

Associations with visual acuity outcomes after 12 months of treatment in 9401 eyes with neovascular AMD

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ABSTRACT

Objective To record visual acuity outcomes after 12 months of treatment for neovascular age-related macular degeneration (NvAMD), investigate variation between sites and explore associations with baseline characteristics and care processes.

Methods and analysis Anonymised demographic and clinical data were extracted from electronic medical records at treating National Health Service (NHS) Trusts. Associations with acuity outcomes were investigated using multivariate linear and logistic regression.

Results Analysis included 9401 eyes (7686 patients) treated at 13 NHS Trusts. From baseline to month 12, median acuity improved from LogMAR 0.50 (IQR 0.30–0.80) to 0.40 (0.22–0.74) and the proportion of eyes with LogMAR ≥ 0.3 increased from 34.5% to 39.8%. Baseline visual acuity was the strongest predictor of visual acuity outcomes. For each LogMAR 0.1 worsening of baseline acuity, the acuity at 12 months was improved by LogMAR 0.074 (95% CI 0.073 to 0.074) and the odds of a 'poor' acuity outcome was multiplied by 1.66 (95% CI 1.61 to 1.70). Younger age, independent living status, lower socioeconomic deprivation, timely loading phase completion and higher number of injections were associated with better acuity outcomes. Despite case-mix adjustments, there was evidence of significant variation in acuity outcomes between sites.

Conclusions Even after adjustment for other variables, variation in acuity outcomes after NvAMD treatment within the NHS remains. Meaningful comparison of outcomes between different providers requires adjustment for a range of baseline characteristics, not visual acuity alone. Identifying best practice at sites with better outcomes and adapting local care processes are required to tackle this health inequality.

Visual acuity change and state after intravitreal therapy for neovascular age-related macular degeneration (NvAMD) are associated with baseline patient characteristics, the ocular phenotype and key care processes.^{1–5} The strongest association is with baseline visual acuity.^{6,7} Early diagnosis, prompt initiation of treatment and adherence to the treatment plan are important to maximise the likelihood of retaining or achieving a good visual acuity state.^{4,5,8,9} Providers also need to ensure sufficient capacity to maintain

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Real-world outcomes after neovascular age-related macular degeneration treatment rarely match those seen in randomised clinical trials. Some of this can be explained by differences in baseline characteristics and the care pathway. Variation in outcomes between individual treatment sites is less well studied.

WHAT THIS STUDY ADDS

⇒ In real-world practice, baseline acuity is the strongest predictor of both visual acuity change and state but age, deprivation care processes and site are also important.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ Starting treatment while acuity is still good is key to achieving good outcomes. Identifying best practice at sites with better outcomes will also help to maximise acuity outcomes.

treatment intervals and develop care pathways to suit the local population.¹⁰

Real-world data suggest ongoing variation in acuity outcomes between centres, despite an intention to provide the same care pathway.^{11,12} Comparing outcomes with local and national benchmarks may help identify best practice and potential areas for concern.¹⁰ Given the influence of baseline characteristics on visual acuity outcomes, this needs take account of any differences in these characteristics. Only after adjustment for variation in baseline acuity and other, relevant variables will benchmarking identify important differences in the care pathway. By investigating variability in and associations with visual acuity outcomes, this study aimed to determine the relative contribution of baseline characteristics and care processes on acuity outcomes after NvAMD treatment.

MATERIALS AND METHODS

Anonymised demographic and clinical data were extracted from the Medisoft EMR

(Medisoft Ophthalmology, Leeds, UK) at 13 National Health Service (NHS) Trusts, identified in the analysis by the letters A–M. Eligibility criteria required treatment to have started in one or both eyes between 2017 and 2018 and to be aged 55 years or older at the time of the first injection.

Prior to data extraction in February 2021, written approval from both the medical retina lead and Caldicott Guardian (responsible for data protection) at each site was obtained. Analyses of anonymised databases are classified as service evaluations by the Health Research Authority and so NHS research ethics committee is not required (<http://www.hra-decisiontools.org.uk/research/>).

From the extracted data, age at the start of treatment, sex, any systemic or chronic ocular comorbidity and first or second-treated eye status were recorded for all patients. Index of multiple deprivation (IMD), an indicator of socioeconomic status and assisted or independent living status were determined from the first half of and the full patient postcode, respectively, at the time of data extraction. Completion of the loading phase of 3, monthly injections was rounded up or down to the nearest whole week and classified as fast (≤ 8 weeks), medium (9–10 weeks), slow (> 10 weeks) or incomplete.

Visual acuity was recorded with an Early Treatment Diabetic Retinopathy Study (ETDRS) or Snellen chart, using habitual correction. Acuties of count fingers or worse were converted to LogMAR 1.7, equivalent to an EDTRS acuity of zero letters. Acuties converted from Snellen were allocated a LogMAR score to 1 decimal place. For each site, the number of eyes treated in the study period was identified and, as the acuity distribution was not normally distributed, the median LogMAR acuties at baseline and 12 months (± 56 days) were calculated. The proportion of eyes with ‘good’ (LogMAR ≤ 0.3) (≥ 70 ETDRS letters) and ‘poor’ acuity (LogMAR > 0.3) was also determined for each site.

Statistical analysis

Associations between the chosen variables and visual acuity state at 12 months from the start of treatment, measured both as a continuous variable and dichotomised into a binary outcome (‘good’ and ‘poor’ state), were investigated using multivariate generalised linear models.

A variety of variables captured in the patient record were used for prediction. Baseline acuity, age and the number of injections to month 12 were analysed as continuous variables. First or second-treated eye status, sex, independent living status, IMD quintile, treatment site, systemic comorbidity, ocular comorbidity and time to complete the loading phase of treatment were analysed as categorical variables.

For both models, the use of splines (non-linear effects) was considered for the continuous variables but did not lead to an improvement in the Akaike Information Criterion (AIC) and, therefore, linear terms were used.¹³

Similarly, an interaction term between age and sex led to no improvement of the AIC. Random effects for treatment site and hierarchical random effects for eyes within patients were considered but did not improve the AIC and were, therefore, dropped from the final model.

Model fit was checked using plots of the residuals, calibration plots and the C-index. Bootstrap sampling was used to estimate a global shrinkage factor for each model, which was applied to the model coefficients shown in the results tables.

Patient and public involvement

Patients and members of the public were not involved in the design, conduct and dissemination plans for this research.

RESULTS

From the 9116 people (12 414 eyes) with baseline visual acuity data, 7686 (9401 eyes) were still in active follow-up after 12 months. Baseline characteristics for the full cohort and those with follow-up to month 12 are presented in table 1.

Median visual acuity for the 9401 eyes with 12-month follow-up was LogMAR 0.50 (IQR: 0.30–0.80) or 60 ETDRS letters at baseline and LogMAR 0.40 (IQR: 0.22–0.74) or 65 ETDRS letters after 12 months. Median visual acuity change was LogMAR -0.06 (IQR: -0.2 – 0.1). Across sites, the median acuity change at month 12 ranged from LogMAR -0.1 (Sites B, C, F) or $+5$ ETDRS letters to LogMAR 0.0 (Sites K and L).

The proportion of eyes with ‘good’ visual acuity increased from 34.5% at baseline to 39.8% at month 12. Overall, 40.9% of eyes gained at least 0.1 LogMAR in acuity and 90.5% avoided losing at least 0.3 LogMAR or 15 ETDRS letters. Median LogMAR acuity at baseline and month 12 for the treated eyes at each site and the proportion with acuity gains and losses and in each visual acuity category are shown in online supplemental table 4.

Median visual acuity at baseline and month 12 was better for second-treated eyes, with 47.9% achieving a ‘good’ visual acuity state (see online supplemental table 5).

A total of 72 416 injections were given before month 12. This comprised 52 052 injections of aflibercept (71.9%), 18 751 injections of ranibizumab (25.9%) and 1491 injections of bevacizumab (2.1%). For the remaining 122 injections, the drug used was not readily identifiable. Completion of the loading phase of three initial injections was fast in 2046 eyes (21.8%), medium in 5343 (56.8%), slow in 1770 (18.8%) and incomplete in 242 (2.6%). The median number of injections in the first 12 months was 8.0 (IQR: 6.0–9.0). Variation between sites for time to complete the loading phase and the total number of injections is shown in figure 1.

Visual acuity prediction

The results of the multivariate linear regression exploring associations with visual acuity at month 12 are shown in table 2.

Table 1 Baseline characteristics and care processes for the full cohort of 9116 people (12 414 eyes) starting treatment and the 7686 people (9401 eyes) with 12 month follow-up data

	Characteristic	Full cohort starting treatment	Cohort with month 12 data
Median age in years (IQR)		81.4 (75.3, 86.4)	81.0 (74.9, 86.1)
Sex n (%)	Female	5711 (62.6%)	4858 (63.2%)
	Male	3405 (37.4%)	2828 (36.8%)
Chronic systemic comorbidity n (%)	Present	5734 (46.2%)	3582 (46.6%)
Living status n (%)	Assisted	524 (5.8%)	384 (5.0%)
	Independent	8578 (94.1%)	7302 (95.0%)
Index of multiple deprivation n (%)	Quintile 1 (most deprived)	1899 (20.8%)	1586 (20.6%)
	Quintile 2	1500 (16.4%)	1262 (16.4%)
	Quintile 3	1704 (18.7%)	1439 (18.7%)
	Quintile 4	1948 (21.4%)	1657 (21.6%)
	Quintile 5 (least deprived)	2040 (22.3%)	1742 (22.7%)
	Unknown	25 (0.3%)	0
Median baseline LogMAR acuity (IQR)		0.46 (0.26, 0.80)	0.50 (0.30, 0.80)
Chronic ocular comorbidity n (%)	Present	3385 (27.3%)	2530 (26.9%)
First-treated eye status n (%)		9182 (74.0%)	6909 (73.5%)

The effects shown are those found after shrinkage by the global shrinkage factor of 0.95, indicative of a good initial model fit. Predicted visual acuity was most strongly associated with baseline visual acuity. For each LogMAR 0.1

(5 EDTRS letters) worsening of baseline acuity, median acuity at 12 months was improved by LogMAR 0.074 (95% CI 0.073 to 0.076) or approximately 3.5 ETDRS letters. Compared with the eyes of people in assisted living, predicted visual acuity was better by LogMAR 0.03 (95% CI 0.056 to 0.005), approximately 1.5 ETDRS letters, in the eyes of people living independently. Similarly, when compared with the eyes of people living in the most deprived areas (IMD 1), visual acuity in the eyes of people from the least deprived areas (IMD 5) was better by LogMAR 0.029 (95% CI 0.049 to 0.011) or approximately 1.5 ETDRS letters (see figure 2A). Smaller effects on visual acuity were also associated with first-treated eye status and each additional injection. By contrast, visual acuity was worse in eyes with an incomplete loading phase of treatment by LogMAR 0.078 (95% CI 0.039 to 0.12), approximately four ETDRS letters, when compared with eyes with fast loading phase completion (see figure 2B). For every decade of increasing age at the start of treatment, predicted visual acuity was worse by LogMAR 0.044 (95% CI 0.04 to 0.05), approximately two ETDRS letters. Despite case-mix adjustments, there was evidence of significant variation in the predicted visual acuity between sites. Compared with site A, eyes treated at site B were associated with an improvement of 0.075 LogMAR (95% CI 0.11 to 0.041), approximately four ETDRS letters, while eyes treated at site K were associated with worsening vision of 0.085 LogMAR (95% CI 0.051 to 0.12), approximately four EDTRS letters (see figure 2C).

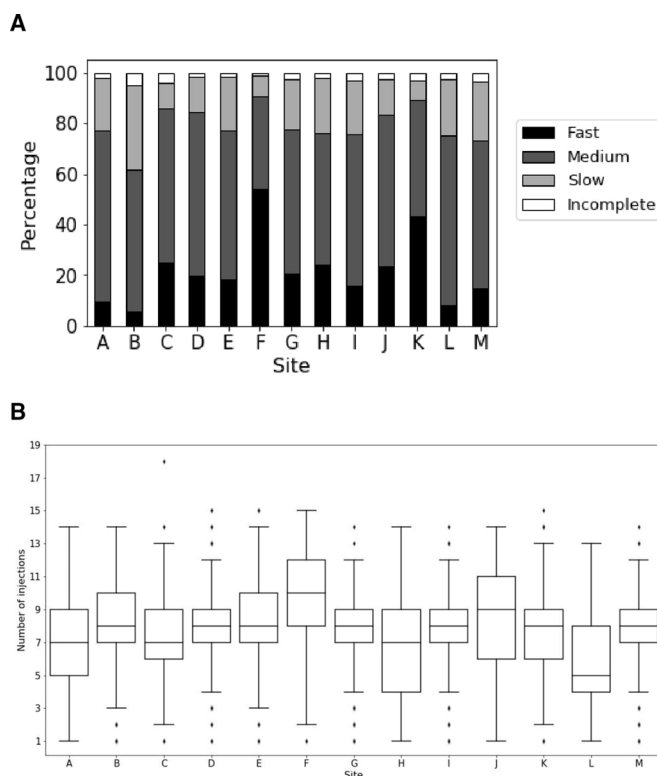


Figure 1 Bar chart and box and whisker plot to show variation between sites for (A) the time to complete the loading phase of 3 initial injections and (B) the number of intra-vitreous injections before the month 12 visit.

Visual acuity state

The results of the multivariate linear regression exploring associations with visual acuity state at month 12 are shown in table 3.

Table 2 Multivariate regression analysis to explore associations with median visual acuity change at month 12

Parameter		Estimate	95% CI	P value
Intercept		-0.13	(-0.21 to 0.059)	
Age (decades)		0.044	(0.04 to 0.05)	<0.001
Sex (male vs female)		0.0038	(-0.008 to 0.015)	0.52
Independent living status (vs assisted)		-0.0300	(-0.056 to 0.005)	0.02
First eye (vs second eye)		-0.0145	(-0.027 to 0.0016)	0.028
Ocular comorbidity (present vs absent)		0.0120	(-0.0021 to 0.0250)	0.098
Systemic comorbidity (present vs absent)		0.0068	(-0.0054 to 0.02)	0.28
Baseline visual acuity (0.1 LogMAR)		0.0740	(0.073 to 0.076)	<0.001
Site (relative to A)	Site B	-0.0750	(-0.11 to -0.041)	<0.001
	Site C	-0.0003	(-0.038 to 0.037)	0.99
	Site D	-0.0042	(-0.04 to 0.031)	0.82
	Site E	0.0130	(-0.017 to 0.043)	0.39
	Site F	0.0058	(-0.028 to 0.039)	0.74
	Site G	0.0150	(-0.014 to 0.044)	0.31
	Site H	0.0032	(-0.026 to 0.033)	0.83
	Site I	0.0570	(0.027 to 0.087)	<0.001
	Site J	-0.0130	(-0.044 to 0.018)	0.41
	Site K	0.0850	(0.051 to 0.12)	<0.001
IMD (quintiles relative to 1 (most deprived))	IMD 2	0.0091	(-0.0094 to 0.028)	0.34
	IMD 3	-0.0082	(-0.026 to 0.0098)	0.37
	IMD 4	-0.0130	(-0.031 to 0.0048)	0.15
	IMD 5	-0.0290	(-0.049 to -0.011)	0.001
Number of injections (for each additional injection over 0)		-0.0130	(-0.015 to -0.011)	<0.001
Completion of loading phase of treatment (relative to fast completion)	Medium (9–10 weeks)	0.0046	(-0.0098 to 0.019)	0.53
	Slow (>10 weeks)	0.0170	(-0.0013 to 0.035)	0.069
	Incomplete	0.0780	(0.039 to 0.12)	<0.001

Spline used to correct for number of days away from 365 (nuisance variable so not in table).

This is using a linear model, so we are attempting to predict the actual VA score in 12 months time. If 12 month VA >0.3 LogMar in T4. These estimates are post-optimism adjustment using bootstrap sampling. Optimism factor was 0.95 AdjR²=0.514.

IMD, index of multiple deprivation.

The effects shown are those found after shrinkage by the global shrinkage factor of 0.986, indicative of a good initial model fit. Data are presented to show association with a 'poor' outcome, defined as LogMAR >0.3 at month 12, and indicating that a 'good' visual acuity state was not achieved. The strongest association was again with baseline visual acuity. For each 0.1 LogMAR worsening of baseline visual acuity, the odds of a 'poor' acuity state was multiplied by 1.66 (95% CI 1.61 to 1.70).

Similarly, for each additional decade of age at the start of treatment, the odds of a 'poor' acuity state at month 12 was multiplied by 1.45 (95% CI 1.40 to 1.50). Eyes with slow completion of the loading phase of treatment were more likely to achieve a 'poor' acuity state at month 12 (OR=1.26 (95% CI 1.01 to 1.48)) compared with fast completion. A medium speed and incomplete loading phase completion were associated with 'poor' visual acuity state but did not reach statistical significance. In

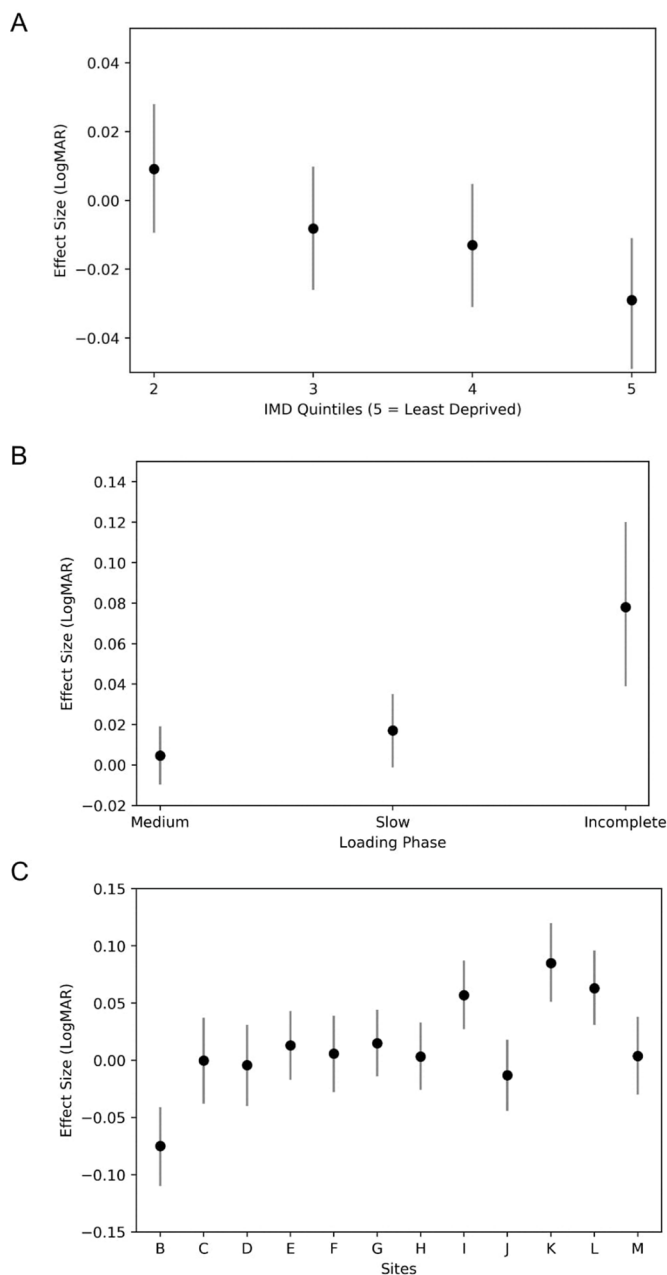


Figure 2 Impact of index of multiple deprivation (A) time to complete the loading phase of treatment (B) and site (C) on visual acuity outcome.

contrast, the odds of a ‘poor’ acuity outcome for first-treated eyes were 0.89 (95% CI 0.79 to 0.99) times that of second-treated eyes. For eyes from people in the least deprived quintile, the odds of a ‘poor’ visual acuity state were 0.77 (95% CI 0.65 to 0.90) times that of eyes from people in the most deprived quintile. Despite case-mix adjustments, there was evidence of significant variation between sites in the odds for a ‘poor’ visual acuity state at month 12. Compared with the reference, site A, the odds of a ‘poor’ outcome was significantly lower at three other sites, namely B, C and E. For site B, with the best outcomes, the odds of a ‘poor’ acuity state was 0.44 (95% CI 0.32 to 0.60) times that of site A.

DISCUSSION

This analysis of NvAMD treatment outcomes, within the publicly funded NHS, identified trajectories of visual acuity that are broadly in line with other large, real-world data sets. Visual acuity outcomes were associated with both baseline characteristics and key clinical care processes. Even with adjustment for other variables, there was evidence of variation in outcomes between sites.

For both visual acuity outcomes and state at month 12, the strongest association was with baseline visual acuity. With each 0.1 LogMAR (five ETDRS letter) worsening of baseline acuity, visual acuity at 12 months increased by 0.074 LogMAR, equivalent to 3.5 ETDRS letters. Likewise, for the same worsening of baseline acuity, the odds of having a ‘poor’ visual acuity state at month 12 was 1.66 times higher, reinforcing the need for prompt referral, diagnosis and initiation of treatment. This trend for bigger gains but worse outcomes for eyes with lower baseline acuity has been well documented.^{5 6} Relative to eyes with baseline acuity of 50–59 ETDRS letters, Talks *et al* reported ORs of 0.24 and 10.52 for achieving a ‘good’ acuity state for eyes with baseline acuities of <45 or ≥75 letters.¹² Tufail *et al* found a linear relationship between baseline acuity and achieving a ‘good’ acuity state, with every extra letter of acuity at baseline increasing the OR of a ‘good’ acuity outcome by 10%.¹⁴ These findings are likely to explain the better visual acuity state typically reported for second eyes. The lower and statistically significant OR of achieving a ‘poor’ acuity state for first eyes reported here was unexpected after including baseline visual acuity in the model. However, the effect size for first versus second-treated eyes is small and the finding may be due to chance. Alternatively, there may be a small effect of first or second-treated eye status on visual acuity outcomes above and beyond the effect of baseline visual acuity.

Other baseline characteristics associated with visual acuity outcomes and state were age, independent living and socioeconomic deprivation. For every extra 10 years of age, visual acuity at 12 months reduced by LogMAR 0.044, approximately two ETDRS letters, and the odds of having a ‘poor’ acuity state increased by almost 50%. Compared with the eyes of people living in the most deprived areas, eyes of people in the least deprived areas had greater acuity gains and were more likely to avoid a ‘poor’ visual acuity outcome, even after adjustment for baseline acuity and age. A non-significant trend existed, suggesting similar outcomes for eyes in the third and fourth quintiles. These findings have not been reported before but are consistent with the broader literature on socioeconomic deprivation and health outcomes. More *et al* reported a greater risk of presenting with lower acuity levels in people living in areas of high deprivation, after adjustment for age, gender and distance to the treatment centre.¹⁵ However, Acharya *et al* found that deprivation was not associated with baseline visual acuity.¹⁶

Key care processes were also found to be associated with acuity outcomes and state. In this data set, more

Table 3 Multivariate regression analysis to explore associations with ‘poor’ visual acuity state at month 12

Parameter		Estimate (OR)	95% CI	p-value
Intercept		0.100	(0.051 to 0.21)	
Age (decades)		1.450	(1.40 to 1.50)	<0.001
Sex (male vs female)		1.037	(0.93 to 1.15)	0.51
Independent living status (vs assisted)		0.840	(0.65 to 1.073)	0.16
First-treated eye (vs second eye)		0.890	(0.79 to 0.99)	0.04
Ocular comorbidity (present vs absent)		0.950	(0.84 to 1.079)	0.44
Systemic comorbidity (present vs absent)		0.980	(0.87 to 1.094)	0.69
Baseline visual acuity (0.1 LogMAR)		1.660	(1.61 to 1.7)	<0.001
Site (relative to A)	Site B	0.440	(0.32 to 0.6)	<0.001
	Site C	0.610	(0.43 to 0.86)	0.005
	Site D	0.870	(0.62 to 1.2)	0.39
	Site E	0.740	(0.56 to 0.97)	0.03
	Site F	0.780	(0.57 to 1.061)	0.11
	Site G	0.840	(0.64 to 1.096)	0.2
	Site H	0.920	(0.7 to 1.21)	0.56
	Site I	1.210	(0.91 to 1.61)	0.18
	Site J	0.750	(0.57 to 1.0)	0.05
	Site K	1.100	(0.8 to 1.51)	0.55
	Site L	1.320	(0.98 to 1.79)	0.07
	Site M	0.890	(0.66 to 1.21)	0.46
	IMD (quintiles relative to 1 (most deprived))	IMD 2	1.079	(0.91 to 1.28)
IMD 3		0.880	(0.75 to 1.041)	0.14
IMD 4		0.950	(0.81 to 1.12)	0.54
IMD 5		0.770	(0.65 to 0.9)	0.002
Number of injections (for each additional injection over 0)			0.980	(0.96 to 1.0053)
Completion of loading phase of treatment (relative to fast completion)	Medium (9–10 weeks)	1.120	(0.98 to 1.28)	0.09
	Slow (>10 weeks)	1.260	(1.066 to 1.48)	0.007
	Incomplete	1.340	(0.88 to 2.034)	0.18

than 75% of eyes complete the loading phase of three initial injections within 10 weeks. For those eyes with an incomplete loading phase, visual acuity was worse by almost 0.08 LogMAR, or four ETDRS letters, when compared with eyes with fast completion of the loading phase and a non-significant trend also suggested worse outcomes in eyes with medium or slow completion. Similarly, the likelihood of a ‘poor’ acuity outcome increased in eyes without fast completion of the loading phase, but statistical significance was reached only for the eyes with slow completion. For these eyes, the odds ratio of a ‘poor’ acuity outcome was 1.26 times that of eyes with fast completion. Mean visual acuity change was greater in eyes with loading phase completion under 90 days in the Rainbow study, regardless of whether subsequent treatment was given regularly.^{3 17} Similarly, acuity outcomes at both 3 and 12 months were greater in the eyes receiving

three or more loading phase injections within 3 months (defined as 104 days) of starting treatment.¹⁸ In contrast, both visual acuity outcomes and state were better in eyes with regular treatment both during and after the loading phase in the Perseus study.⁴ Both studies reported better outcomes with more injections.^{4 17} Talks *et al* reported that each additional injection increased the likelihood of a ‘good’ acuity state and Ciulla *et al* also reported a linear improvement in visual outcomes with more injections, before a plateau was reached at 10 injections.^{5 12} In this study, each additional injection resulted in an 0.13 LogMAR acuity improvement, less than one ETDRS letter, but similar to the effect reported by Chandra *et al*.¹⁹

Despite case-mix adjustment for baseline characteristics and care processes, these data provide evidence of ongoing variation in acuity outcomes between sites. Compared with those treated at the reference site A,

eyes with the same characteristics and care but treated at sites B and I had better acuity gains of 0.075 and 0.057 LogMAR, respectively, equivalent to 3.5 and 2.5 ETDRS letters. Conversely, acuity outcomes for eyes treated at sites K and L were worse by 0.085 and 0.063 LogMAR or four and three ETDRS letters. The likelihood of a 'poor' acuity state was reduced at sites B, C and E when compared with 'identical' eyes treated at site A. The ORs were 0.44 and 0.74 at sites B and E. The data analysed in this study cannot explain this variation. It may result from either baseline characteristics or care processes not studied here, such as tolerance of persistent intra-retinal or subretinal fluid.²⁰ In an earlier study involving 12 sites, Talks *et al* found significant variation in baseline and month 12 acuities. After adjustment, the odds of achieving a 'good' acuity state at the 'best' site was 1.53 (95% CI 1.15 to 2.05).¹²

The use of pooled data from multiple sites with wide geographical coverage adds validity to the findings of this study and improves the generalisability of study findings to the wider NHS NvAMD population. Real-world evidence can help shape and improve clinical practice.²¹ Many of the key findings are supported by other publications, but the associations with independent living status and socioeconomic status are novel. Loss to follow-up before the month 12 visit is a potential weakness. However, almost 85% of patients did reach this milestone and this figure compares favourably to other real-world data sets.^{11 12 17}

As the data extracted for this study was collected as part of routine clinical practice in the publicly funded NHS, the findings may not be applicable to other healthcare systems. Different, licensed therapies were used, but there is little data to suggest meaningful differences in visual outcomes.^{22 23} In addition, other factors that may be associated with visual acuity outcomes, such as smoking history, time to diagnosis and adherence to treatment, were not included in the analysis given concerns about the quality of data entry. Data entry for smoking history in this study suggested a prevalence much lower than the estimated prevalence of 14.9% among UK adults in 2017 and 2018.²⁴ Lesion type and the preferred treatment regimen were also not recorded, although the stated regimen at all sites was 'treat and extend', according to the clinical leads for medical retina. Similarly, the times from the onset of symptoms to initial presentation, referral from primary care, diagnosis and the start of treatment are not recordable within the current version of the Medisoft EMR and the contribution of these variables to acuity outcomes is not known. Finally, the use of median values for acuity at baseline and month 12 may have underestimated the population level visual acuity change when compared with the use of mean letter score change.

Although baseline visual acuity was the strongest predictor of both visual acuity outcome and state, several other baseline characteristics and care processes were also associated with visual acuity outcomes. Benchmarking of acuity outcomes should adjust for baseline acuity, age and

socioeconomic deprivation. These characteristics appear more important than the care processes. Despite case-mix adjustment, there was evidence of variation in visual acuity outcomes between sites. Additional investigation is required to identify other baseline characteristics or care processes that explain this variation. Sharing of best practice may help to address the causes of this health inequality.

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Contributors The authors SDR, GCC, RMW and MM were all involved in the design of the study, data analysis and initial preparation of the manuscript. AL and all the named collaborators in the Real World AMD treatment outcomes User Group helped to secure local permissions for data extraction and had the opportunity to review and amend early drafts of the manuscript. Each contributorship statement must make clear who is responsible for the overall content as guarantor. MM acted as guarantor and accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by University of Leeds Medicine and Health Faculty Research Ethics Committee (MREC 19008). Permission for the release and transfer of anonymised data at each site was provided by the local Caldicott Guardians.

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement No data are available. Access to the anonymised data from each collaborating site data required local Caldicott Guardian and/or Information Governance approval. The approval specified that the data would not be shared with any third parties. Reasonable requests for additional analysis of the data will be considered. Due to the nature of this research, the Caldicott guardians at each participating site of this study did not agree for the data to be shared publicly, so supporting data is not available.

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