UNMET NEEDS IN DME MANAGEMENT:

Latest Findings From the DME AWARE Delphi Study

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With the DME AWARE Delphi Steering Committee

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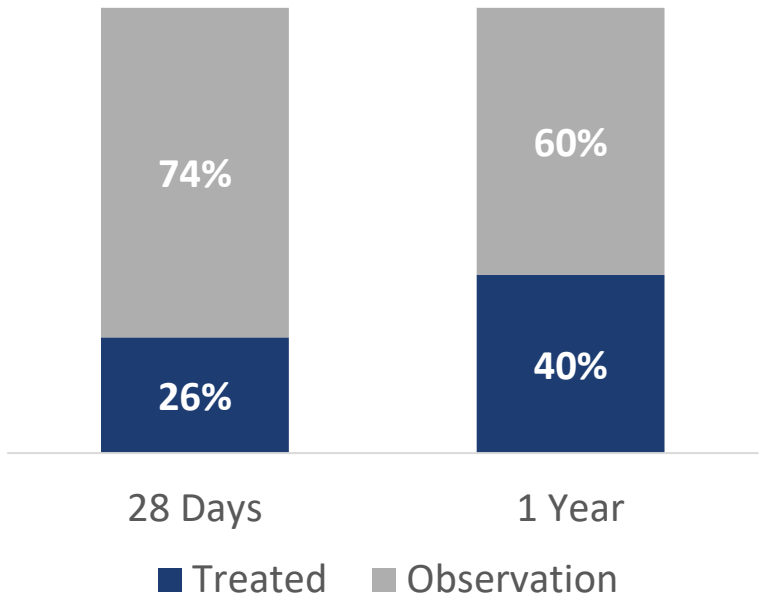
DME Is a Leading Cause of Vision Loss in Working-Age Adults, but Many Patients Are Left Untreated[1]

TREATMENT RATE IN NEWLY DIAGNOSED DME[2,a]



DME affects a **working-age population** and is typically **diagnosed at** an average age of **52 years** [1,2]

Patients with less severe and early-stage DME are not often treated due to the risk/benefit of the invasive therapy options[3]

Of those treated with an anti-VEGF, **40% have an inadequate treatment response** defined as BCVA gain < 5-letters[4]

[a]Real-world data from the American Academy of Ophthalmology (AAO) IRIS Registry. DME, diabetic macular edema; VEGF, vascular endothelial growth factor.

1. Ciulla TA, et al. *Diabetes Care.* 2003;26:2653–2664. 2. Petrella RJ, et al. *J Ophthalmol.* 2012;2012:159167. 3. Baker CW, et al. *JAMA.* 2019;321(19):1880-1894. 4. Gonzalez VH, et al. *Am J Ophthalmol.* 2016;172:72-79.

DME AWARE Delphi Study

Establishing consensus across three specific areas of unmet needs in the continuum of DME patient management:

1

Patient Journey

Early-stage patients, suboptimal responders, refractory patients, and reducing the burden associated with treatment

2

Early Detection, Diagnosis, Monitoring, and Management

Current and future management of DME patients

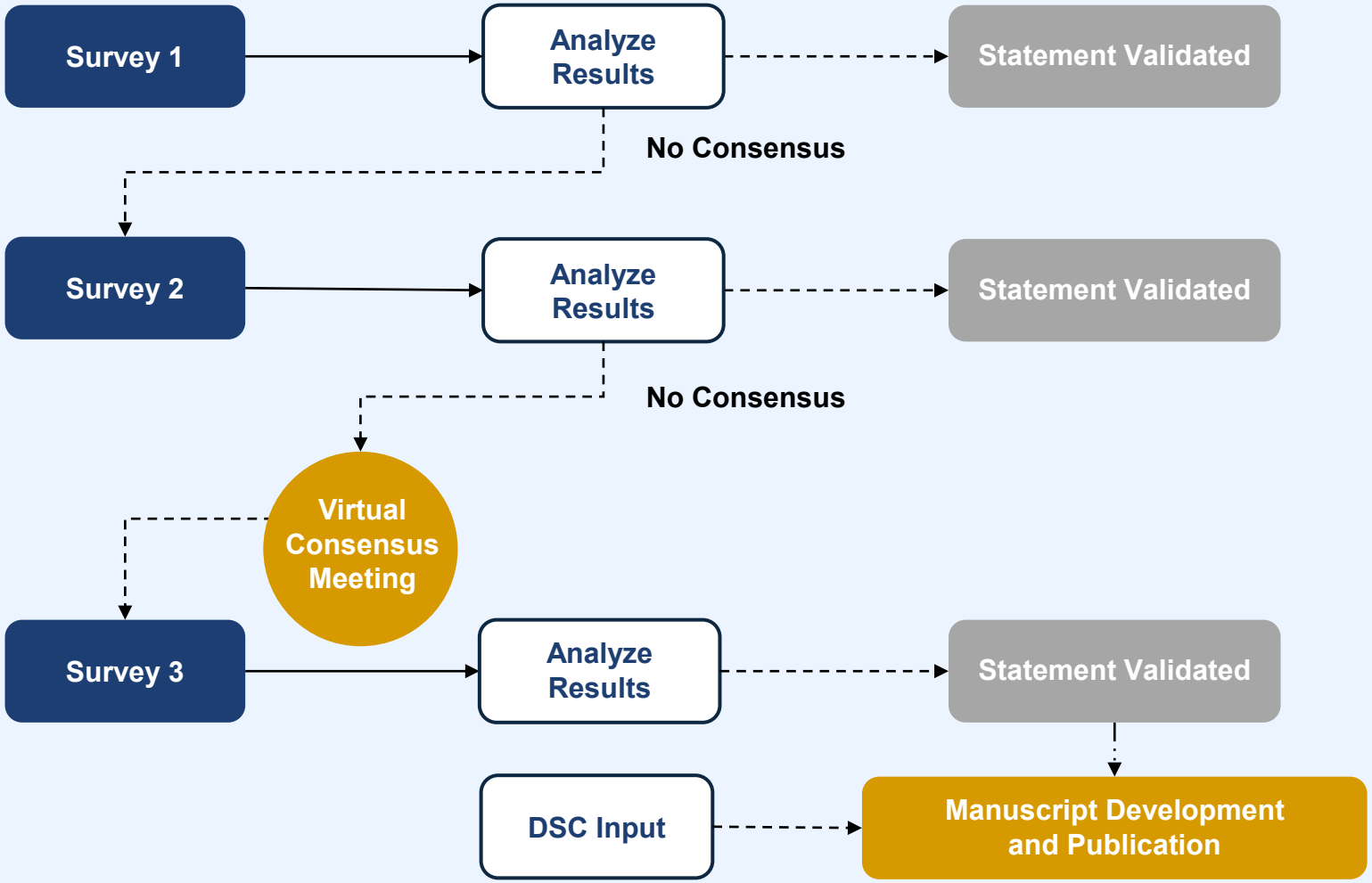
3

Ideal Attributes for Current and Future Treatments Across Patient Segments

Comprised of 25 leading global retina and ophthalmology experts
Delphi Steering Committee (DSC) and Delphi Panel (DP)

DSC: Arshad Khanani, David Boyer, Anat Loewenstein, Frank G. Holz, and Eric Donnenfeld
DP: Barry Kuppermann, Peter Kaiser, Jeffrey Heier, Veeral Sheth, Diana Do, Quan Nguyen, Sophie Bakri, Christina Weng, Adrienne Scott, Carl Danzig, Courtney Crawford, Eric Souied, Jordi Mones, Thomas Wolfensberger, Giovanni Staurenghi, Sobha Sivaprasad, Kuldev Singh, Chris Starr, Zaina Al-Mohtaseb, John Berdahl, Marjan Farid, Preeya Gupta, Liz Yeu

DME AWARE Modified Delphi Methodology

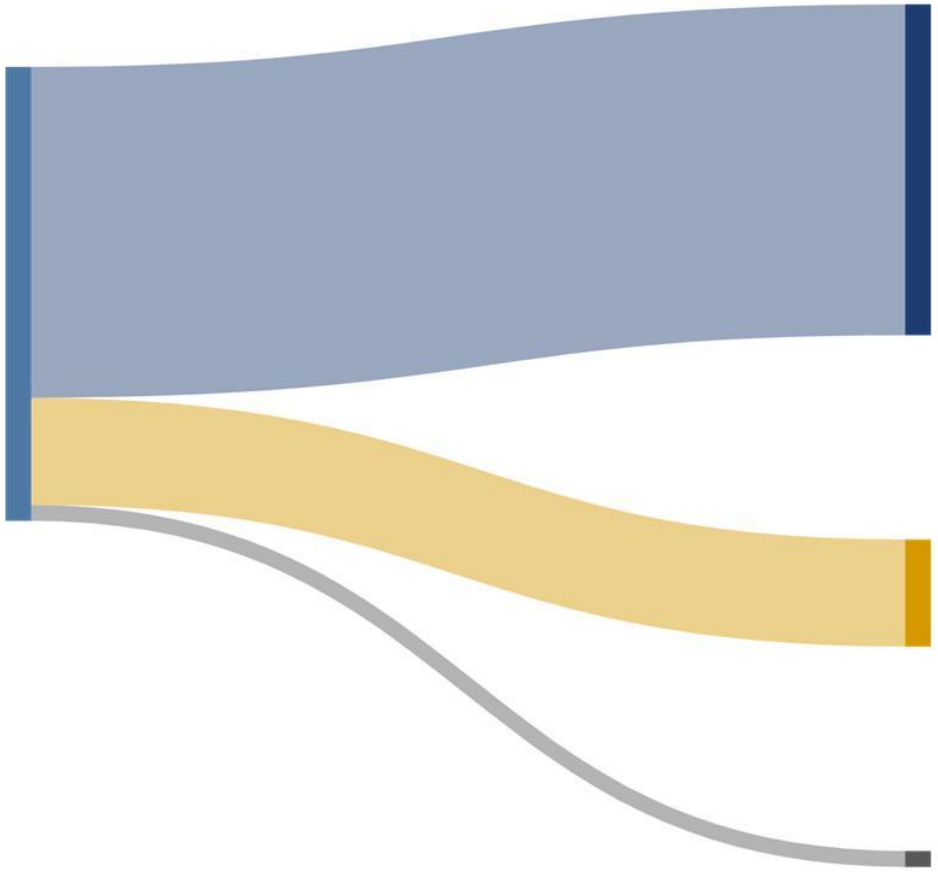


DSC: Delphi Steering Committee

20 Global Experts Responded to 284 Statements Across 3 Surveys

284

Total Statements



Survey 1
207 Statements

Survey 2
67 Statements

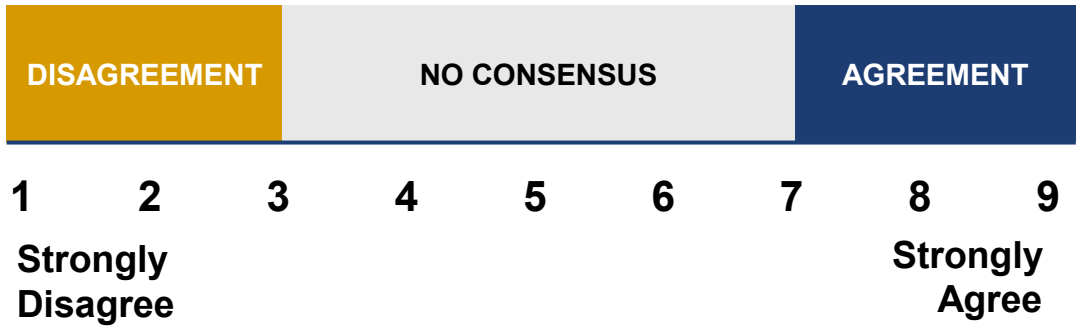
Survey 3
10 Statements

DME AWARE Modified Delphi Methodology

QUESTION TYPES

1. **Likert statements and multiple-choice questions**: for consensus
2. **Open-response questions:** to generate insights and refine subsequent surveys

9-POINT LIKERT SCALE STATEMENTS



Median Likert score reflects **decisiveness**
(1 = Strongly disagree, 9 = Strongly agree)

Disagreement index (DI) reflects **alignment**
(≤1 = Significant Alignment, >1 = Significant Variability)

CONSENSUS REQUIREMENTS

LIKERT STATEMENT

Decisive	+	Aligned
Median Likert Score ≤3 or ≥7		DI ≤1

MULTIPLE CHOICE

≥70% agreement

67%

(190/284)

consensus achieved in surveys 1 to 3

DME AWARE Modified Delphi Methodology

Understanding Consensus for Likert-Scale Statements

For each statement, experts selected a number from 1 to 9

Lower scores means disagreement.

Higher scores means agreement.

Considering n=20 experts, results were calculated as follows

5 | 6 | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9

MEDIAN

Median was calculated as the average of the 10th and 11th values.

8 | 8 = **8** (Average)

Agreement

DISAGREEMENT INDEX (DI)

Measures how much expert responses vary.

DI <1 indicates **alignment** (no significant variation)

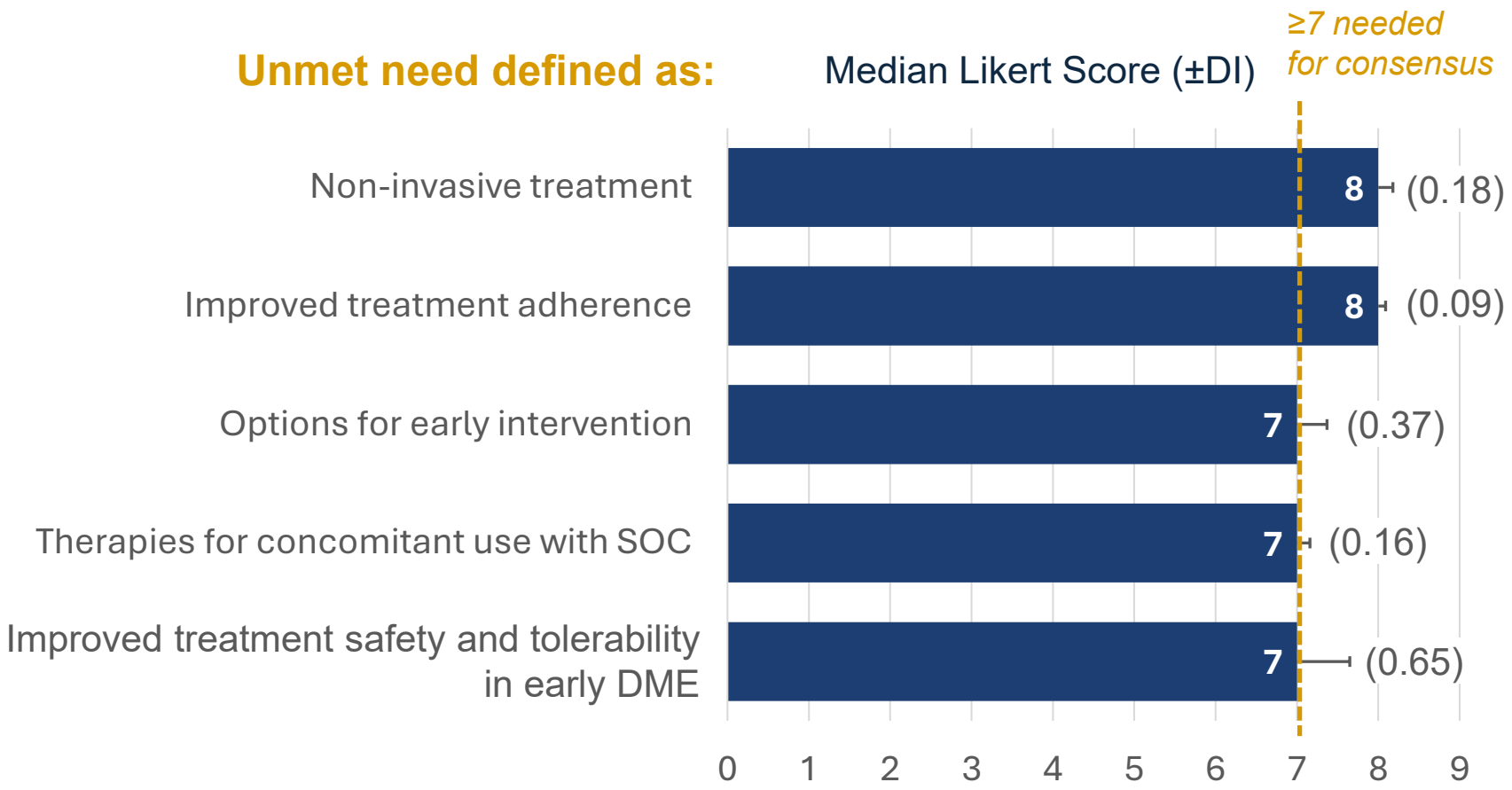
Consensus: Median Likert Score ≤3 or ≥7 and DI <1

Overview of Key Consensus Findings

1. **Significant Unmet Needs in DME**
2. **Goals of Early Intervention in DME**
3. **Definition of Early Detection and Intervention in DME**
4. **Definition of Poor and Non-response in DME**
5. **Preferred Treatment Approach for Early Intervention in DME**

Global Consensus on **Significant Unmet Needs in DME**

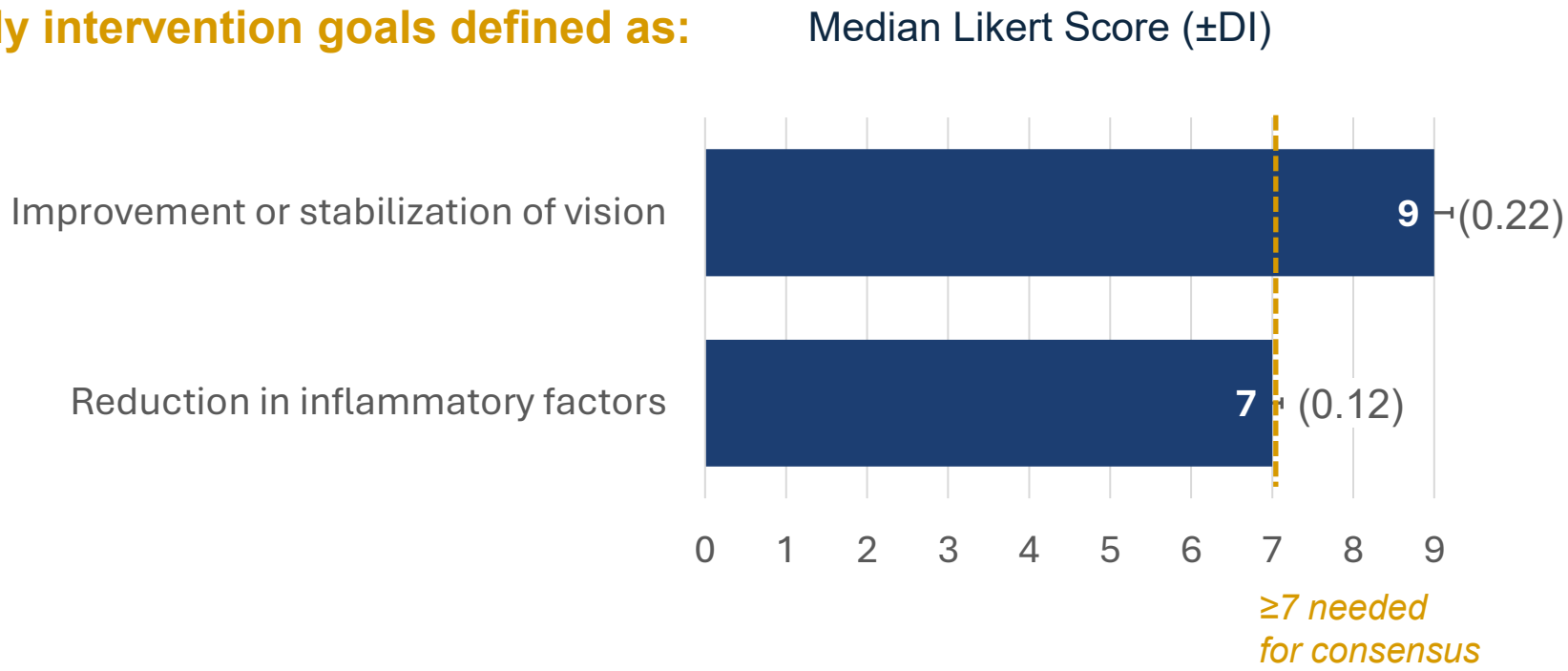
Unmet need for **non-invasive therapies, early intervention** and **concomitant use** with current standard of care



Global Consensus on **Early Intervention Goals in DME**

Early treatment intervention aims to **improve or stabilize vision and reduce** inflammation

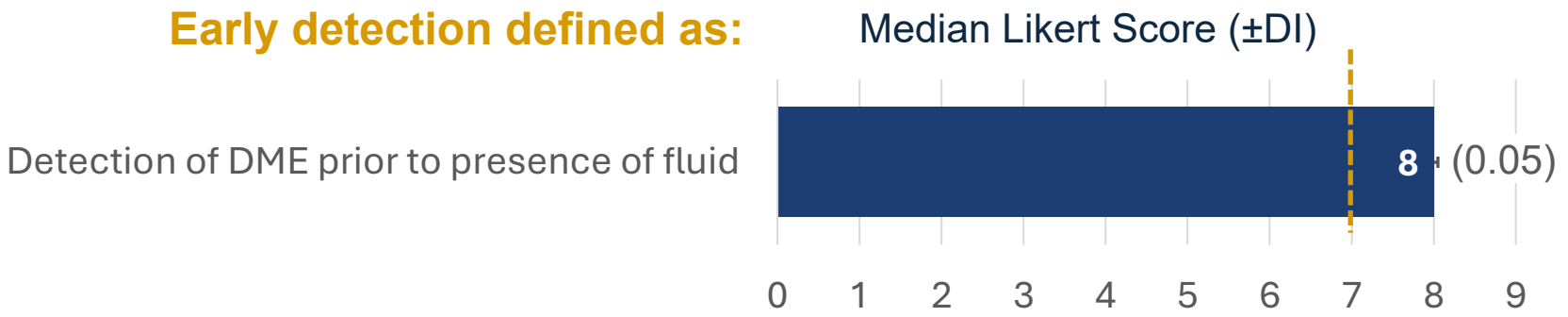
Early intervention goals defined as:



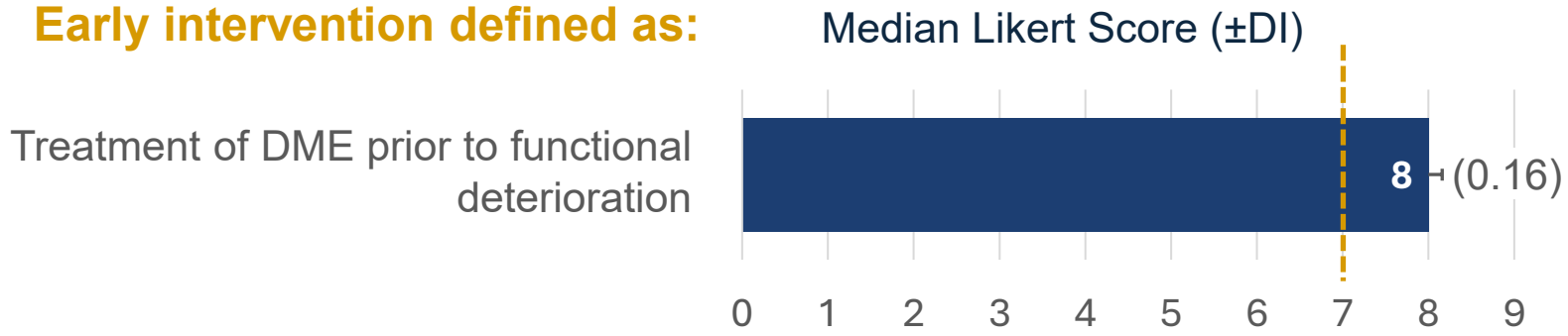
Global Consensus on Early Detection and Intervention in DME

Consensus on **early detection** prior to presence of fluid and **early intervention** prior to functional deterioration

Early detection defined as:



Early intervention defined as:



≥7 needed for consensus

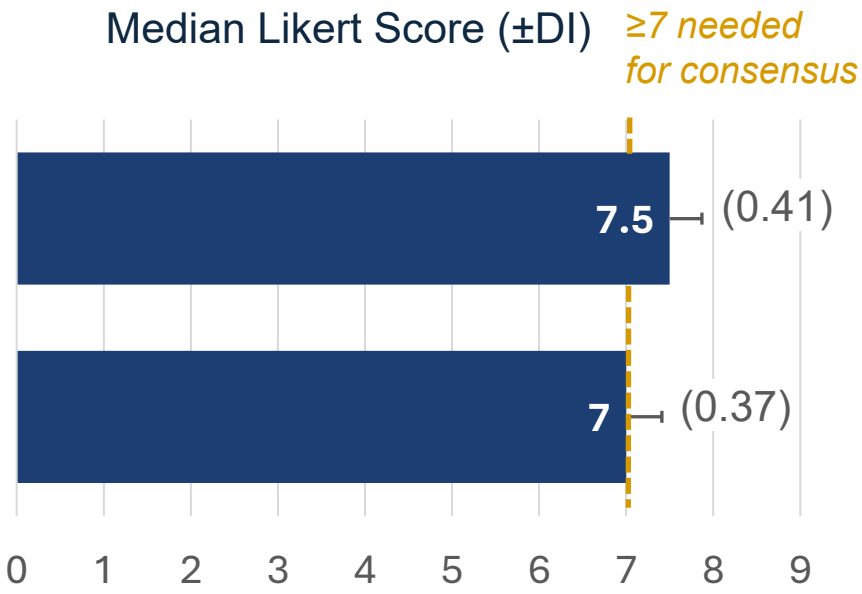
Global Consensus on **Response to Treatment Evaluation**

Response to treatment evaluation guided by both **visual function** and **retinal thickening**

Poor/Non-response to treatment definition/statement:

Poor response to treatment can be defined as <10% reduction in retinal thickness from baseline CST ≥350 µm

Visual function should be used to help define non-response to DME treatment



75% rely on intraretinal fluid (IRF) over subretinal fluid (SRF) as a key factor beyond macular volume in assessing/defining retinal thickening in DME

Global Consensus on **Early Intervention in DME**

Strong need for **non-invasive treatment options** **for early intervention** in DME

≥1-line loss BCVA (from 20/20)

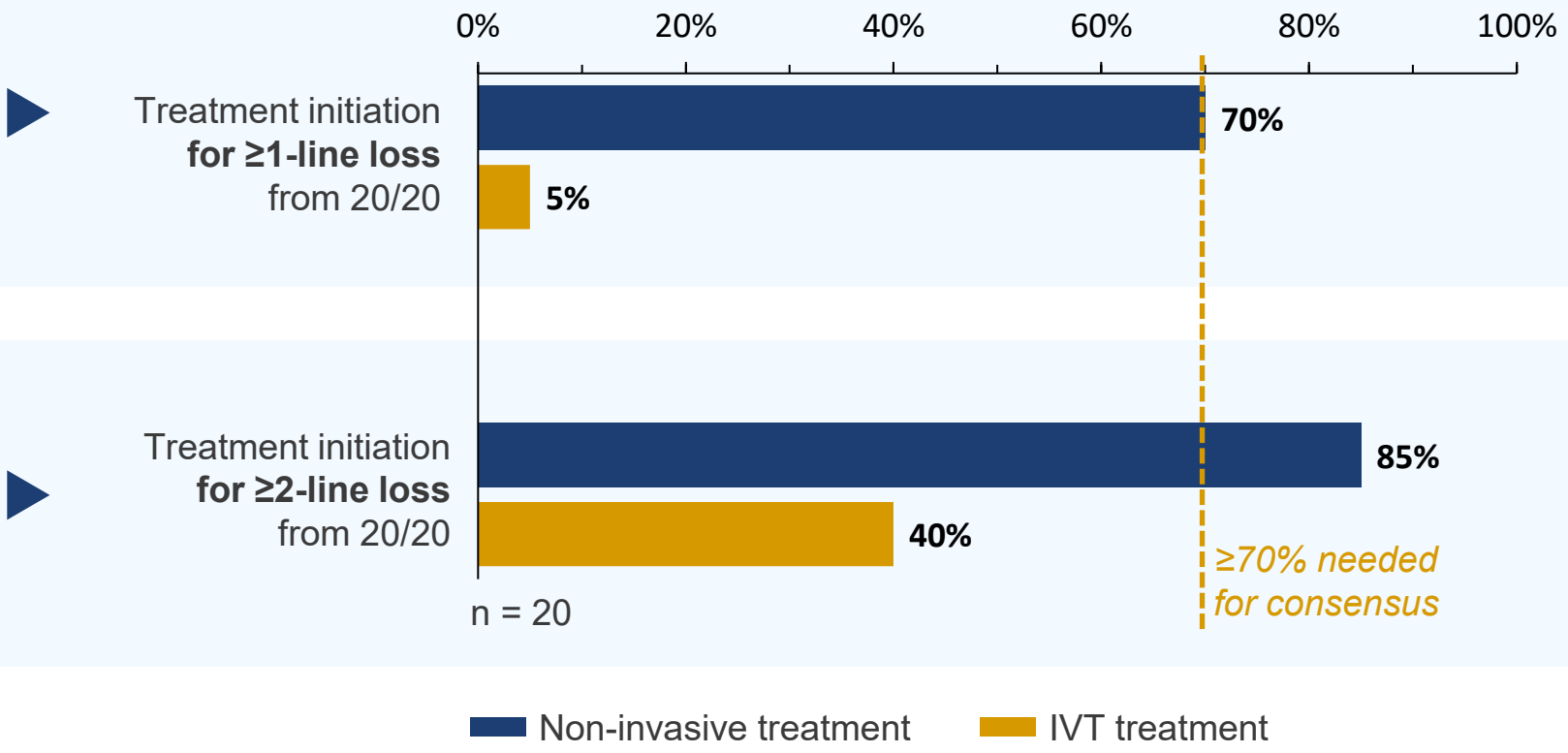
70% agreed on early intervention **with non-invasive treatment**

5% agreed on early intervention **with IVT treatment**

≥2-line loss BCVA (from 20/20)

85% agreed on early intervention **with non-invasive treatment**

40% agreed on early intervention **with IVT treatment**



Highlights from the DME AWARE Delphi Study

1. **Significant unmet needs for early intervention and concomitant treatments**
2. **Early intervention aims to improve or stabilize vision and reduce inflammation**
3. **Strong need for non-invasive treatment options for early intervention**

A manuscript detailing the complete results of the DME Aware Delphi Study is underway.

Thank You!

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