AVID: Complete results of all published data analyses for BCVA

This document presents tables and figures for all analyses, including meta-analyses, network meta-analyses and threshold analyses using data from publications of included RCTs for the outcome BCVA (measured either using ETDRS or logMAR scales).

Proliferative diabetic retinopathy

All figures and tables relate to the trials of proliferative diabetic retinopathy (PDR), excluding the two trials (PANORAMA, PROTOCOL W) of non-proliferative retinopathy. For their results, see the end of this document.

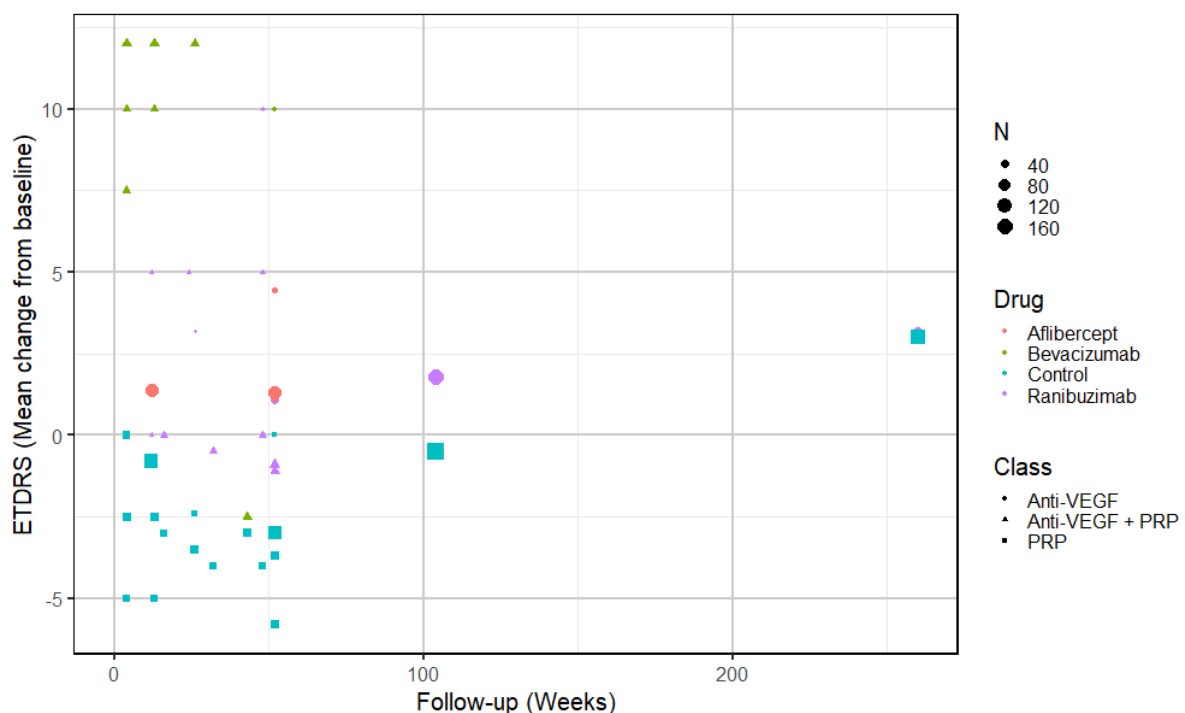## 1 FIGURES AND FOREST PLOTS SUMMARISING BCVA DATA

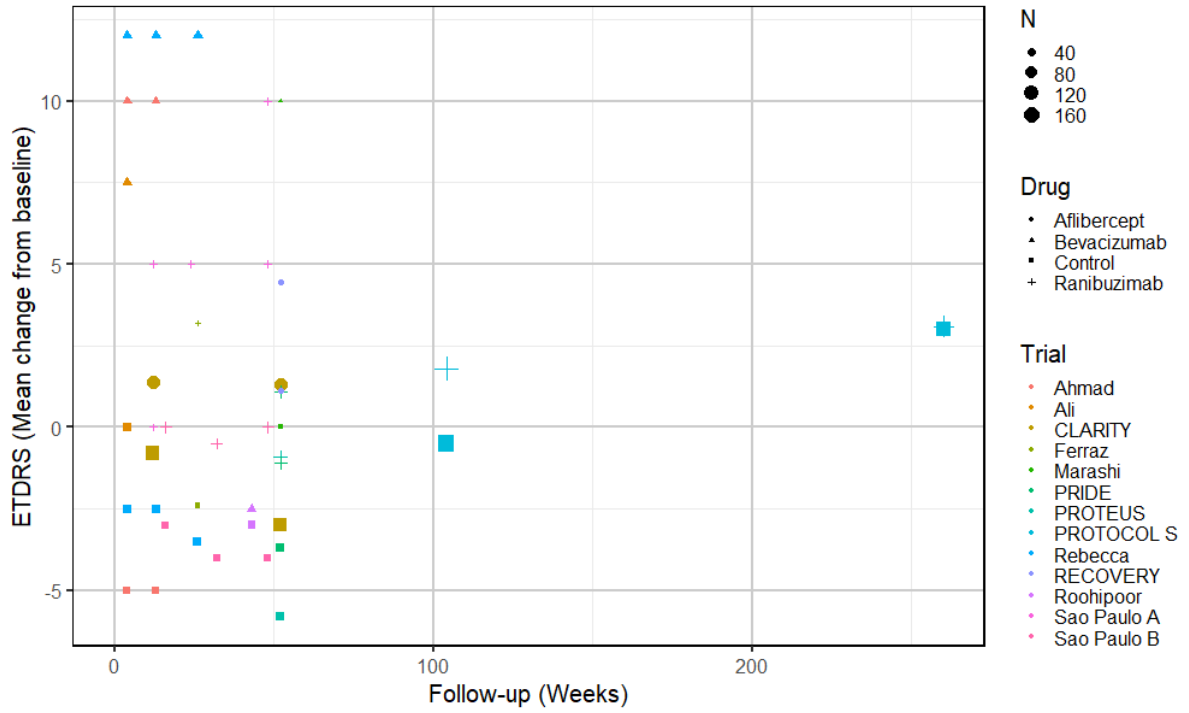*Figure 1 All ETDRS data (as mean change from baseline) by drug and type of intervention*

Figure 2 All ETDRS data (as mean change from baseline) by trial and drug type
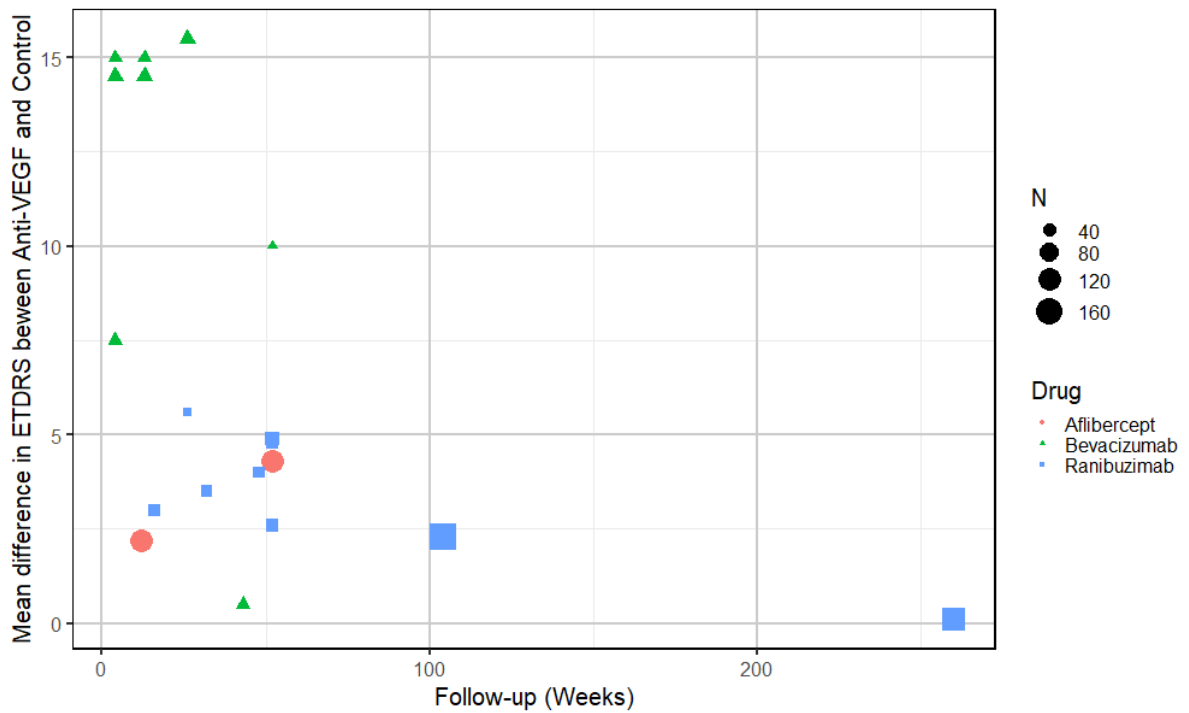
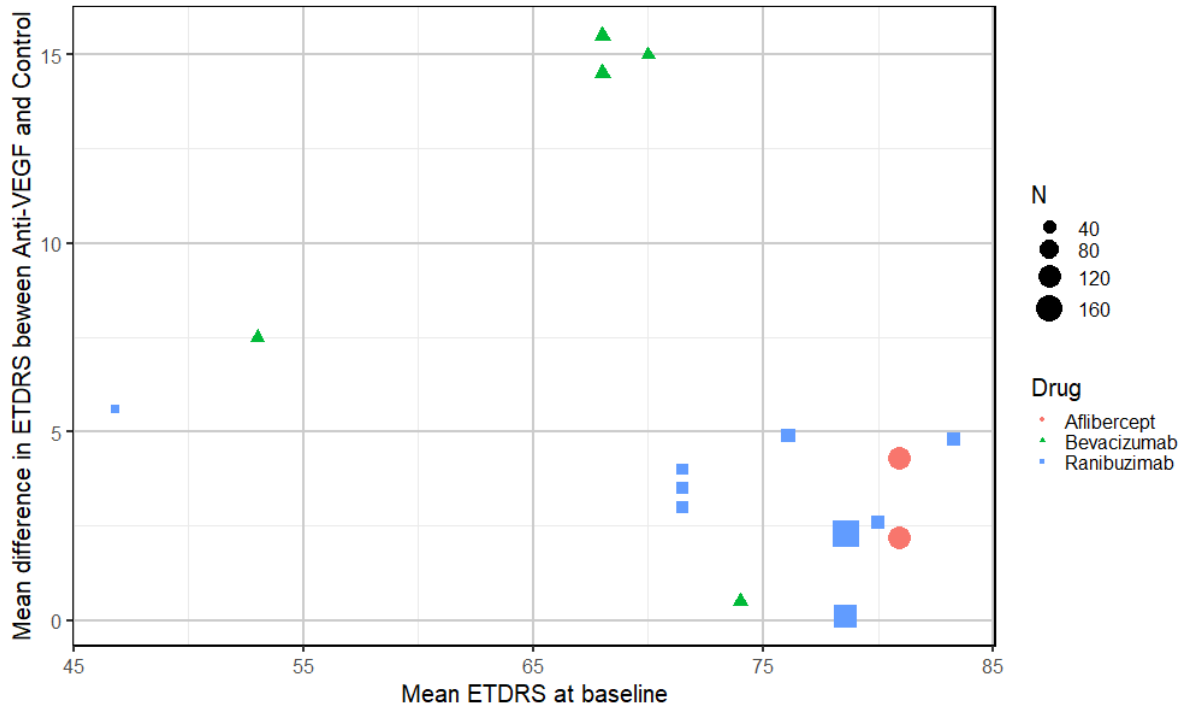*Figure 3 Mean difference in ETDRS between anti-VEGF and control arms over time*

Figure 4 Mean difference between anti-VEGF and control arms by ETDRS at randomisation

Note from these figures that there appears to be a possible decline in benefit to vison over time, and that the benefit of ant-VEGF may be greater in people with poorer initial vision, but these difference may be confounded by differences between types of anti-VEGF.
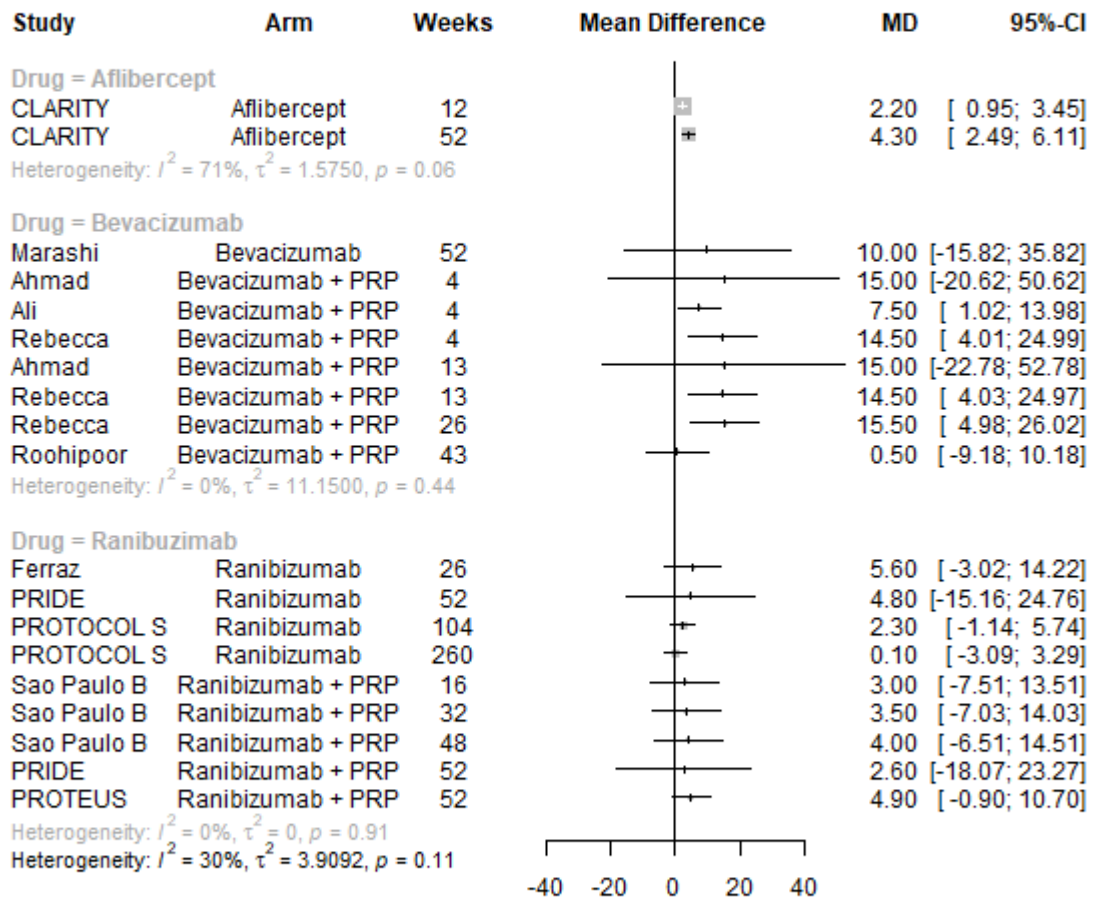
Study	Arm	Weeks	Mean Difference	MD	95%-CI
Drug = Aflibercept					
CLARITY	Aflibercept	12		2.20	[0.95; 3.45]
CLARITY	Aflibercept	52		4.30	[2.49; 6.11]
Heterogeneity: I^2 = 71%, τ^2 = 1.5750, p = 0.06					
Drug = Bevacizumab					
Marashi	Bevacizumab	52		10.00	[-15.82; 35.82]
Ahmad	Bevacizumab + PRP	4		15.00	[-20.62; 50.62]
Ali	Bevacizumab + PRP	4		7.50	[1.02; 13.98]
Rebecca	Bevacizumab + PRP	4		14.50	[4.01; 24.99]
Ahmad	Bevacizumab + PRP	13		15.00	[-22.78; 52.78]
Rebecca	Bevacizumab + PRP	13		14.50	[4.03; 24.97]
Rebecca	Bevacizumab + PRP	26		15.50	[4.98; 26.02]
Roohipoor	Bevacizumab + PRP	43		0.50	[-9.18; 10.18]
Heterogeneity: I^2 = 0%, τ^2 = 11.1500, p = 0.44					
Drug = Ranibuzimab					
Ferraz	Ranibizumab	26		5.60	[-3.02; 14.22]
PRIDE	Ranibizumab	52		4.80	[-15.16; 24.76]
PROTOCOL S	Ranibizumab	104		2.30	[-1.14; 5.74]
PROTOCOL S	Ranibizumab	260		0.10	[-3.09; 3.29]
Sao Paulo B	Ranibizumab + PRP	16		3.00	[-7.51; 13.51]
Sao Paulo B	Ranibizumab + PRP	32		3.50	[-7.03; 14.03]
Sao Paulo B	Ranibizumab + PRP	48		4.00	[-6.51; 14.51]
PRIDE	Ranibizumab + PRP	52		2.60	[-18.07; 23.27]
PROTEUS	Ranibizumab + PRP	52		4.90	[-0.90; 10.70]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91					
Heterogeneity: I^2 = 30%, τ^2 = 3.9092, p = 0.11					

-40 -20 0 20 40

Figure 5 Forest plot of all mean differences in ETDRS between anti-VEGF and control (right side favours anti-VEGF)

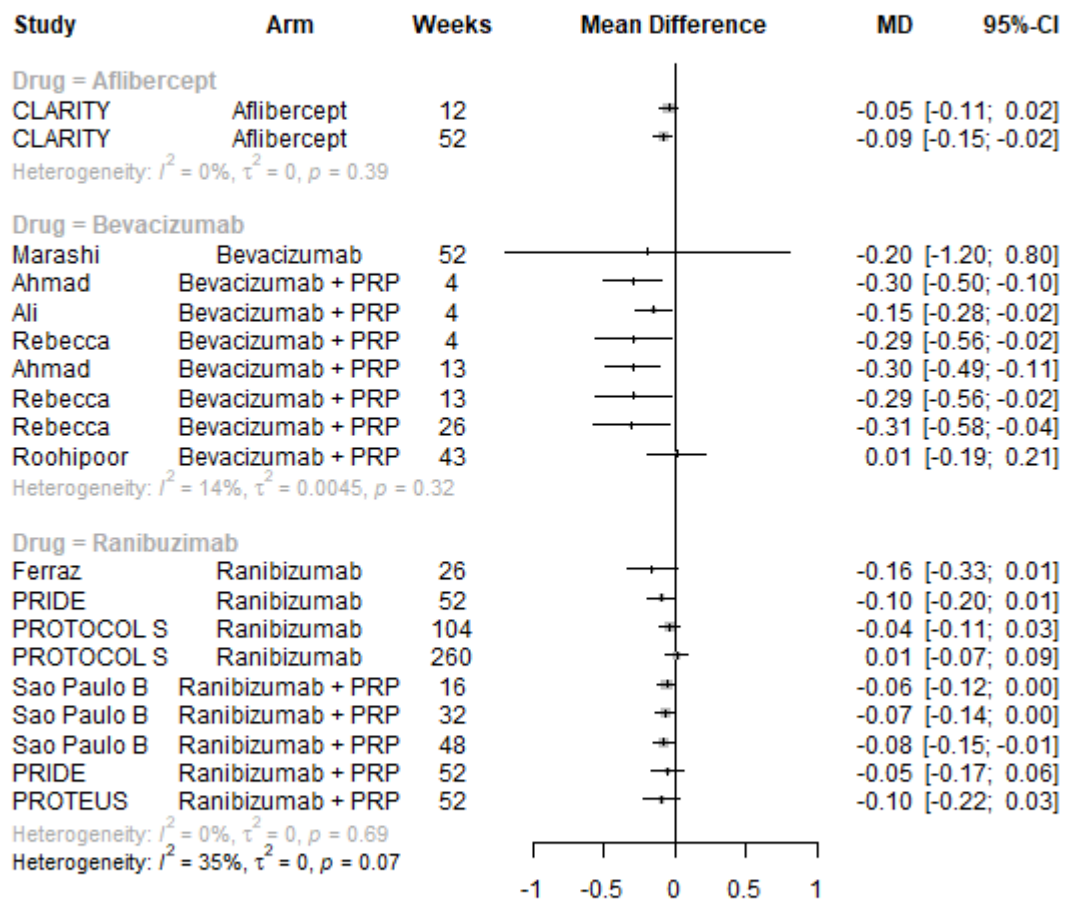| Study	Arm	Weeks	Mean Difference	MD	95%-CI
Drug = Aflibercept					
CLARITY	Aflibercept	12		-0.05	[-0.11; 0.02]
CLARITY	Aflibercept	52		-0.09	[-0.15; -0.02]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.39					
Drug = Bevacizumab					
Marashi	Bevacizumab	52		-0.20	[-1.20; 0.80]
Ahmad	Bevacizumab + PRP	4		-0.30	[-0.50; -0.10]
Ali	Bevacizumab + PRP	4		-0.15	[-0.28; -0.02]
Rebecca	Bevacizumab + PRP	4		-0.29	[-0.56; -0.02]
Ahmad	Bevacizumab + PRP	13		-0.30	[-0.49; -0.11]
Rebecca	Bevacizumab + PRP	13		-0.29	[-0.56; -0.02]
Rebecca	Bevacizumab + PRP	26		-0.31	[-0.58; -0.04]
Roohipoor	Bevacizumab + PRP	43		0.01	[-0.19; 0.21]
Heterogeneity: I^2 = 14%, τ^2 = 0.0045, p = 0.32					
Drug = Ranibuzimab					
Ferraz	Ranibizumab	26		-0.16	[-0.33; 0.01]
PRIDE	Ranibizumab	52		-0.10	[-0.20; 0.01]
PROTOCOL S	Ranibizumab	104		-0.04	[-0.11; 0.03]
PROTOCOL S	Ranibizumab	260		0.01	[-0.07; 0.09]
Sao Paulo B	Ranibizumab + PRP	16		-0.06	[-0.12; 0.00]
Sao Paulo B	Ranibizumab + PRP	32		-0.07	[-0.14; 0.00]
Sao Paulo B	Ranibizumab + PRP	48		-0.08	[-0.15; -0.01]
PRIDE	Ranibizumab + PRP	52		-0.05	[-0.17; 0.06]
PROTEUS	Ranibizumab + PRP	52		-0.10	[-0.22; 0.03]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69					
Heterogeneity: I^2 = 35%, τ^2 = 0, p = 0.07					

-1   -0.5   0   0.5   1

Figure 6 Forest plot of all mean differences in logMAR between anti-VEGF and control (left side favours anti-VEGF)

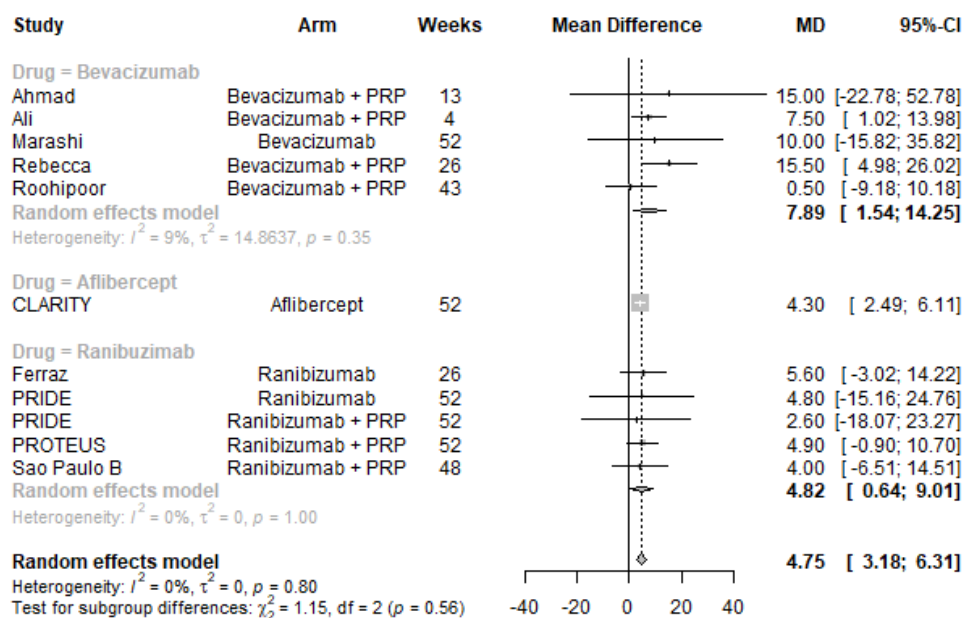# 2 STANDARD META-ANALYSES OF BCVA

2.1 UP TO 1 YEAR

Figure 7 Meta-analysis of mean differences in ETDRS between anti-VEGF and control up to 1 year of follow-up (right side favours anti-VEGF)
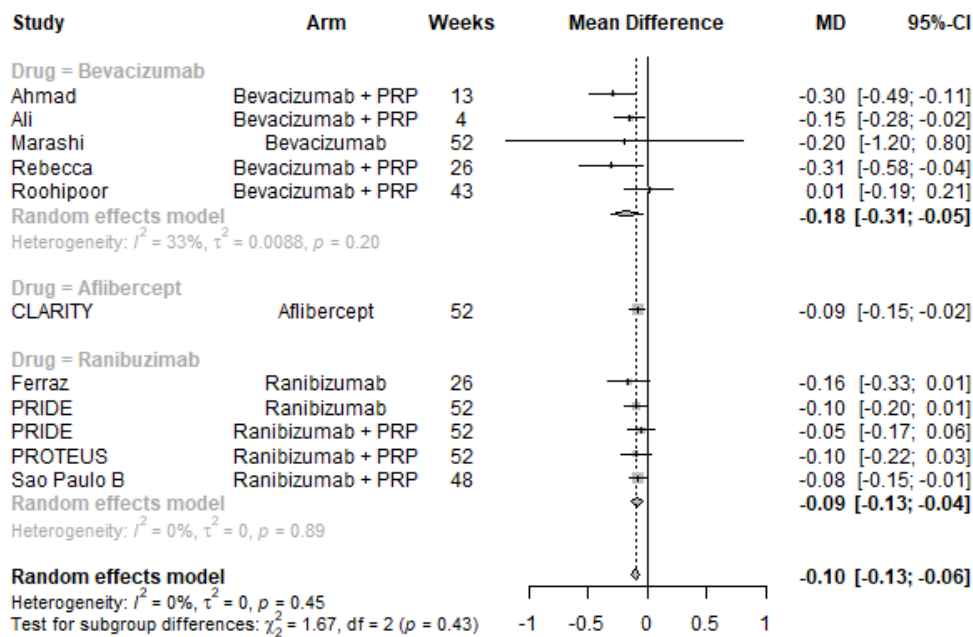

Figure 8 Meta-analysis of mean differences in logMAR between anti-VEGF and control up to 1 year of follow-up (left side favours anti-VEGF)
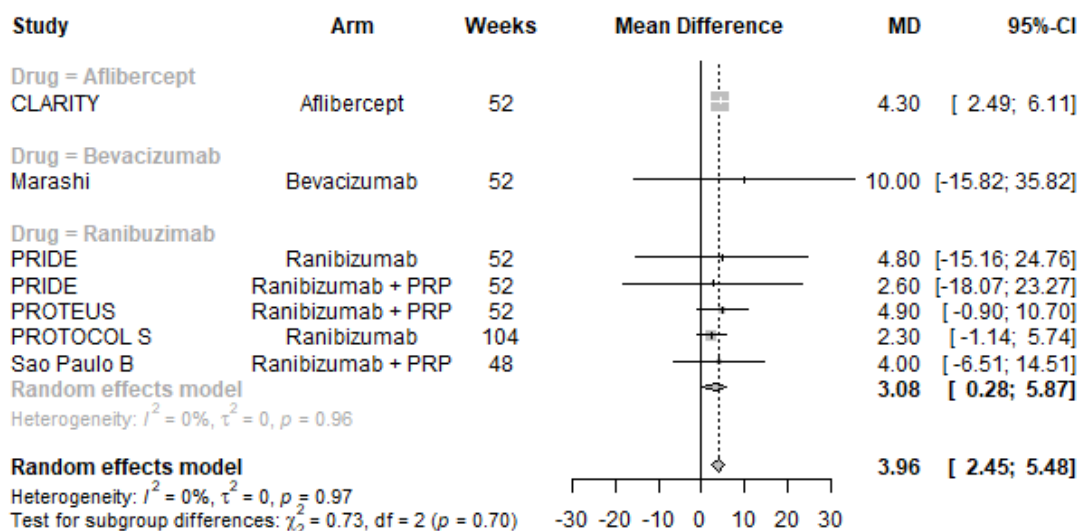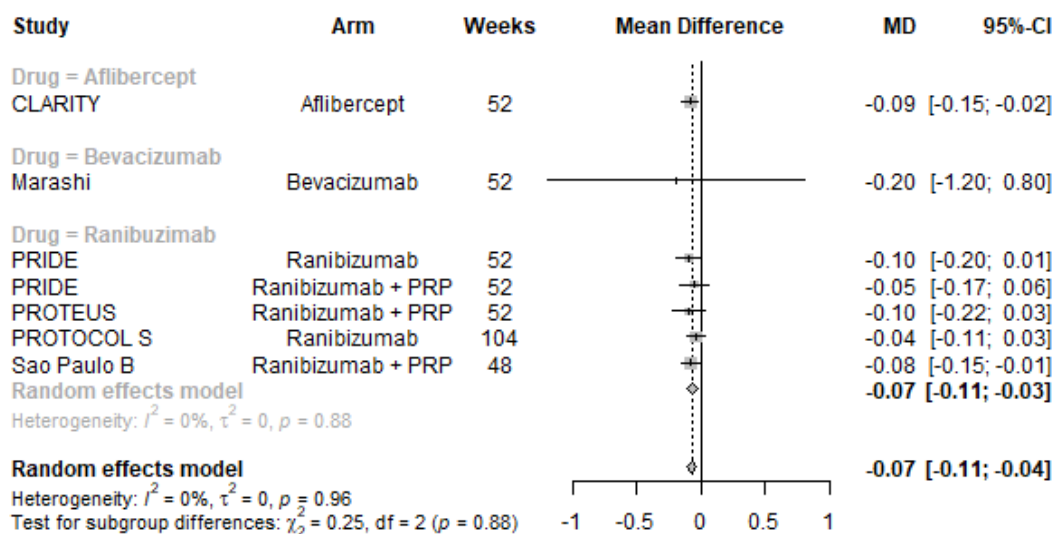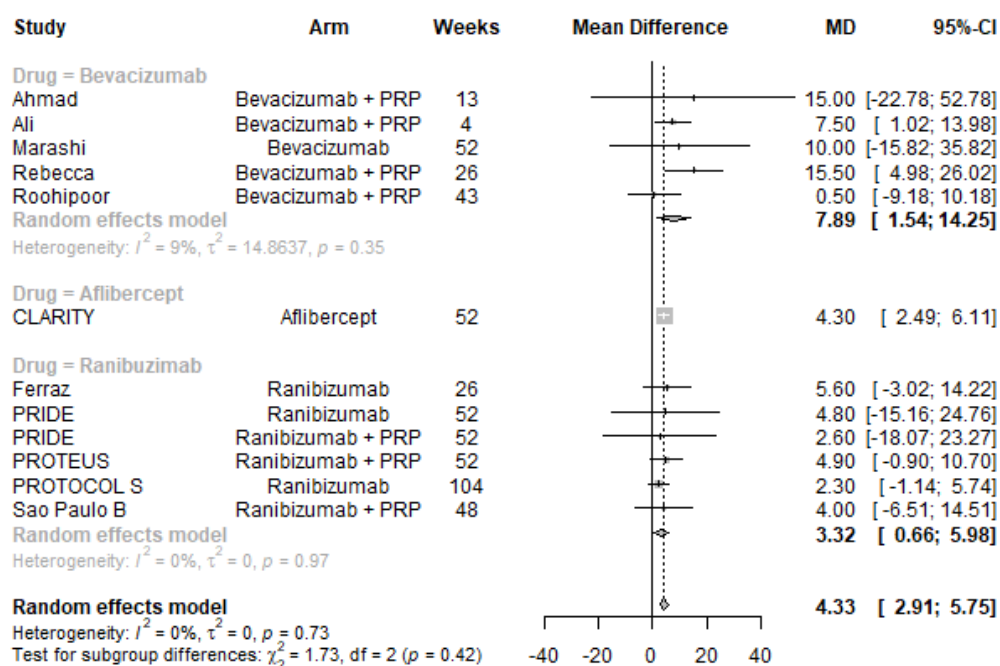
2.2 1 TO 2 YEARS' FOLLOW-UP

Figure 9 Meta-analysis of mean differences in ETDRS between anti-VEGF and control with 1 to 2 years' of follow-up (right side favours anti-VEGF)

Figure 10 Meta-analysis of mean differences in logMAR between anti-VEGF and control with 1 to 2 years' of follow-up (left side favours anti-VEGF)

2.3 MAXIMUM FOLLOW-UP IN TRIAL (UP TO 2 YEARS)

Figure 11 Meta-analysis of mean differences in ETDRS between anti-VEGF and control at end of trial (right side favours anti-VEGF)
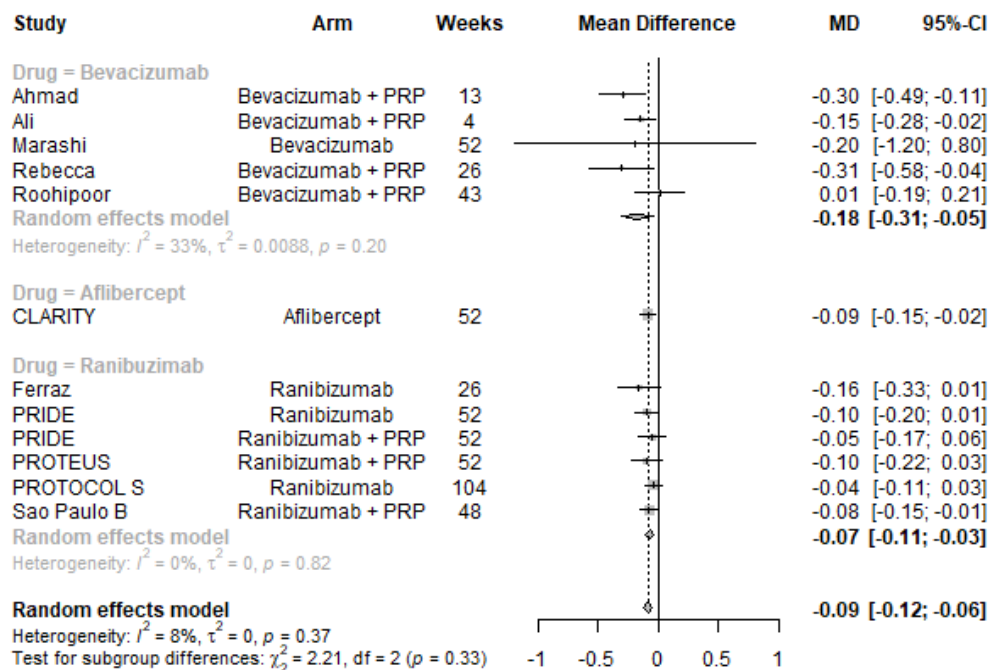
Figure 12 Meta-analysis of mean differences in logMAR between anti-VEGF and control at end of trial (left side favours anti-VEGF)

3 STANDARD NETWORK META-ANALYSES OF BCVA (AS LOGMAR)

Note: From this point forward on meta-analyses of BCVA measured using logMAR are presented. Some analyses using ETDRS were performed, but are not included here to save space and because they are less mathematically robust. Similarly, only random effects analyses are presented for simplicity, as differences between random and fixed effect analyses were minimal.
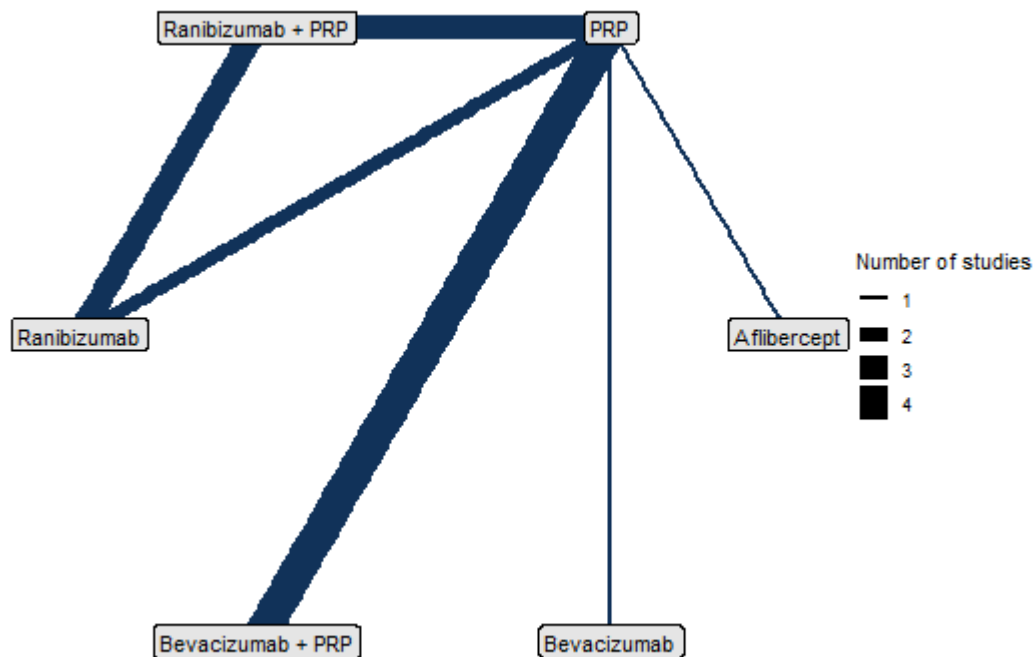
3.1 ANALYSES AT UP TO 1 YEAR OF FOLLOW-UP

Figure 13 Network diagram of BCVA at up to 1 year of follow-up
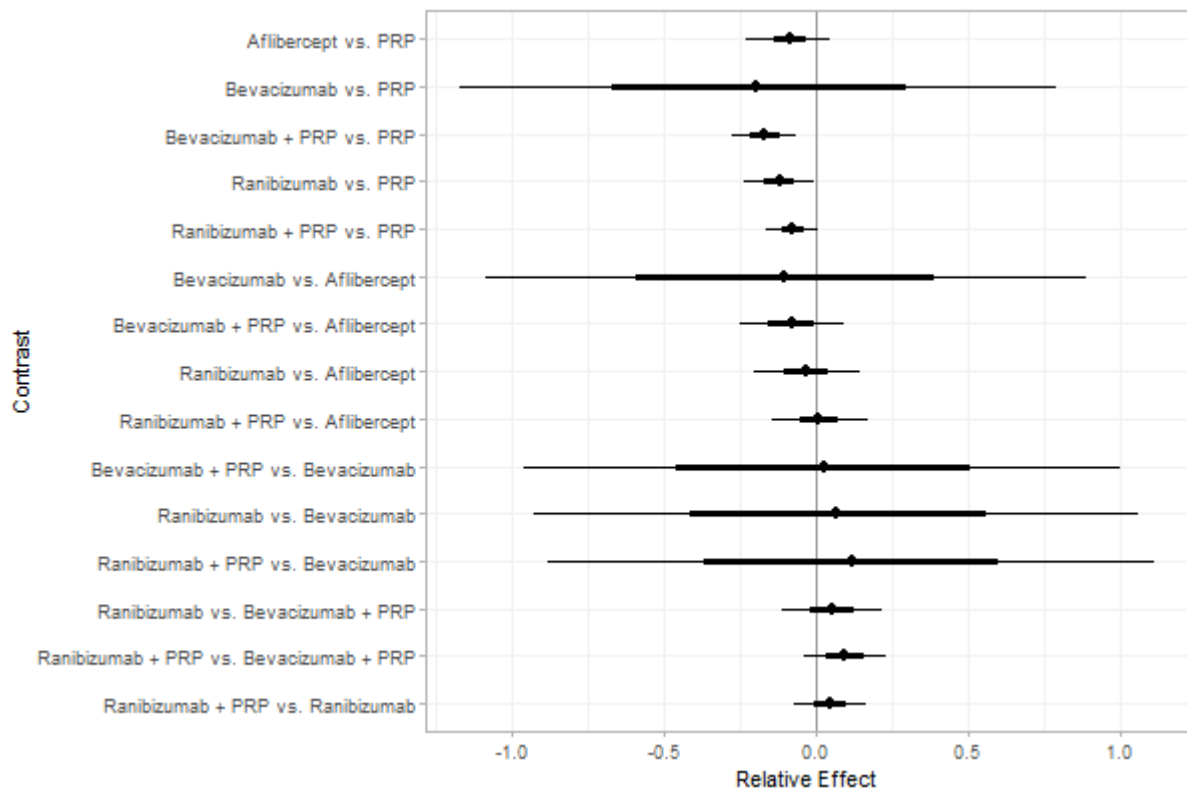
Figure 14 All treatment comparisons for 1-year random-effects NMA of logMAR
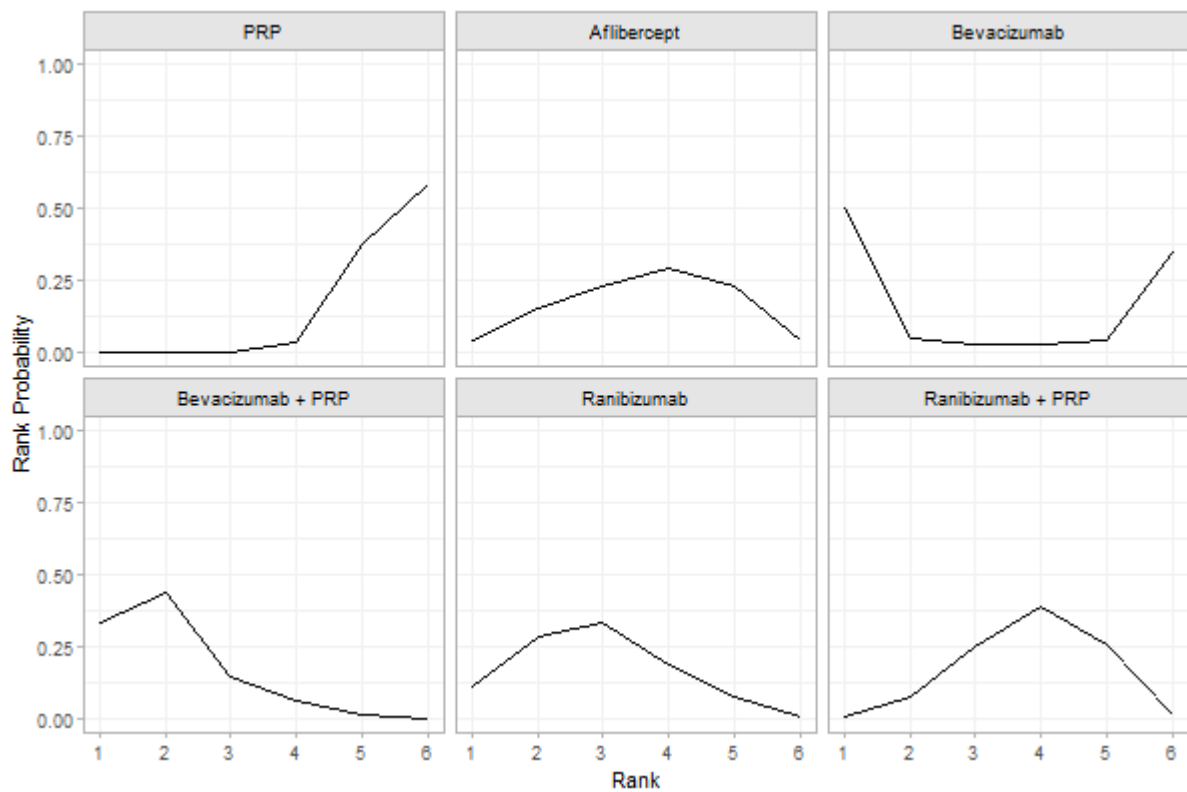

Figure 15 Probability of treatments for 1-year random-effects NMA of logMAR

Table 1 Results of NMA of logMAR up to 1 year - comparisons between treatments

Comparison	Mean difference	95% CI	
d[Aflibercept vs. PRP]	-0.088	-0.232	0.042
d[Bevacizumab vs. PRP]	-0.193	-1.172	0.786
d[Bevacizumab + PRP vs. PRP]	-0.172	-0.282	-0.065
d[Ranibizumab vs. PRP]	-0.123	-0.237	-0.011
d[Ranibizumab + PRP vs. PRP]	-0.080	-0.163	0.003
d[Bevacizumab vs. Aflibercept]	-0.105	-1.084	0.885
d[Bevacizumab + PRP vs. Aflibercept]	-0.084	-0.251	0.088
d[Ranibizumab vs. Aflibercept]	-0.034	-0.204	0.145
d[Ranibizumab + PRP vs. Aflibercept]	0.008	-0.144	0.167
d[Bevacizumab + PRP vs. Bevacizumab]	0.021	-0.963	0.998
d[Ranibizumab vs. Bevacizumab]	0.071	-0.927	1.053
d[Ranibizumab + PRP vs. Bevacizumab]	0.113	-0.881	1.107
d[Ranibizumab vs. Bevacizumab + PRP]	0.050	-0.111	0.217
d[Ranibizumab + PRP vs. Bevacizumab + PRP]	0.092	-0.041	0.230
d[Ranibizumab + PRP vs. Ranibizumab]	0.042	-0.077	0.162

Table 2 Results of NMA of logMAR up to 1 year – ranking probabilities

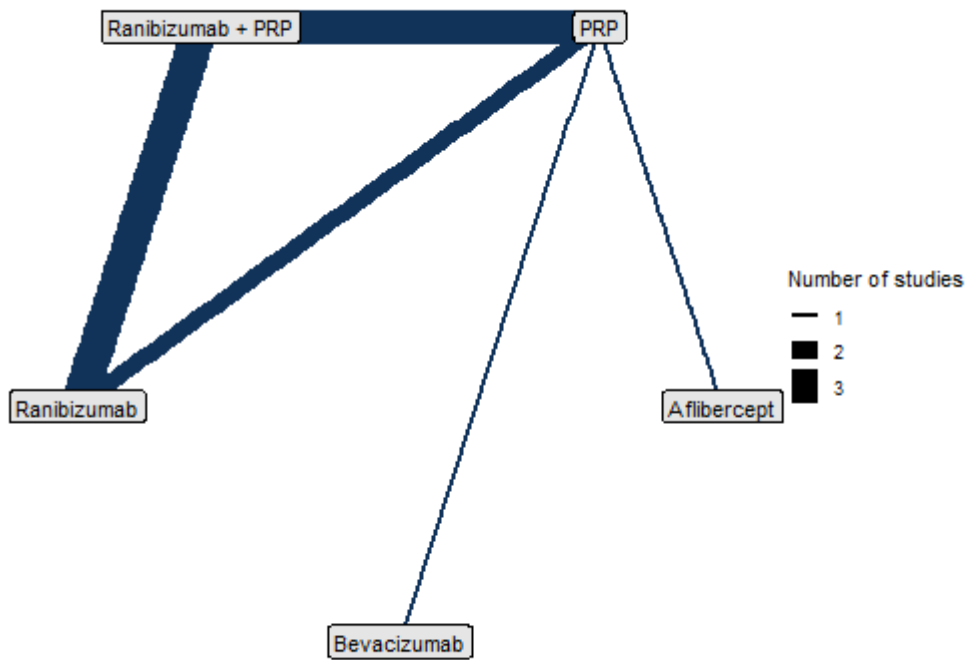| Treatment arm	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]	p_rank[5]	p_rank[6]
d[PRP]	0.00%	0.00%	0.48%	3.53%	37.90%	58.10%
d[Aflibercept]	4.48%	15.08%	23.28%	29.48%	23.15%	4.55%
d[Bevacizumab]	50.23%	4.93%	3.25%	2.83%	3.98%	34.80%
d[Bevacizumab + PRP]	33.50%	44.03%	14.75%	6.25%	1.35%	0.13%
d[Ranibizumab]	10.88%	28.58%	33.10%	18.98%	7.68%	0.80%
d[Ranibizumab + PRP]	0.93%	7.40%	25.15%	38.95%	25.95%	1.63%

3.2 ANALYSES AT 1 TO 2 YEARS' FOLLOW UP

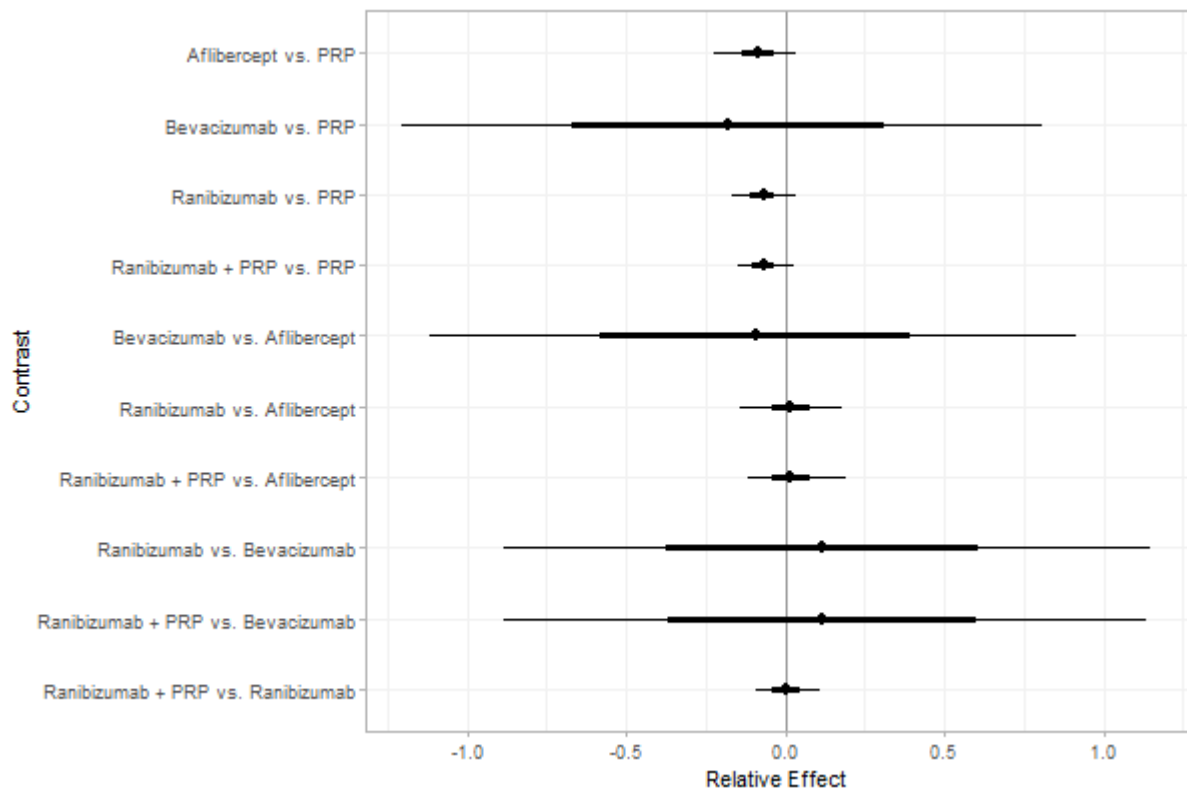*Figure 16 Network diagram of BCVA at up to 1 to 2 years of follow-up*

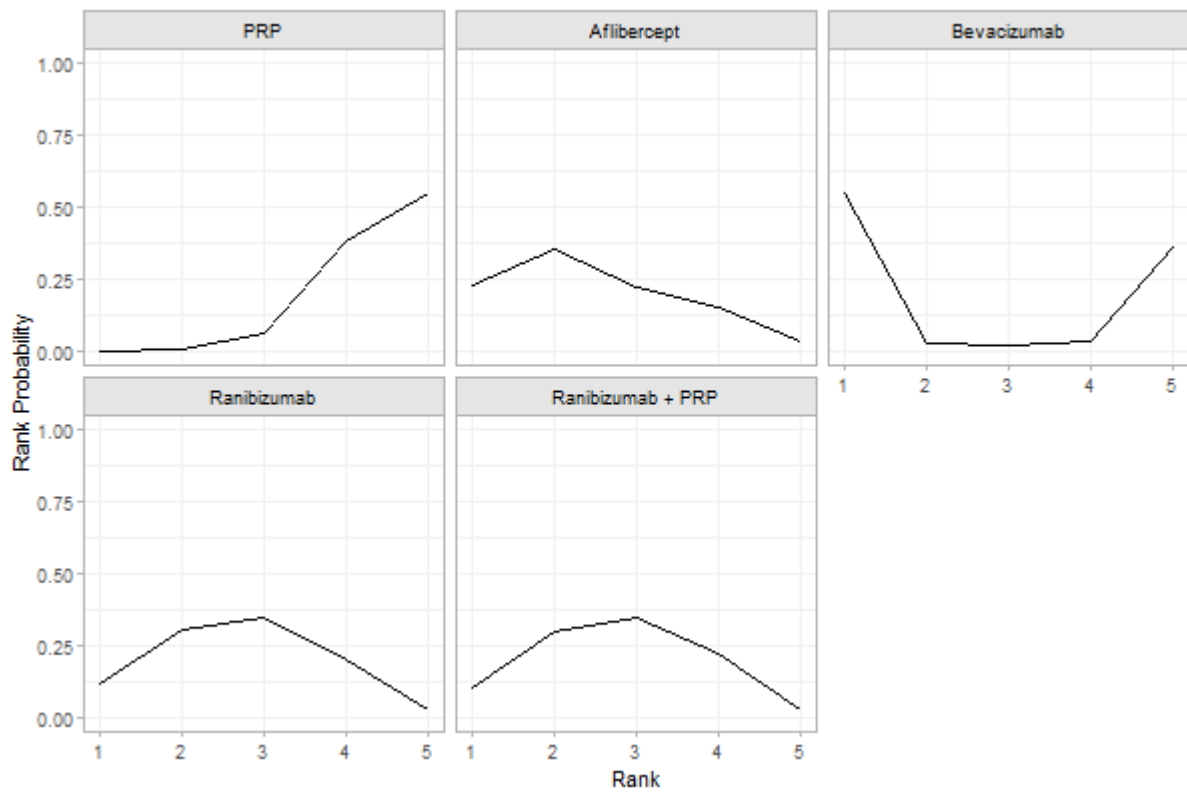*Figure 17 All treatment comparisons for 1 to 2 year random-effects NMA of logMAR*

Figure 18 Probability of treatments for 1 to 2 year random-effects NMA of logMAR

Table 3 Results of NMA of logMAR 1 to 2 years - comparisons between treatments

Comparison	Mean difference	95% CI	
d[Aflibercept vs. PRP]	-0.088	-0.224	0.035
d[Bevacizumab vs. PRP]	-0.183	-1.204	0.807
d[Ranibizumab vs. PRP]	-0.071	-0.167	0.034
d[Ranibizumab + PRP vs. PRP]	-0.068	-0.147	0.029
d[Bevacizumab vs. Aflibercept]	-0.095	-1.117	0.912
d[Ranibizumab vs. Aflibercept]	0.017	-0.143	0.181
d[Ranibizumab + PRP vs. Aflibercept]	0.020	-0.120	0.191
d[Ranibizumab vs. Bevacizumab]	0.112	-0.884	1.149
d[Ranibizumab + PRP vs. Bevacizumab]	0.115	-0.884	1.136
d[Ranibizumab + PRP vs. Ranibizumab]	0.003	-0.093	0.108

Table 4 Results of NMA of logMAR 1 to 2 years – ranking probabilities

parameter	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]	p_rank[5]
d[PRP]	0.10%	0.70%	6.08%	38.53%	54.60%
d[Aflibercept]	22.90%	35.68%	22.38%	15.65%	3.40%
d[Bevacizumab]	54.88%	3.20%	2.23%	3.58%	36.13%
d[Ranibizumab]	11.75%	30.65%	34.43%	20.05%	3.13%
d[Ranibizumab + PRP]	10.38%	29.78%	34.90%	22.20%	2.75%

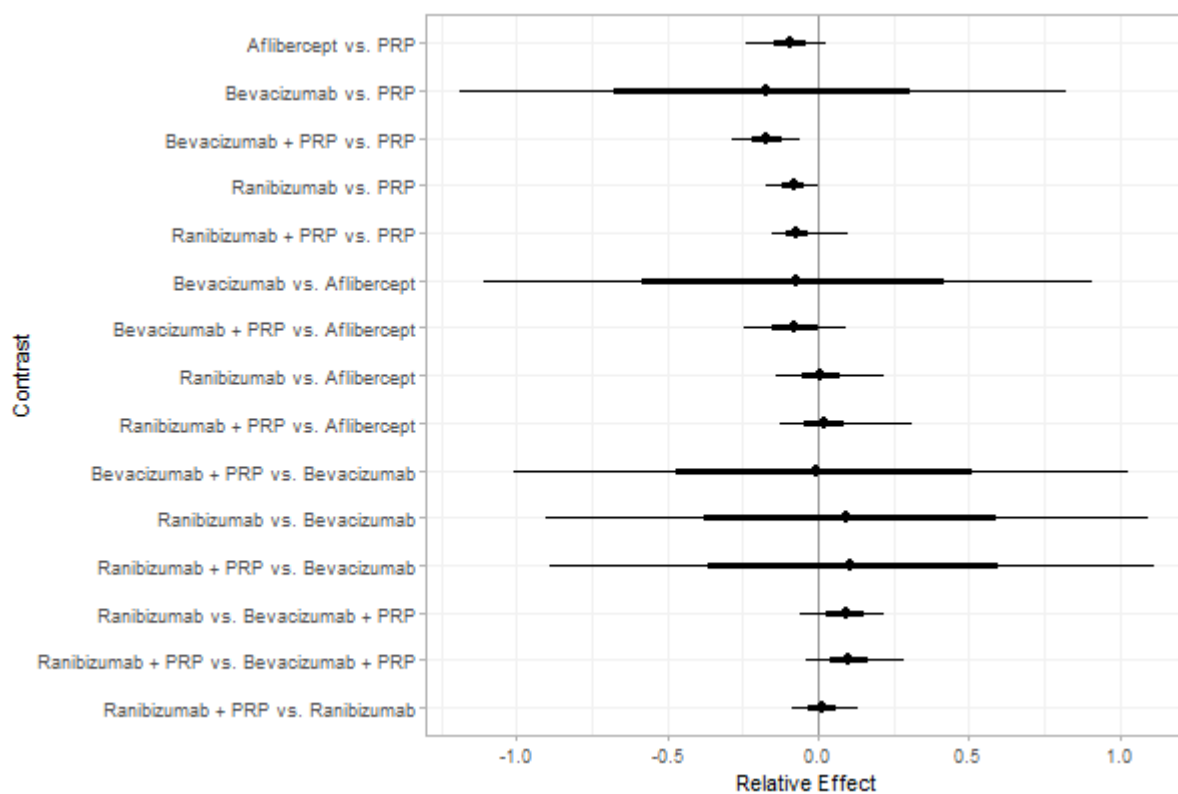## 3.3 ANALYSIS AT MAXIMUM FOLLOW-UP TIME (UP TO 2 YEARS)

Figure 19 All treatment comparisons for end-of-trial random-effects NMA of logMAR
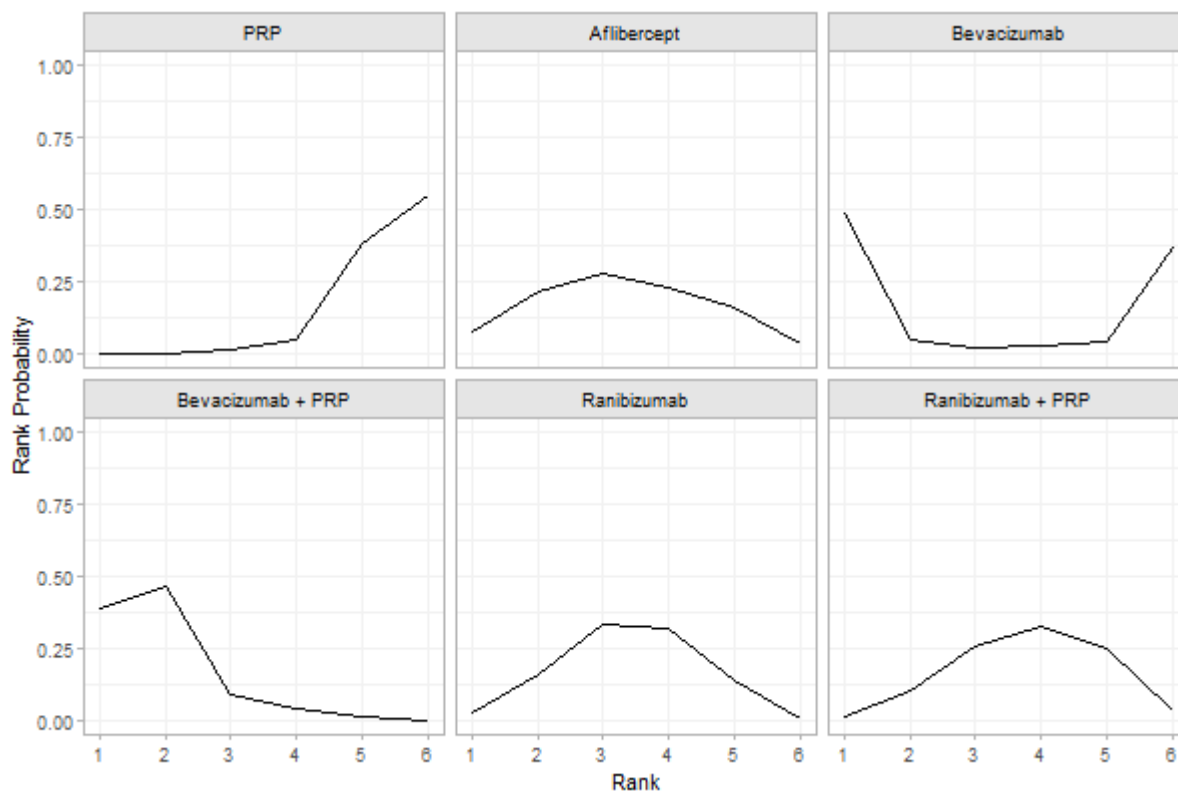

Figure 20 Probability of treatments for end-of-trial random-effects NMA of logMAR

Table 5 Results of NMA of logMAR at end of trial - comparisons between treatments

Comparison	Mean difference	95% CI	
d[Aflibercept vs. PRP]	-0.094	-0.242	0.029
d[Bevacizumab vs. PRP]	-0.180	-1.188	0.822
d[Bevacizumab + PRP vs. PRP]	-0.171	-0.284	-0.058
d[Ranibizumab vs. PRP]	-0.082	-0.172	0.004
d[Ranibizumab + PRP vs. PRP]	-0.066	-0.155	0.103
d[Bevacizumab vs. Aflibercept]	-0.087	-1.109	0.907
d[Bevacizumab + PRP vs. Aflibercept]	-0.078	-0.243	0.094
d[Ranibizumab vs. Aflibercept]	0.011	-0.141	0.217
d[Ranibizumab + PRP vs. Aflibercept]	0.028	-0.125	0.315
d[Bevacizumab + PRP vs. Bevacizumab]	0.009	-1.010	1.027
d[Ranibizumab vs. Bevacizumab]	0.098	-0.902	1.099
d[Ranibizumab + PRP vs. Bevacizumab]	0.114	-0.892	1.113
d[Ranibizumab vs. Bevacizumab + PRP]	0.089	-0.061	0.219
d[Ranibizumab + PRP vs. Bevacizumab + PRP]	0.105	-0.040	0.285
d[Ranibizumab + PRP vs. Ranibizumab]	0.016	-0.087	0.134

Table 6 Results of NMA of logMAR at end of trial – ranking probabilities

Treatment arm	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]	p_rank[5]	p_rank[6]
d[PRP]	0.00%	0.03%	1.48%	5.25%	38.33%	54.93%
d[Aflibercept]	8.03%	21.68%	27.83%	22.80%	16.08%	3.60%
d[Bevacizumab]	48.88%	4.90%	2.55%	2.68%	4.30%	36.70%
d[Bevacizumab + PRP]	38.63%	46.45%	8.83%	4.18%	1.73%	0.20%
d[Ranibizumab]	2.88%	16.20%	33.43%	32.30%	14.30%	0.90%
d[Ranibizumab + PRP]	1.60%	10.75%	25.90%	32.80%	25.28%	3.68%

4 NMAS ALLOWING FOR TIME-VARYING EFFECTS

4.1 ALLOWING FOR VARIATION OVER TIME

Network meta-analyses incorporating all follow-up times, allowing for time-varying effect of anti-VEGF. Time variation is assumed to be the same for all types of anti-VEGF. A selection of output plots are presented. Results are presented for the predicted effects after 2 years of follow-up.

Figure 21 All treatment comparisons for time-adjusted random-effects NMA of logMAR

Table 7 Results of NMA of logMAR adjusting for time - comparisons between treatments

Comparison	Mean difference	95% CI	
d[New 1: Aflibercept vs. PRP]	-0.010	-0.106	0.100
d[New 1: Bevacizumab vs. PRP]	-0.159	-1.165	0.866
d[New 1: Bevacizumab + PRP vs. PRP]	-0.184	-0.505	0.112
d[New 1: Ranibizumab vs. PRP]	-0.058	-0.131	0.000
d[New 1: Ranibizumab + PRP vs. PRP]	-0.040	-0.295	0.198
d[New 1: Bevacizumab vs. Aflibercept]	-0.149	-1.156	0.870
d[New 1: Bevacizumab + PRP vs. Aflibercept]	-0.175	-0.520	0.128
d[New 1: Ranibizumab vs. Aflibercept]	-0.049	-0.174	0.052
d[New 1: Ranibizumab + PRP vs. Aflibercept]	-0.031	-0.312	0.230
d[New 1: Bevacizumab + PRP vs. Bevacizumab]	-0.025	-1.092	1.025
d[New 1: Ranibizumab vs. Bevacizumab]	0.101	-0.912	1.127
d[New 1: Ranibizumab + PRP vs. Bevacizumab]	0.119	-0.924	1.165
d[New 1: Ranibizumab vs. Bevacizumab + PRP]	0.126	-0.178	0.437
d[New 1: Ranibizumab + PRP vs. Bevacizumab + PRP]	0.144	0.039	0.257
d[New 1: Ranibizumab + PRP vs. Ranibizumab]	0.018	-0.229	0.271

Table 8 Results of NMA of logMAR adjusting for time – ranking probabilities

Treatment arm	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]	p_rank[5]	p_rank[6]
d[PRP]	0.10%	1.83%	8.90%	25.58%	40.30%	23.30%
d[Aflibercept]	1.88%	6.73%	16.38%	27.30%	29.30%	18.43%
d[Bevacizumab]	47.13%	7.73%	3.95%	2.90%	2.73%	35.58%
d[Bevacizumab + PRP]	44.75%	38.88%	5.15%	5.58%	5.40%	0.25%
d[Ranibizumab]	6.15%	23.08%	38.78%	25.75%	5.68%	0.58%
d[Ranibizumab + PRP]	0.00%	21.78%	26.85%	12.90%	16.60%	21.88%

4.2   ALLOWING FOR VARIATION OVER TIME AND BY LOGMAR AT RANDOMISATION

Network meta-analyses incorporating all follow-up times, allowing for time-varying effect of anti-VEGF and varying effect by trial mean logMAR at randomisation. Time and logMAR variation are assumed to be the same for all types of anti-VEGF. A selection of output plots are presented. Results are presented for the predicted effects after 2 years of follow-up and at mean baseline BCVA across trials.
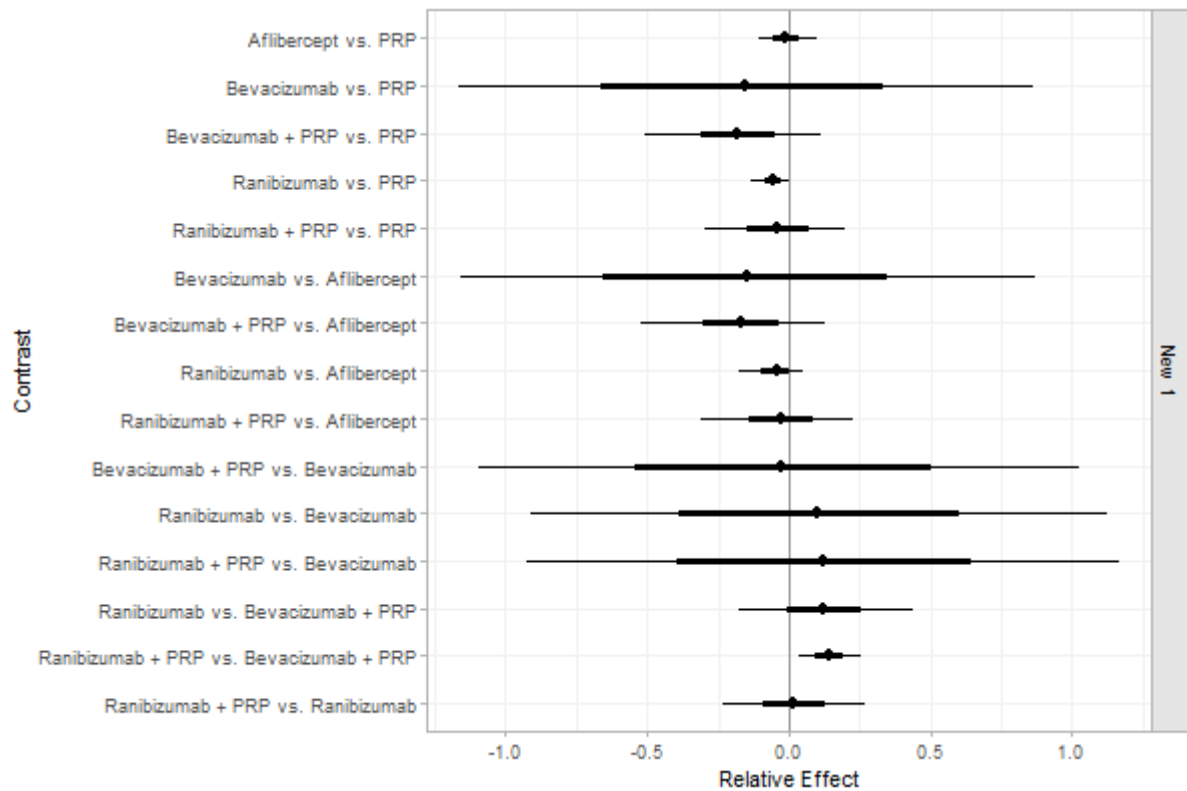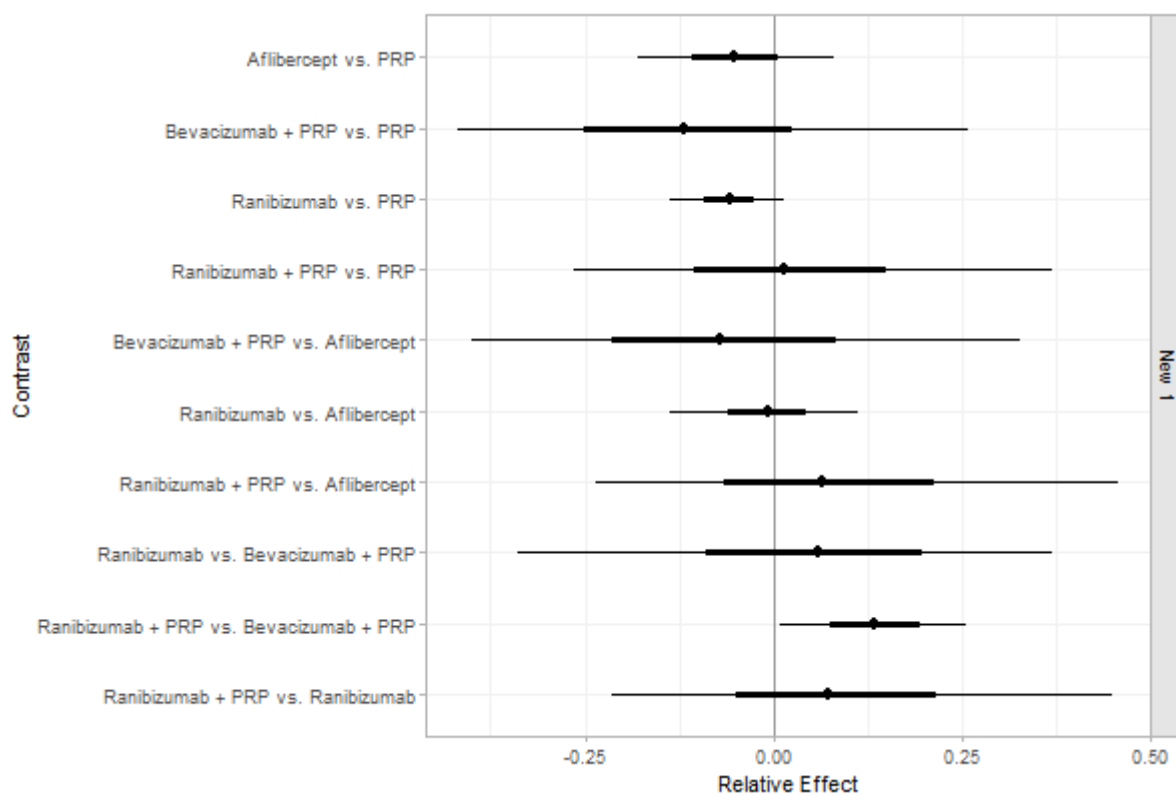

Figure 22 All treatment comparisons for time-adjusted and baseline BCVA adjusted random-effects NMA of logMAR

Table 9 Results of NMA of logMAR adjusting for time and baseline BCVA - comparisons between treatments

Comparison	Mean difference	95% CI	
d[New 1: Aflibercept vs. PRP]	-0.051	-0.178	0.080
d[New 1: Bevacizumab + PRP vs. PRP]	-0.111	-0.418	0.258
d[New 1: Ranibizumab vs. PRP]	-0.060	-0.137	0.014
d[New 1: Ranibizumab + PRP vs. PRP]	0.023	-0.264	0.369
d[New 1: Bevacizumab + PRP vs. Aflibercept]	-0.060	-0.400	0.328
d[New 1: Ranibizumab vs. Aflibercept]	-0.009	-0.138	0.112
d[New 1: Ranibizumab + PRP vs. Aflibercept]	0.074	-0.234	0.457
d[New 1: Ranibizumab vs. Bevacizumab + PRP]	0.052	-0.338	0.370
d[New 1: Ranibizumab + PRP vs. Bevacizumab + PRP]	0.135	0.008	0.257
d[New 1: Ranibizumab + PRP vs. Ranibizumab]	0.083	-0.215	0.449

Table 10 Results of NMA of logMAR adjusting for time and baseline BCVA – ranking probabilities

Treatment	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]	p_rank[5]
d[PRP]	0.78%	4.78%	23.25%	34.80%	36.40%
d[Aflibercept]	19.25%	26.28%	26.55%	17.55%	10.38%
d[Bevacizumab]	61.25%	8.75%	9.83%	18.93%	1.25%
d[Bevacizumab + PRP]	18.25%	35.38%	31.43%	13.88%	1.08%
d[Ranibizumab]	0.48%	24.83%	8.95%	14.85%	50.90%

Table 10 Results of NMA of logMAR adjusting for time and baseline BCVA – ranking probabilities

	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]	p_rank[5]

5 NMAs of reduced networks

5.1 Assuming anti-VEGF and anti-VEGF+PRP are equivalent

This analysis assumes that anti-VEGF only arms and anti-VEGF+PRP arms have equal effect. To be used to assess differences between anti-VEGF types. A model allowing effect to vary with time and baseline logMAR was used. Results are presented for the predicted effects after 2 years of follow-up and at mean baseline BCVA across trials.
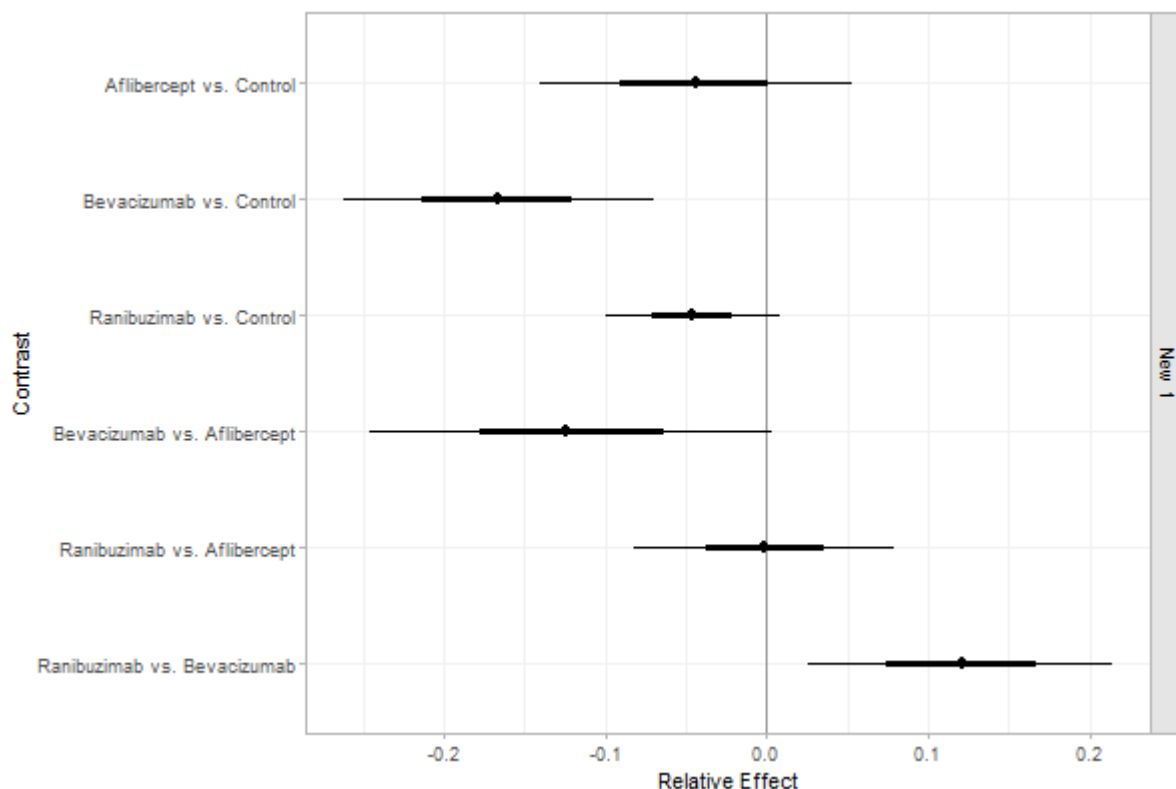

Figure 23 Results from a reduced network to compare anti-VEGFs

Table 11 Results of reduced network to compare anti-VEGFs - comparisons between treatments

Comparison	Mean difference	95% CI	
d[New 1: Aflibercept vs. PRP]	-0.044	-0.140	0.053
d[New 1: Bevacizumab vs. PRP]	-0.167	-0.262	-0.070
d[New 1: Ranibuzimab vs. PRP]	-0.046	-0.099	0.008
d[New 1: Bevacizumab vs. Aflibercept]	-0.122	-0.246	0.003
d[New 1: Ranibuzimab vs. Aflibercept]	-0.002	-0.083	0.079
d[New 1: Ranibuzimab vs. Bevacizumab]	0.121	0.026	0.214

Table 12 Results of reduced network to compare anti-VEGFs - ranking probabilities

Treatment	p_rank[1]	p_rank[2]	p_rank[3]	p_rank[4]
d[New 1: PRP]	0.00%	2.95%	16.15%	80.90%
d[New 1: Aflibercept]	2.63%	45.80%	34.65%	16.93%
d[New 1: Bevacizumab]	97.05%	2.43%	0.53%	0.00%
d[New 1: Ranibuzimab]	0.33%	48.83%	48.68%	2.18%

5.2 ASSUMING ALL TYPES OF ANTI-VEGF ARE EQUIVALENT

This analysis assumes that all three anti-VEGF drugs have equal effect. To be used to assess the overall effect of anti-VEGF. A model allowing effect to vary with time and baseline logMAR was used.
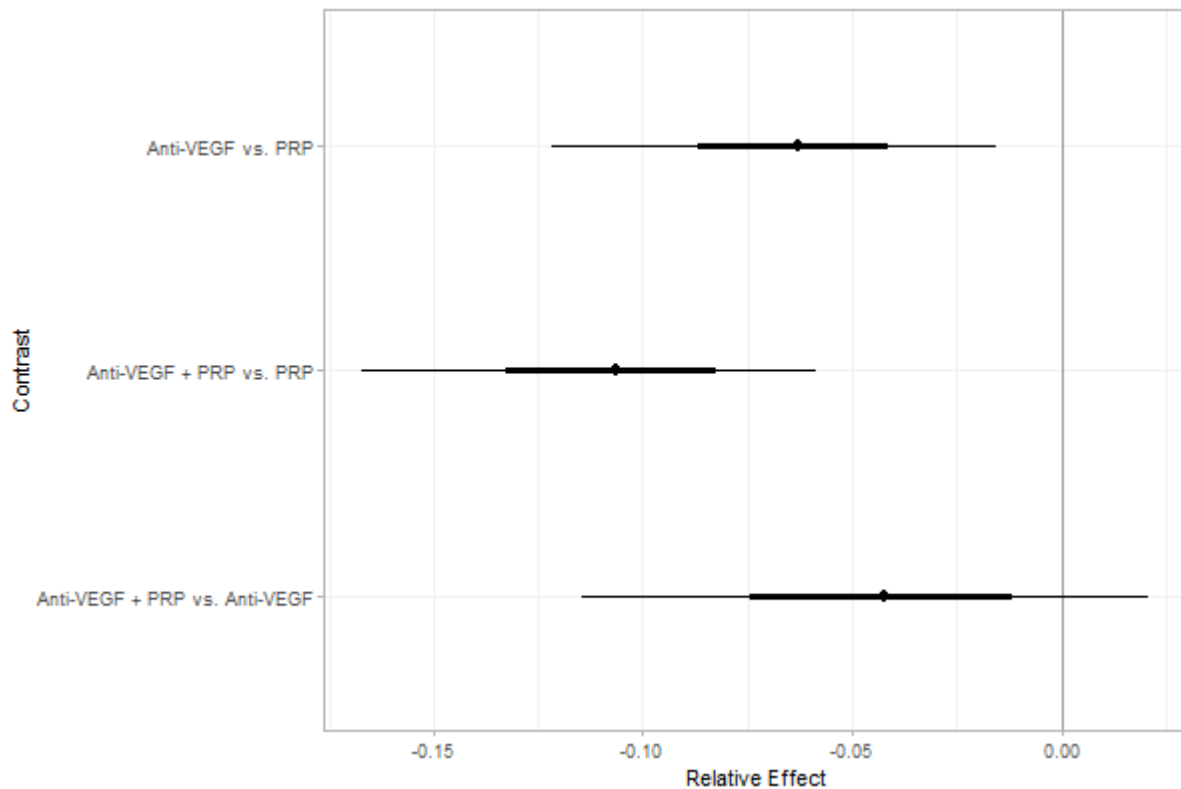
Figure 24 Results from a reduced network to compare treatment classes

Table 13 Results of reduced network to compare treatment classes - comparisons between treatments

Comparison	Mean difference	95% CI	
d[Anti-VEGF vs. PRP]	-0.064	-0.122	-0.015
d[Anti-VEGF + PRP vs. PRP]	-0.108	-0.167	-0.059
d[Anti-VEGF + PRP vs. Anti-VEGF]	-0.044	-0.115	0.021

Table 14 Results of reduced network to compare treatment classes - ranking probabilities

Treatment	p_rank[1]	p_rank[2]	p_rank[3]
d[PRP]	0.00%	0.90%	99.10%
d[Anti-VEGF]	9.48%	89.63%	0.90%
d[Anti-VEGF + PRP]	90.53%	9.48%	0.00%

6 THRESHOLD ANALYSES

Up to 1 year

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Ranibizumab + PRP vs. PRP	-0.08	(-0.13, -0.03)	Ranibizumab + PRP	(-0.45, -0.03)	Bevacizumab + PRP
Bevacizumab + PRP vs. PRP	-0.17	(-0.26, -0.08)	Bevacizumab + PRP	(-0.21, 0.09)	Ranibizumab
Ranibizumab vs. PRP	-0.12	(-0.20, -0.04)	Bevacizumab + PRP	(-0.17, NT)	–
Aflibercept vs. PRP	-0.09	(-0.15, -0.02)	Bevacizumab + PRP	(-0.11, NT)	–
Bevacizumab vs. PRP	-0.20	(-1.18, 0.81)	–	(NT, -0.17)	Bevacizumab + PRP
Ranibizumab vs. Ranibizumab + PRP	-0.04	(-0.13, 0.04)	Bevacizumab + PRP	(-0.09, NT)	–

◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 25 Threshold analyses of data up to 1 year of follow-up

1 to 2 years

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Ranibizumab + PRP vs. PRP	-0.07	(-0.12, -0.02)	Ranibizumab + PRP	(-0.19, NT)	–
Ranibizumab vs. PRP	-0.07	(-0.12, -0.01)	Ranibizumab	(-0.14, NT)	–
Aflibercept vs. PRP	-0.09	(-0.15, -0.02)	–	(NT, 0.05)	Ranibizumab + PRP
Bevacizumab vs. PRP	-0.22	(-1.19, 0.78)	–	(NT, -0.09)	Aflibercept
Ranibizumab vs. Ranibizumab + PRP	0.00	(-0.07, 0.07)	Ranibizumab	(-0.54, NT)	–

◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 26 Threshold analyses of data with 1 to 2 years of follow-up

Maximum follow-up (up to 2 years)

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Ranibizumab + PRP vs. PRP	-0.07	(-0.13, -0.02)	–	(NT, -0.04)	Bevacizumab + PRP
Bevacizumab + PRP vs. PRP	-0.17	(-0.26, -0.08)	Bevacizumab + PRP	(-0.22, 0.29)	Aflibercept
Ranibizumab vs. PRP	-0.08	(-0.13, -0.02)	Ranibizumab	(-0.55, -0.02)	Bevacizumab + PRP
Aflibercept vs. PRP	-0.09	(-0.15, -0.02)	Bevacizumab + PRP	(-0.17, NT)	–
Bevacizumab vs. PRP	-0.21	(-1.20, 0.80)	–	(NT, -0.17)	Bevacizumab + PRP
Ranibizumab vs. Ranibizumab + PRP	-0.00	(-0.07, 0.06)	Bevacizumab + PRP	(-0.51, 3.24)	Ranibizumab + PRP

◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 27 Threshold analyses of data at end of trial (up to 2 years)

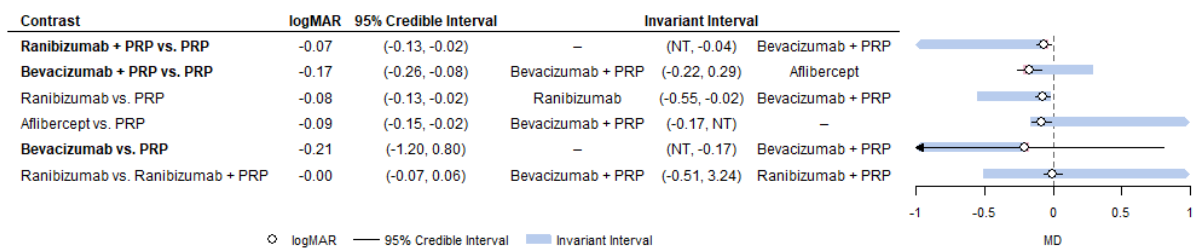## Allowing for effect variation with time and baseline logMAR

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Bevacizumab + PRP vs. PRP	-0.02	(-0.18, 0.14)	Bevacizumab + PRP	(-0.85, 0.01)	Ranibizumab
Ranibizumab + PRP vs. PRP	-0.16	(-0.34, 0.03)	–	(NT, -0.13)	Aflibercept
Ranibizumab vs. PRP	-0.06	(-0.11, 0.00)	Ranibizumab	(-0.14, 2.21)	PRP
Aflibercept vs. PRP	-0.05	(-0.15, 0.04)	Aflibercept	(-0.12, NT)	–
Ranibizumab vs. Bevacizumab + PRP	-0.04	(-0.20, 0.14)	–	(NT, NT)	–

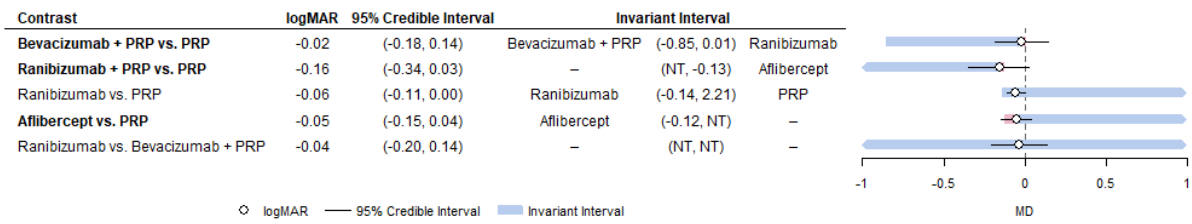◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 28 Threshold analyses of model adjusting for effect of time and baseline logMAR

Reduced network (for comparing anti-VEGFs)

At end-of-trial

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Ranibuzimab vs. Control	-0.06	(-0.09, -0.03)	Ranibuzimab	(-0.23, 1.11)	Aflibercept
Bevacizumab vs. Control	-0.21	(-0.28, -0.13)	–	(NT, -0.06)	Aflibercept
Aflibercept vs. Control	-0.06	(-0.11, -0.02)	Aflibercept	(-0.22, 2.64)	Ranibuzimab

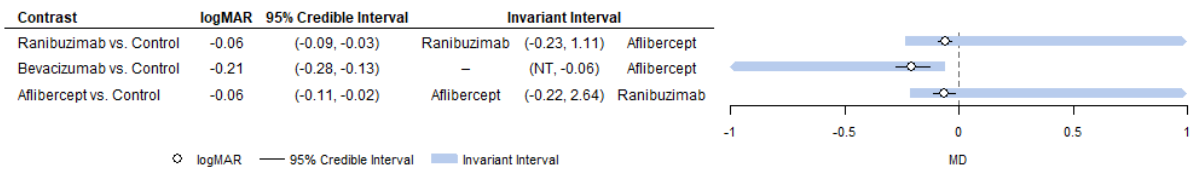◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 29 Threshold analysis of simplified network to compare anti-VEGF types, at end of trial

Adjusted for follow-up time and BCVA at baseline

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Ranibuzimab vs. Control	-0.04	(-0.09, -0.00)	Aflibercept	(-0.19, 0.13)	Control
Bevacizumab vs. Control	-0.17	(-0.25, -0.08)	–	(NT, -0.04)	Aflibercept
Aflibercept vs. Control	-0.05	(-0.13, 0.04)	Aflibercept	(-0.14, 0.54)	Control

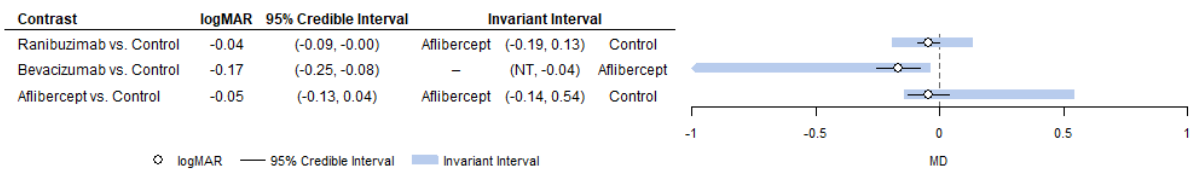◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 30 Threshold analysis of simplified network to compare anti-VEGF types, with time and baseline BCVA adjustment

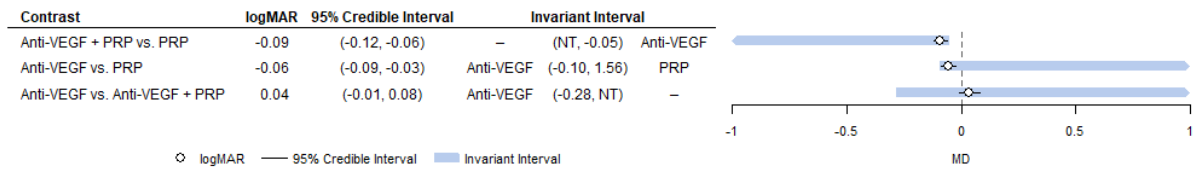### Reduced network (comparing anti-VEGF to PRP)

At end-of-trial

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Anti-VEGF + PRP vs. PRP	-0.09	(-0.12, -0.06)	–	(NT, -0.05)	Anti-VEGF
Anti-VEGF vs. PRP	-0.06	(-0.09, -0.03)	Anti-VEGF	(-0.10, 1.56)	PRP
Anti-VEGF vs. Anti-VEGF + PRP	0.04	(-0.01, 0.08)	Anti-VEGF	(-0.28, NT)	–

◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 31 Threshold analyses of simplified network to compare anti-VEGF to PRP, at end of trial

Adjusted for follow-up time and BCVA at baseline

Contrast	logMAR	95% Credible Interval	Invariant Interval		
Anti-VEGF + PRP vs. PRP	-0.09	(-0.13, -0.06)	–	(NT, -0.06)	Anti-VEGF
Anti-VEGF vs. PRP	-0.06	(-0.09, -0.02)	Anti-VEGF	(-0.09, NT)	–
Anti-VEGF vs. Anti-VEGF + PRP	0.04	(-0.01, 0.09)	–	(NT, NT)	–

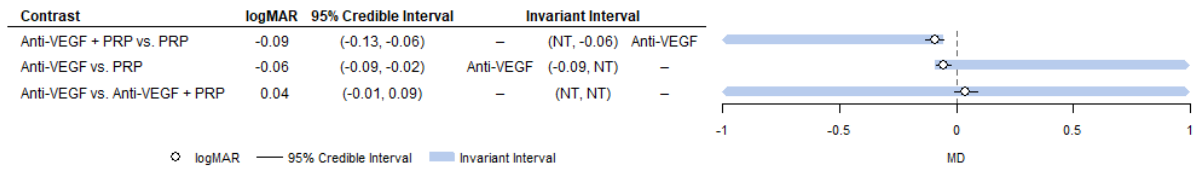◇ logMAR —— 95% Credible Interval ▬ Invariant Interval

Figure 32 Threshold analyses of simplified network to compare anti-VEGF to PRP, adjusted for follow-up time and baseline BCVA

Non-proliferative diabetic retinopathy

This section reports the findings of the two trials in non-proliferative retinopathy. As both trials compared aflibercept to sham injection no NMAs were performed. PANORAMA had two aflibercept arms: injections every 8 weeks or every 16 weeks. Only the 16 week arm is analysed here, as that was the schedule used in PROTOCOL W.
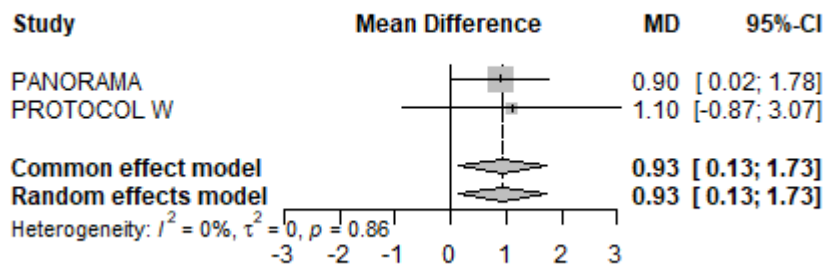

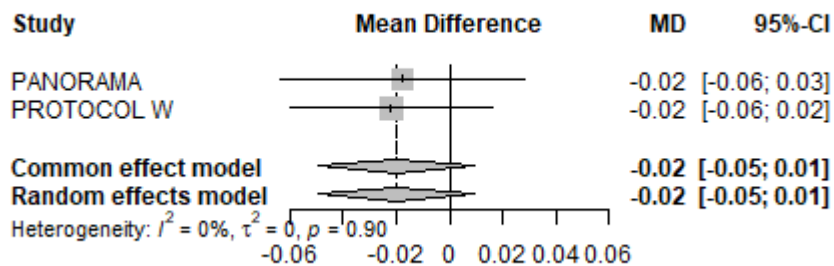*Figure 33 Mean difference in ETDRS after 2 years in NPDR trials*

Figure 34 Mean difference in logMAR after 2 years in NPDR trials