Appendix

This appendix contains supplementary data for the paper:

Henrik Vorum, Thorbjørn Kruse Olesen, Jette Zinck & Morten Størling Hedegaard (2016): Real world evidence of use of anti-VEGF therapy in Denmark, Current Medical Research and Opinion, [DOI: 10.1080/03007995.2016.1221803](https://doi.org/10.1080/03007995.2016.1221803).

Frequency of injections

Table A1 provides supplementary statistical data of the median (lower and upper quartiles) and the smallest and largest values (excluding outliers) for the injection frequency of patients with neovascular age-related macular edema (nAMD), diabetic macular edema (DME, n=76) and retinal vein occlusion (RVO, n=82) who initiated anti-vascular endothelial growth factor (anti-VEGF) treatment between 1 January 2012 and 30 June 2014 and who were treated for at least one year. For nAMD patients, the table presents values for patients who received a loading phase, defined as at least three injections during the first four months of treatment (n=500).

Table A1: Frequency of anti-VEGF injections in year 1 of treatment in treatment-naïve nAMD patients who received a loading dose (a), diabetic macular edema (b) and retinal vein occlusion patients (c)

a. nAMD patients

Grouping year/half year	Number of patients (n=500)	Median (lower and upper quartile)	Smallest and largest values (excluding outliers)
2012/1	155	6.0 (5.0; 7.0)	3.0; 10.0
2012/2	58	6.0 (5.0; 7.0)	3.0; 10.0
2013/1	60	6.0 (5.0; 7.75)	3.0; 11.0
2013/2	142	6.0 (5.0; 7.0)	3.0; 10.0
2014/1	85	7.0 (6.0; 8.0)	3.0; 11.0

b. DME patients

Grouping year/half year	Number of patients (n=76)	Median (lower and upper quartile)	Smallest and largest values (excluding outliers)
2012/1	7	5.0 (4.0; 6.0)	2.0; 9.0
2012/2	16	4.0 (2.0; 5.0)	1.0; 7.0
2013/1	10	4.5 (1.75; 7.0)	1.0; 10.0
2013/2	29	5.0 (3.0; 7.5)	1.0; 10.0
2014/1	14	6.0 (4.75; 8.0)	2.0; 9.0

c. RVO patients

Grouping year/half year	Number of patients (n=82)	Median (lower and upper quartile)	Smallest and largest values (excluding outliers)
2012/1	1	-	-
2012/2	6	5.0 (3.75; 5.5)	3.0; 7.0
2013/1	10	4.0 (3.0; 4.0)	2.0; 5.0
2013/2	41	5.0 (4.5; 7.0)	2.0; 10.75
2014/1	24	6.0 (5.0; 7.0)	3.0; 9.0

Sensitivity analysis for nAMD patients

A sensitivity analysis was performed for nAMD patients who did not receive a loading phase (n=616) and all nAMD patients (n=1,116), irrespective of loading phase. Table A2 provides supplementary statistical data of the median (lower and upper quartiles) and the smallest and largest values (excluding outliers) for the injection frequency of patients who initiated anti-vascular endothelial growth factor (anti-VEGF) treatment between 1 January 2012 and 30 June 2014 and who were treated for at least one year.

Table A2: Frequency of anti-VEGF injections in year 1 of treatment in treatment-naïve nAMD patients without a loading dose (a) and all nAMD patients (b)

a. nAMD without loading

Grouping year/half year	Number of patients (n=616)	Median (lower and upper quartile)	Smallest and largest values (excluding outliers)
2012/1	91	5.0 (3.0; 6.0)	1.0; 10.0
2012/2	12	4.0 (2.0; 5.0)	1.0; 9.0
2013/1	71	5.0 (4.0; 6.0)	1.0; 9.0
2013/2	311	5.0 (4.0; 6.0)	1.0; 9.0
2014/1	131	5.0 (4.0; 6.0)	1.0; 9.0

b. All nAMD patients

Grouping year/half year	Number of patients (n=1,116)	Median (lower and upper quartile)	Smallest and largest values (excluding outliers)
2012/1	246	6.0 (4.0; 7.0)	1.0; 11.0
2012/2	70	6.0 (4.75; 7.0)	1.0; 10.0
2013/1	131	6.0 (5.0; 7.0)	2.0; 10.0
2013/2	453	5.0 (4.0; 6.0)	1.0; 9.0
2014/1	216	6.0 (5.0; 7.0)	2.0; 10.0

nAMD patients without loading

Multiple t-tests with Bonferroni corrections identified three pairwise comparisons that were significantly different (2012/1 and 2012/2 versus 2013/1, $p=0.041$ and 0.017 , and 2012/2 versus 2014/1 $p=0.044$) in patients who did not receive a loading phase. The Shapiro-Wilks tests found the data to be non-normal ($p<0.05$ for four of five six-month periods), thus data were log-transformed, but were still not normally distributed ($p<0.05$ for four of five six-month periods). Kruskal-Wallis testing found a p -value of 0.013 , suggesting the median number of injections vary over time. A robustness check using the Mann Whitney U test was performed due to non-normality and the mean number of injections in 2012 were found to be fewer than the mean in 2014/1 ($p=0.021$).

All nAMD patients

Similar to the nAMD patient populations with and without a loading dose, the Shapiro-Wilks test and ANOVA testing on log transformed data found the data for all nAMD patients was not normally distributed ($p < 0.05$ for all six-month periods).

Multiple t-tests with Bonferroni correction found no significant differences between any of the time periods. The Kruskal-Wallis test showed the median number of injections vary over time ($p = 0.041$). However, the Mann Whitney U robustness test found the mean number of injections in 2012 was not fewer than the mean in 2014 ($p = 0.311$).