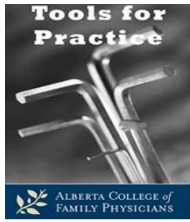


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## **Taking a hard look at the evidence: Phosphodiesterase-5-inhibitors in erectile dysfunction**

**Clinical Question: What is the efficacy and safety of phosphodiesterase-5-inhibitors (PDE5 inhibitors) for erectile dysfunction?**



**Bottom Line: PDE5 inhibitors increase the proportion of successful sexual intercourse attempts to ~65% versus ~30% for placebo. For every 3 men given a PDE5 inhibitor compared to placebo, an additional 1 will have "improved erections".**

### **Evidence:**

- All results statistically significant unless indicated.
  - Systematic review, 130 randomized controlled trials (RCTs) of most PDE5 inhibitors (sildenafil, vardenafil, tadalafil, mirodenafil, udenafil), over 30,000 patients with erectile dysfunction of any cause.<sup>1,2</sup> After ~12 weeks:
    - Proportion of successful sexual intercourse attempts (erection sufficiently hard and long lasting for satisfactory intercourse):
      - ~65% versus ~30% (placebo).
    - Proportion of patients with self-reported "improved erections" using PDE5 inhibitors:
      - ~78% versus 31% (placebo), Number Needed to Treat (NNT)=3.
  - Systematic review, 118 RCTs, n=31,195, all PDE5 inhibitors:<sup>3</sup>
    - Proportion of patients with "improved erections": ~79% versus ~29% (placebo); NNT=2.
  - Systematic review, 8 RCTs, n=1759, men with diabetes:<sup>4</sup>
    - Proportion of patients with "improved erections": ~58% for PDE5 inhibitors versus ~15% placebo; NNT=3.
  - Adverse effects:
    - Any adverse event:<sup>1</sup> ~44% versus ~24% (placebo), mainly headache, flushing, dyspepsia.
    - Withdrawal due to adverse effects: Sildenafil<sup>5</sup>, vardenafil<sup>2</sup> not different from placebo, tadalafil 1.6-3.2% versus 1.3% placebo<sup>5</sup>, number needed to harm=52-333.

- Limitations:
  - Majority of RCTs unclear randomization concealment/blinding methods.<sup>1,6,7</sup>
  - Many RCTs industry supported.<sup>1,2</sup>
  - Other systematic reviews inadequately reported symptom scores or used scales with limited clinical meaning.<sup>5,6,8,9</sup>

**Context:**

- Prevalence of erectile dysfunction is ~30-50% in men aged 40–70; increases with age and comorbidities.<sup>1,5</sup>
- Contraindicated with concurrent nitrate use.<sup>2</sup>
- All PDE5 inhibitors: \$50-\$65 for 4 tabs (or \$13-\$16/tablet independent of dose) and not generally covered by public drug plans.<sup>10</sup>
  - Cost may be reduced by pill splitting.
- On-demand versus daily dosing of tadalafil: no clinically meaningful difference in change of erectile function and no difference in adverse event discontinuation rates.<sup>6,7</sup>

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