

# Prevalence, Burden, and Pharmacoeconomics of Dry Eye Disease

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## Prevalence of DED

Dry eye disease (DED) prevalences ranging from <0.1% to as high as 33% have been reported (see [Table](#)).<sup>1-9</sup> This wide variation among studies is, at least in part, the result of different DED definitions and study populations.<sup>10</sup> For example, because many people with DED symptoms may self-treat rather than seek care, estimated prevalence may depend on whether the data came from general population surveys or physician assessments. Among patients diagnosed by physicians, estimated prevalence may vary depending on the diagnostic criteria used and the clinicians' subjective assessments.<sup>8</sup>

The highest reported prevalence of 33% came from a population-based study using a self-diagnosis questionnaire. Of the subjects with self-reported DED, only 11% had sought medical care for their symptoms.<sup>4</sup>

The lowest reported prevalence of <0.1% was derived from interviews with a sample of consultant ophthalmologists (ie, ophthalmologists with a special interest in DED). Therefore, this estimate excludes patients seen by general ophthalmologists and primary care physicians, as well as those not seeking medical care.<sup>8</sup>

Claims data from a large US managed care database (reflecting only individuals who seek medical care and are diagnosed with DED) suggest that the prevalence of clinically diagnosed DED is 0.4% to 0.5% overall, and is highest among women and the elderly.<sup>6</sup>

A similar estimate was obtained from the Dry Eye Management Outcomes Simulation (DEMOS). In this study, data from multiple sources were used in a Markov model to estimate medical costs and outcomes of DED. The DED prevalence in a typical managed care population was estimated at approximately 1%. Of these cases, about 60% are mild in severity, 30% moderate, and 10% severe. Of individuals with mild DED, only about 20% seek medical care, compared with 50% of those with moderate disease and 100% of those with severe disease.<sup>11</sup> This suggests that approximately 0.37% of individuals in a typical managed care population seek medical care for and are diagnosed with DED.

The largest cross-sectional survey studies, the Women's Health Study (WHS) and the Physicians' Health Study (PHS), included only older age groups, and defined DED as either a clinical diagnosis or self-reported severe symptoms. The age-adjusted prevalences among women and men age >50 years in the United States were

## Abstract

Data from a large US managed care database suggest that the prevalence of clinically diagnosed dry eye disease (DED) is 0.4% to 0.5% overall, and is highest among women and the elderly. The burden of DED to the patient can be substantial, impacting visual function, daily activities, social and physical functioning, workplace productivity, and quality of life (QOL). Preliminary analysis suggests that DED also has a considerable economic impact in terms of both direct and indirect costs. A number of therapies have been shown to improve DED signs and symptoms, but few clinical trials have addressed QOL and economic issues. Limited data suggest that topical cyclosporine has the potential to reduce physician visits and use of other medications, including artificial tears; however, further research is needed to clarify its impact on both the direct and indirect costs of DED.

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For author information and disclosures, see end of text.

■ **Table.** Prevalence of Dry Eye Disease (DED)

Reference	Country	Population or Data Source	Criteria	Prevalence (%)
Bjerrum, 1997 <sup>1</sup>	Denmark (Copenhagen)	504 subjects, ages 30-60 years, randomly selected from population-based Copenhagen City Heart Study	Preliminary European criteria	8
			Copenhagen criteria	11
Schein et al, 1997 <sup>2</sup>	United States (Salisbury, MD)	2520 subjects, age ≥65 years, selected from population-based Health Care Financing Administration Medicare database	≥1 symptoms	14.6
			≥1 symptoms + low Schirmer score	2.2
			≥1 symptoms + high rose bengal score	2
			≥1 symptoms + low Schirmer score + high rose bengal score	0.7
McCarty et al, 1998 <sup>3</sup>	Australia (Melbourne)	926 subjects, ages 40-97 years, participating in population-based Melbourne Visual Impairment Project	Schirmer test	16.3
			TBUT	8.6
			Fluorescein staining	1.5
			≥2 signs	7.4
			Any severe symptom not attributed to hay fever	5.5
Shimmura et al, 1999 <sup>4</sup>	Japan	2500 subjects, the majority (86%) ages 20-49 years, randomly chosen from general population	Self-diagnosis questionnaire	33
Moss et al, 2000 <sup>5</sup>	United States (Beaver Dam, WI)	3722 subjects, ages 48-91 years, participating in population-based Beaver Dam Eye Study	Self-reported history	14.4 overall (11.4% of men and 16.7% of women, age-adjusted)
Yazdani et al, 2001 <sup>6</sup>	United States	PharMetrics claims data, covering 10 million individuals in 22 managed care plans	DED diagnosis or punctal occlusion (based on ICD-9-CM or CPT-4 codes)	0.48 (1997) and 0.39 (1998)
Schaumberg et al, 2003 <sup>7</sup>	United States	Cross-sectional survey of 36,995 female health professionals, ages 49-89 years, participating in Women's Health Study	History of clinically diagnosed DED, or severe symptoms constantly or often	7.8 (age-adjusted) for women ages ≥50 years in the United States
Clegg et al, 2006 <sup>8</sup>	France, Germany, Italy, Spain, Sweden, United Kingdom	Interviews with 23 consultant ophthalmologists with special interest in DED	—	<0.1, ranging from 0.02% (Sweden) to 0.07% (Germany)
Miljanovic et al, 2007 <sup>9</sup>	United States	Cross-sectional survey of 25,444 male physicians, age ≥50 years, participating in Physicians' Health Study	History of clinically diagnosed DED, or severe symptoms constantly or often	4.34 (age-adjusted) for men ages ≥50 years in the United States
TBUT indicates tear breakup time; ICD-9-CM, <i>International Classification of Diseases, Ninth Revision, Clinical Modification</i> ; CPT, <i>Current Procedural Terminology</i> .				

7.8% and 4.34%, respectively. This translates to a total of approximately 4.9 million Americans age >50 years with DED.<sup>7,9</sup>

### Burden of DED

The burden of DED to the patient is not trivial. Studies suggest that DED can have a considerable impact on visual function, daily activities, social and physical functioning, workplace productivity, and quality of life (QOL).<sup>10,12</sup>

Three survey studies—2 in which the majority of patients had Sjögren syndrome<sup>13,14</sup> and 1 in which DED etiology was not specified<sup>15</sup>—found that the impact of DED on daily activities (including work) and healthcare utilization is substantial. In these studies (conducted before the US Food and Drug Administration approval of topical cyclosporine in 2002), treatment often did not provide adequate symptom relief or prevent disease progression.

Data from a subset of WHS and PHS participants demonstrated that people with DED are significantly more likely than people without DED to report problems with reading (odds ratio [OR] 3.64, 95% confidence interval [CI] 2.45-5.40), performing professional work (OR 3.49, 95% CI 1.72-7.09), computer use (OR 3.37, 95% CI 2.11-5.38), television watching (OR 2.84, 95% CI 1.05-7.74), daytime driving (OR 2.80, 95% CI 1.58-4.96), and nighttime driving (OR 2.20, 95% CI 1.48-3.28).<sup>16</sup>

Two utility assessment studies found that the impact of severe DED on patients' lives is in the range of that reported in other studies for moderate to severe angina.<sup>17,18</sup> For the most severe DED cases (requiring tarsorrhaphy), the utility was lower (worse) than that reported for disabling hip fracture.<sup>18</sup>

Although economic data are scarce, preliminary analysis suggests that the economic impact of DED is also substantial. Potential cost drivers include direct medical costs (eg, office visits; prescription and over-the-counter medications; specialized eyewear; humidifiers; surgical procedures), direct non-medical costs (eg, patient transportation), indirect costs (eg, lost work time and productivity; changes in type of work), and intangible costs (eg, reduced QOL; lost leisure time; impaired social, emotional, and physical functioning).<sup>19,20</sup>

Case-control data from a large managed care database in 1997-1998 showed DED-specific charges of \$228 per patient over 6 months, of which >70%

was for physician visits.<sup>21</sup> In addition, surveys have shown out-of-pocket costs to the patient of approximately \$25 per month.<sup>13-15</sup>

In a survey of 78 patients with Sjögren syndrome, DED symptoms interfered with work an average of 200 days per year, and caused 5 days of absenteeism per year.<sup>13</sup> Another survey of 70 patients (the majority with non-Sjögren syndrome DED) found that DED symptoms interfered with work an average of 191 days and resulted in 2 days of absenteeism per year.<sup>22</sup> Still other survey data from 74 patients with DED (etiology unspecified) showed that DED symptoms interfered with work 184 days per year, with an estimated productivity loss of >\$5000 per patient per year.<sup>15</sup>

In a study conducted in the United Kingdom in 2001, healthcare utilization and direct healthcare costs for 129 patients with primary Sjögren syndrome were compared with similar data for 91 rheumatoid arthritis (RA) patients and 92 healthy controls. Costs of ophthalmology visits were significantly higher for patients with primary Sjögren syndrome compared with either RA patients or healthy subjects. Costs associated with optician visits also were higher for primary Sjögren syndrome patients compared with either RA patients or healthy controls, but the difference was statistically significant only for the comparison with RA patients.<sup>23</sup>

### Impact of cyclosporine

A number of therapies have been shown to improve the signs and symptoms of DED, as discussed by Lemp in an accompanying article in this supplement.<sup>24</sup> Although it seems likely that these therapies would also improve QOL and productivity and reduce overall healthcare utilization, few clinical studies have included QOL and economic data.

Using Markov modeling with data from multiple sources, it has been estimated that a new, more effective DED treatment could reduce nondrug direct medical costs by as much as 30%, primarily by reducing physician visits and the need for punctal plugs.<sup>11</sup>

Although most DED treatments are palliative rather than disease-modifying, topical cyclosporine addresses the underlying inflammatory process in DED. Limited data suggest that topical cyclosporine has the potential to decrease the economic burden of DED. For example:

- In phase 3 trials, cyclosporine decreased the need for artificial tears.<sup>25</sup> Because DED patients may require artificial tears multiple times per day—and, in severe cases, even multiple times per hour—a reduction in their use can potentially have a substantial impact on QOL and productivity, as well as artificial tear costs.
- In a retrospective medical record review, DED symptoms and corneal staining scores improved after initiation of cyclosporine; this was accompanied by decreased resource utilization, including fewer patient-initiated ophthalmologist visits for DED and fewer prescriptions of concomitant medications.<sup>26</sup>
- A survey study enrolling 14,927 DED patients examined the patients' experiences with cyclosporine in a real-world setting. Patients were asked to complete the survey at baseline, 30 days, and 60 days after initiating cyclosporine. Fifty-three percent of patients completed the first and third surveys (the second survey was optional). Among the 5884 patients (39%) who completed all 3 surveys, cyclosporine significantly reduced symptom severity and activity impairment compared with baseline. These reductions were observed at both the 30- and 60-day follow-ups. Patient-reported artificial tear use was also reduced (no statistical analysis given).<sup>27</sup> The reasons for the high noncompletion rate were not reported.
- A retrospective analysis of a large US managed care database found that, among DED patients using cyclosporine, a majority (73%) used 1 vial per day rather than the labeled 2 vials per day. The reasons for this nonadherence were not determined; however, possible reasons might include either re-use of vials (despite labeling for single use) or efficacy at less than the labeled dosage. Either way, this suggests that the real-world acquisition cost of cyclosporine may be less than that estimated based on the recommended regimen.<sup>28</sup>

Further research is needed to determine the extent to which the acquisition cost of cyclosporine is offset by decreases in other direct medical costs, and to ascertain the impact of cyclosporine on indirect costs of DED.

## Summary

DED prevalences ranging from <0.1% to as high as 33% have been reported. This wide variation is, at least in part, the result of different study populations and DED definitions. Claims data from a large US managed care database suggest that the prevalence

of clinically diagnosed DED is 0.4% to 0.5% overall, and is highest among women and the elderly.

The burden of DED to the patient is not trivial. Studies suggest that DED can have a considerable impact on visual function, daily activities, social and physical functioning, workplace productivity, and QOL. Furthermore, several surveys found that treatment often did not provide adequate symptom relief or prevent disease progression.

Preliminary analysis suggests that the economic impact of DED is also substantial, in terms of both direct medical costs (eg, for medications and physician visits) and indirect costs (eg, lost work time and impaired productivity).

A number of therapies have been shown to improve DED symptoms. Although it seems likely that these therapies would also improve QOL and productivity and reduce overall healthcare utilization, few clinical studies have included QOL and economic data. It has been estimated that a new, more effective DED treatment could reduce nondrug direct medical costs by as much as 30%. Unlike most DED treatments, which are palliative, topical cyclosporine addresses the underlying inflammatory process in DED. Limited data suggest that cyclosporine has the potential to decrease the economic burden of DED by reducing physician visits and use of other medications, including artificial tears. Further research is needed to determine the extent to which the acquisition cost of cyclosporine is offset by decreases in other direct medical costs, and to ascertain the impact of cyclosporine on the indirect costs of DED.

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