recommends that cerclage should be considered if cervical length is <25 mm before 24 weeks of gestation with a woman who had a prior preterm delivery before 34 weeks of gestation (Level 1, based on randomized controlled trials).

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.


A 2007 systematic review of 13 RCTs with 1,557 COPD patients also analyzed the clinical benefit of antibiotics for COPD exacerbations. Five trials with 593 patients showed no statistically significant effect on treatment failure rate in mild to moderate exacerbations, defined as 1 or 2 of the Winnipeg symptoms of dyspnea, increased sputum volume, and sputum purulence (OR 1.1; 95% CI, 0.75–1.6). Antibiotic use was associated with a lower likelihood of treatment failure in severe exacerbations (defined as all 3 Winnipeg criteria) compared with placebo (4 trials, N=472; OR 0.25; 95% CI, 0.16–0.3; NNT=4). Antibiotics also reduced mortality in patients hospitalized with severe exacerbations compared with placebo (4 trials, NNT=401; OR 0.20; 95% CI, 0.06–0.62; NNT=14).

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What are the most effective nonpharmacologic treatments for urinary incontinence in women?

A 2009 Cochrane review of 11 RCTs with 917 patients examined the benefit of antibiotic use during a COPD exacerbation. The COPD exacerbations were characterized by increased cough, sputum volume, purulence, or any combination of these symptoms. Mortality risk was significantly lower with antibiotic use than with placebo in hospitalized patients (4 trials, N=356; RR 0.23; 95% CI, 0.10–0.52; NNT=8). The risk of treatment failure was also significantly decreased with antibiotics in hospitalized patients (4 trials, N=321; RR 0.47; 95% CI, 0.36–0.62; NNT=3). Compared with placebo, antibiotics also resulted in successful resolution of sputum purulence (3 trials, N=456; RR 0.56; 95% CI, 0.41–0.77; NNT=8). Antibiotic choice did not affect outcomes. The risk of diarrhea was increased in patients with antibiotics compared with placebo (2 trials, N=363; RR 2.9; 95% CI, 1.1–7.8; NNH=20).

A Cochrane review of 14 RCTs (N=672) evaluated the effectiveness of PFMT in women with stress, urge, or mixed UI. The type of UI in 3 studies was based on signs and symptoms, and 11 trials reported a urodynamic diagnosis. Most studies performed multiple PFMT (30–200 contractions/relaxation in sets of 10) ranging from 8 weeks to 6 months in duration (most used 12 weeks).

PFMT in nonpooled data increased perception of cure or improvement in stress UI compared with sham or no treatment (1 trial, N=55; risk ratio [RR] 14; 95%...
PFMT in nonpooled data significantly decreased daily leakage episodes in stress UI compared with the control group, with a mean difference ranging from −0.8 to −2.9 episodes/day in 4 trials with less than 100 patients each. PFMT decreased daily leakage episodes in all types of UI combined (1 trial, N=125; MD −0.77; 95% CI, −1.2 to −0.32).¹

PFMT in nonpooled data resulted in lower volume of leaked urine compared with sham or no treatment in stress UI (1 trial, N=61; MD −30 g; 95% CI, −48 to −12; and in a second trial, N=50; MD −12 g; 95% CI, −22 to −3.0). There was no difference with PFMT regarding volume of leaked urine compared with sham or no treatment in all types of UI, although the confidence interval was wide (1 trial, N=29; MD −5.1 mL; 95% CI, −11 to 1.1).¹

A Cochrane review of 21 RCTs of 1,490 women with stress, urge, or mixed UI involved comparison of 11 different PFMT interventions.² The average age of participants was 50 and most had only stress UI. Ten of the trials excluded elderly participants. The authors found confounding factors and/or poor study design in many of the trials and concluded that evidence was insufficient to recommend 1 type of PFMT over another. The data were both pooled and not pooled (due to heterogeneity of the study design and chosen outcomes). This review was limited by blinding issues, selection bias, and lack of intention-to-treat analysis.

Another Cochrane review examined the efficacy of mechanical devices, such as pessaries, to treat incontinence in 7 randomized parallel and crossover studies that included 732 women.² Two small trials (N=6 and 18) compared mechanical devices with no treatment during exercise and found pessaries were better than no treatment (MD of pad weight −6.6 g; 95% CI, −11 to −1.9); but no difference with a tampon versus no treatment (MD of pad weight −14 g; 95% CI, −38 to 9.8). Four trials compared different devices against each other and found no evidence of superiority of 1 device over another. One trial compared mechanical devices with behavioral interventions and found no lasting difference between the groups. The authors concluded that the evidence is insufficient to recommend mechanical devices for the treatment of incontinence in women.

Evidence-Based Answer

Does long-term use of metformin cause vitamin B₁₂ deficiency?

Evidence-Based Answer

Probably. Long-term treatment with metformin is associated with an increased risk of vitamin B₁₂ deficiency (SOR: C, RCT and cohort studies using disease-oriented outcomes).

A RCT in 390 patients with type 2 diabetes examined the effects of long-term metformin on vitamin B₁₂ levels.¹ Compared with placebo, metformin 850 mg TID for a mean period of 4.3 years was associated with a mean decrease in vitamin B₁₂ concentration of 19% (95% CI, 0.24–0.14; P<.001) and a nonsignificant increase in homocysteine concentration of 5% (95% CI, −0.01 to 0.11; P=.091). The absolute risk of vitamin B₁₂ deficiency (<150 pmol/L) at the end of the study was 9.9% in the metformin group compared with 2.7% in the placebo group (mean difference [MD] 7.7%; 95% CI, 0.023–0.12; P=.004; NNH=14 over 4.3 years). The absolute risk of low vitamin B₁₂ concentration (150–220 pmol/L) was higher in in the metformin group (18%) compared with the placebo group (7%) (MD 11%; 95% CI, 0.046–0.18; P=.001; NNH=9 over 4.3 years).

In a nested case-control study 155 patients with diabetes taking metformin and with vitamin B₁₂ deficiency were compared with 310 matched controls, selected from the cohort who did not have vitamin B₁₂ deficiency while taking metformin.² After adjusting for confounders, each 1-g/d increment in metformin dose increased the risk of developing a vitamin B₁₂ level less than 150 pmol/L (OR 2.9; 95% CI, 2.2–3.9) compared with matched controls. Using metformin for more than