H.6.1.6 Treatment frequency: PRN vs routine injection

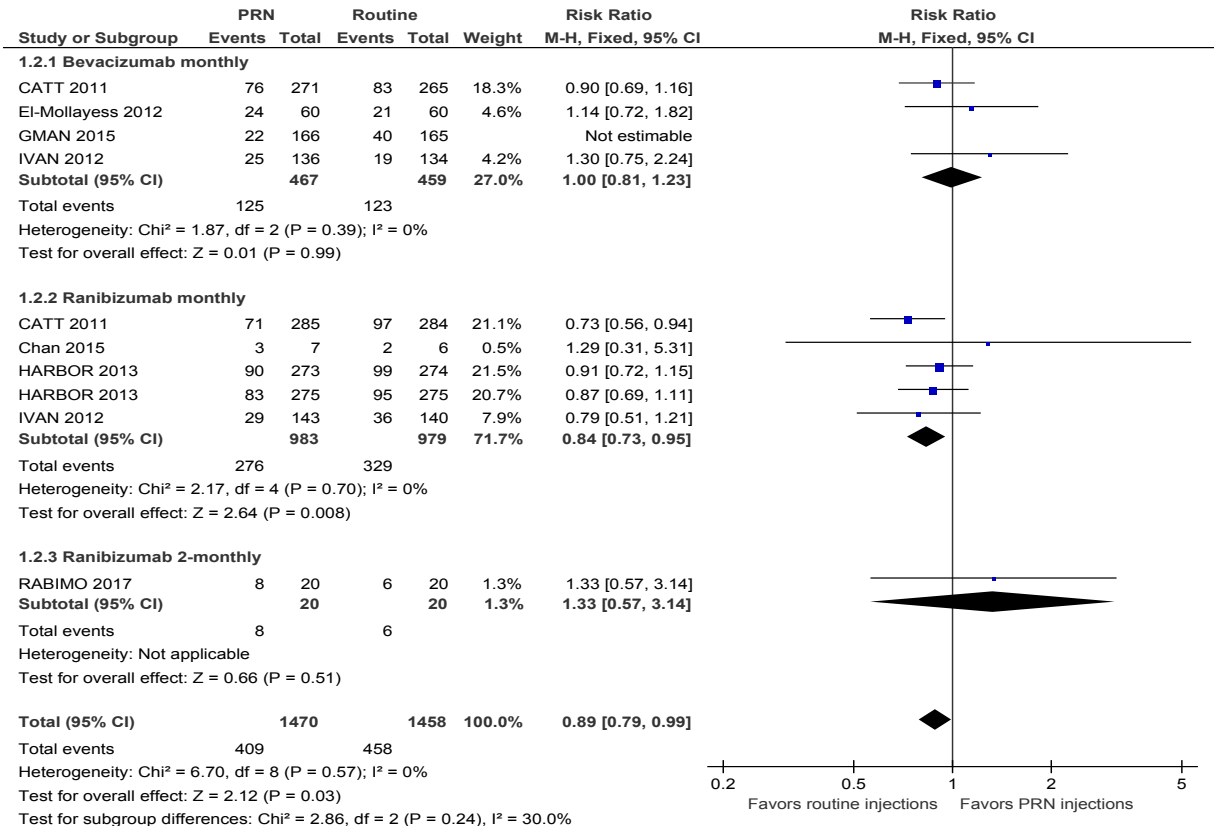
Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
PRN vs routine injections							
Gain of ≥15 letters at one year							
6 studies (CATT 2011, HARBOUR 2013, El-Mollayess 2012, IVAN 2012, Chan 2015, RABIMO 2017)	Serious[1]	Not serious	Not serious	serious[3]	2928	RR 0.89 (0.79, 0.99)	LOW
Loss of <15 letters at one year							
4 studies (CATT 2011, IVAN 2012, HARBOUR 2013, RABIMO 2017)	Serious[1,2]	Not serious	Not serious	Not serious	2795	RR 0.99 (0.97, 1.01)	MODERATE
Mean change in BCVA in ETDRS letters at one year (higher values indicate better vision)							
4 studies (CATT 2011, HARBOUR 2013, , El-Mollayess 2012, IVAN 2012)	Serious[1]	Not serious	Not serious	Not serious	2874	MD -1.45 (-2.45, -0.45)	MODERATE
Mean number of injections at one year							
2 studies (CATT 2011, , HARBOUR 2013)	Serious[1]	Serious[4]	Not serious	Not serious	2202	MD -4.22 (-4.72, -3.73)	LOW
Adverse events (serious systemic events at one year)							
2 studies (CATT 2011, HARBOUR 2013,)	Serious[1]	Serious[4]	Not serious	Serious[5]	2280	RR 1.07 (0.70, 1.63)	VERY LOW
Adverse events (serious ocular events at one year)							
2 studies (CATT 2011, HARBOUR 2013,)	Serious[1]	Serious[4]	Not serious	not serious	2280	RR 0.31 (0.13, 0.78)	LOW

1. Downgraded one level for risk of bias due to masking of participants (either not reported in the study or participants were not blinded in the study)
2. Downgraded one level for risk of bias due to incomplete data (IVAN)
3. Downgraded one level for imprecision due to 95%CI of estimated effect crossing1 line of a defined minimal important difference

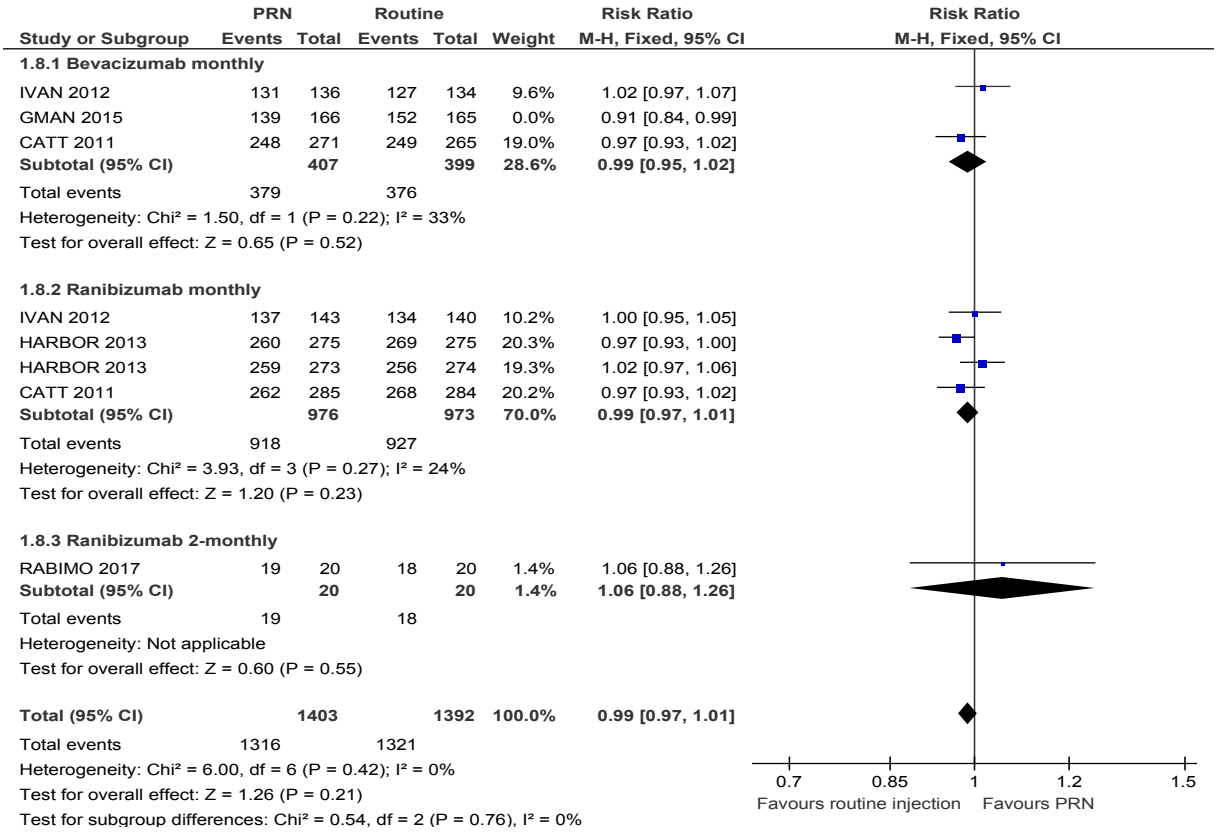
Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
4. Downgraded for inconsistency due to heterogeneity (i2>50%) 5. Downgrade one level for imprecision due to 95%CI of the effect cannot be estimated							

PRN vs routine injections

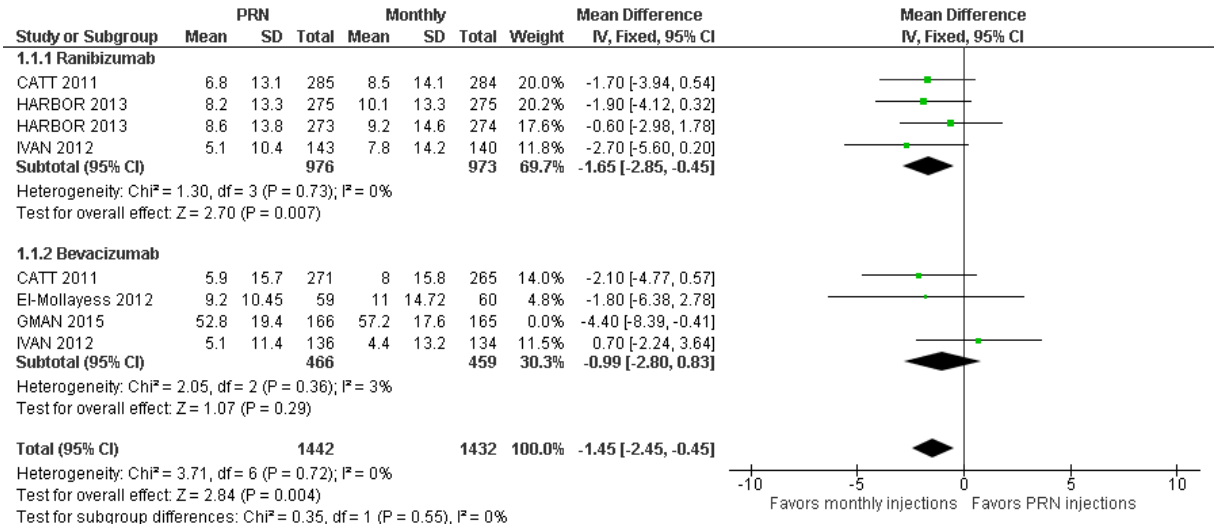
Gain of 15 or more letters ETDRS



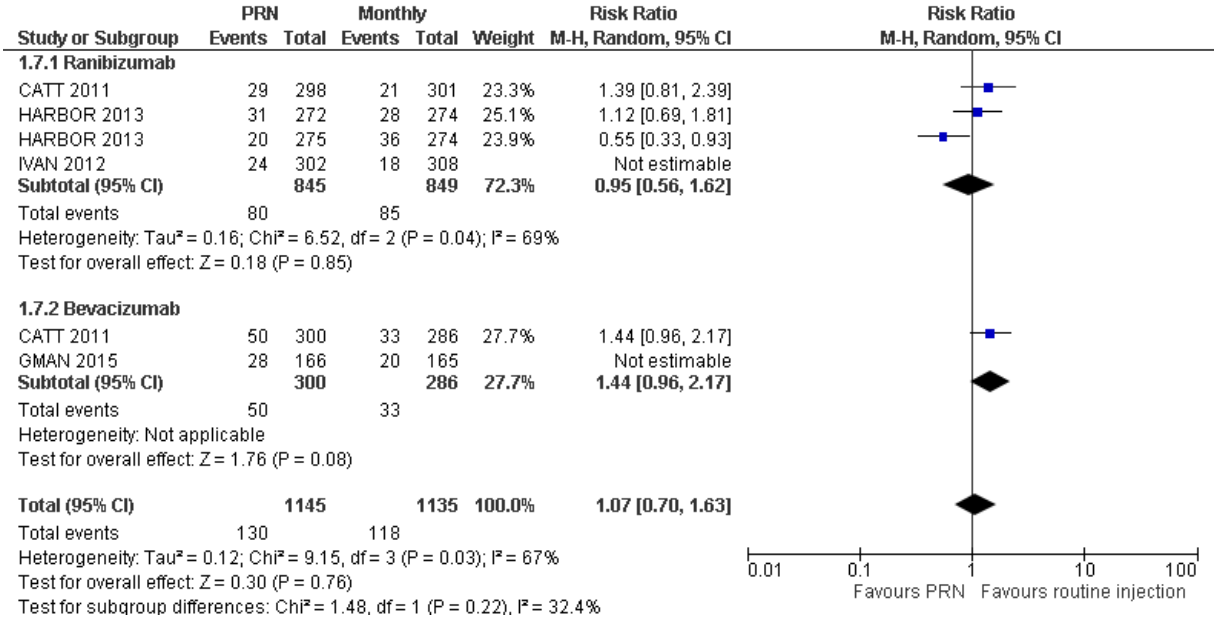
Loss of fewer than 15 letters ETDRS



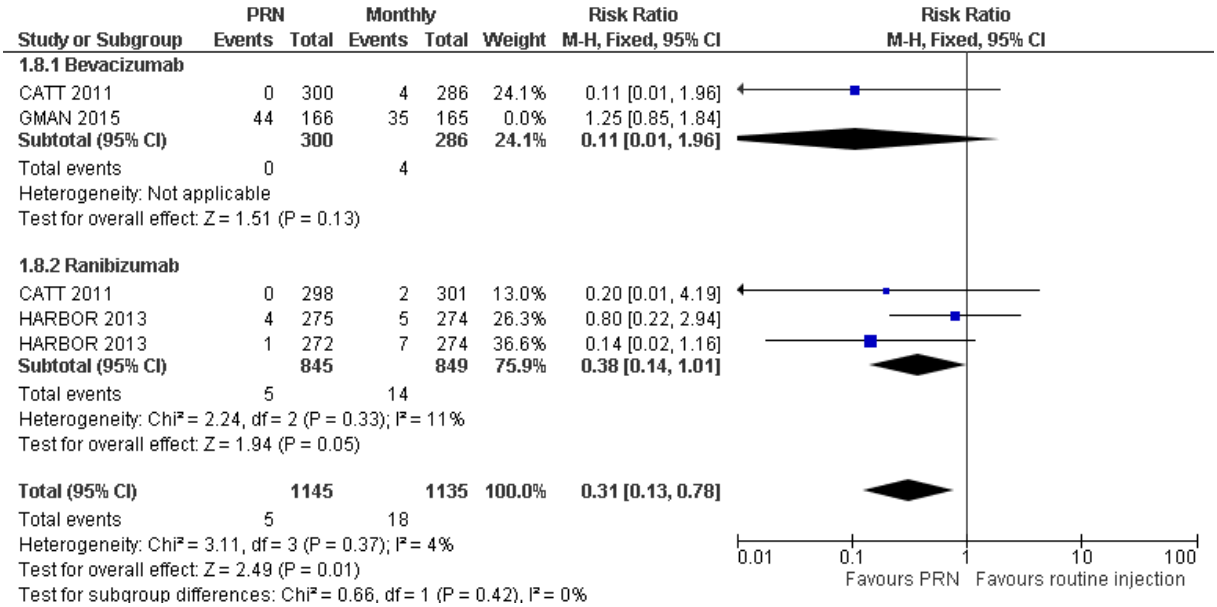
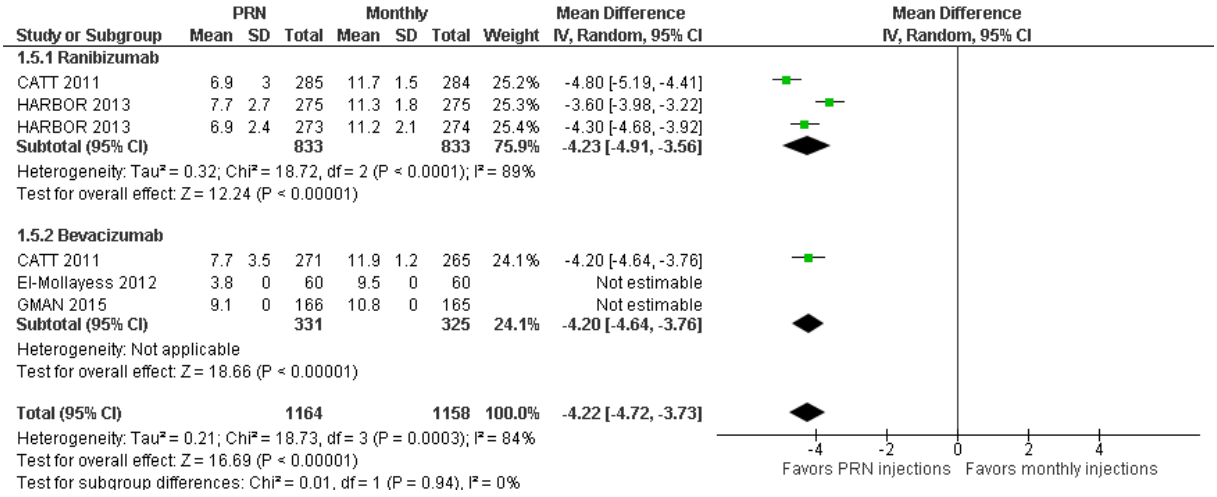
Mean change in BCVA of EDTRS letters



Serious systemic events



Serious ocular events



Number of injections