The American College of Cardiology and the American Heart Association (ACC/AHA) 2013 evidence-based guidelines3 recommend use of the new Pooled Cohort Equations calculator to estimate 10-year CVD risk in adults, and identified 4 groups most likely to benefit from statins to reduce CVD events in both primary and secondary prevention:

- Patients with clinical atherosclerotic CVD (Grade A, strong recommendation with high certainty based on the evidence that the benefits are substantial)
- Patients with primary elevations of LDL cholesterol of ≥190 mg/dL (Grade B, with moderate certainty based on evidence that the net benefit is moderate to substantial)
- Adults with diabetes aged 40 through 75 years with LDL levels between 70 and 189 mg/dL (Grade A)
- Adults aged 40 through 75 who have LDL levels 70 to 189 mg/dL and estimated 10-year CVD risk of ≥7.5% (Grade A)

The guidelines state that moderate-intensity statin therapy can be considered in individuals with a 5% to 7.5% 10-year atherosclerotic CVD risk (Grade C, with at least moderate certainty based on evidence that there is a small net benefit).3

Makristy Caratao, MD
John Van Buskirk, DO
Tacoma FMR
Tacoma, WA


Does nasal saline irrigation decrease the symptoms of seasonal allergic rhinitis when used as adjunctive therapy?

Evidence-Based Answer
It appears likely, although the magnitude of any additional effect is unclear. Saline nasal irrigation decreases symptoms of allergic rhinitis, but does not improve quality of life in children and adults compared with a heterogeneous collection of control treatments (SOR: B, extrapolated from a meta-analysis with some nonactive comparators). In children, saline nasal irrigation as adjunctive therapy to nasal steroids decreases symptoms more than either therapy individually (SOR: B, single RCT).

A 2012 meta-analysis of 10 RCTs and prospective cohort studies (N=406) assessed the efficacy of 1.5 to 500 mL nasal saline irrigation used every 4 to 12 hours in 275 adults, 86 children, and 45 pregnant women with allergic rhinitis.1 Control groups consisted of patients using no intervention, oil drops, nasal steroid spray, or cetirizine. The primary outcome was improvement of allergy symptoms, using various severity scales ranging from 0 to 5 points per symptom. Scores were translated to percentages of improvement after nasal irrigation. A secondary outcome was quality of life, using the validated Rhinitis Quality of Life Questionnaire (28 questions, 0–6 scale) and validated Rhinasthma Questionnaire (30 questions, 0–5 scale).

Over 1 to 12 weeks, saline irrigation improved nasal symptom scores by 30.1% (95% CI, 15.7–44.4) compared with control, while quality-of-life scores did not change significantly.1
A 2014 open-label RCT compared the efficacy of using intranasal corticosteroid spray and saline spray together and separately for allergic rhinitis in children treated by a referral clinic (N=61). The study enrolled children (age range 2–15 years) with moderate to severe allergic rhinitis and a positive skin prick test for common allergens. Patients were excluded if they had marked septum deviation, prior nasal surgery, nasal polyposis, or active infection. Intranasal fluticasone was started at 200 mcg/d and decreased by half every 4 weeks to 50 mcg/d. For nasal saline irrigation, 4–6 sprays of nasal saline spray were applied twice daily using a positive pressure applicator. Patients visited the clinic at 4, 8, and 12 weeks and were assessed for nasal symptoms, based on a 12-point scale ranging from 0 to 3 for itching, rhinorrhea, nasal congestion, and sneezing. The average initial symptom score ranged from 7 to 7.2 (numerical values estimated from graphs). After 12 weeks, the average symptom score was 6.6 for the irrigation group (7% decrease in symptoms, no \( P \) value reported), 4.2 for the steroid group (41% decrease in symptoms, no \( P \) value reported), and 3.3 for the steroid and irrigation group (64% decrease in symptoms, \( P < .05 \)).

Liya Milgram, DO
Margaret Wiedmann, MD
Advocate Illinois Masonic FMR
Chicago, IL

Do macrolides have long-term clinical benefits in patients with severe asthma?

**Evidence-Based Answer**

Macrolide antibiotics given for at least 6 weeks improve asthma symptom scores, quality of life (QOL), peak expiratory flow, and airway hyperreactivity (SOR: A, meta-analysis of RCTs). In patients with severe asthma, macrolide therapy does not decrease the number of asthma exacerbations (SOR: B, single RCT).

A 2013 meta-analysis of 12 RCTs (N=831) examined the effectiveness of a prolonged course of macrolide antibiotics (clarithromycin, erythromycin, roxithromycin, or troleandomycin) versus placebo or standard treatment for the long-term management of asthma. Ten studies included adults and 2 included children. Five studies included patients with mild to moderate asthma, 3 studies included patients with severe asthma, and 4 did not specify.

Azithromycin and clarithromycin were the most common antibiotics, and duration of treatment varied from 6 to 26 weeks (mean 8 weeks). Outcomes evaluated included forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF), airway hyperactivity (measured by dose or concentration of methacholine needed to reduce the FEV1 by 20%), symptom scores, and QOL measures. Details of symptom scores were not given and QOL was measured using the asthma QOL questionnaire, which included asthma symptoms and activity restrictions, with 0.5 indicating a clinically meaningful change.

Macrolides improved final asthma symptom scores (5 trials, n=199; weighted mean difference [WMD] –0.56; 95% CI, –0.73 to –0.39) and QOL (5 trials, n=346; WMD 0.18; 95% CI, 0.001–0.37). Macrolides also improved PEF (4 trials, n=419; WMD 6.70 L/min; 95% CI, 1.35–12.06), but on subgroup analysis PEF was improved in adults only and not children. Macrolides decreased airway hyperactivity (2 trials, n=131; standardized mean difference [SMD] 1.99; 95% CI, 0.46–3.52), although there was significant heterogeneity between the studies. (A SMD of 0.2 is considered small, 0.6 moderate, and 1.2 large.) No improvement was noted in FEV1 (8 trials, n=381; SMD 0.05; 95% CI, –0.14 to 0.25).

Patients on macrolides had more nausea (3 trials, n=403; RR 2.47; 95% CI, 1.22–5.0). Study quality on the 0 to 5 Jadad scale ranged from 3 to 5 (5 being the highest quality score).

A 2013 RCT examined the effect of azithromycin 250 mg 3 times weekly versus placebo over 26 weeks in 109 adult patients, 18 to 75 years old, with severe asthma. Severe asthma was defined as patients on inhaled steroids and long-acting beta-agonists for at least 6 months, and 2 exacerbations requiring corticosteroids in the past 12 months. Current smokers and ex-smokers with a >10 pack-year smoking history were excluded. The primary outcome was the rate of exacerbations over the duration of macrolide therapy. The rate of exacerbations over 6 months in the azithromycin group was 0.75 compared with 0.81 in the placebo group (\( P = .682 \)). The strict exclusion criteria of smokers and any noncompliance with inhaled steroid