Preprints.org

Article

Not peer-reviewed version

Treat-and-Extend as a Threshold Search Problem—A Deterministic Model of Injection Interval Strategies

Kevin Gallagher *

Posted Date: 12 May 2026

doi: 10.20944/preprints202605.0588.v1

Keywords: age-related macular degeneration; anti-VEGF; treat and extend

Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC, OpenAlex.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 12 May 2026 doi:10.20944/preprints202605.0588.v1

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Article

Treat-and-Extend as a Threshold Search Problem—A Deterministic Model of Injection Interval Strategies

Kevin Gallagher

Cwm Taf Morgannwg University Health Board, Llantrisant, Wales CF72 8XR, UK;
Kevin.gallagher@wales.nhs.uk; ORCID ID: 0000-0002-7751-5569; tel.: 01443 443 443

Abstract

Background and Objective: Treat-and-extend(TREX) dosing is widely used for anti-VEGF therapy in macular disease but no principled basis exists for choosing interval-change rules. We frame TREX as a threshold-search problem and compare rules in terms of search efficiency and overshoot. **Patients and Methods:** A deterministic model represented TREX as a threshold search for the true maximum dry interval(T_{max}) on a 1-week grid(4–16 weeks). Four rules were evaluated:+2/−2,+4/−2,+4/−4 with midpoint refinement, and a midpoint binary-like rule. Visits to maintenance interval and overshoot metrics were calculated for each rule and T_{max}. **Results:** No single rule was optimal. The +2/−2 rule minimised overshoot (maximum 2 weeks) but required most visits. The +4/−2 rule was fastest. In long-durability eyes, midpoint search matched +4/−2 in speed with overshoot comparable to +2/−2. **Conclusion:** Framing TREX as a threshold search makes the speed-overshoot trade-off explicit and provides a principled basis for choosing and justifying interval-change rules.

Keywords: age-related macular degeneration; anti-VEGF; treat and extend

---

Introduction

Anti-VEGF agents are the mainstay of treatment for several retinal diseases, but treatment burden at both patient and service levels is high. Various dosing strategies have been used, including fixed-interval dosing, pro re nata (PRN) treatment, and treat-and-extend (TREX)[1–3]. In TREX, the interval between injections is increased while disease activity remains controlled, and shortened again if activity recurs. The aim is to reduce clinic and injection burden while maintaining disease control [2,3].

In routine practice, different interval-change rules are used. Historically, 2-week interval changes have been common. Trials such as ALTAIR have shown that 4-week extension rules can be employed safely and that a maintenance interval can be reached with fewer steps than with 2-week extensions [4]. Other trials have shown safety and efficacy using an initial 8-week extension after loading doses [5]. Although these trials show that longer extension strategies work, they do not provide a principled basis for choosing between rules or evaluating novel strategies. With newer longer-acting agents permitting extensions to 24 weeks, larger interval changes may be used. For example, the posology for 8 mg Eylea allows interval adjustments of 8-16 weeks "at clinician discretion". This delegates extension rule selection to the clinician but without criteria to guide that choice [6–8].

How should different extension rules be chosen, compared, justified, or criticised? On what basis should a clinician choose 2-week rather than 4-week or longer increments? We suggest these questions become clearer if TREX is viewed as a threshold-search problem. Threshold search is already familiar in ophthalmology. In automated perimetry and visual acuity testing, prior information such as age-matched norms or previous responses speeds up threshold estimation. In pan-retinal photocoagulation, laser power is titrated upward while balancing speed of titration against the risk of an overly intense burn. TREX is analogous. Once disease control has been achieved

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

after loading, the clinician knows the eye is controlled at a short interval but does not know the longest interval that will still maintain control. Each interval extension therefore tests for that unknown threshold between continued control ("dry") and recurrence ("wet").

Framed in this way, different TREX rules can be understood as different search strategies for the dry/wet threshold. These rules can then be compared in terms of the trade-off they create between the speed of finding a practical maintenance interval and the risk of overshooting beyond the disease-controlling interval. The purpose of this paper is to describe the underlying structure and decision logic of the interval-selection problem. It is not intended to provide a biologically complete model of macular disease behaviour, nor to validate or recommend a specific TREX regimen. We developed a deterministic model of the TREX search phase under simplified assumptions to compare example search rules on these metrics.

Methods

This was a deterministic modelling study and did not involve human participants, human-derived data or animals. Institutional Review Board approval was therefore not required.

We modelled the following typical clinical pathway during the initial TREX search phase. A patient has received a course of loading doses at 4-week intervals and disease stability has been achieved. The interval between injections is then increased while disease remains controlled, up to a pre-defined maximum interval (16 weeks in the present model). If disease activity recurs at any point, the injection interval is shortened to re-establish control, and treatment is then continued at a disease-controlling interval (maintenance interval). In clinical practice, the gap between the interval at which disease activity first recurs and the maintenance interval is usually small, typically 1–2 weeks (the maintenance interval is defined formally below). Once this maintenance interval is identified, the modelled search pathway for that eye is considered complete. In routine clinical practice, eyes are often re-extended after a period of stability at the maintenance interval to test whether longer intervals can be tolerated. The purpose of the study was to model the initial search phase of TREX. The subsequent maintenance phase or later re-extension after a period of stability were not modelled.

Model assumptions:

1. Eyes were assumed to be dry/stable after 4-week loading injections.
2. Each eye was assumed to have a true maximum dry interval (T_{max}), unknown to the clinician at the outset of treatment, representing the "dry" boundary of the dry/wet threshold.
3. T_{max} was assumed to be fixed during the initial search phase.
4. Disease activity was assumed to recur immediately once T_{max} is exceeded. For example, if T_{max} is 10 weeks and the tested interval is 12 weeks, overshoot is calculated as 2 weeks.
5. Once injected, disease control was assumed to be immediate.

These assumptions simplify the biology to clarify the structure of the search problem.

The shortest interval at which recurrence was observed was denoted i_w (shortest wet interval) and the longest dry interval i_d. At the start of TREX, i_d = 4 weeks and i_w was undetermined. Each observation updated i_d or i_w accordingly.

The maintenance interval (M) was the point at which the dry/wet threshold had been bracketed such that $i_w - i_d \leq 2$ weeks. A gap of 2 weeks was chosen as this represents a clinically meaningful degree of threshold resolution. At this point the patient is maintained at i_d (i_d = M) as any interval longer than i_d has already been shown to result in disease recurrence.

TREX search rules evaluated

Four rules were evaluated to demonstrate that the framework supports explicit comparison between TREX rules, not to recommend any particular rule. For each rule, testing continued until the maintenance interval criterion was met ($i_w - i_d \leq 2$ weeks).

+2/-2 rule: Interval extended by 2 weeks when dry; reduced by 2 weeks when wet.

+4/-2 rule: Interval extended by 4 weeks when dry; reduced in 2-week steps when wet until a dry interval is re-established.

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

+4/-4 rule with midpoint refinement: Interval extended by 4 weeks when dry; reduced by 4 weeks when wet to the last dry interval, followed by a single midpoint refinement step testing the interval halfway between the last dry and first wet.

Midpoint (binary-like) rule: The next interval is the integer midpoint of the current search bracket [i_d, i_w], with initial bounds [4, 16]. Dry observations update i_d; wet observations update i_w.

Because the model uses a 1-week grid, and test intervals were restricted to integer values, exact halving was not always possible. As such this rule was considered binary-like rather than a pure binary search. Where no integer midpoint exists, a 2-week step is taken followed by a 1-week refinement if needed. Figure 1 shows example pathways for each rule for T_{max} = 8 weeks. The full deterministic pathways for all values of T_{max} are provided in Supplementary file 1.

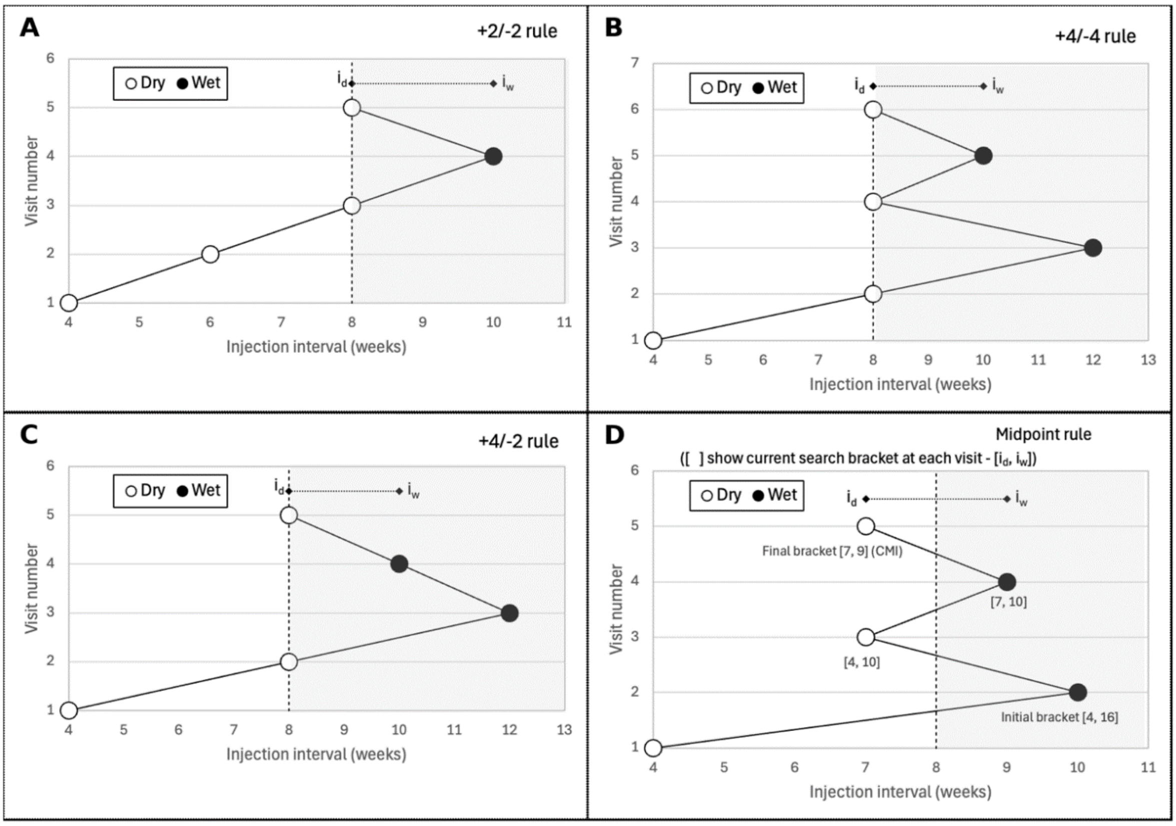
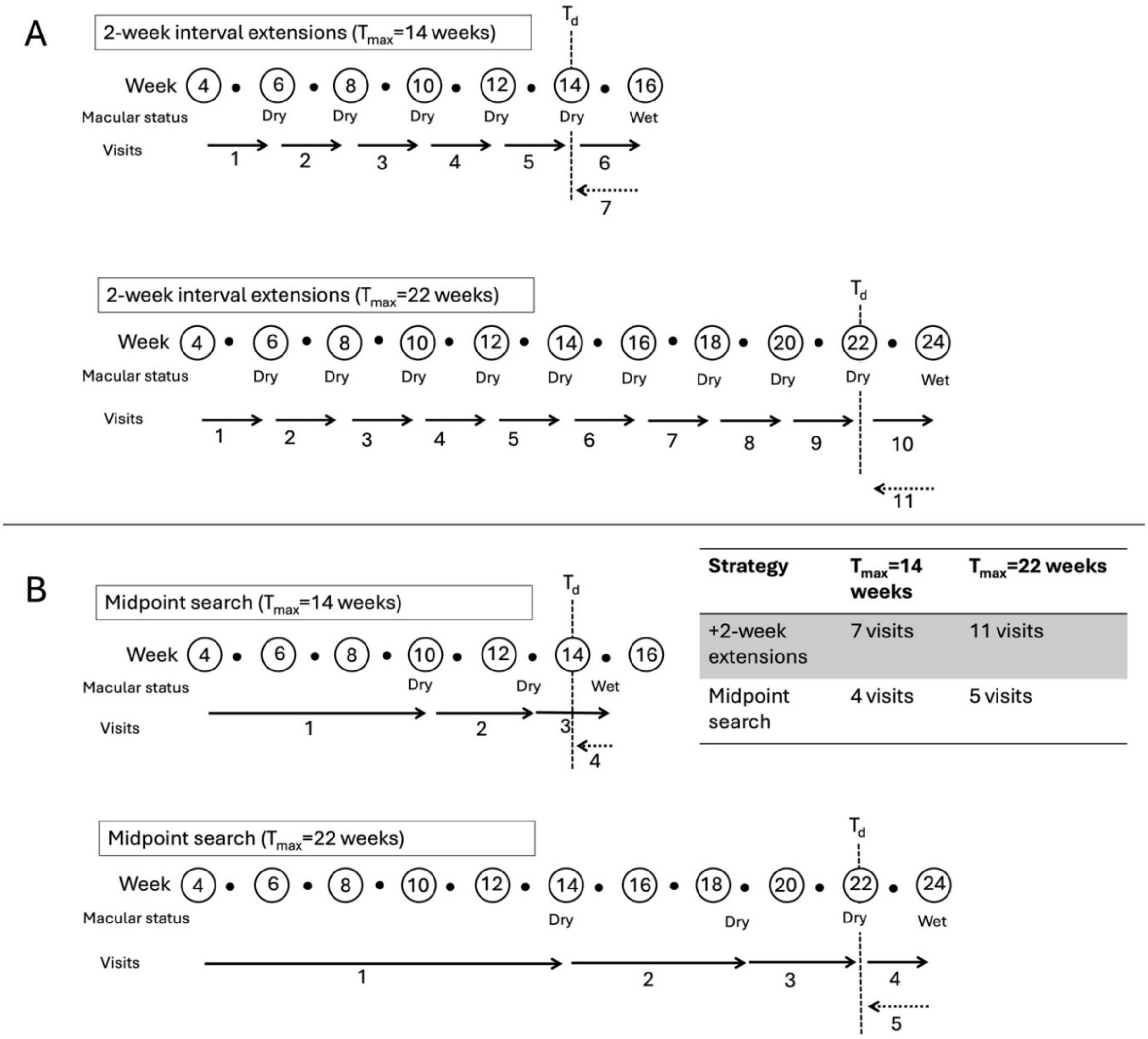


Figure 1. Example paths for each strategy when T_{max} = 8 weeks. For full pathways for all assessed values of T_{max}, see supplementary file 1. The vertical dashed line shows T_{max}. i_d and i_w are the longest dry and shortest wet intervals, respectively.

Binary search is a theoretically optimal threshold-search strategy for speed. In general, it identifies the threshold in approximately $\log_2(N)$ steps (where N is the total number of possible test intervals). For a 4–16-week range, this is approximately 3.7 steps, making it increasingly efficient compared with linear search rules (e.g. +2/-2) as the search range widens with longer-acting agents. Figure 2 illustrates this scaling advantage.

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.



Strategy	T_{max}=14 weeks	T_{max}=22 weeks
+2-week extensions	7 visits	11 visits
Midpoint search	4 visits	5 visits

Figure 2. Threshold search strategy comparison - +2-week extensions scale linearly as the search range is increased. For midpoint search, each doubling of the search space requires just one additional step.

Outcome measures

Each TREX rule was applied deterministically to model eyes for each possible value of T_{max} in the 4–16-week range. For each rule and each value of T_{max}, we determined the number of visits (and therefore injections) required to reach a maintenance interval.

Overshoot metrics

Overshoot was treated as a process metric representing time spent beyond the disease-controlling interval. The following metrics were calculated:

- Maximum single overshoot - defined as the largest number of weeks by which any tested interval exceeded T_{max}
- Cumulative overshoot - defined as the sum, in weeks, of all overshoots at visits where the tested interval exceeded T_{max}

Mean, median, and range were calculated for each outcome metric across all values of T_{max} combined. Equal weighting was assigned to each value of T_{max} across the 4–16-week range as a neutral benchmark within the model. In biological reality, the true distribution of T_{max} is likely to depend on the disease and anti-VEGF agent under consideration and is unlikely to be uniform across the 4–16-week range. To explore the impact of underlying durability, performance was also stratified for eyes with short durability (T_{max} <12 weeks) and long durability ($T_{max} \geq 12$ weeks).

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

Results

Overall performance across all values of T_{max} is summarised in Table 1. Stratified results for short (T_{max} < 12 week) and long ($T_{max} \geq 12$ weeks) durability are summarised in Table 2.

Table 1. Performance of four TREX search strategies across all true dry intervals (T_{max} = 4–16 weeks). +4/-2 was fastest. +2/-2 had the least overshoot. Midpoint had the highest overshoot.

Search strategy	Mean injections to maintenance (n)	Median injections to maintenance (n) (all T_{max}) (range)	Median cumulative overshoot (weeks) (range)	Maximum single overshoot (weeks)
+2/-2	4.6	5 (2-7)	1 (0-2)	2.0
+4/-4	4.4	4 (3-6)	2 (0-6)	4
+4/-2	3.5	3 (2-5)	2 (0-6)	4
Midpoint	3.8	4 (3-5)	2 (0-10)	6

Table 2. Performance of each search strategy grouped by short durability (T_{max} <12 weeks) and long durability (T_{max} ≥12 weeks).

T_{max} group	Search strategy	Mean injections to maintenance (n)	Median injections to maintenance (n) (range)	Median cumulative overshoot (weeks) (range)	Maximum single overshoot (weeks)
<12 weeks	+2/-2	3.5	3.5 (2-5)	1.5 (1-2)	2
	+4/-4	4.0	4 (3-5)	3 (1-6)	4
	+4/-2	3.0	3 (2-4)	3 (1-6)	4
	Midpoint	3.6	4 (3-4)	4.5 (1-10)	6
≥ 12 weeks	+2/-2	6.4	6 (6-7)	1 (0-2)	2
	+4/-4	5.0	5 (3-6)	2 (0-6)	4
	+4/-2	4.2	4 (3-5)	2 (0-6)	4
	Midpoint	4.0	4 (3-5)	1 (0-2)	2

Across the full range of T_{max}, the +2/-2 rule was safest - maximum single or cumulative overshoot did not exceed 2 weeks - but at the cost of additional visits when durability was long. The +4/-2 rule was fastest (mean 3.5 visits to maintenance). The +4/-4 rule had identical overshoot metrics to +4/-2 but was slower. The midpoint rule was similarly fast but with higher overshoot overall (maximum single overshoot of 6 weeks), driven by its performance in short-durability eyes.

In short-durability eyes (T_{max} <12 weeks), +4-week rules were similar in speed to +2/-2 but with higher overshoot. The midpoint rule performed poorly. For example, for T_{max} = 4 weeks, the initial 10-week midpoint test produced a maximum overshoot of 6 weeks and cumulative overshoot of 10 weeks.

In long-durability eyes (T_{max} ≥12 weeks), relative rule performance shifted. The +2/-2 rule required approximately 60% more visits than the midpoint rule (mean 6.4 vs 4 visits) while the midpoint rule was fastest overall (mean 4 visits to maintenance) and showed an overshoot profile comparable to +2/-2.

No TREX rule was “best” across all eyes. There is a trade-off between speed and overshoot, and rule performance depends on underlying durability, suggesting rule choice should be informed by prior expectations about treatment durability.

Discussion

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 12 May 2026 doi:10.20944/preprints202605.0588.v1

By framing TREX as a threshold search, common clinical "rules of thumb" correspond to simple algorithms with predictable, comparable behaviour. No strategy is universally optimal - each represents a trade-off between speed and overshoot.

When consequences of overshoot are high e.g. aggressive disease, previous rapid reactivation, only-seeing eye, the +2/-2 rule is most appropriate, capping overshoot at 2 weeks. Where overshoot may be less consequential, such as in a retinal vein occlusion where macular edema often resolves promptly after interval shortening, longer extensions offer a useful compromise, arriving at a maintenance interval faster and with an acceptable overshoot profile.

When 4-week extensions are used, our model shows no difference in overshoot between +4/-4 and +4/-2, but +4/-2 reaches the maintenance interval faster. Where reactivation is minor, +4/-2 is therefore the more efficient choice. A larger shortening step may still be appropriate where reactivation is clinically significant.

When T_{max} is anticipated to be longer (e.g. using longer-acting agents (faricimab or aflibercept 8mg))[9,10], midpoint bracketing combines fast search speed with a favourable overshoot profile. Our model shows midpoint search performs close to the theoretical optimum – mean 4 visits to maintenance versus the 3.7 predicted by binary search theory. Approaches sharing this logic have already appeared in practice. Patwardhan *et al* extended patients immediately to 12 weeks after faricimab loading doses, implicitly testing towards the midpoint of a presumed longer-durability bracket [5]. Our framework provides the theoretical basis for why this is close to optimal under longer-durability expectations.

This framework is not intended as a set of specific recommendations but as a principled basis for comparing and justifying TREX strategies. Rather than asking whether +2 or +4-week extensions are "better," the question becomes: for this patient, with this disease and these consequences of overshoot, using this agent, which strategy balances speed and safety best?

The model rests on the simplifying assumption of immediate disease reactivation beyond T_{max} and immediate disease control after injection. This was chosen to clarify the structure of the search problem rather than to simulate disease biology. The model measures overshoot duration: the time spent beyond the disease-controlling interval within which all reactivation events necessarily occur. Although the relationships between overshoot duration, fluid recurrence, and clinical harm are complex and likely non-linear, overshoot is the upstream metric directly determined by rule choice and the outcome the search strategy directly influences. Minimising overshoot is therefore a rational basis for rule comparison, even if downstream consequences vary between eyes and clinical contexts. These assumptions are most likely to affect absolute overshoot values while the relative comparison between rules is more stable.

T_{max} was treated as a fixed property during the search phase. In reality it may drift over time or be influenced by treatment intensity. For the relatively short horizon of the search phase, this is a reasonable simplifying assumption.

Equal weighting of T_{max} across the 4–16-week range was used as a neutral benchmark rather than a realistic durability distribution. Our results show that rule performance depends on underlying treatment durability. Consequently, future rule choice should be improved by more accurate and realistic estimates of expected durability. A companion paper in preparation addresses this using Monte Carlo simulation with trial-derived durability priors.

A fundamental challenge is that T_{max} is also unknown in advance - clinicians must choose a rule under uncertainty, drawing on disease type, agent, and trial data. Durability analyses from trials or local cohorts could formalise this, shifting rule choice towards an evidence-based footing. Prospective studies comparing rules head-to-head with pre-specified efficiency and overshoot metrics alongside clinical outcomes are needed to validate this modelling. Framing TREX as a threshold search provides a principled basis for comparing and justifying interval-change rules in routine practice.

Supplementary content - full deterministic pathways for all values of T_{max} are provided. () show overshoot in weeks at each interval:

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 12 May 2026 doi:10.20944/preprints202605.0588.v1

True dry interval (Tmax)	+2/-2	Status:wet/dry (overshoot in weeks)					Injections to maintenance	Mean cumulative overshoot	Maximum single overshoot
4	dry at 4	wet at 6 (2)	dry at 4				2	2	2
5	dry at 4	wet at 6 (1)	dry at 4				2	1	1
6	dry at 4	dry at 6	wet at 8 (2)	dry at 6			3	2	2
7	dry at 4	dry at 6	wet at 8 (1)	dry at 6			3	1	1
8	dry at 4	dry at 6	dry at 8	wet at 10 (2)	dry at 8		4	2	2
9	dry at 4	dry at 6	dry at 8	wet at 10 (1)	dry at 8		4	1	1
10	dry at 4	dry at 6	dry at 8	dry at 10	wet at 12 (2)	dry at 10	5	2	2
11	dry at 4	dry at 6	dry at 8	dry at 10	wet at 12 (1)	dry at 10	5	1	1
12	dry at 4	dry at 6	dry at 8	dry at 10	dry at 12	wet at 14 (2)	6	2	2
13	dry at 4	dry at 6	dry at 8	dry at 10	dry at 12	wet at 14 (1)	6	1	1
14	dry at 4	dry at 6	dry at 8	dry at 10	dry at 12	dry at 14	7	2	2
15	dry at 4	dry at 6	dry at 8	dry at 10	dry at 12	dry at 14	7	1	1
>=16	dry at 4	dry at 6	dry at 8	dry at 10	dry at 12	dry at 14	6	0	2
True dry interval (Tmax)	+4-4								
4	dry at 4	wet at 8 (4)	dry at 4	wet at 6 (2)	dry at 4		4	6	4
5	dry at 4	wet at 8 (3)	dry at 4	wet at 6 (1)	dry at 4		4	4	3
6	dry at 4	wet at 8 (2)	dry at 4	dry at 6			3	2	2
7	dry at 4	wet at 8 (1)	dry at 4	dry at 6			3	1	1
8	dry at 4	dry at 8	wet at 12 (4)	dry at 8	wet at 10 (2)	dry at 8	5	6	4
9	dry at 4	dry at 8	wet at 12 (3)	dry at 8	wet at 10 (1)	dry at 8	5	4	3
10	dry at 4	dry at 8	wet at 12 (2)	dry at 8	dry at 10		4	2	2
11	dry at 4	dry at 8	wet at 12 (1)	dry at 8	dry at 10		4	1	1
12	dry at 4	dry at8	dry at 12	wet at 16 (4)	dry at 12	wet at 14 (2)	6	6	4
13	dry at 4	dry at 8	dry at 12	wet at 16 (3)	dry at 12	wet at 14 (1)	6	4	3
14	dry at 4	dry at 8	dry at 12	wet at 16(2)	dry at 12	dry at 14	5	2	2
15	dry at 4	dry at 8	dry at 12	wet at 16 (1)	dry at 12	dry at 14	5	1	1
>=16	dry at 4	dry at 8	dry at 12	dry at 16			3	0	0

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 12 May 2026 doi:10.20944/preprints202605.0588.v1

True dry interval (Tmax)	+4/-2								
4	dry at 4	wet at 8 (4)	wet at 6 (2)	dry at 4			3	6	4
5	dry at 4	wet at 8 (3)	wet at 6 (1)	dry at 4			3	4	3
6	dry at 4	wet at 8 (2)	dry at 6				2	2	2
7	dry at 4	wet at 8 (1)	dry at 6				2	1	1
8	dry at 4	dry at 8	wet at 12 (4)	wet at 10 (2)	dry at 8		4	6	4
9	dry at 4	dry at 8	wet at 12 (3)	wet at 10 (1)	dry at 8		4	4	3
10	dry at 4	dry at 8	wet at 12 (2)	dry at 10			3	2	2
11	dry at 4	dry at 8	wet at 12 (1)	dry at 10			3	1	1
12	dry at 4	dry at 8	dry at 12	wet at 16 (4)	Wet at 14 (2)	dry at 12	5	6	4
13	dry at 4	dry at 8	dry at 12	wet at 16 (3)	Wet at 14 (1)	dry at 12	5	4	3
14	dry at 4	dry at 8	dry at 12	wet at 16 (2)	dry at 14		4	2	2
15	dry at 4	dry at 8	dry at 12	wet at 16 (1)	dry at 14		4	1	1
>=16	dry at 4	dry at 8	dry at 12	dry at 16			3	0	0
True dry interval (Tmax)	Midpoint								
4	dry at 4	wet at 10 (6)	wet at 7 (3)	wet at 5 (1)	dry at 4		4	10	6
5	dry at 4	wet at 10 (5)	wet at 7 (2)	dry at 5			3	7	5
6	dry at 4	wet at 10 (4)	wet at 7 (1)	dry at 5	dry at 6		4	5	4
7	dry at 4	wet at 10 (3)	dry at 7	wet at 9 (2)	dry at 7		4	5	3
8	dry at 4	wet at 10 (2)	dry at 7	wet at 9 (1)	dry at 7		4	3	2
9	dry at 4	wet at 10 (1)	dry at 7	dry at 9			3	1	1
10	dry at 4	dry at 10	wet at 13 (3)	wet at 11 (1)	dry at 10		4	4	3
11	dry at 4	dry at 10	wet at 13(2)	dry at 11			3	2	2
12	dry at 4	dry at 10	wet at 13(1)	dry at 11			3	1	1
13	dry at 4	dry at 10	dry at 13	wet at 15 (2)	dry at 13		4	2	2
14	dry at 4	dry at 10	dry at 13	wet at 15 (1)	dry at 13		4	1	1
15	dry at 4	dry at 10	dry at 13	dry at 15	wet at 16(1)	dry at 15	5	1	1
>=16	dry at 4	dry at 10	dry at 13	dry at 15	dry at 16		4	0	0

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 12 May 2026 doi:10.20944/preprints202605.0588.v1

Conflicts of Interest: The authors have no conflicts of interest to disclose.

References

1. Lalwani GA, Rosenfeld PJ, Fung AE, et al. A variable-dosing regimen with intravitreal ranibizumab for neovascular age-related macular degeneration: year 2 of the PrONTO study. *Am J Ophthalmol.* 2009;148(1):43-58.
2. Wykoff CC, Croft DE, Brown DM, et al. Prospective trial of treat-and-extend versus monthly dosing for neovascular age-related macular degeneration: TREX-AMD 1-year results. *Ophthalmology.* 2015;122(12):2514-2522.
3. Rufai SR, Almuhtaseb H, Paul RM, et al. A systematic review to assess the treat-and-extend dosing regimen for neovascular age-related macular degeneration using ranibizumab. *Eye (Lond).* 2017;31(9):1337-1344.
4. Ohji M, Takahashi K, Okada AA, Kobayashi M, Matsuda Y, Terano Y. Efficacy and safety of intravitreal aflibercept treat-and-extend regimens in exudative age-related macular degeneration: 52-and 96-week findings from ALTAIR: a randomized controlled trial. *Advances in therapy*. 2020 Mar;37(3):1173-87.
5. Patwardhan A, Ali N, Law S. Intravitreal Faricimab in treatment-naïve neovascular age-related macular degeneration: real-world outcome of 12-week extension after the loading dose from a UK centre. *Eye*. 2025 Mar;39(4):766-70.
6. American Academy of Ophthalmology Retina/Vitreous Panel. Age-Related Macular Degeneration Preferred Practice Pattern®. San Francisco, CA: American Academy of Ophthalmology; 2024. Accessed 18 Nov 2025 Available at: https://www.aao.org/education/preferred-practice-pattern/age-related-macular-degeneration-ppp
7. Lai TY, Kataoka K, Hsieh YT, et al. International consensuses and guidelines on etiology, diagnosis, treatment, and future developments of neovascular age-related macular degeneration by the Asia-Pacific Vitreo-retina Society, Asia-Pacific Ocular Imaging Society, and Academy of the Asia-Pacific Professors of Ophthalmology. *Asia Pac J Ophthalmol (Phila).* 2025;14(5):100242.
8. Chaudhary V. Treat and extend in neovascular age-related macular degeneration: how we got here and where do we go next? *Eye.* 2023;37(4):581-583.
9. Heier JS, Khanani AM, Ruiz CQ, et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomized, double-masked, phase 3, non-inferiority trials. *Lancet.* 2022;399(10326):729-740.
10. Lanzetta P, Korobelnik JF, Heier JS, et al. Intravitreal aflibercept 8 mg in neovascular age-related macular degeneration (PULSAR): 48-week results from a randomized, double-masked, non-inferiority, phase 3 trial. *Lancet.* 2024;403(10432):1141-1152.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© 2026 by the author(s). Distributed under a Creative Commons CC BY license.