Effectiveness and safety of corneal crosslinking for progressive keratoconus

Background
Keratoconus is a non-inflammatory disease manifested by a breakdown of corneal collagen leading to corneal thinning and causing development of a cone-like corneal architecture. The corneal bulging leads often to regular and irregular astigmatism and deterioration of visual acuity. The etiology and pathogenesis of keratoconus remains partly unknown.

Aim
The aim of this systematic review was to study the effectiveness, safety and costs of corneal collagen cross-linking (CXL) using the Dresden method compared to no treatment in patients aged under 35 years with progressive keratoconus.

Methods
A literature search was performed in January 2013 without time limit from Medline-, Cochrane central-, Cochrane Database of Systematic Reviews-, Psychinfo- and CRD- (DARE, HTA and NHS EED) databases. Inclusion criteria were controlled clinical trials and prospective follow-up studies including at least 20 patients and with a follow-up of at least 12 months. For the effectiveness assessment, 125 titles were identified and for the safety evaluation the Canadian health technology assessment report was included.

Effectiveness
Three case series were identified including altogether 118 patients and 151 eyes of which 129 eyes were diagnosed with keratoconus and 22 with post-LASIK ectasia. Based on these studies it was not possible to conclude whether keratoconus progression was halted since only average corneal steepness was given. Best corrected visual acuity (BCVA) improved in the treated eyes in all three studies on average by one LogMAR line. Astigmatism decreased in one study, but not in the others.

Safety
Infections and noninfectious keratitis with signs of corneal melting were the most common complications following CXL and may lead to permanent deterioration of visual performance necessitating keratoplasty. The overall prevalence of complications cannot be estimated because of poor scientific data.

Conclusions
Males were outstandingly over-represented in the studies. The assessment of the one-year effectiveness of CXL is based only on case series. CXL may be an effective treatment to halt progression of keratoconus. Research evidence of CXL safety and long-term effectiveness is uncertain because effectiveness analysis is based only on small case series. Risk of bias for the research evidence is high. Small case series may lead to overestimating the effect of the intervention and to underestimating harms, especially of rare complications. Studies are often financed by device or drug companies. There is a need for well-conducted large trials recruiting patients with progressive keratoconus with several years of follow-up.