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Research Questions and Outcomes Prioritized by Patients With Dry Eye

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Abstract

IMPORTANCE—Dry eye is a common ocular surface condition with significant influence on patient quality of life and societal economic burden. There is an urgent need to prioritize new research for dry eye.

OBJECTIVE—To identify and rank research questions and outcomes important to patients with dry eye.

DESIGN, SETTING, AND PARTICIPANTS—This study was conducted using the following 6 steps:(1) identifying research questions from a previous survey of clinicians who treat patients with dry eye; (2) identifying outcomes from existing research (systematic reviews and their cited clinical trials in the Cochrane Eyes and Vision US Satellite database of eyes and vision reviews,

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and National Eye Institute–funded clinical trials registered on ClinicalTrials.gov) as of June 13, 2017; (3) identifying a sample of patients with dry eye from the email subscribers to the online newsletter *KeratoScoop*; (4) and (5) conducting a 2-round Delphi survey of those patients online in November and December 2017, respectively; and (6) designating and ranking questions and outcomes as important.

MAIN OUTCOMES AND MEASURES—Importance assigned to research questions and outcomes for dry eye. A research question or outcome ranked by at least 75% of patients as 6 or higher on a scale of 0 to 10 was considered important.

RESULTS—Among the 420 patients from 15 countries who completed both rounds of the Delphi survey, most were 60 years of age or older (233 [56%]), female (348 [83%]), white (393 [94%]), and of non-Hispanic ethnicity (398 [95%]). Among the 12 questions that clinicians had previously prioritized, patients rated 8 as important. The top 3 questions pertained to effectiveness of patient education, environmental modifications, and topical anti-inflammatory eye drops for dry eye. Among the 109 outcomes identified in existing research on dry eye, patients rated 26 as important. Ten of these 26 were unpopular in existing research, with fewer than 10% of 158 studies reporting these outcomes. Of the 10 most important outcomes, 9 were associated with symptoms or quality of life. The 3 outcomes rated most important by patients were ocular burning or stinging, ocular discomfort, and ocular pain.

CONCLUSIONS AND RELEVANCE—This study identified research questions and outcomes important to patients with dry eye. A considerable gap was noted between outcomes in existing research on dry eye and outcomes patients consider important. Future research on dry eye should consider addressing the important research questions and outcomes identified herein, taking into account the patient perspective.

Dry eye is a multifactorial ocular surface condition that occurs when tear film homeostasis is disturbed. One of the most frequent ocular conditions (prevalence 5% to 50% globally[1]), dry eye is more common among women and with increasing age.[1] Dry eye negatively impacts quality of life[1–4] and functional capacity, such as reading ability.[5,6] Another major impact is economic: $3.8 billion per year is spent on managing this condition in the United States ($783 per patient).[7] When productivity loss, physician visits, and other costs are considered, societal and per patient expenditures on dry eye approximate $55.4 billion per year and $11 302 per year, respectively.[7]

Current dry eye treatment algorithms are mostly based on expert opinion, rather than on reliable evidence of improvement in specific outcomes.[8–10] This field urgently needs prioritization of new research so that effective treatments are brought to bear on patient care. We previously surveyed clinicians managing dry eye to identify their most important unanswered clinical questions.[11] Most questions pertained to topical and other treatments already being used clinically.[11] Dry eye research prioritization efforts must also incorporate patient perspectives,[12] in part because assessments of both the disease process and treatment outcomes include the use of patient reports. In addition, patient voices must also inform outcome prioritization efforts.[3,12–14] Our objective in the present study was to identify and rank research questions and outcomes important to patients with dry eye.

Methods

We followed the 6-step approach described below (eAppendix 1 in the Supplement). The Johns Hopkins Bloomberg School of Public Health Institutional Review Board (Baltimore, Maryland) approved this study. Written patient informed consent was obtained as part of the survey.

Step 1: Selecting Research Questions for Patient Prioritization

We previously identified 24 research questions (hereinafter referred to as questions) important to clinicians treating patients with dry eye.[11] We selected the 12 questions rated as most important by the clinicians to be prioritized by patients in the present study.

Step 2: Selecting Outcomes for Patient Prioritization

A completely specified outcome has 5 elements: domain, specific measurement, specific metric, method of aggregation, and time points.[15,16] In the present study, we focused on the domain (eg, visual acuity). For instances in which a study used a single instrument (eg, Ocular Surface Disease Index) to aggregate and present multiple domains, we considered the domain representing the aggregated outcome (eg, patient overall assessment of ocular surface symptoms). For instances in which a study separately considered the aggregated outcome and its individual domains (eg, ocular itching), we determined that the study had included both the domain representing the aggregated outcome and the individual domains. In other words, we deconstructed aggregated outcomes only when the study investigators did.

We identified all outcomes in existing research assessing interventions for dry eye reported as of June 13, 2017. We defined *existing research* as systematic reviews (hereinafter called reviews), published clinical trials, and National Eye Institute–funded trials registered on ClinicalTrials.gov (hereinafter called registered trials).

Outcomes in Reviews—We identified reviews assessing intervention effectiveness for dry eye through the Cochrane Eyes and Vision US Satellite database of eyes and vision reviews. This database, which supports our work with the American Academy of Ophthalmology's Preferred Practice Patterns, includes both Cochrane and non-Cochrane reviews. We extracted each outcome named in each review's Methods or Results sections.

Outcomes in Published Trials—We examined each published randomized trial that each review included. For each trial, we examined the journal article cited in the review, and when multiple journal articles were cited, we examined the first article cited. We extracted each outcome named in the Methods or Results section of each trial.

Outcomes in Registered Trials—We identified each outcome examined in National Eye Institute–funded trials registered on ClinicalTrials.gov. To be more inclusive of outcomes for rating by patients, we used a low cutoff to define popularity of an outcome. We defined an outcome as *popular* in existing research if 10% or more of studies (ie, reviews, published trials, and registered trials) examined it; otherwise, the outcome was defined as *unpopular*.

Step 3: Identifying Survey Participants(Patients With Dry Eye)

We surveyed subscribers to *KeratoScoop*, a weekly online newsletter created by one of us (R.P.), who is the sole proprietor and president of the Dry Eye Company LLC, which does not accept any commercial funding. The Dry Eye Company LLC includes the Dry Eye Zone, an online information portal for dry eye.[17] Individuals typically subscribe to *KeratoScoop* after visiting Dry Eye Zone's blog posts, webpages, or Facebook groups. While subscription to *KeratoScoop* is free and open to anyone, most subscribers are patients with dry eye. Given the absence of an established sampling theory for Delphi surveys, we did not conduct a priori sample size or power calculations.

Step 4: Conducting Delphi Round 1

In November 2017, we sent a website link for our survey (designed using Qualtrics survey software) by email to all current subscribers to *KeratoScoop*, an online newsletter generated by one of us (R.P.). We asked subscribers whether they or someone for whom they are a caregiver (eg, family member) were currently experiencing or had previously experienced dry eye, restricting participation in the present study to those who answered affirmatively. We asked caregivers to complete the survey on behalf of the person for whom they were providing care. For simplicity, we refer to all survey respondents hereinafter as patients. We followed the initial email with reminder emails 2 and 3 weeks later. We accepted responses up to 4 weeks after the first invitation.

Round 1 of the survey included 5 groups of items: (1) demonstration of understanding the purpose of the survey; (2) patient characteristics and email address; (3) ratings of importance of the questions prioritized by clinicians (eAppendix 2 in the Supplement); (4) ratings of importance of popular outcomes (eAppendix 3 in the Supplement); and (5) consideration of any of the unpopular outcomes as important. For outcomes, we also asked for preferred periods for measurement after starting treatment in a trial in the event the patient was to participate in a trial testing a new treatment of dry eye. The options included less than 3 months, 3 to 6 months, 7 to 12 months, more than 12 months, all periods, or no opinion (eAppendix 3 in the Supplement).

To facilitate patient comprehension and the provision of informed ratings, we accompanied all technical terms and concepts with lay language clarification. A long-term patient with dry eye (R.P.) helped develop the lay language.

Step 5: Conducting Delphi Round 2

For round 2 of the survey, we compiled the ratings of each outcome using a histogram (with the median) and an anonymized list of any patient comments regarding that outcome from round 1. In round 2, patients re-rated each outcome by taking into account their own response and those of their peers from round 1. Patients also provided ratings and preferred measurement periods for the 10 outcomes that were unpopular in existing research but most often preferred in round 1. In December 2017, one of us (I.J.S.) emailed to all patients who had completed round 1 a website link for round 2, with reminder emails sent 2 and 3 weeks later. We did not compensate patients for their participation.

Step 6: Designating and Ranking Important Research Questions and Outcomes

We analyzed the median, interquartile range (IQR), and range for each question and outcome, classifying as important all questions or outcomes that at least 75% of patients rated 6 or higher on a scale of 0 to 10 and classifying as moderately important all questions or outcomes that at least 75% of patients rated 5 or higher. To rank the questions or outcomes, we sorted them in decreasing order of the median, and when the median was tied, in decreasing order of the 25th percentile.

Results

Steps 1 and 2: Selecting Research Questions for Patient Prioritization and Selecting Outcomes for Patient Prioritization

For step 1, we selected the 12 highest-rated questions by the clinicians[11] for rating by the patients. For step 2, we identified 20 systematic reviews, published between 2009 and 2017, inclusive, that examined 63 unique outcomes (median, 7.0 outcomes per review; IQR, 4.5–10.5). The reviews included 134 published trials (median, 6.5 trials per review; IQR, 3.0–13.5). The 134 trials presented in the included reviews, published between 1984 and 2015, inclusive, examined 96 unique outcomes (median, 6.0 outcomes per trial; IQR, 4.0–19.0).

We identified 4 registered trials, which examined 35 unique outcomes (median, 7.5 outcomes per trial; IQR, 3.8–11.2). Together, the published and registered trials examined1.7 times as many unique outcomes as examined in the reviews (105 vs 63).

Across all 158 studies denoted as existing research for dry eye (ie, 20 reviews, 134 published trials, and 4 trials registered on ClinicalTrials.gov; eAppendix 4 in the Supplement), we identified 109 unique outcomes (eAppendix 5 in the Supplement). We organized the outcomes into the following 6 mutually exclusive categories: 35 symptoms, 28 signs or clinical testing, 29 laboratory measurements, 4 safety outcomes, 7 quality-of-life–related outcomes, and 6 other outcomes (eAppendix 5 in the Supplement). Among the 109 unique outcomes, we categorized 18 as popular and 91 as unpopular in existing research. The 18 popular outcomes included 6 of 35 symptoms, 7 of 28 signs or clinical testing, 2 of 29 laboratory measurements, 2 of 4 safety outcomes, and 1 of 6 other outcomes (eAppendix 6 in the Supplement). No popular outcomes were categorized as associated with quality of life.

Steps 3 to 5: Identifying Survey Participants and Conducting Delphi Rounds 1 and 2

We sent round 1 of the Delphi survey to 13 761 persons who were email subscribers to *KeratoScoop* (Figure 1). The email was opened by 4211 subscribers (31%), of which 741 subscribers (18%) clicked through to the survey website for further information and began round 1. Among those who accessed the website through the email link, 622 patients (84%) and 420 patients (57%) completed rounds 1 and 2, respectively. The 420 persons who completed round 2 resided in 15 countries and included 414 patients (99%) and 6 caregivers (1%).

The self-reported characteristics of patients were similar between those who completed rounds 1 and 2 (Table). Among the 420 patients completing round 2, most were 60 years of

age or older (233 [56%]), female (348 [83%]), white individuals (393 [94%]), non-Hispanic ethnicity (398 [95%]), and currently residing in the United States (358 [85%]) or Canada (32 [8%]). More than two-thirds of the patients (290 [69%]) had been living with dry eye for 6 years or longer. Blepharitis was the most common underlying diagnosis (178 [43%]). In addition, 158 patients (38%) had received no underlying diagnosis (Table).

Step 6: Designating and Ranking Important Research Questions and Outcomes

Rating of Questions—Patients rated 8 of 12 questions as important and 4 of 12 as moderately important (Figure 2). Among the 8 questions rated as important, 4 (50%) addressed topical treatments, 1 (13%) an environmental intervention, 1 (13%) an educational intervention, 1 (13%) a systemic treatment, and 1 (13%) a general treatment. The 3 most important questions pertained to effectiveness of patient education, environmental modifications, and topical anti-inflammatory eye drops.

Ranking of Questions by Underlying Diagnosis—Most rankings did not appear to differ by patient subgroups defined by underlying diagnosis (Figure 2). For example, the question on patient education was top ranked by all subgroups, except by patients with rheumatoid arthritis, who ranked it second. When questions were specific to certain conditions (eg, autologous serum for Sjögren syndrome), they were top ranked by patients with those conditions.

Rating of Outcomes—The medians, IQRs, and ranges of ratings of outcomes in round 2 of the survey were very similar to those in round 1 (eAppendix 7 in the Supplement). In round 2, patients rated 28 outcomes (ie, 18 popular outcomes plus 10 unpopular outcomes selected in round 1). Figure 3 shows ratings for these 28 outcomes in round 2 in decreasing order of the 25th percentile. We classified 26 of 28 outcomes as important and 2 of 28 as not important. The 10 most important outcomes included 6 symptoms, 3 outcomes associated with quality of life, and 1 sign or clinical testing outcome. Among these 10 outcomes, 4 were unpopular in existing research. The 3 most important outcomes were ocular burning or stinging, ocular discomfort, and ocular pain.

Both outcomes classified as not important pertained to salivary function (dryness of the mouth and salivary flow), which is generally compromised in patients with Sjögren syndrome. Compared with patients without Sjögren syndrome, those with it assigned statistically significantly higher ratings for dryness of the mouth (median, 10.0; IQR, 3.8–11.2 vs median, 6.0; IQR, 3.0–8.0; $P < .001$) and for salivary flow (median, 9.0; IQR 7.0–10.0 vs median, 5.0; IQR, 2.0–8.0; $P < .001$).

Ranking of Outcomes by Underlying Diagnosis—Rank ordering of outcomes was consistent across diagnostic subgroups (Figure 3). Of note, salivary function outcomes (dryness of the mouth and salivary flow) classified by the overall group as not important were also ranked lowest by patients with Sjögren syndrome. Although patients with Sjögren syndrome assigned a high rating to these salivary function outcomes (see preceding paragraph), they rated outcomes pertaining to the eye higher.

Period Preferences for Outcome Measurements—For 12 of 28 outcomes (43%), and notably for 7 of 11 symptom outcomes (64%), 75% or more of all patients preferred measurement within 3 months of starting treatment in a trial (Figure 4). For all 28 outcomes, 50% or more of patients preferred measurement within 6 months. For some outcomes (eg, all 4 outcomes associated with quality of life), patients preferred measurement during all periods. For 9 of 10 outcomes rated lowest (eg, conjunctival staining and conjunctival impression cytology), fewer than 50% wanted measurement beyond 6 months after starting treatment (Figure 4).

Discussion

Using a 2-round Delphi survey of 420 patients with dry eye, we identified 8 important research questions and 26 important outcomes for dry eye. Patients rated effectiveness of patient education, environmental modifications, and topical anti-inflammatory eye drops as most important. The 10 highest-rated outcomes included 6 symptoms, 3 outcomes associated with quality of life, and 1 sign or clinical testing outcome. Among these top 10 outcomes, we determined 4 to be unpopular in existing research on dry eye. Given their preeminence to both treating clinicians and patients, the important questions and outcomes we identified should be considered in trials and reviews.

Our results add to a growing body of work showing that researchers often do not report outcomes important to patients, the most directly affected stakeholders.[18–22] Among the 26 outcomes that patients deemed important in the present study, 10 were unpopular in existing research, suggesting that patients and researchers do not agree on what outcomes matter most or that patient relevance is not being adequately considered as a factor in the choice of outcomes for research or both. For example, the US Food and Drug Administration approved 2 drugs for dry eye based on evidence of improvement in 1 symptom and 1 sign in trials.[23–25] However, there is only a limited correlation between symptoms and signs in dry eye.[26–28] Such limited correlation and the evolution of newer clinical measurements might have, at least in part, accounted for the discrepancy in outcomes considered important by patients and researchers. Most funding agencies now encourage, and some require, inclusion of patient-important outcomes in trials. The findings of our study, by identifying patient-important outcomes for dry eye, could help trialists satisfy this requirement.

While diverging perspectives between researchers and patients are not unique to dry eye, they make a compelling and urgent case for developing a core outcome set for this burdensome and expensive condition. Core outcome sets are agreed on minimum sets of outcomes that should be reported by all trials in a given disease area.[29] They promote consistency across trials, thereby facilitating evidence synthesis and evidence-based health care.[30] By identifying 109 outcomes examined in existing research and prioritizing the 26 outcomes among them most important to patients, we have completed 2 early steps of core outcome set development.[31] Multi-stakeholder consensus development efforts are now needed to narrow the list of 26 important outcomes into a core outcome set. Such efforts should also consider outcomes discussed in recent reports of the Tear Film and Ocular Surface Society.[23,32]

We also identified likely differences in perspectives among researchers studying dry eye, that is, discrepancies among those conducting trials, and discrepancies between those conducting trials and those conducting reviews. Indeed, there were1.7 times as many unique outcomes across the trials than across the reviews. This finding is consistent with what we reported previously for 4 other prevalent eye conditions.[33] In the present study, this multiplicity in outcomes likely accounted for the large proportion of unpopular outcomes among all outcomes in existing research (91 of 109 [83%]).

Strengths

First, to our knowledge, this is the only study to systematically engage patients with dry eye in determining priorities for research questions and outcomes. Second, the patients had received a range of underlying diagnoses. This enabled us to meaningfully examine whether the assigned ratings differed by underlying diagnosis. Third, we had a relatively large sample size, with 420 patients completing both Delphi rounds. Fourth, patients were predominantly older women, a population known to disproportionately experience dry eye.[10] Fifth, most patients had lived with dry eye for a long time (69% for more than 6 years). This allowed more experience-informed ratings of the importance of questions and outcomes than that which might have been feasible with a sample of patients who had more recently received this diagnosis. Sixth, we used the Delphi method to conduct online surveys of geographically dispersed patients. The anonymity of responses likely promoted honest ratings that were unaffected by dominant voices, a common challenge during in-person group deliberations. A particular benefit of engaging patients exclusively was that their voices were not readily influenced by clinicians or other experts. Seventh, although the survey contained technical terms, we added detailed clarifying lay language. A long-term patient with dry eye (R.P.) helped develop this clarifying language to ensure survey accessibility. Finally, we also obtained from patients their preferences regarding when during trials for dry eye they would like each important outcome to be measured.

Limitations

First, it is possible that we missed some outcomes in existing randomized trials addressing dry eye because we searched only for trials included in systematic reviews and in the ClinicalTrials.gov registry. We did not conduct a comprehensive search of all dry eye trials. Second, perhaps because of the regionality of the *KeratoScoop* newsletter, only small proportions of patients were of Asian race (2%) or Hispanic ethnicity (4%). Because dry eye is also common in these populations,[10,34–36] future research should examine whether our results apply to them. Third, although 31% of recipients of *KeratoScoop* opened our invitation email, only 18% of those who opened it clicked through to the website and began round 1 of the survey. However, of the 741 individuals who began round 1 of the survey, 84% and 68% completed rounds 1 and 2, respectively. Some factors might have contributed to survey noncompletion: (1) although we included detailed clarifying language for all technical terms, the survey's complexity might have discouraged some patients, and (2) dry eye symptoms themselves might have interfered with survey completion. Finally, we identified all survey patients through the *KeratoScoop* newsletter. We do not know whether the priorities of patients with dry eye who do not subscribe to *KeratoScoop* are similar or different.

Conclusions

Through a 2-round Delphi survey of 420 patients with dry eye, we identified 8 research questions and 26 outcomes important to patients. Those conducting research and developing core outcome sets for dry eye should consider these priorities, which have also been informed by clinicians and existing research addressing dry eye.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points

Question

What are patient priorities for future dry eye research?

Findings

A 6-step process (identifying research questions from a prior survey of clinicians and identifying outcomes from existing research, followed by a 2-round online Delphi survey of 420 patients with dry eye) was used to identify 8 research questions and 26 outcomes important to patients with dry eye. The top 3 questions pertained to effectiveness of patient education, environmental modifications, and topical anti-inflammatory drops, and the top 3 outcomes included ocular burning or stinging, ocular discomfort, and ocular pain.

Meaning

Results of this study may refine future research assessing dry eye treatments.

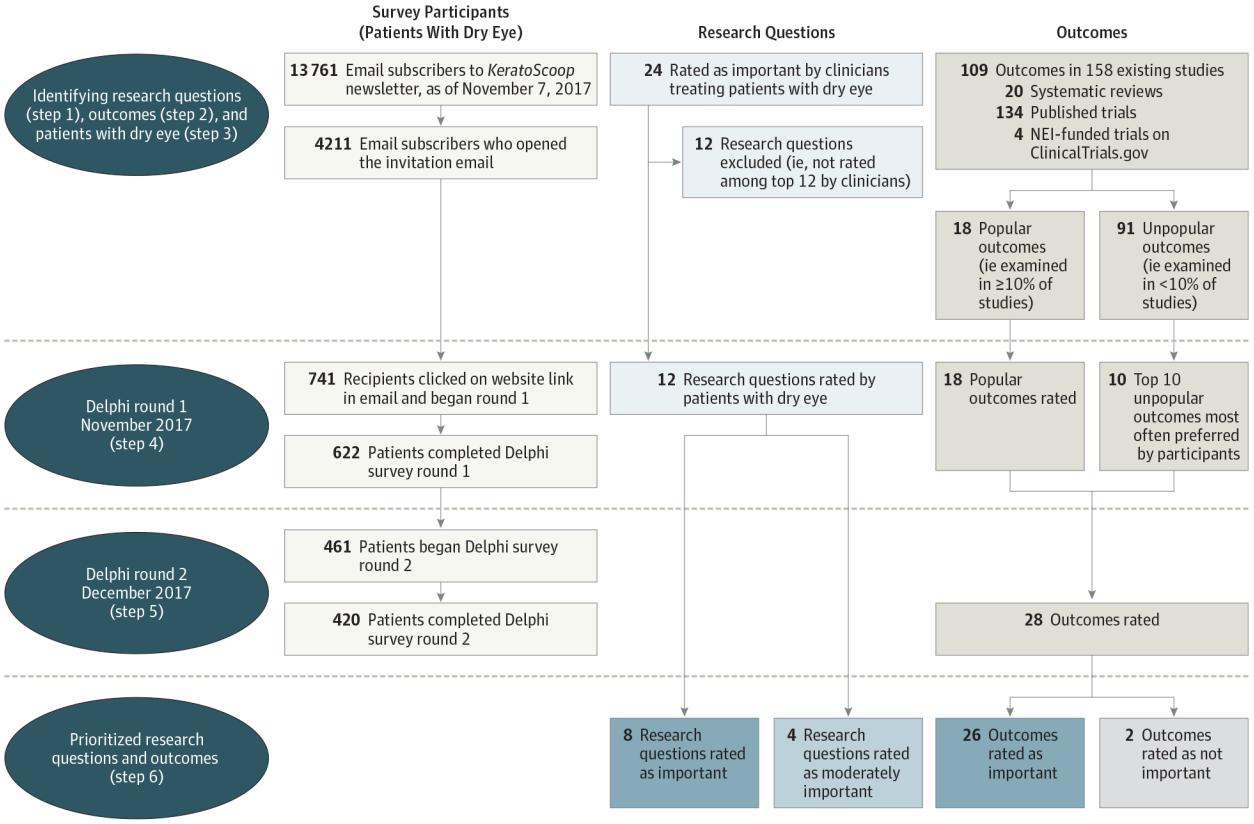
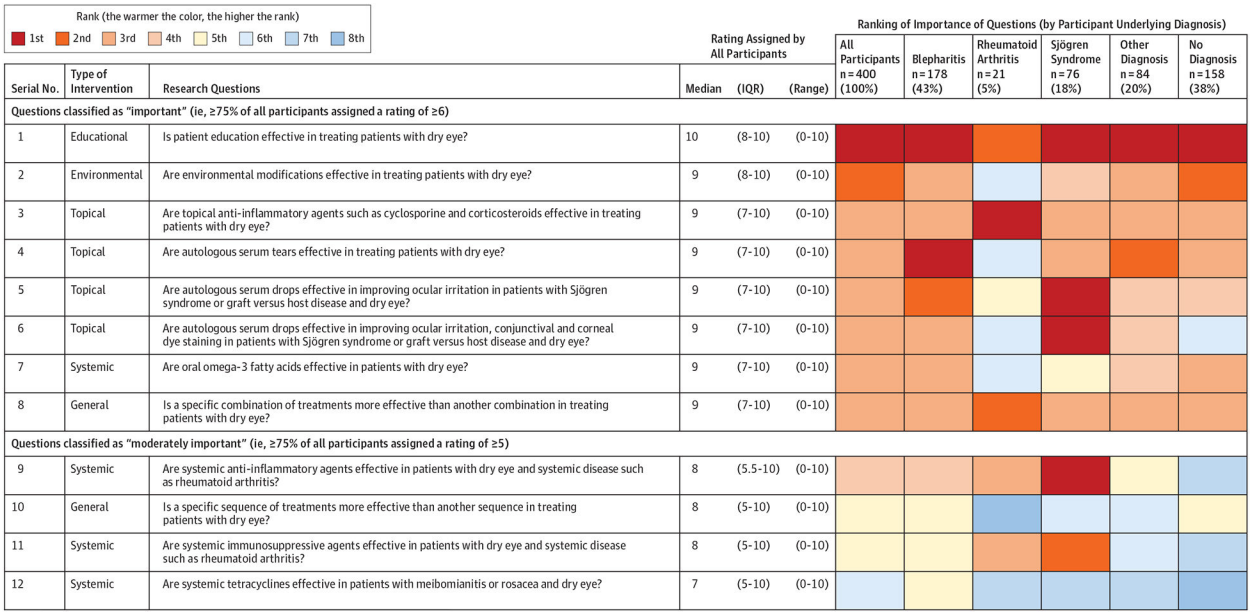


Figure 1. Steps and Flow of Survey Participants, Research Questions, and Outcomes in This Study

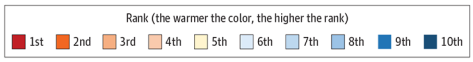
NEI indicates National Eye Institute.



Serial No.	Type of Intervention	Research Questions	Rating Assigned by All Participants: Median	(IQR)	(Range)	Ranking of Importance of Questions (by Participant Underlying Diagnosis): All Participants n = 400 (100%)	Blepharitis n = 178 (43%)	Rheumatoid Arthritis n = 21 (5%)	Sjögren Syndrome n = 76 (18%)	Other Diagnosis n = 84 (20%)	No Diagnosis n = 158 (38%)
Questions classified as "important" (ie, ≥75% of all participants assigned a rating of ≥6)											
1	Educational	Is patient education effective in treating patients with dry eye?	10	(8-10)	(0-10)	1st	1st	2nd	1st	1st	1st
2	Environmental	Are environmental modifications effective in treating patients with dry eye?	9	(8-10)	(0-10)	2nd	4th	6th	5th	4th	2nd
3	Topical	Are topical anti-inflammatory agents such as cyclosporine and corticosteroids effective in treating patients with dry eye?	9	(7-10)	(0-10)	4th	4th	1st	4th	4th	4th
4	Topical	Are autologous serum tears effective in treating patients with dry eye?	9	(7-10)	(0-10)	4th	1st	6th	4th	2nd	4th
5	Topical	Are autologous serum drops effective in improving ocular irritation in patients with Sjögren syndrome or graft versus host disease and dry eye?	9	(7-10)	(0-10)	4th	2nd	5th	1st	5th	5th
6	Topical	Are autologous serum drops effective in improving ocular irritation, conjunctival and corneal dye staining in patients with Sjögren syndrome or graft versus host disease and dry eye?	9	(7-10)	(0-10)	4th	4th	6th	1st	5th	6th
7	Systemic	Are oral omega-3 fatty acids effective in patients with dry eye?	9	(7-10)	(0-10)	4th	4th	6th	5th	5th	4th
8	General	Is a specific combination of treatments more effective than another combination in treating patients with dry eye?	9	(7-10)	(0-10)	4th	4th	2nd	4th	4th	4th
Questions classified as "moderately important" (ie, ≥75% of all participants assigned a rating of ≥5)											
9	Systemic	Are systemic anti-inflammatory agents effective in patients with dry eye and systemic disease such as rheumatoid arthritis?	8	(5.5-10)	(0-10)	5th	5th	4th	1st	5th	6th
10	General	Is a specific sequence of treatments more effective than another sequence in treating patients with dry eye?	8	(5-10)	(0-10)	5th	5th	7th	6th	6th	5th
11	Systemic	Are systemic immunosuppressive agents effective in patients with dry eye and systemic disease such as rheumatoid arthritis?	8	(5-10)	(0-10)	5th	5th	4th	2nd	6th	6th
12	Systemic	Are systemic tetracyclines effective in patients with meibomianitis or rosacea and dry eye?	7	(5-10)	(0-10)	6th	5th	6th	6th	6th	7th

Figure 2. Research Questions, Ratings of Importance, and Ranking in Round 1 of the Delphi Survey

IQR indicates interquartile range.



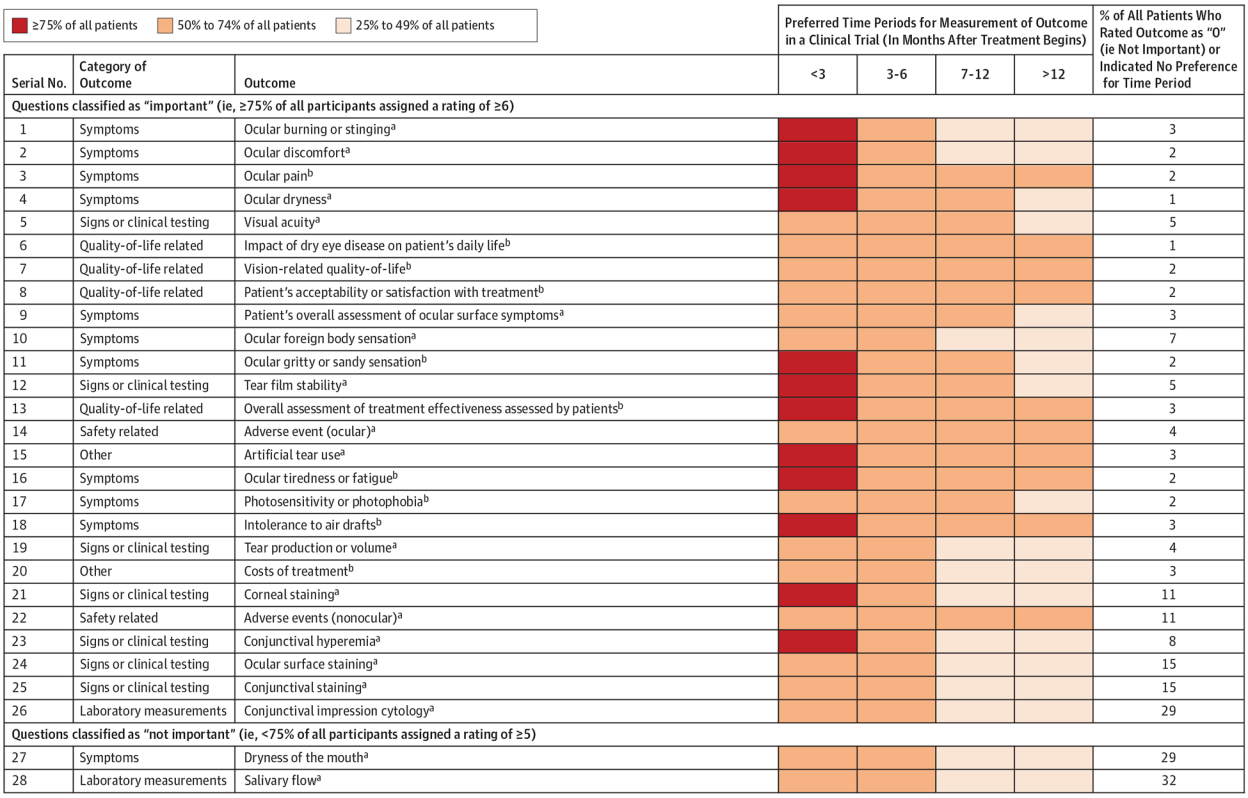
Serial No.	Category of Outcome	Outcome	Rating Assigned by All Participants: Median	(IQR)	(Range)	Ranking of Importance of Questions (by Participant Underlying Diagnosis): All Participants n = 400 (100%)	Blepharitis n = 178 (43%)	Rheumatoid Arthritis n = 21 (5%)	Sjögren Syndrome n = 76 (18%)	Other Diagnosis n = 84 (20%)	No Diagnosis n = 158 (38%)
Questions classified as "important" (ie, ≥75% of all participants assigned a rating of ≥6)											
1	Symptoms	Ocular burning or stinging[a]	10	(10-10)	(2-10)						
2	Symptoms	Ocular discomfort[a]	10	(10-10)	(0-10)						
3	Symptoms	Ocular pain[b]	10	(10-10)	(0-10)						
4	Symptoms	Ocular dryness[a]	10	(10-10)	(0-10)						
5	Signs or clinical testing	Visual acuity[a]	10	(10-10)	(0-10)						
6	Quality-of-life related	Impact of dry eye disease on patient's daily life[b]	10	(10-10)	(0-10)						
7	Quality-of-life related	Vision-related quality-of-life[b]	10	(10-10)	(0-10)						
8	Quality-of-life related	Patient's acceptability or satisfaction with treatment[b]	10	(10-10)	(0-10)						
9	Symptoms	Patient's overall assessment of ocular surface symptoms[a]	10	(9-10)	(2-10)						
10	Symptoms	Ocular foreign body sensation[a]	10	(9-10)	(0-10)						
11	Symptoms	Ocular gritty or sandy sensation[b]	10	(9-10)	(0-10)						
12	Signs or clinical testing	Tear film stability[a]	10	(9-10)	(0-10)						
13	Quality-of-life related	Overall assessment of treatment effectiveness assessed by patients[b]	10	(9-10)	(0-10)						
14	Safety related	Adverse event (ocular)[a]	10	(9-10)	(1-10)						
15	Other	Artificial tear use[a]	10	(9-10)	(0-10)						
16	Symptoms	Ocular tiredness or fatigue[b]	10	(8-10)	(0-10)						
17	Symptoms	Photosensitivity or photophobia[b]	10	(8-10)	(0-10)						
18	Symptoms	Intolerance to air drafts[b]	10	(8-10)	(0-10)						
19	Signs or clinical testing	Tear production or volume[a]	10	(8-10)	(0-10)						
20	Other	Costs of treatment[b]	10	(8-10)	(0-10)						
21	Signs or clinical testing	Corneal staining[a]	9	(8-10)	(0-10)						
22	Safety related	Adverse events (nonocular)[a]	9	(8-10)	(1-10)						
23	Signs or clinical testing	Conjunctival hyperemia[a]	9	(7-10)	(0-10)						
24	Signs or clinical testing	Ocular surface staining[a]	8	(7-10)	(0-10)						
25	Signs or clinical testing	Conjunctival staining[a]	8	(7-10)	(0-10)						
26	Laboratory measurements	Conjunctival impression cytology[a]	8	(7-10)	(0-10)						
Questions classified as "not important" (ie, 75% of all participants assigned a rating of ≥5)											
27	Symptoms	Dryness of the mouth[a]	5	(4-8)	(0-10)						
28	Laboratory measurements	Salivary flow[a]	5	(3-8)	(0-10)						

Figure 3. Outcomes, Ratings of Importance, and Ranking in Round 2 of the Delphi Survey

IQR indicates interquartile range.

[a] The 18 popular outcomes in existing research are ocular burning or stinging; ocular discomfort; ocular dryness; visual acuity; patient's overall assessment of ocular surface symptoms; ocular foreign body sensation; tear film stability; ocular adverse events; artificial tear use; tear production or volume; corneal staining; nonocular adverse events; conjunctival hyperemia; ocular surface staining; conjunctival staining; conjunctival impression cytology; dryness of the mouth; and salivary flow.

[b]The 10 unpopular outcomes in existing research are ocular pain; influence of dry eye disease on patient's daily life; vision-related quality of life; patient's acceptability or satisfaction with treatment; ocular gritty or sandy sensation; overall assessment of treatment effectiveness assessed by patients; ocular tiredness or fatigue; photosensitivity or photophobia; intolerance to air drafts; and treatment cost.



Serial No.	Category of Outcome	Outcome	Preferred Time Periods for Measurement of Outcome in a Clinical Trial (In Months After Treatment Begins) <3	3-6	7-12	>12	% of All Patients Who Rated Outcome as "0" (ie Not Important) or Indicated No Preference for Time Period
Questions classified as "important" (ie, ≥75% of all participants assigned a rating of ≥6)							
1	Symptoms	Ocular burning or stinging[a]					3
2	Symptoms	Ocular discomfort[a]					2
3	Symptoms	Ocular pain[b]					2
4	Symptoms	Ocular dryness[a]					1
5	Signs or clinical testing	Visual acuity[a]					5
6	Quality-of-life related	Impact of dry eye disease on patient's daily life[b]					1
7	Quality-of-life related	Vision-related quality-of-life[b]					2
8	Quality-of-life related	Patient's acceptability or satisfaction with treatment[b]					2
9	Symptoms	Patient's overall assessment of ocular surface symptoms[a]					3
10	Symptoms	Ocular foreign body sensation[a]					7
11	Symptoms	Ocular gritty or sandy sensation[b]					2
12	Signs or clinical testing	Tear film stability[a]					5
13	Quality-of-life related	Overall assessment of treatment effectiveness assessed by patients[b]					3
14	Safety related	Adverse event (ocular)[a]					4
15	Other	Artificial tear use[a]					3
16	Symptoms	Ocular tiredness or fatigue[b]					2
17	Symptoms	Photosensitivity or photophobia[b]					2
18	Symptoms	Intolerance to air drafts[b]					3
19	Signs or clinical testing	Tear production or volume[a]					4
20	Other	Costs of treatment[b]					3
21	Signs or clinical testing	Corneal staining[a]					11
22	Safety related	Adverse events (nonocular)[a]					11
23	Signs or clinical testing	Conjunctival hyperemia[a]					8
24	Signs or clinical testing	Ocular surface staining[a]					15
25	Signs or clinical testing	Conjunctival staining[a]					15
26	Laboratory measurements	Conjunctival impression cytology[a]					29
Questions classified as "not important" (ie, <75% of all participants assigned a rating of ≥5)							
27	Symptoms	Dryness of the mouth[a]					29
28	Laboratory measurements	Salivary flow[a]					32

Figure 4. Preferred Outcome Measurement Periods for All 28 Outcomes Rated in Round 2 of the Delphi Survey

[a]For the 18 popular outcomes in existing research (ocular burning or stinging; ocular discomfort; ocular dryness; visual acuity; patient's overall assessment of ocular surface symptoms; ocular foreign body sensation; tear film stability; ocular adverse events; artificial tear use; tear production or volume; corneal staining; nonocular adverse events; conjunctival hyperemia; ocular surface staining; conjunctival staining; conjunctival impression cytology; dryness of the mouth; and salivary flow), we obtained preferred measurement periods during Delphi round 1 (n = 622 patients). For each outcome, we allowed patients to indicate multiple measurement periods.

[b]For the 10 unpopular outcomes in existing research (ocular pain; influence of dry eye disease on patient's daily life; vision-related quality of life; patient's acceptability or satisfaction with treatment; ocular gritty or sandy sensation; overall assessment of treatment effectiveness assessed by patients; ocular tiredness or fatigue; photosensitivity or photophobia; intolerance to air drafts; and treatment cost), we obtained preferred measurement periods during Delphi round 2 (n = 420 patients). For each outcome, we allowed patients to indicate multiple measurement periods.

Table

Demographic and Clinical Characteristics of Survey Participants (ie, Patients With Dry Eye) Stratified by Delphi Round

	Patients, No. (%)	
Characteristic	**Completed Delphi Round 1 (n = 622)**	**Completed Delphi Rounds 1 and 2 (n = 420)**
Age category, y		
20–29	13 (2)	12 (3)
30–39	28 (5)	17 (4)
40–49	71 (11)	42 (10)
50–59	150 (24)	99 (24)
60–69	224 (36)	153 (37)
70–79	103 (17)	73 (17)
≥80	9 (1)	7 (2)
Prefer not to answer	24 (4)	17 (4)
Gender		
Female	506 (81)	348 (83)
Male	110 (18)	71 (17)
Other	1 (0)	1 (0)
Prefer not to answer	5 (1)	0
Race[a]		
White	582 (94)	393 (94)
Black or African American	11 (1)	7 (2)
American Indian or Alaskan Native	7 (1)	3 (1)
Asian	9 (1)	8 (2)
Native Hawaiian or Pacific Islander	0	0
Other	17 (3)	12 (3)
Prefer not to answer	7 (1)	2 (1)
Ethnicity		
Hispanic	26 (4)	16 (4)
Non-Hispanic	584 (94)	398 (95)
Not sure	3 (1)	2 (1)
Prefer not to answer	9 (1)	4 (1)
Country of current residence		
Australia	9 (1)	5 (1)
Canada	38 (6)	32 (8)
United Kingdom	15 (2)	8 (2)
United States	533 (86)	358 (85)
Other	18 (4)	12 (3)
Prefer not to answer	9 (1)	5 (1)

	Patients, No. (%)	
Characteristic	**Completed Delphi Round 1 (n = 622)**	**Completed Delphi Rounds 1 and 2 (n = 420)**
Duration of dry eye, y		
<1	9 (1)	6 (1)
1–2	58 (9)	37 (9)
3–5	119 (19)	80 (19)
6–10	170 (28)	116 (28)
>10	256 (41)	174 (41)
Cannot remember	6 (1)	3 (1)
Prefer not to answer	4 (1)	4 (1)
Underlying diagnosis[a]		
Blepharitis	264 (42)	178 (43)
Rheumatoid arthritis	33 (5)	21 (5)
Sjögren syndrome	105 (17)	76 (18)
Other	126 (20)	84 (20)
None of the above	237 (38)	158 (38)
Prefer not to answer	0	0

[a]Patients could select more than one category. Percentages were calculated using the column totals (ie, 622 and 420) as the denominator