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REVIEW

What we have learnt from 30 years living with positive dysphotopsia after intraocular lens implantation?: a review

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ABSTRACT

Introduction: Positive dysphotopsia (PD) is a topic of great interest in intraocular lens (IOL) field. Several approaches have been developed from the physics, psychophysics and psychometry fields to measure PD. However, the complexity of characterizing this phenomenon and the lack of standardization have resulted in a considerable bias between studies that avoid its inclusion in systematic reviews and meta-analysis.

Areas Covered: The purposes of this review were first to suggest a definition and classification of PD that minimize the bias between studies that use different questions to rate PD prevalence. Second, to describe the limitations found in psychophysical studies. Finally, to identify the associations between photic phenomena (PP) and the design of monofocal and multifocal IOLs. A non-systematic literature review was conducted from the last 30 years.

Expert Opinion: PD can be defined as any bothering bright artifact perceived by patients along or around direct bright lights or reflected over objects located in the visual field. If the patient is not bothered by the artifact, the term PP should be used instead. Psychophysical approaches measure PP and not PD. Whereas LED approaches are preferable, these really measure Light Disturbance because the classification of PP cannot be differentiated.

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1. Introduction

The term dysphotopsia can be defined as the abnormal, difficult or bad (dys-) light (-photo-) vision (-opsia) [1]. Despite two classifications have been coined depending on the increase (positive) or decrease (negative) of light within the patient's visual field, in this review we are going to focus in positive dysphotopsia (PD) after intraocular lens (IOL) implantation [2]. PD was originally described with monofocal IOLs [3] in patients reporting light sensitivity, halos, central flash and arcs of light [4]. The topic, specifically related to monofocal IOLs, was reviewed by Masket et al. [5] in 2020.

Multifocal intraocular lenses (MIOLs) increased the prevalence of patients who perceived halos in comparison to monofocal IOLs [6] and nowadays are one of the main concerns of patients implanted with this type of IOLs [7]. Although PD started to be a topic of great interest nearly 30 years ago [3,6,8], there are still problems to conduct systematic reviews and meta-analysis with results reported from randomized clinical trials on this issue due to the lack of standardization [9]. Several methods have been historically proposed to assess photic phenomena (PP) through in-vitro, psychophysical and psychometric approaches. The aim of the current article was to review the advantages, limitations and results provided from these approaches and to provide some key points that could help for the development of a standardization in the assessment of PD.

2. Definition of positive dysphotopsia

PD should be considered as a latent variable or latent trait, terms commonly used in the science of measuring variables that cannot be observed directly [10]. The difference between PP and PD lies in PP can be observed directly with the measurement by a psychophysical system but the bothersome to this PP (PD) cannot be observed and requires to use of a questionnaire for estimating this latent variable. PD measurement can have some bias or difference between studies attributed not to variations in the populations but to a systematic error which results from a common practice of using non-validated questionnaires.

People working in the assessment of PD should be conscious of the troubles originated by the simple change of a word in a question. The first problem for standardizing PD symptoms is related to the several meanings attributed to the prefix dys-, such as bad, ill, hard, difficult, abnormal or imperfect [1,11]. Different studies evaluating PD use several terms that can lead to different prevalences of symptoms and signs: notice [6], problems [12], difficulties [13,14], limitation [12], frequency [15], bothersome [16,17], annoying [18], debilitating [18], and unspecified in some cases [19,20]. Solicited questions can lead to higher prevalence than unsolicited questions [21] (i.e., *Do you have problems with your vision?* Versus *Do you sometimes see halos?*) and some authors interviewed only patients who were bothered about their vision, and later described their symptoms [22]. In these cases, the prevalence of PD can decrease in

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Article Highlights

- Photic phenomena, a psychophysical term, should be differentiated from dysphotopsia, a psychometric term. Photic phenomena can be perceived by the patient but it should be considered as dysphotopsia only if these bother the patient.
- No positive dysphotopsia is present if there is no point of light or object on which light is reflected, this should be discerned from other perceptions of flashes of light associated to some diseases.
- Halo, glare and starburst are the most commonly reported photic phenomena in the literature with intraocular lens.
- Several options for measuring photic phenomena and dysphotopsia have been proposed but a lack of consensus and standard protocols avoid a reliable comparison between clinical studies.
- Although these phenomena could be minimized with an appropriate intraocular lens design, there is a gap between lab studies and evidence provided by clinical research. Scientific associations should work in a consensus for standardizing the measurement and report of clinical results.

comparison to other studies on which all patients are directly asked about PP with direct questions [23,24].

Clinical trials for FDA approval of new MIOLs include patient-reported outcome (PRO) measurements with questionnaires that should demonstrate their validity [25]. In the clinical trial of the AcrySof ReSTOR in 2005, a visual disturbance questionnaire was used including questions related to difficulties with dysphotopsia [19,26]. McAlinden developed afterward a questionnaire to measure the quality of vision (QoV) latent trait, including some PD-related items and helping the patient to understand the items by means of example figures [27].

The QoV measurement through questionnaires [14] and the understanding of PP with images [17,28] were approaches previously used by other authors but McAlinden was the first using the item response theory (IRT) for validating the QoV latent trait, something not required by the FDA for which validation through the classic test theory (CTT) was enough [25]. McAlinden also included three subscales of frequency, severity and bothersome, which were not interchangeable [29]. These three domains described by McAlinden are in agreement with our suggestion of differentiating between PP and PD, even though some experts might argue that simply evaluating PD from none to very bothersome might be enough, just to answering none in this question will not answer to the PP perception which was covered by McAlinden through the frequency domain.

Latest FDA clinical trials for Tecnis Symfony and AcrySof IQ PanOptix IOLs also used questionnaires for assessing visual disturbances including PD [30,31]. Symfony clinical trial assessed bothersomeness associated to glare, halos, starbursts, streaks of light and sensitivity to light, with spontaneously-reported subject responses, considering 'none' in the scale for those cases not experiencing symptoms or experienced them but not bothering. Non-directed spontaneous questions related to difficulties with halos, night glare and starburst were also included [30]. AcrySof IQ PanOptix clinical trial included evaluation of halos, starburst and glare as PD, asking first if the patient experienced a particular disturbance and later rating the severity, frequency and bothersomeness. However, only bothersomeness and severity were included in the report [31].

Although the definition of PD can be difficult considering the lack of uniformity, an attempt of defining it are going to be presented, even knowing that some of the previous cited experts did not completely agree. PD can be defined as bothering bright artifacts perceived by patients along or around direct bright lights or reflected over objects located in the visual field [32,33]. It is important to remark that no PD is present if there is no point of light or object on which light is reflected, helping this to discern PD from other perceptions of flashes of light associated to some diseases [28,34]. Likewise, no PD is present if it does not bother the patient even though the patient perceives some abnormal artifacts.

The simplification of the definition is required to obtain uniform results for conducting systematic reviews and meta-analysis [9]. It could be argued that the term dys- also includes the abnormal or imperfect perception, and PP, such as halos, are an abnormal perception of light secondary to the implantation of a MIOL. Therefore, PD might be also defined without bothersomeness arguing that there is abnormality, but this causes bias between studies using different types of questions, which is the current problem [9]. In addition, it can be also argued that the term difficulty instead of bothersomeness is also frequently used in clinical trials, but it should be considered that PP can bother the patient without causing any difficulty. Considering cataract surgery with MIOL implantation as a premium surgery, we believe that asking about the term bothersomeness can be more conservative than using the term difficulty and therefore more centered on patient concerns.

3. Photic phenomena classification

In the previous section, we concluded that in favor to look for a single uniform terminology, the term PD should be only used when the patient is bothered, even though an abnormal perception of light is experimented. In case of not being bothered, the term PP should be only used [34]. A second problem for standardization is what type of PP can result in PD or what type of PP can bother the patient. Types of PP emerged from the experiences reported by patients:

- Glare: Reduced sharpness of vision with bright lights that can be translated as the sensation of a white veil in front of the actual image [24]. Despite some authors pointed out that if a decrease on visual performance in the presence of increased luminance is not present [35], the term glare should not be used [34], this is a psychophysical definition. In agreement with this definition, a questionnaire evaluating glare should be correlated with visual performance metrics to demonstrate the construct validity [27]. Glare can be explained by high order aberrations [36], residual refractive errors [36], posterior capsular opacification [37], IOL material [38] and IOL opacification [39].

- Halo: Circular or large arcuate ring around a point source of light that is usually seen in darkness or dim lighting. Examples of light sources generating halos are car headlights or streetlights [17,28,34,40].

- Starbursts: Spikes emerging from a light source produced by diffraction effects for instance due to non-regular edges in apertures [41]. Despite many questionnaires do not include starburst, they should be evaluated because it is one of the most common PP together with glare and halo [30,31].
- Flare: The use of the term flare has been very confused along history, because it is commonly combined with glare and starburst, with the main difference of appearing with ghosting bright shapes [26,28,34,42,43]. Some old studies used the term flare for referring to effects that are currently better defined as streaks of light [40,-,44–46]. This effect usually appears by reflections in complex optical systems and it is not currently used in modern questionnaires [27,30,31].
- Streak of light: Defined as an arc, semicircle or tail of light usually seen in darkness or dim lighting and lasting only seconds and also named central flashes [2,28]. As it was described in the previous point, some old studies wrongly used the term flare instead of streaks of light. It has been attributed to the edge of an optic exposed within the pupillary aperture [40]. Streaks of light have been reported with the 3-piece AcrySof IOL and attributed to its edge or haptics [44–46].

According to the scientific literature revised, halo (Figure 1(a)), starburst (Figure 1(b)), and glare (Figure 1(c)) should be included in any questionnaire evaluating visual symptoms with MIOLs, as they are the most common PP with this kind of implants [30,31]. However, other PP, such as flare or streaks of light, might not be considered mandatory in the evaluation of MIOLs because the first one is more commonly associated to complex optical structures with multiple surfaces and the second one produces temporal artifacts that do not bother the patient and that are attributed to other aspects beyond the optical zone. Streaks of light should be considered in studies on which the target of evaluation are the holes, borders, or transitions between optic/haptic in the IOL or platform design [2]. Sensitivity of light also included in some FDA studies is a confusing term with the visual disturbances perceived in some diseases and is not directly related to IOL design [30,47]. Indeed, it should not be classified as PP, not being necessary its consideration as an item for PD latent trait evaluation. This approach disagrees with FDA studies for which the latent trait is the visual disturbance and not the PD.

4. Methods of measurement

According to the definition used in the previous sections, PD is a PP that bothers the patient. Therefore, it should be considered a single latent trait or a domain from quality of vision or visual disturbance, which requires from an instrument with a bothersome scale. However, there are other approaches requiring that patient evaluate the PP perception without considering the level of bothersomeness, as the PP simulators. Both are considered psychometric approaches to measure PD or PP. PP can be also assessed by physics through optical bench measurements on which neural processing is not considered or psychophysics on which the PP is induced by a physical stimulus and a method is designed to measure the characteristics of such PP. Considering this, it is important to note that PD can be only measured through psychometry whereas PP through psychometry, physics and/or psychophysics.

4.1. Questionnaires

Questionnaires should be validated and two approaches can be used for this purpose, the CTT and the modern IRT [48]. The FDA requires that sponsors demonstrate the validity of their questionnaires through statistical approaches according to the CTT [25]. Researchers that are non-familiarized with psychometric validation procedures can be very confused about the validity of questionnaires for assessing a latent trait. First, it is important to know that PP are considered items from a latent trait, therefore halos, glare, etc. can be items for the PD latent trait.

Nowadays, there is no IRT validated questionnaire that evaluates directly PD as latent trait. The most similar IRT validated is the QoV questionnaire that does not consider only PD as items of QoV. Therefore, not only items from PD domain are considered by the final scoring derived from this instrument [27,49]. This means that only items corresponding to the PD domain would be enough to assess PD. This is important to understand because all the current questionnaires that include PP as items are not designed for the specific latent trait of PD, but are designed for QoV [27], visual disturbances [26,30,31], quality of life [50,51], visual disability [52], night driving [53], and others. Likewise, questionnaires validated through CTT failed in IRT analysis for the specific latent trait for which were designed, such as the cataract symptom score [54].

The lack of standardization is a problem for considering PD in systematic reviews and meta-analysis. Evans et al. [9] proposed to include the proportion of people reporting visual symptoms as a method of aggregation, each symptom reported separately. This means that bothersomeness due to halo, starburst and glare should be included in any research study with MIOLs. Since proportion is measured through a dichotomous variable and questionnaires usually use a Likert scale, it should be standardized which level to use to dichotomize the variable. The correlation of these questions with the patients who would not be implanted again with the same IOL due to the PD if they have to take the decision again could help in the future to determine the cutoff to transform the polytomous variable to a dichotomous variable. Another approach would be to directly meta-analyze the proportion of answers at each one of the levels of the scale.

4.2. Simulators

Some questionnaires as the QoV use images to help patients to differentiate between different PP [27]. Others use images combining PP in order to globally understand the patient's vision [17]. Computers have allowed the creation of simulators that allows the patient to select size and intensity of PP, such as the Halos and Glare simulator (Eyeland-Design Network GmbH, Vreden, Germany) [55] or the EyeVisPod programme

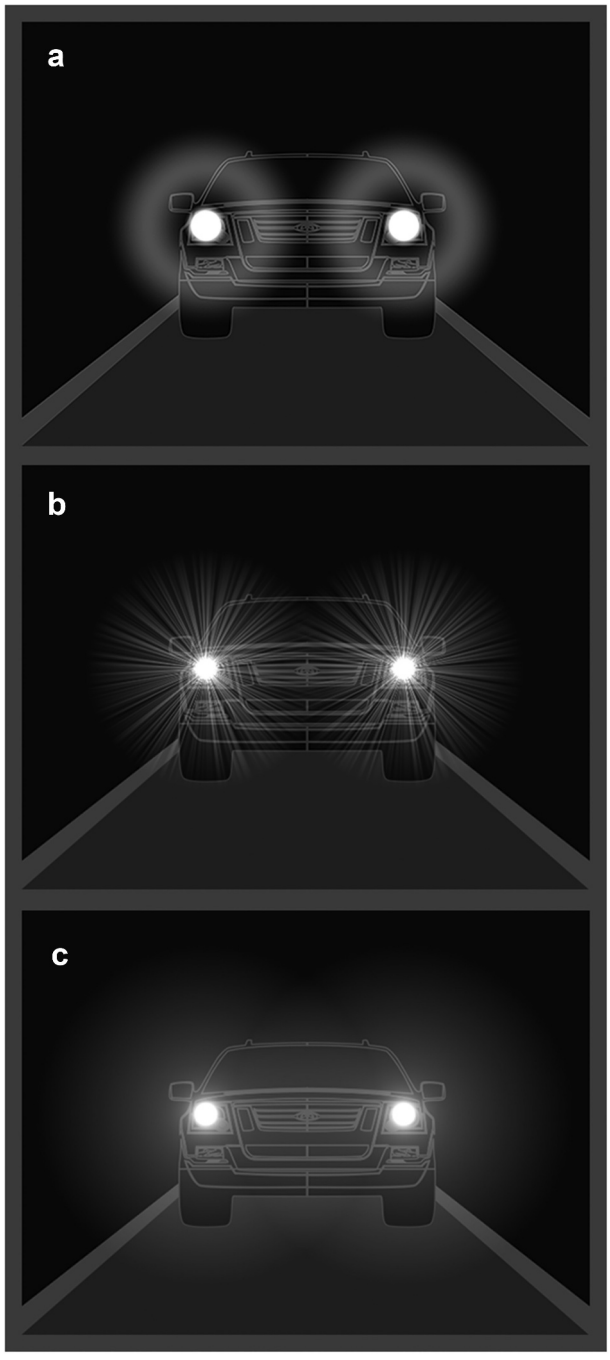

Figure 1. Simulation of halos (A), starburst (B) and glare (A) over car headlights.

(PGB, Milan, Italy) [56]. The Halos and Glare simulator classifies three types of halo, being H1 and H3 diffused and striated halos, respectively. However, H2 type should not be named as halo in agreement with other questionnaires, being more compatible with starburst [57]. The same happens for Glare, with G2 subtype being a combination of glare and starburst. A main limitation of simulators used in non-calibrated displays is that they might provide differences between studies that might be attributed to the luminance properties of the display instead of the MIOL. In fact, some inconsistencies have been reported in studies using the same MIOL [58,59]. Kretz et al. [58] reported a predomination of the starbust type in eyes implanted with the trifocal diffractive IOL AT Lisa Tri, whereas Alió et al. [59] reported that either ring or starburst predominated equally at 1 month after surgery. Conversely, difficulties associated to starbust were referred by only 10% of patients in comparison to the 65% of patients who perceived halos when were asked through a questionnaire [60]. Savini et al. [57] also reported controversial results using images of QoV and the simulator with regard to the PP type described by the patients. Therefore, results obtained from different scientific articles in terms of PP should be interpreted with caution. This kind of simulators should be combined with questionnaires that grade how these PP bother the patient, and then measuring PD instead of PP.

4.3. Psychophysical assessment

First efforts trying to measure halo size dates from late nineties through a computer software with a central circle of 86.6 cd/m^2 and a small mark moved through to 12 meridians until the exterior border of the halo was achieved [61]. Unfortunately, no significant differences were obtained between monofocal IOLs and refractive MIOLs although higher prevalence in refractive MIOLs was obtained through questionnaires [62]. The lack of differences was explained by not considering the intensity or halo shape [28]. However, the same procedure resulted in significant differences between monofocal refractive and diffractive MIOLs, and cataract patients, with the last group experiencing the bigger halo size [61]. This method also resulted in no significant differences between monofocal and refractive MIOLs after capsulotomy [63]. Similar approach was followed by Pieh et al. [64], but with less intensity of the circular light (56.6 cd/m^2) and resulting in differences between monofocal and multifocal IOLs.

The method described above involved a task on which the patient defined the limits of the halo. Another approach described was to use a circular stimulus on a computer screen of 175.6 cd/m^2 and a dot in movement (61.4 cd/m^2) from center to periphery. This method consists of a detection task in such a way the patient indicates the location on which the halo intensity decreases up to 61.4 cd/m^2. This method resulted in significant differences between diffractive MIOLs, but only for bifocals of high addition (+4.00 D) in comparison to trifocal and bifocals of low addition [65].

The main limitation of the previous methods was the stimuli used to generate the halo. It is unknown if methods that use a computer display to generate a circle with such as low luminance and considering that the light is not scattered in similar way that traffic or car lights, are really measuring PP or the ghosting image. Other methods have proposed to use LED or fiber optics light with higher intensity and more scattered than the produced by a display [66,67]. Gutierrez et al. measured the size of light disturbance with a central LED intensity of 3000 cd/m^2 and 4000 cd/m^2 and low intensity peripheral LEDs in a detection task [68]. Later, Ferreira-Neves et al. used a similar method but including the size, shape, regularity, and location of the light disturbance (Light Distortion Analyzer, CEORLab-University of Minho, Portugal) [67]. The Aston Halometer [69] also proposed the measurement considering

a central LED and a peripheral recognition task with letters, such as performed with the MonCV3 system (Metrovision, Pérenchies, France) [70].

There are several conclusions to remark about the previous mentioned psychophysical methods. First, the measurement of halos using computer displays as has been historically conducted, is not really an appropriate method, providing possibly a measurement of the ghosting image. Second, despite the advantages of methods using sources of light with higher intensity (around 10 times higher than computer displays), it cannot be differentiated when there is a halo as a ring of light, starburst or glare. The term light disturbance should be used instead.

5. IOL design and photic phenomena

5.1. Monofocal IOLs

Monofocal IOL designs were studied for understanding the factors leading to an increase of the prevalence of PD. For instance, halos were found to be explained by high positive eye spherical aberration (>0.5 µm) [22], whereas glare was attributed to shape-factor and material [71,72], and arcs of light to edge shape [73]. Aslam et al. [28] reviewed the principles of some pseudophakic PP, including the following main reasons for monofocal IOLs: ovoid lenses, positioning holes [74], smaller optic size and square edge design lenses [28].

In an unequal biconvex hydrophobic IOL design, the highest refractive index and flat anterior radius of curvature can explain an increase of glare [71,72,75,76]. Less glare symptoms have been also reported with hydrophilic compared to hydrophobic IOLs, probably due to the lower refractive index and equi-convex design [76]. However, other study comparing two hydrophobic IOLs of refractive indexes of 1.55 vs 1.47 reported the opposite trend in terms of the difference of glare due to refractive index [77]. The symptoms of glare could be also attributed to IOL related adverse events such as glistenings and subsurface nanoglistenings, observed mainly in hydrophobic IOLs [78].

The particular type of PP associated to the edge of the IOL can appear in the peripheral visual field opposite to the image of the glare source due to the reflection on the internal surface of the edge [79]. This was described as an arc-like pattern, with an intensity that can be reduced with a rounded-edge design instead of a sharp-edge [79]. Edge designs, such as sigma-edged, have been also proposed to reduce the arc-like pattern [80]. Other PP related to IOL edge were solved in the past texturizing the border [44]. Beyond edge shape, non-imaging features within the optic body that reduce the functional optic diameter can influence on edge-reflected glare and secondary image on peripheral retina [2]. For IOLs with peripheral non-imaging features, edge-reflected glare has been reported at 30º and edge-transmitted at 45º. For evaluating the impact of edge glare in clinical practice, it is important to note that major part of simulations had been conducted for pupils of 5 mm [2,81,82], although Das et al. [2] reported a similar trend at large off-axis angles of illumination for smaller pupil sizes. Furthermore, these symptoms can be reduced in weeks probably due to fibrosis of the rhexis edge around the IOL [44]. A case report has been also reported for a three-piece IOL with unwanted glare images due to the junction of haptic and optic [44]. Recently, Masket et al. [83] demonstrated, in agreement to the previously described, that by exchanging the monofocal IOL for one with a lower index of refraction or different edge design, an approximate 85% success rate could be achieved in the treatment of PD.

5.2. Multifocal IOLs

Although the previous PP can also appear with MIOLs, the findings obtained at previous section were derived from studies using monofocal IOLs. Multifocal IOLs increased the prevalence of some PP, such as halos, which was mainly seen with monofocal IOLs in the presence of high positive spherical aberration [22]. On the other hand, theoretical explanation of halo with diffractive MIOLs was first documented by Simpson et al. and afterward dealt by other authors [8,64,84]. Halo can be seen in the point spread function (PSF) at the two primary focus planes of a bifocal IOL. The PSF will consist on the focused component surrounded by a large halo resulting from the other primary image and fainter halos which extend to larger off-axis distances than the primary halo due to light in the higher diffraction orders [8]. According to theory, an easy approach for reducing PP size would be to reduce the area inside the pupil assigned to the non-focused image (i.e. by means of reducing the number of rings in a conventional diffractive MIOL or the zones in a refractive MIOL) and to reduce the intensity for the non-focused image in certain conditions (i.e. light energy for near at far distance tasks, such as night driving) [84,85].

Randomized clinical trials have not offered evidence up to date in PROs about the theoretically expected benefits of some designs, such as apodization (comparison of AT LISA tri and SN6AD1 IOLs) [86] or diffractive EDOF (comparison between Symfony and Panoptix IOLs) [87]. On the other hand, despite theoretical studies reported comparable haloes between Symfony and monofocal IOLs [88], clinical trials have resulted in significant PD scores between monofocal and either Symfony or Panoptix IOLs [87]. Cross-sectional observational studies have reported significant lower size of the starburst with the EDOF IOL Mini WELL than with Restor SV25T IOL, but non-significant differences were found in glare size and intensity [57]. Table 1 includes a revision of the results reported by studies with some commercially available MIOLs. A considerable bias was found between studies even using the same MIOL.

6. Neuroadaptation and personality

Vryghem et al. [24] reported that the population reporting halos were younger than those who did not see halos (66 vs 72 years old). Perception of glare and haloes have been reported to decrease from 1 month to 3 month [21,58,94]. This decrease is related to the process of neuroadaptation which is associated with an initial increased activity of cortical areas involved in visual attention, procedural learning, effortful cognitive control, and goal-oriented behavior that is

Table 1. Review of studies with current commercial MIOLs that report positive dysphotopsia results using several approaches.

Author	Study type	n	Follow-up (months)	Age	MIOL	Halo	Starburst	Glare	Reported Grading	Method
Giers et al.(2019) [55]	Non-RCT	14	2–4	66	Mini WELL	23%	23%	70%	Mean None-Mild Problems	Non-validated questionnaire and Halo & Glare Simulator
Savini et al.(2018) [57]	Observational	20	1–2	66	Mini WELL	5%	0%	10%	Mild for halo and glare	QoV and Halo & Glare Simulator with controversial results
Savini et al.(2018) [57]	Observational	37	1–2	64	ReSTOR SV25T	27%	27%	5.4%	Mild to moderate for halo and starburst Mild for glare	QoV and Halo & Glare Simulator with controversial results
Vryghem et al. (2013) [24]	Observational	25	1–2	70	FineVision	32%	-	-	Not considered bothersome	Non-validated questionnaire Yes/Not experienced
Mendicute et al. (2016) [21]	Observational	104	1	-	AT LISA tri	~80%	~35%	~42%	Not bothersome in 75%	QoV
Law et al.(2010) [94]	Observational	30	1	61	AT LISA tri	80%	-	73.3%	Medium or more difficulty	Non-validated questionnaire
Law et al.(2010) [94]	Observational	30	6	61	AT LISA tri	40%	-	13.3%	Medium or more difficulty	Non-validated questionnaire
Maurino et al.(2015) [86]	RCT	94	4–8	67	AT LISA tri	44%	11.9%	35%	A little bothersome in 29.8%, quite in 8.3% and very in 6.0% for Halo	QoV
Maurino et al.(2015) [86]	RCT	94	4–8	68	Restor SN6AD1	36.9%	16.7%	28.6%	A little bothersome in 22.6%, quite in 8.3% and very in 6.0% for Halo	QoV
Kretz et al.(2015) [58]	Observational	38	1	62	AT LISA tri	90%	-	-	Disturbing for 10%	Non-validated questionnaire. Yes/Not experienced and disturbing
Alió et al.(2018) [59]	RCT	17	1 6	63	AT LISA bi	35.3% 47.1%	35.3% 35.3%	-	Not considered bothersome for great majority	Halo & Glare Simulator
Alió et al.(2018) [59]	RCT	15	1 6	63	AT LISA tri	40% 26.7%	46.7% 66.7%	-	Not considered bothersome for great majority	Halo & Glare Simulator
Alió et al.(2018) [59]	RCT	17	1 6	63	Restor SN6AD1	47.1% 41.2%	41.2% 47.1%	-	Not considered bothersome for great majority	Halo & Glare Simulator
Peng et al.(2012) [19]	RCT	50	6	66	ReSTOR SN6AD1	-	-	-	Mean rated as minimal difficulty	Used in FDA clinical trial [26]
Monaco et al.(2017) [87]	RCT	20	4	66	Panoptix	-	-	-	Halo moderate and quite in 15% bothersome	Used in FDA clinical trial [26]
Monaco et al.(2017) [87]	RCT	20	4	67	Symfony	-	-	-	Halo moderate and quite in 20% bothersome	Used in FDA clinical trial [26]
Böhm et al.(2018) [60]	Observational	20	3	63	AT LISA tri	65%	10%	20%	Not specified	Modified from used in FDA clinical trial [26]
Böhm et al.(2018) [60]	Observational	20	3	63	Panoptix	90%	0%	15%	Not specified	Modified from used in FDA clinical trial [26]
Kohnen et al.(2017) [89]	Observational	27	3	63	Panoptix	89%	-	11%	Not bothersome in the majority of cases	Used in FDA clinical trial [26]
Kohnen et al.(2016) [90]	Observational	27	3	64	AT LISA tri	60%	8%	28%	Not specified	Non-validated
Kohnen et al.(2009) [91]	Observational	93	1 6	62	ReSTOR SN6AD1	-	-	-	8% severe difficulty for halo, 5% for glare	FDA used [26]
Liu et al.(2018) [92]	Observational	25	3	50	AT LISA tri	84%	-	40%	Not bothered at all or slightly bothered in 88%	Non-validated Yes/Not experienced and bothered
Liu et al.(2018) [92]	Observational	30	3	50	AT LISA bi	86.7%	-	33.3%	Not bothered at all or slightly bothered in 86.7%	Non-validated Yes/Not experienced and bothered
FDA (2005) [26]	Non-RCT	126	6	69	ReSTOR SA60D3	-	-	-	Moderate or severe 30.4% for halos and 9% for glare	FDA used [26]
FDA (2005) [26]	Non-RCT	440	6	69	ReSTOR MA60D3	-	-	-	Moderate or severe 22.4% for halos and 25% for glare	FDA used [26]
FDA (2016) [30]	RCT	135	6	68	Symfony	59.2%	57.8%	57.2%	Bothered quite a bit or very 15.6% for halos 17% for starburst and 12.4% for glare	FDA used [30]
FDA (2019) [31]	Non-RCT	243	6	66	Panoptix	48.8%	44.8%	45.2%	Bothered quite a bit or very 11.1% for halos, 12% for starburst and 8.7% for glare	FDA used [30]
Hayashi (2019) [93]	Observational	32	3	67	Panoptix	65.6%	-	43.7%	Severe 15.6% for halos, 12% for starburst and 6.3%% for glare	Non-validated

normalized at 6 months [95]. Specifically, patients with more bothersome PP after multifocal IOL implantation have shown in another study increased activity in several regions in frontoparietal circuits, as well as cingulate gyrus and caudate nucleus [96]. This suggests that training involving visual attention and procedural learning networks may be potentially beneficial for promoting the neuroadaptation in eyes implanted with multifocal IOLs, especially if it is combined with the additional benefit of videogames in terms of neuroplasticity [97]. There is a minimal previous experience evaluating the benefit of visual training using sinusoidal gratings as stimuli in patients implanted with multifocal IOL, showing a significantly faster and larger improvement of orientation visual acuity, contrast sensitivity and near vision in trained eyes compared to control eyes, with a mean duration of training sessions of 30 ± 5 minutes [98]. This type of training combining different type of stimuli to promote a visual improvement and the activation of brain areas associated to neuroadaptation may be a promising option to minimize the prevalence of PD after cataract surgery with implantation of multifocal IOL. However, this should be corroborated in future clinical trials validating this potential approach.

Personality has been suggested to be another factor with the potential of contributing to the perception of PD in a similar way than other visual performance measurements such as tolerance of blur [99]. Specifically, the personality characteristics of compulsive checking, orderliness, competence, and dutifulness have been found to be statistically significantly correlated to subjective disturbance by glare and halos in a multicenter study assessing personality characteristics that may influence patient satisfaction after implantation of MIOLs [100]. Rudalevicius et al. [101] on the other hand reported weak or none linear relationships between glare and halos and latent traits measured with the Five Factor Inventory scale.

7. Expert opinion

A lack of uniformity is currently present in the definition and methods of measuring PD, although after the blurred vision it is one of the main sources of patient's complains after MIOL implantation [102]. PD specifically can be defined as bothering bright artifacts perceived by patients along or around direct bright lights or reflected over objects located in the visual field. Therefore, no PD is present if it is not bothering although the patient perceives some abnormal artifacts. No specific test has been developed to this date to characterize each specific type of PD, including halos, glare, starburst and streaks of light. Simulators and subjective questionnaires can provide some estimations that are not directly related to PD, and psychophysical tests allows the clinician to obtain a more adequate measurement of light disturbance but without differentiating between PD types. Future developments should be performed to design a more specific test to characterize clinically PD. Finally, in terms of prevention, these phenomena can be minimized with an appropriate IOL design from the optical and geometrical perspective even though there is a gap between lab studies and evidence provided by clinical research which should be joined in the future after improving the clinical research methods for assessment of PD. Likewise, visual training is another promising option to reduce the negative impact of PD, but this approach still requires more development and research. A standardized definition of dysphotopsia, methods for assessing and reporting should come through consensus in order to improve the bias found between studies. In fact, we would like to thank suggestions provided by the reviewers which clearly showed the need of an international consensus with them claiming for the need of bridging the gap between lab findings and clinical results, new terms for differentiation between PD derived from monofocal and diffractive IOLs, such as 'Diffractive Dysphotopsia (DD)'.The current review does not pretend to be a standard but intends to provide some historical background that helps to achieve this expert consensus in the future.

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