

Improving Clinical Management of Diabetic Macular Edema: Insights from a Global Survey of Patients, Healthcare Providers, and Clinic Staff

Focke Ziemssen,¹ Michelle Sylvanowicz,² Winfried M. Amoaku,³ Tariq Aslam,⁴ Bora Eldem,⁵ Robert P. Finger,⁶ Richard P. Gale,⁷ Laurent Kodjikian,⁸ Jean-François Korobelnik,⁹ Xiaofeng Lin,¹⁰ Anat Loewenstein,¹¹ Paul Mitchell,¹² Moira Murphy,¹³ David R. Owens,¹⁴ Nick Parker,¹⁵ Ian Pearce,¹⁶ Francisco J. Rodríguez,¹⁷ Jude Stern,¹⁸ S. James Talks,¹⁹ David T. Wong,²⁰ Tien Yin Wong,²¹ Jane Barratt²²

¹Department of Ophthalmology, University Hospital Leipzig, Leipzig, and Centre for Ophthalmology, Eberhard Karl

University of Tübingen, Tübingen, Germany; ²Bayer Consumer Care AG, Basel, Switzerland; ³Queen's Medical

Centre, Nottingham, UK; ⁴Manchester Royal Eye Hospital, NHS Central Manchester University Hospitals and

University of Manchester, Manchester, UK; ⁵Department of Ophthalmology, Hacettepe University, Ankara, Turkey;

⁶Department of Ophthalmology, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany;

⁷York and Scarborough Teaching Hospital NHS Foundation Trust, York, UK; ⁸Service d'Ophtalmologie, Hôpital

Universitaire de la Croix-Rousse, Hospices Civils de Lyon, Lyon, France, and Laboratoire UMR-CNRS 5510 MATEIS,

INSA, Université Lyon 1, Villeurbanne, France; ⁹Service d'Ophtalmologie, CHU Bordeaux, Bordeaux, France, and

Universitaire Bordeaux, INSERM, BPH, UMR1219, F-33000 Bordeaux, France; ¹⁰Zhongshan Ophthalmic Center, Sun

Yat-sen University, Guangdong Provincial Key Laboratory of Ophthalmology and Visual Science, Guangzhou, China;

¹¹Department of Ophthalmology, Tel Aviv Medical Center, Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel;

¹²University of Sydney (Westmead Institute for Medical Research), Sydney, NSW, Australia; ¹³Exploristics Ltd,

Belfast, Northern Ireland, UK; ¹⁴Swansea University Medical School, Swansea, Wales, UK; ¹⁵The International

Agency for the Prevention of Blindness, London, UK; ¹⁶Royal Liverpool University Hospital, Liverpool, UK;

¹⁷Fundación Oftalmología Nacional, Escuela de Medicina y Ciencias de la Salud, Universidad del Rosario, Bogotá,

Colombia; ¹⁸The International Agency for the Prevention of Blindness, Sydney, Australia; ¹⁹The Newcastle upon Tyne

Hospitals NHS Foundation, Newcastle upon Tyne, UK; ²⁰Department of Ophthalmology and Vision Sciences,

University of Toronto and Unity Health Toronto, St. Michael's Hospital, Toronto, ON, Canada; ²¹Tsinghua Medicine,

School of Clinical Medicine, Beijing, China and Singapore Eye Research Institute, Singapore National Eye Center,

Singapore; ²²International Federation on Ageing, Toronto, ON, Canada.

Corresponding author:

Professor Focke Ziemssen

University Eye Clinic

University of Leipzig

Leipzig

Germany

Telephone: +49 (0) 341 97 216 50

Fax: +49 (0) 341 97 216 59

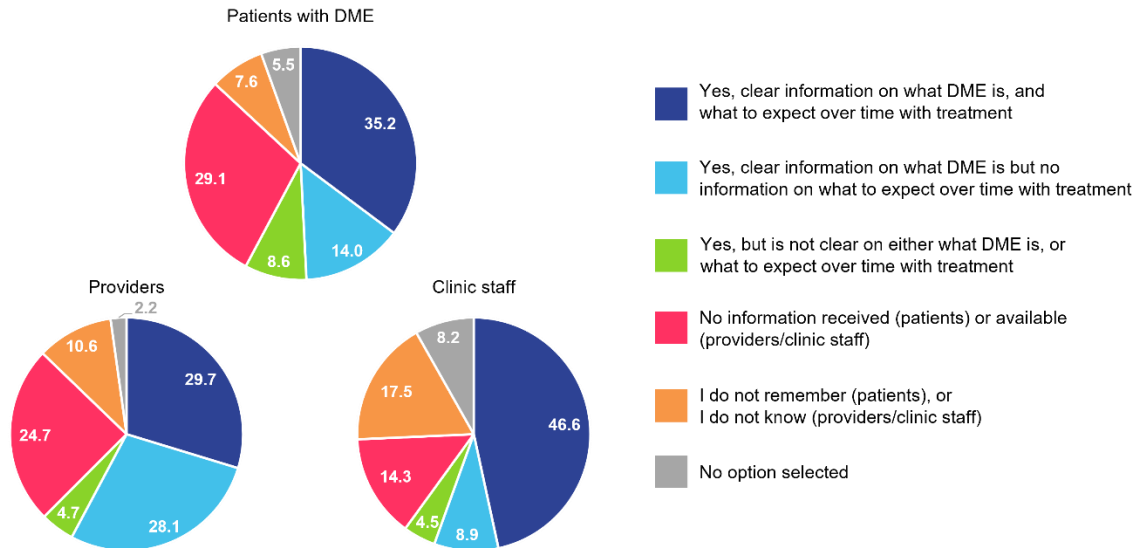
focke.ziemssen@medizin.uni-leipzig.de

Contents

Supplementary materials	3
Figure S1.....	3
Figure S2.....	4
Table S1.....	5
Table S2.....	6
Table S3.....	7
Table S4.....	12
Table S5.....	13
Appendices	14
Appendix 1. The opening pages of the survey (including covering informed consent).....	14
Appendix 2. List of clinics.	18
Appendix 3. Survey information and definitions.	20
Appendix 4. Additional demographics information.	22

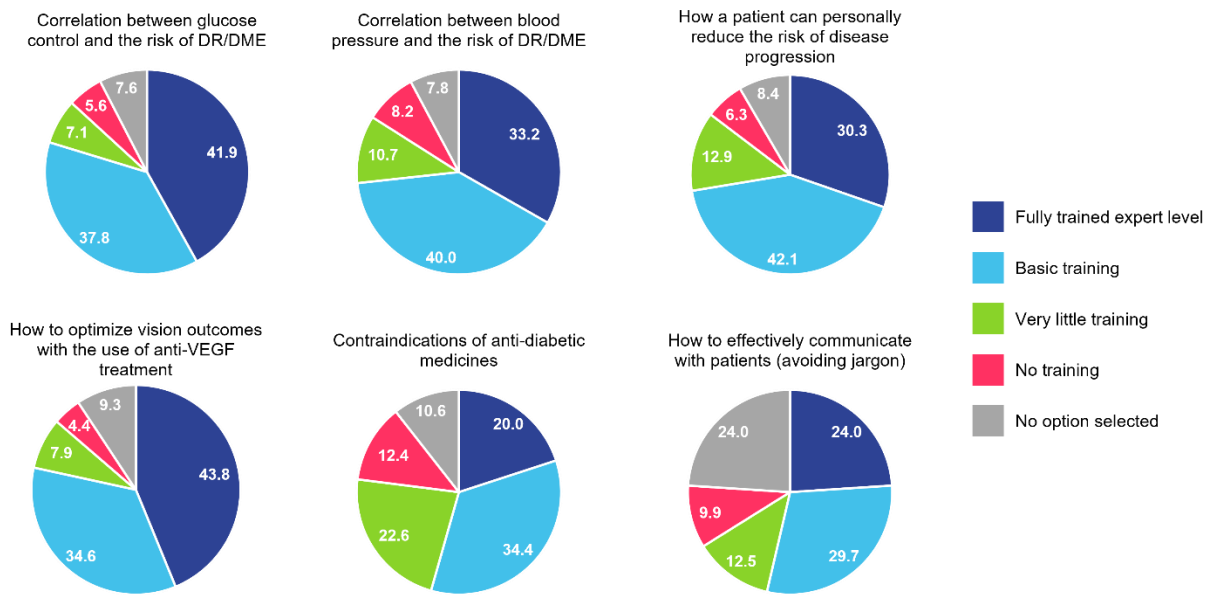
Supplementary materials

Figure S1. Levels of information received, or available, for patients concerning their disease and/or treatment.



Patients, providers, and clinic staff were asked about the level of information they either received or could provide on DME. DME, diabetic macular edema.

Figure S2. Providers' level of agreement with formal training received on aspects of DR/DME patient care.



DME, diabetic macular edema; DR, diabetic retinopathy; VEGF, vascular endothelial growth factor.

Table S1. Survey completion by country and participant type.

	Total number of DME patients (%) (N=3752)	Total number of providers (%) (N=680)	Total number of clinic staff (%) (N=1249)
Overall	3752 (100.0)	680 (100.0)	1249 (100.0)
Australia	100 (2.7)	2 (0.3)	13 (1.0)
Brazil	75 (2.0)	18 (2.6)	35 (2.8)
Canada	107 (2.9)	4 (0.6)	29 (2.3)
China	527 (14.0)	105 (15.4)	0 (0.0)
Colombia	325 (8.7)	56 (8.2)	199 (15.9)
Croatia	23 (0.6)	0 (0.0)	3 (0.2)
Ethiopia	203 (5.4)	3 (0.4)	16 (1.3)
France	28 (0.7)	7 (1.0)	20 (1.6)
Germany	77 (2.1)	39 (5.7)	34 (2.7)
Ghana	38 (1.0)	2 (0.3)	12 (1.0)
Greece	130 (3.5)	4 (0.6)	3 (0.2)
India	417 (11.1)	55 (8.1)	144 (11.5)
Indonesia	267 (7.1)	25 (3.7)	111 (8.9)
Israel	54 (1.4)	15 (2.2)	14 (1.1)
Kenya	61 (1.6)	4 (0.6)	11 (0.9)
Kuwait	63 (1.7)	14 (2.1)	39 (3.1)
Mexico	558 (14.9)	122 (17.9)	206 (16.5)
Nigeria	188 (5.0)	37 (5.4)	132 (10.6)
Portugal	97 (2.6)	25 (3.7)	54 (4.3)
Russia	188 (5.0)	88 (12.9)	109 (8.7)
Saudi Arabia	38 (1.0)	0 (0.0)	0 (0.0)
Switzerland	18 (0.5)	3 (0.4)	10 (0.8)
Turkey	151 (4.0)	46 (6.8)	34 (2.7)
UAE	19 (0.5)	6 (0.9)	21 (1.7)

DME, diabetic macular edema; UAE, United Arab Emirates.

Table S2. Summary of key clinic demographic characteristics.

	Parameter	Total n (%) (N=78)
Clinic setting	Standalone eye clinic independent of another medical department	41 (52.6)
	Eye clinic within a hospital	21 (26.9)
	Eye clinic within a multi-discipline clinic	14 (17.9)
	Other	2 (2.6)
Clinic location	Urban setting (i.e., large metropolis city)	70 (89.7)
	Suburban setting (i.e., residential area outside of a large city)	5 (6.4)
	Rural setting (i.e., countryside)	3 (3.8)
Clinic sector	Public	31 (39.7)
	Private	29 (37.2)
	Combined/mixed (e.g., public/private)	18 (23.1)
	<25% private	3 (16.7)
	≥25% and <50% private	5 (27.8)
	≥50% and <75% private	4 (22.2)
	≥75% private	5 (27.8)
Number of staff in clinics	Missing	1 (5.6)
	Eye surgeon(s)	1334 (17.4)
	Nurse(s)	1322 (17.2)
	General ophthalmologist(s)	1247 (16.3)
	Resident medical student(s)	1059 (13.8)
	Medical assistant(s)	886 (11.6)
	Optometrist(s)	564 (7.4)
	Retinal specialist(s)	524 (6.8)
	Scheduling administrator(s)	442 (5.8)
	OCT technician(s)	292 (3.8)

Data collected from clinic primer. OCT, optical coherence tomography.

Table S3. Summary of the importance of opportunities to provide better support for managing DME from the patients', providers', and clinic staff's perspectives.

Statement	Total number of DME patients n (%) N=3752	Total number of providers n (%) N=680	Total number of clinic staff n (%) N=1249
Appointment reminders sent by the clinic			
Extremely important	1941 (51.7)	314 (46.2)	732 (58.6)
Very important	1077 (28.7)	292 (42.9)	377 (30.2)
Slightly important	330 (8.8)	66 (9.7)	86 (6.9)
Not important	292 (7.8)	4 (0.6)	24 (1.9)
No option selected	112 (3.0)	4 (0.6)	30 (2.4)
Transportation assistance to attend treatment/office visits			
Extremely important	1284 (34.2)	182 (26.8)	375 (30.0)
Very important	1118 (29.8)	283 (41.6)	436 (34.9)
Slightly important	613 (16.3)	168 (24.7)	326 (26.1)
Not important	581 (15.5)	41 (6.0)	77 (6.2)
No option selected	156 (4.2)	6 (0.9)	35 (2.8)
Financial assistance with office/parking fees			
Extremely important	1193 (31.8)	167 (24.6)	321 (25.7)
Very important	960 (25.6)	238 (35.0)	390 (31.2)
Slightly important	607 (16.2)	185 (27.2)	359 (28.7)
Not important	814 (21.7)	84 (12.4)	135 (10.8)
No option selected	178 (4.7)	6 (0.9)	44 (3.5)
Financial assistance with DR/DME drug/prescription costs			
Extremely important	1702 (45.4)	294 (43.2)	441 (35.3)
Very important	1039 (27.7)	265 (39.0)	489 (39.2)
Slightly important	431 (11.5)	92 (13.5)	220 (17.6)
Not important	421 (11.2)	23 (3.4)	57 (4.6)
No option selected	159 (4.2)	6 (0.9)	42 (3.4)
Ability to monitor vision accurately with a home monitoring machine			
Extremely important	1384 (36.9)	182 (26.8)	353 (28.3)
Very important	1131 (30.1)	332 (48.8)	500 (40.0)
Slightly important	646 (17.2)	140 (20.6)	274 (21.9)
Not important	413 (11.0)	23 (3.4)	75 (6.0)
No option selected	178 (4.7)	3 (0.4)	47 (3.8)

Medical services/treatment that travel to or near the patient's home			
Extremely important	1388 (37.0)	183 (26.9)	362 (29.0)
Very important	1205 (32.1)	308 (45.3)	518 (41.5)
Slightly important	579 (15.4)	154 (22.6)	271 (21.7)
Not important	414 (11.0)	28 (4.1)	53 (4.2)
No option selected	166 (4.4)	7 (1.0)	45 (3.6)
Dedicated nurse in the clinic to provide guidance to improve diabetes management and answer questions about DR/DME			
Extremely important	1566 (41.7)	240 (35.3)	516 (41.3)
Very important	1254 (33.4)	308 (45.3)	498 (39.9)
Slightly important	486 (13.0)	63 (20.7)	159 (12.7)
Not important	283 (7.5)	5 (1.6)	39 (3.1)
No option selected	163 (4.3)	4 (1.3)	37 (3.0)
More time for the doctor to answer questions/concerns at each appointment			
Extremely important	1695 (45.2)	269 (39.6)	565 (45.2)
Very important	1277 (34.0)	330 (48.5)	535 (42.8)
Slightly important	404 (10.8)	67 (.9)	107 (8.6)
Not important	233 (6.2)	5 (0.7)	11 (0.9)
No option selected	143 (3.8)	9 (1.3)	31 (2.5)
Extra time with the doctor to plan the next 6 months of treatment			
Extremely important	1485 (39.6)	212 (31.2)	433 (34.7)
Very important	1406 (37.5)	342 (50.3)	568 (45.5)
Slightly important	468 (12.5)	61 (20.0)	178 (14.3)
Not important	235 (6.3)	3 (1.0)	29 (2.3)
No option selected	158 (4.2)	5 (1.6)	41 (3.3)
Phone consultations to answer any questions/concerns			
Extremely important	1615 (43.0)	171 (25.1)	490 (39.2)
Very important	1295 (34.5)	281 (41.3)	489 (39.2)
Slightly important	429 (11.4)	178 (26.2)	207 (16.6)
Not important	253 (6.7)	40 (5.9)	29 (2.3)
No option selected	160 (4.3)	10 (1.5)	34 (2.7)
Always having the same clinic staff and doctor treating the patient			
Extremely important	1948 (51.9)	230 (33.8)	427 (34.2)
Very important	1165 (31.1)	295 (43.4)	471 (37.7)
Slightly important	404 (10.8)	119 (17.5)	265 (21.2)
Not important	107 (2.9)	23 (3.4)	50 (4.0)
No option selected	128 (3.4)	13 (1.9)	36 (2.9)

Proactive discussion by doctor/clinic staff about any challenges the patient may have			
Extremely important	1822 (48.6)	241 (35.4)	476 (38.1)
Very important	1319 (35.2)	346 (50.9)	582 (46.6)
Slightly important	358 (9.5)	72 (10.6)	131 (10.5)
Not important	101 (2.7)	5 (0.7)	16 (1.3)
No option selected	152 (4.1)	16 (2.4)	44 (3.5)
If DME in both eyes, treat both eyes on the same day			
Extremely important	1390 (37.0)	207 (30.4)	439 (35.1)
Very important	935 (24.9)	185 (27.2)	429 (34.3)
Slightly important	547 (14.6)	158 (23.2)	243 (19.5)
Not important	703 (18.7)	121 (17.8)	99 (7.9)
No option selected	177 (4.7)	9 (1.3)	39 (3.1)
Less frequent appointments without losing vision			
Extremely important	1531 (40.8)	270 (39.7)	361 (28.9)
Very important	1283 (34.2)	335 (49.3)	558 (44.7)
Slightly important	504 (13.4)	22 (7.2)	259 (20.7)
Not important	233 (6.2)	2 (0.7)	36 (2.9)
No option selected	201 (5.4)	2 (0.7)	35 (2.8)
Longer time in between treatments without losing vision			
Extremely important	1586 (42.3)	296 (43.5)	395 (31.6)
Very important	1200 (32.0)	293 (43.1)	529 (42.4)
Slightly important	524 (14.0)	73 (10.7)	253 (20.3)
Not important	245 (6.5)	9 (1.3)	32 (2.6)
No option selected	197 (5.3)	9 (1.3)	40 (3.2)
Lifting of reimbursement restrictions			
Extremely important	1391 (37.1)	262 (38.5)	399 (31.9)
Very important	1028 (27.4)	258 (37.9)	438 (35.1)
Slightly important	492 (13.1)	108 (15.9)	267 (21.4)
Not important	495 (13.2)	31 (4.6)	74 (5.9)
No option selected	346 (9.2)	21 (3.1)	71 (5.7)
Regular treatment (monthly/bi-monthly) in the 1st year and then reduced treatment (couple of times a year) afterwards			
Extremely important	1409 (37.6)	321 (47.2)	591 (47.3)
Very important	1270 (33.8)	300 (44.1)	521 (41.7)
Slightly important	619 (16.5)	43 (6.3)	74 (5.9)
Not important	251 (6.7)	5 (0.7)	25 (2.0)
No option selected	203 (5.4)	11 (1.6)	38 (3.0)

An information pack for a supervisor/teacher to explain DR/DME and the need for frequent eye appointments to justify missed time at work/school			
Extremely important	1064 (28.4)	218 (32.1)	524 (42.0)
Very important	1065 (28.4)	320 (47.1)	529 (42.4)
Slightly important	667 (17.8)	114 (16.8)	137 (11.0)
Not important	712 (19.0)	19 (2.8)	20 (1.6)
No option selected	244 (6.5)	9 (1.3)	39 (3.1)
Opportunity to join a peer-to-peer support group			
Extremely important	907 (24.2)	199 (29.3)	382 (30.6)
Very important	964 (25.7)	303 (44.6)	518 (41.5)
Slightly important	821 (21.9)	152 (22.4)	259 (20.7)
Not important	850 (22.7)	16 (2.4)	56 (4.5)
No option selected	210 (5.6)	10 (1.5)	32 (2.7)
More involvement of the person who accompanies the patient in their care			
Extremely important	1052 (28.0)	230 (33.8)	446 (35.7)
Very important	1304 (34.8)	334 (49.1)	575 (46.0)
Slightly important	727 (19.4)	102 (15.0)	168 (13.5)
Not important	440 (11.7)	6 (0.9)	19 (1.5)
No option selected	229 (6.1)	8 (1.2)	41 (3.3)
Better material available to improve understanding of DR/DME			
Extremely important	1408 (37.5)	252 (37.1)	542 (43.4)
Very important	1305 (34.8)	320 (47.1)	555 (44.4)
Slightly important	624 (16.6)	91 (13.4)	103 (8.2)
Not important	221 (5.9)	7 (1.0)	12 (1.0)
No option selected	194 (5.2)	10 (1.5)	37 (3.0)
Coordination of diabetes appointments by a professional			
Extremely important	1517 (40.4)	269 (39.6)	531 (42.5)
Very important	1291 (34.4)	313 (46.0)	532 (42.6)
Slightly important	509 (13.6)	86 (12.6)	120 (9.6)
Not important	226 (6.0)	3 (0.4)	25 (2.0)
No option selected	209 (5.6)	9 (1.3)	41 (3.3)
Providing diabetes care services within the eye clinic			
Extremely important	1646 (43.9)	252 (37.1)	532 (42.6)
Very important	1228 (32.7)	288 (42.4)	491 (39.3)
Slightly important	481 (12.8)	114 (16.8)	133 (10.6)
Not important	216 (5.8)	17 (2.5)	36 (2.9)
No option selected	181 (4.8)	9 (1.3)	57 (4.6)

Providing eye care services within the diabetes clinic			
Extremely important	1573 (41.9)	280 (41.2)	559 (44.8)
Very important	1185 (31.6)	293 (43.1)	464 (37.1)
Slightly important	463 (12.3)	88 (12.9)	125 (10.0)
Not important	237 (6.3)	11 (1.6)	43 (3.4)
No option selected	294 (7.8)	8 (1.2)	58 (4.6)

DME, diabetic macular edema; DR, diabetic retinopathy.

Table S4. Summary of how informed patients feel regarding their disease, treatment, and available support options.

Statement	Total number of DME patients n (%) N=3752
Basic explanation of what DME is Agreement Disagreement	2967 (79.1) 478 (12.7)
Risk that DME could result in vision loss Agreement Disagreement	3003 (80.0) 431 (11.5)
Why DME is a chronic condition requiring long-term regular treatment Agreement Disagreement	2917 (77.7) 510 (13.6)
What to expect with vision changes over time with treatment Agreement Disagreement	2688 (71.6) 685 (18.3)
Different treatment options available Agreement Disagreement	2579 (68.7) 817 (21.8)
How the treatment works within the eye Agreement Disagreement	2334 (62.2) 1036 (27.6)
How often you would need treatment Agreement Disagreement	2629 (70.1) 720 (19.2)
How long you may need treatment for Agreement Disagreement	2470 (65.8) 861 (22.9)
What to expect after completing the first year of treatment Agreement Disagreement	2325 (62.0) 993 (26.5)
How treatment may reverse the progression of DME Agreement Disagreement	2483 (66.2) 854 (22.8)
How improved diabetes control may protect your vision Agreement Disagreement	2956 (78.8) 451 (12.0)
Personal steps you could take to reduce disease progression Agreement Disagreement	2786 (74.3) 598 (15.9)
How to include your family/friends in your care Agreement Disagreement	2500 (66.6) 908 (24.2)
Where to find more information on DME or support services Agreement Disagreement	1973 (52.6) 1276 (34.0)

Questions specifically regarding disease asked to appropriate cohort. DME, diabetic macular edema.

Table S5. Summary of anti-VEGF treatment regimens employed following initial monthly injections for the majority of patients with DME, according to clinics.

	For the first year of treatment (N=78)	Beyond the first year of treatment (N=78)
PRN with extended monitoring – as needed with extension of monitoring visits if deemed stable	20 (25.6)	32 (41.0)
Treat-and-extend type regimen – injection performed at every visit, with extension of visits if stable	18 (23.1)	16 (20.5)
PRN with monthly monitoring – as needed based on monthly monitoring	17 (21.8)	10 (12.8)
Fixed treatment intervals (e.g. 2q4, 2q8)	12 (15.4)	5 (6.4)
No set regimen – it varies by patient and/or physician choice	9 (11.5)	12 (15.4)
Treatment regimen is driven by clinic capacity	2 (2.6)	3 (3.8)

2q4, 2 mg anti-VEGF every 4 weeks; 2q8, 2 mg anti-VEGF every 8 weeks; DME, diabetic macular edema; PRN, pro re nata; VEGF, vascular endothelial growth factor.

Appendices

Appendix 1. The opening pages of the survey (including covering informed consent).

DR Barometer

Shifting the needle



DR Barometer Survey Diabetic Macular Edema Patient Survey

WHAT IS THE DR BAROMETER PROGRAMME?

- The DR Barometer is a programme dedicated to improving the vision health of people living with diabetes
- The survey has been developed by a group of experts that includes doctors and leaders from patient groups, in partnership with Bayer Pharmaceuticals
- The results will help to develop:
 - Resources and services to help support people living with DME
 - Guidance and tools to support doctors and staff who treat people living with DME

WHAT DOES THE SURVEY ASK ABOUT?

- We want to better understand your experience of living with DME and the care you receive
- We recognise the burden that comes with treatment, so we would like to understand what challenges you face and explore opportunities to support you
- The survey therefore includes questions on the following topics:
 - A little bit about yourself
 - Looking back to when you were diagnosed with DME
 - Discussions with the doctor who treats your DME
 - Treatment satisfaction so far
 - Challenges with attending appointments
 - A few more questions about yourself
- These questions refer to your experience in managing your condition outside of the Covid-19 pandemic, **please answer the questions based on 'normal' experiences (non-Covid-19).**
- If you have any questions, please let a member of the staff know

DO YOU QUALIFY FOR THIS SURVEY?

Firstly, it is important to make sure you qualify; this survey is intended for people who:

- have been diagnosed with Diabetic Retinopathy with macular edema also known as Diabetic Macular Edema (DME)*.



- **Diabetic macular edema is a condition where there is fluid and swelling in the back of an eye which may affect a person with diabetes' vision.*



- are currently being treated, or have been in the past, for their DME.

If you do not meet the above description, or if you are unsure, please see your healthcare team as there is a different survey available for those with Diabetic Retinopathy (DR) without macular edema.

INSTRUCTIONS

- This survey should take, on average, 30 minutes to complete
- Please use **PENCIL** only on this answer sheet.
- Please **DO NOT FOLD OR CREASE THIS SHEET**.
- Record your answers by making a heavy black mark that fills the circle.
- If you make a mistake please use a rubber eraser to remove your incorrect selection

RIGHT



WRONG



TERMS:

- When we refer to "**DME**", we mean your eye condition Diabetic Macular Edema.
- When we refer to your "**Doctor**", we mean the doctor who is treating you here in this clinic for your DME.
- When we refer to "**Treatment**", we mean the treatment for your DME (e.g. either an anti-VEGF treatment or steroid implant).

CONSENT TO PARTICIPATE:

Thank you for agreeing to participate in this market research survey conducted by Exploristics Research on behalf of the 'nAMD & DR Barometer Leadership Coalition', sponsored by Bayer, a pharmaceutical company.

- I understand that the aim of this research is to gain my views for market research purposes in the development of educational materials and is not intended as a promotional exercise.
- Any information presented during the course of this research is done so solely to explore reactions to such information and should be assumed to represent hypotheses of what can be said about a disease area
- I understand that I have the right to refuse to answer questions or withdraw at any time
- I understand that any information I disclose will be treated in the strictest confidence and the results of the research aggregated to provide an overall picture of attitudes to the areas being covered in this survey. This survey will not collect any personally identifying information, therefore I, and my responses, will remain anonymous

By completing this questionnaire, you are confirming that you have read, understood and accept the points above, and are happy to proceed with the market research survey on this basis.

Thank you for taking the time to help us to better understand your experience of living with DME and the areas in which your care could be improved.

Your participation will provide valuable insights allowing for meaningful improvements in future care.

TELL US A BIT ABOUT YOURSELF

1. How old are you?

- ☐ Less than 18 years [THANK YOU FOR YOUR TIME BUT YOU DO NOT QUALIFY]
- ☐ 18 - 29
- ☐ 30 - 39
- ☐ 40 - 49
- ☐ 50 - 59
- ☐ 60 - 69
- ☐ 70 - 79
- ☐ 80 - 89
- ☐ 90 years and above

2. Have you been diagnosed with Diabetic Macular Edema (DME) and are receiving, or have received in the past, treatment for your DME?

- ☐ Yes
- ☐ No [PLEASE SEE THE CLINIC STAFF TO CONFIRM YOUR DIAGNOSIS]
- ☐ I do not know [PLEASE SEE THE CLINIC STAFF TO CONFIRM YOUR DIAGNOSIS]

3. Which type of regular treatment are you currently receiving for your DME?

(Check all the apply)

- ☐ Anti-VEGF eye Injections (e.g. EYLEA, Lucentis, Avastin) which are injections in your eye given on a regular, frequent basis, such as monthly or every other month
- ☐ Steroids (e.g. Ozurdex) which is a treatment implanted in your eye requiring, on average, treatment every 6-8 months
- ☐ Laser Therapy
- ☐ I do not know [PLEASE SEE THE CLINIC STAFF TO CONFIRM WHICH TREATMENT YOU ARE CURRENTLY RECEIVING]

Appendix 2. List of clinics.

Country	Clinic
Australia	Australian Eye Specialists
	Retina Specialists Victoria
	Sydney West Retina
Brazil	CBV – Centro Brasileiro da Visão
	CEROF – Centro de Referência em Oftalmologia
	CRESEP – Hospital de Olhos de Araraquara
	Hospital Oftalmologico de Sorocaba
Canada	Eye Care Center NB
	Retina Center of Ottawa
	Unity Health Toronto
China	Henan Provincial People's Hospital
	Shanghai General Hospital
	The First Affiliated Hospital of Dalian Medical University
	The First Affiliated Hospital of Kunming Medical University
	Xi'an People's Hospital
	Zhongshan Ophthalmic Center of Sun Yat-sen University
Colombia	Cali Ophthalmology Clinic
	Clínica Foscal
	Clínica Oftalmológica del Caribe
	Clínica Oftalmologica Unigarro
	Fundacion Oftalmologica Nacional
Croatia	KBC Zagreb
Ethiopia	Biruh Vision Specialized Eye Care Center
	La Vista Speciality Eye Clinic
	Nisir Specialized Eye Clinic
	Roha Specialized Eye Clinic
France	Centre PO2 (Pôle Oise Ophtalmologie)
	Centre Rétine Gallien
	Hôpital de la Croix Rousse
Germany	Augenzentrum am St. Franziskus-Hospital
	Klinikum der Universitaet Muenchen
	Universitätsklinikum Bonn
	Universitätsklinikum Tübingen
Ghana	Tamale Teaching Hospital
Greece	Ophthalmological Clinic of University Hospital of Alexandroupolis
India	Hyderabad Eye Research Foundation, L V Prasad Eye Institute
	ICARE Eye Hospital
	Narayana Nethralaya Eye Hospital
	Prakash Netra Kendra
	Sankara Nethralaya
	Shroff Charity Eye Hospital
	Synergy Eye Care (previously called Visitech Eye Institute)

Indonesia	JEC Eye Hospitals & Clinics
	Netra Klinik Spesialis Mata - Bandung
	RS Khusus Mata Prov. Sumatera Selatan
	Sumatera Eye Center
Israel	The Medical Research, Infrastructure, and Health Services Fund of the Tel-Aviv Sourasky Medical Center
Kenya	City Eye Hospital
	Eldo Eye Clinic
	Lighthouse for Christ Eye Centre
Kuwait	Kuwait Specialized Eye Center
Mexico	Asociación para Evitar la Ceguera en México
	Dr. Roberto Nettel Flores General Hospital
	Fundación Hospital Nuestra Señora de la Luz, IAP
	Instituto Mexicano de Oftalmología IAP
	Sala Uno Ophthalmological Center
Nigeria	Department of Ophthalmology University of Uyo Teaching Hospital, Uyo, Akwa-Ibom State
	Department of Ophthalmology, Jos University Teaching Hospital, Jos
	Eye Clinic, Department of Ophthalmology, Faculty of Clinical Sciences, College of Health Sciences, Ahmadu Bello University Zaria
	Eye Foundation Hospital
	MDR-Lighthouse Medical Eye and Specialist Laser Center Lokoja
	University College Hospital, Ibadan
Portugal	ALM - Oftalmologia Médica e Cirúrgica
	Centro Hospitalar de Setúbal
	Centro Hospitalar Universitário de Coimbra
	Centro Hospitalar do Porto
Russia	Federal State Budgetary Institution “National Medical and Surgical Center named after N.I. Pirogov” of the Ministry of Healthcare of the Russian Federation
	Novosibirsk State Region Clinic Hospital
	The S. Fyodorov Eye Microsurgery Federal State Institution (Orenburg branch)
	Ufa Research Institute of Eye Diseases
Saudi Arabia	King Abd el Azez Medical City
Switzerland	Swiss Visio Montchoisi
Turkey	Ankara City Hospital
	Gaziantep University
	Hacettepe University
	Karadeniz Technical University Faculty of Medicine
United Arab Emirates	Medcare Eye Center
	Moorfields Hospital Abu Dhabi

Appendix 3. Survey information and definitions.

The Barometer Global Survey was developed based on a large-scale survey into diabetes. The diabetes survey collected information based on disease awareness, challenges accessing healthcare services, and experience within the clinic and with treatment, and encompassed all people with diabetes, regardless of if they had vision loss due to diabetic retinopathy (DR). Within this diabetes survey, questions on overall healthcare, access to screening, and potential DR were asked. The diabetes survey was a qualitative study, and was not validated systematically. The development of the diabetes survey was supported by the New York Academy of Medicine, in collaboration with the International Federation on Ageing, the International Association for the Prevention of Blindness, and the International Diabetes Federation.

The Barometer Global Survey was co-developed and reviewed by all authors (who are experts in retinal care), and piloted in two distinct studies in four clinics (in local languages): Singapore National Eye Center (SERI), Singapore; Centre for Ophthalmology Eberhard Karl University of Tübingen, Tübingen, Germany; Fundación Oftalmología Nacional, Universidad del Rosario, Bogotá, Colombia; and Department of Ophthalmology and Vision Sciences, St. Michael's Hospital, Toronto, ON, Canada. This ensured fit for purpose across different healthcare systems around the world, and that the survey was well-understood and consistent.

Clinics could select to receive the number of surveys they believed they could complete. For diabetic macular edema (DME) patient surveys, this was up to 100 per clinic (in intervals of 25). It was not possible to capture how many patients were subsequently asked to complete the survey.

Surveys were translated into languages appropriate for the country by a professional and certified translation company. These surveys were reviewed by native speaker experienced in retinal care against the original English version to ensure consistency and comprehension. Survey languages included Amharic, Arabic, Chinese (Simplified), Croatian, English, French, French (Canadian), German, Greek, Hebrew, Hindi, Indonesian, Kannada, Portuguese, Portuguese (Brazilian), Russian, Spanish, Tamil, and Turkish.

Across all surveys, there were a finite number of multiple-choice responses available per question and Likert scale questions to understand strength of opinion towards a statement. No free text answers were collected.

The final version of the patient survey consisted of 41 DME-related questions. Questions included personal characteristics (including, but not limited to, age, gender, race/ethnicity, education level, employment status, and diabetes type); disease information provided at diagnosis; challenges with attending appointments; treatment experiences; interaction with providers; and opportunities for improving support, clarifying expectations, and reducing perceived burden. The patient survey also explored treatment adherence and persistence (to be discussed in a future manuscript).

There were 27 questions in the provider survey, covering personal and practice characteristics; level of detail and frequency of discussion with patients; setting of treatment expectations; opportunities for improving outcomes; and demographic information, including age, profession, number of years in practice, and gender. The clinic staff survey contained 18 questions, covering aspects and perspectives of management of DR/DME. The clinic primer questionnaire had 21 questions, addressing clinic practice; adherence and persistence estimates; use of clinic audits; and demographic information, including clinic setting, location, and number of staff.

Definitions of adherence and persistence were previously developed by the Barometer Leadership Coalition,¹ of which many of the authors of this manuscript are members. These definitions were applied to patients who, at the time of the survey, were receiving or had previously received intravitreal anti-vascular endothelial growth factor (VEGF) treatment for their DME.

Adherent: The patient had missed a maximum of one appointment (treatment or monitoring visit as scheduled by the treating physician) by 2 or more weeks for any reason (not including COVID-19-related reasons) over the course of any given year. **Non-adherent:** The patient had missed two or more appointments (treatment or monitoring visit as scheduled by the treating physician) by 2 or more weeks for any reason (excluding COVID-19-related reasons) over the course of any given year. **Persistent:** The patient had maintained treatment or monitoring as advised by the treating physician and attended the most recent appointment within the last 6 months. **Non-persistent:** The patient did not attend any treatment or monitoring visits for any reason over a period of 6 months, and/or follow-up appointments are not scheduled for any reason for a period of 6 months (excluding COVID-19-related reasons).

The questions within the survey were designed to give guidance to patients as to how to fill in the correct answer regarding their adherence and persistence; however, this is self-reported.

Challenges associated with managing DR/DME were identified using key questions and statements from the patient, provider and clinic staff surveys. These questions and statements were grouped according to challenges associated with managing DR/DME from participants' perspectives.

A similar approach was taken to define opportunities to better support patients in managing their DR/DME. These were opportunities to provide better support for managing DR/DME from (1) participants' perspectives on a scale of importance from extremely important to not important; (2) participants' perspectives where patients, providers, and clinic staff are in agreement, and (3) provider and clinic staff perspectives related to scale of training level.

For additional analysis, the grouping of providers was as follows:

Profession Group A: Retinal Specialist (Medical and Surgery);

Profession Group B: General Ophthalmologist & Resident Doctor (who prescribes or administers anti-VEGF treatment);

Profession Group C: Ophthalmic Nurse (who administers anti-VEGF treatment).

The grouping of clinic staff was as follows:

Profession Group 1: Retina Specialist & Resident Doctor (both do not prescribe nor administer anti-VEGF treatment);

Profession Group 2: Optometrist, Medical Assistant & Ophthalmic Nurse (do not administer anti-VEGF treatment);

Profession Group 3: Scheduling Administrator, Ophthalmology Technician, Research Coordinator/Administrator & Other.

Appendix 4. Additional demographics, challenges, and opportunities information.

Clinic characteristics

Per week, 53.8% of clinics treat up to 50 patients, and 28.2% treat between 51 and 100 patients, with the remaining clinics reporting that they treat 101–≥300 patients. Most providers and clinic staff interact with up to 50 diabetic macular edema (DME) patients (67.1% providers, 60.1% clinic staff) per week.

The average wait time to schedule an appointment for a potential new patient is less than a week for 42.3% of patients, and half of the clinics having an average wait time of a week to less than a month for 47.4% of DME patients. For most patients in their clinic, 62.8% reported a time delay between DME diagnosis and treatment. Most clinics reported a delay of less than a month (less than 1 week: 30.6%, between 1 week to less than 2 weeks: 34.7%, between 2 weeks to less than 1 month: 24.5%); however, a minority reported delays up to 3 months. The most common average length of consultation appointment when a new patient is first diagnosed was between 10 to 15 minutes (30.8%). This was similar to during the maintenance phase of treatment; however, for a higher percentage of clinics (47.4%). Appointments were on average shorter during the maintenance phase of treatment.

Patients are not regularly contacted with appointment reminders for their disease in 43.6% of clinics; however, the remainder did employ reminders for patients. These reminders primarily consisted of a phone call (77.3% of clinics) or text message (45.5% of clinics).

Relevant patient information is shared by 39.7% of clinics with providers outside of the clinic who are responsible for other aspects of patient medical care; however, many clinics (26.9%) only share information concerning diabetes. Most clinics provide disease information about DME (59.0%) in print or digital form to patients, alongside other information resources such as nurse support (35.9%), telemedicine (25.6%), and peer-to-peer patient support groups (20.5%) or local support groups (9.0%). No clinics directed patients to websites with basic disease information.

Optional written protocols/guidelines are available in the clinic for the treatment and management of DME (33.3%); no written protocols/guidelines are available for the treatment of DME in 28.2% of clinics. The remaining clinics have written protocols/guidelines available in the clinic, which are followed strictly with (21.8%) or without (16.7%) electronic record verification. Clinics reported that over 80% of patients with DME receive anti-VEGF therapy as first-line treatment.

Clinic perception of adherence

61.0% of clinics had never conducted a systematic evaluation or audit of whether patients were adhering to scheduled appointments. Of these: 53.2% reported that they did not conduct clinic audits because they take too much time or resources; 34.0% reported that they do not systematically record appointment non-attendance; 21.3% reported they do not have an electronic database to extract data; 17.0% reported they did not know how best to audit patient appointment attendance; 17.0% reported that administration is not supportive of conducting a clinic audit; and 12.8% reported that they did not know how best to audit clinic outcomes. Most clinics (39.7%) estimated non-adherence to DME therapy to be between 11 and 20%.

Patient characteristics

Nearly a quarter of patients with DME received their diagnosis between 3 and 12 months ago (22.8%), and between 12 and 24 months ago (22.8%). In the majority of cases, patients were diagnosed by either the doctor who was treating their DME at the time of the survey (41.5%) or another ophthalmologist/retinal specialist (37.7%).

Most (73.2%) patients received intravitreal anti-VEGF injections for their DME; laser therapy (18.5%) and cortisone/steroids (9.6%) were also received. However, 8.3% of patients did not know the treatment they were receiving at the time of the survey. Patients with DME received their current treatment for less than 3 months (16.6%), 3 to <6 months (18.8%), 6 months to <1 year (20.5%), 1 year to <2 years (16.6%), 2 years to <3 years (9.4%), and 3 or more years (15.1%).

Table A depicts key information on issues surrounding reimbursement.

Table A. Key information on reimbursement for treatment, and educational program attendance

	Total number of DME patients n (%) N=3752
How are the costs for your DME treatment (cost of the drug) paid for?	
You personally cover the full costs	1286 (34.3)
It is fully covered by insurance or government funding	1314 (35.0)
You pay part of the costs and insurance or government covers the rest	1003 (26.7)
No option selected	149 (4.0)
Would you be willing to attend a diabetes and DME educational program if it resulted in financial assistance with your treatment/appointment costs?	
Yes	2656 (70.8)
No	818 (21.8)
No option selected	278 (7.4)

DME, diabetic macular edema.

Additional provider and clinic staff characteristics

The 680 providers comprised 305 (44.9%) retinal specialists (medical and surgery), 192 (28.2%) general ophthalmologists, 145 (21.3%) resident doctors (who prescribed/administered anti-VEGF therapies) and 20 (2.9%) ophthalmic nurses (who administered anti-VEGF therapies). No profession was selected by 18 (2.6%) providers. Of 1249 clinic staff, 282 (22.6%) were ophthalmic nurses who did not administer anti-VEGF therapies, 202 (16.2%) were optometrists, 139 (11.1%) medical assistants, 127 (10.2%) resident doctors who did not prescribe/administer anti-VEGF therapies, 82 (6.6%) scheduling administrators, 58 (4.6%) ophthalmology technicians, 53 (4.2%) research coordinators/administrators, 30 (2.4%) retina specialists who did not prescribe/administer anti-VEGF therapies), 257 (20.6%) who selected other, and 19 (1.5%) who did not select a profession. The majority of providers (63.1%) were under 40 years old; with 22.1% of providers aged between 18 and 29, and 41.0% aged between 30 and 39. Similar percentages of male (49.6%) and female (48.2%) providers responded to the survey; some variation was observed based on occupation (for example, retinal specialists comprised 60.0% male and 39.0% female providers).

Overall, 15.7% of providers had been in their profession less than 2 years, 29.3% between 2 and 5 years, 21.5% between 6 and 10 years, 16.3% between 11 and 20 years, 11.2% between 21 and 30 years, and 5.3% for over 30 years. The majority of clinic staff were under 40 years of age (18 to 29: 34.3%, 30 to 39: 35.1%). Retinal specialists or doctors not prescribing anti-VEGFs had the youngest demographic of clinic staff, with 90.4% aged under 40 years. Overall, there were more female staff (69.3%) than male; and most staff had been in their profession for either between 2 and 5 years (28.6%) or 6 to 10 years (21.2%) with some variation based on profession.

Additional clinic staff data

Clinic staff agreed that other chronic health conditions contributed significantly to how patients managed their disease (81.3%), and personal costs related to treatment posed a challenge to patients (77.8%). Also, clinic staff observed that patients were concerned about being a burden to their family/friends (72.5%) and that it was difficult for the patient's accompanying person to attend appointments (66.2%), or they or their accompanying person could not take time off work (55.2%).

When discussing disease, treatment, and support topics, clinic providers said that they frequently talk about challenges patients might face with attending appointments (31.1%), where to find or access support services to help them to manage their condition (36.8%), and how to engage their caregivers in treatment and care discussions (28.0%), as well as sharing information on where to find resources help to improve both diabetes (23.9%) and DR/DME (22.1%) management.

Further challenges

Patients

Additional challenges faced by patients with respect to their appointments included: too many DME appointments needed (45.0%), too many diabetes appointments needed (42.8%), issues for either themselves or accompanying person to take time off work to attend appointments (36.7%), costs related to office/parking fees (34.1%), problems with rescheduling a new appointment once one is missed (32.9%), and appointments interfering with holiday/vacation (27.7%).

Whilst most patients were comfortable asking their doctor questions regarding their diabetes (86.8%) or DME (91.9%), some thought that their doctor did not always have enough time (18.8%) and reported being uncomfortable asking for additional support services to help manage their diabetes (17.9%) or DME (17.1%). Some patients (17.1%) noted their accompanying person (caregiver) was not included in care/treatment discussions, and 15.0% reported that their doctor was only interested in their DME and not their overall health.

Providers

40.0% of providers reported that their patients did not know how to reduce their risk of disease progression through diabetes control, 38.8% said that patients were not comfortable asking for additional support services to manage their DR/DME, 29.9% reported that patients with DME did not understand their treatment goals and required treatment frequency, 28.5% said that patients were not comfortable asking questions and voicing concerns about their diabetes, 28.1% believed that patients did not understand the need for frequent monitoring or treatment, and 22.5% said that patients did not include caregivers in their DR/DME care. Most providers agreed that patients questioned whether their treatment was necessary (54.1%). Many providers (40.7%) reported that there was not always enough time during an appointment to discuss their patients' questions or concerns, and 25.7% believed that patients did not see their eye treatment as a priority.

Further findings

Treatment-related opportunities

More than 85% of providers agreed with these statements: early, intensive treatment in the first year achieves meaningful vision gain (96.3%); patients receiving the full number of label-mandated initial monthly injections realize better vision gains (92.8%); patients who miss injections in the first year are more likely to have poorer long-term outcomes (90.7%); continued treatment provides clinically meaningful vision gains (85.9%); and increasing the duration between injections would improve patient adherence (85.4%).

Regimens

The majority of providers (60.3%) give 3 intravitreal injections during the loading phase irrespective of prescribing information guidelines. **Table S5** describes the different regimens employed following initial monthly injections for the majority of patients, according to clinics. According to providers, most used either a treat-and-extend regimen (24.6%) or a pro re nata (PRN) regimen with extended monitoring (23.8%). After the first year of treatment, most providers used either PRN with extended monitoring (44.6%), or a treat-and-extend regimen (21.5%). Whilst 67.6% of providers reported that they do not change the treatment scheme if the patient has bilateral disease, the remainder would do so.

REFERENCES

1. Okada M, Wong TY, Mitchell P, et al. Defining nonadherence and nonpersistence to anti-vascular endothelial growth factor therapies in neovascular age-related macular degeneration. *JAMA Ophthalmol.* Jul 1 2021;139(7):769-776.

