Mirabegron
for the treatment of
overactive bladder

Submitted by Astellas

Clarification for NICE
STA submission

3rd December 2012

Section A: Clarification on effectiveness data

A1: priority question

For the following outcomes listed in the final scope:

- ***symptoms of urgency;***
- ***urinary frequency;***
- ***frequency of urge urinary incontinence;***
- ***nocturia;***
- ***health-related quality of life (EQ-5D).***

a) Please provide data from SCORPIO comparing the effectiveness of mirabegron 50 mg versus tolterodine by completing tables such as the one below.

No comparisons of mirabegron 50 mg versus tolterodine were conducted in SCORPIO. Although the study included tolterodine as an active comparator, it was not a head-to-head study and not powered to test any hypotheses of mirabegron versus tolterodine.

b) Please provide the efficacy results of the trials DRAGON, 178-CL-045, 178-CL-048, and TAURUS (please provide results from the 3 month and 12 month time points for TAURUS), for mirabegron 25 and 50 mg versus placebo and versus 4 mg tolterodine by completing tables such as the one below.

Available data is reported for:

- Mean number of micturitions per 24 hours (Table 1)
- Mean number of incontinence episodes per 24 hours (Table 2)
- Mean volume voided per micturition (Table 3)
- Mean number of urgency episodes (Grade 3/4) per 24 hours (Table 4)
- Mean level of urgency (Table 5)
- Mean number of urge incontinence episodes per 24 hours (Table 6)
- Mean number of nocturia episodes per 24 hours (Table 7)

Table 1: Mean number of micturitions per 24 hours

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)*	**N=166**	**N=167**	**N=167**	**N=85**
Adjusted mean CFB (vs placebo)	-1.44	-1.88	-2.08	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	-0.45	-0.64	NR
SE	N/A	0.28	0.28	NR
95% CI	N/A	-0.99; 0.10	-1.19; -0.10	NR
Adjusted mean CFB (vs tolterodine)	-1.48	-1.94	-2.13	-1.99
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	0.52	0.06	-0.14	N/A
SE	0.34	0.34	0.34	N/A
95% CI	-0.15; 1.18	-0.60; 0.72	-0.80; 0.53	N/A
178-CL-045	**N=211**	**N=209**	**N=208**	**N=0**
Adjusted mean CFB	−1.26	−1.92	−2.00	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Mean difference vs placebo	N/A	-0.66	-0.74	N/A
SE	N/A	NR	NR	N/A
95% CI	N/A	-1.04; -0.28	-1.12; -0.36	N/A
178-CL-048	**N=368**	**N=0**	**N=369**	**N=368**
Adjusted mean CFB	-0.82	N/A	-1.68	-1.43
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Mean difference vs placebo	N/A	N/A	-0.86	-0.61
SE	N/A	N/A	NR	NR
95% CI	N/A	N/A	-1.16; -0.57	-0.90; -0.32
Mean difference vs tolterodine	NR	N/A	-0.25	N/A
SE	NR	N/A	NR	N/A
95% CI	NR	N/A	-0.55; 0.04	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=742**	**N=735**
Adjusted mean CFB	N/A	N/A	-1.13	-1.27
SE	N/A	N/A	0.079	0.080
95% CI	N/A	N/A	-1.29; -0.98	-1.42; -1.11
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=789**	**N=791**
Adjusted mean CFB	N/A	N/A	-1.30	-1.50
SE	N/A	N/A	0.089	0.089
95% CI	N/A	N/A	-1.48; -1.13	-1.67; -1.32
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

* Throughout the data reported for DRAGON, the adjusted mean change from baseline (CFB) may differ for the comparisons of mirabegron versus placebo and tolterodine. The ANCOVA analysis was performed twice. The primary analysis versus placebo omitted tolterodine, and the secondary analysis versus tolterodine included tolterodine as a covariate.

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

Table 2: Mean number of incontinence episodes per 24 hours

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)	**N=166**	**N=167**	**N=167**	**N=85**
Adjusted mean CFB	-0.53	-1.36	-1.15	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	-0.84	-0.62	NR
SE	N/A	0.31	0.30	NR
95% CI	N/A	-1.45; -0.23	-1.22; -0.02	NR
Adjusted mean CFB	-0.53	-1.37	-1.15	-0.81
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	0.28	-0.56	-0.34	N/A
SE	0.37	0.37	0.37	N/A
95% CI	-0.45; 1.01	-1.29; 0.18	-1.06; 0.39	N/A
178-CL-045	**N=140**	**N=134**	**N=144**	**N=0**
Adjusted mean CFB	−0.77	−1.16	−1.17	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Mean difference vs placebo	N/A	-0.39	-0.40	N/A
SE	N/A	NR	NR	N/A
95% CI	N/A	-0.67; -0.11	-0.67; -0.13	N/A
178-CL-048	**N=264**	**N=0**	**N=266**	**N=240**
Adjusted mean CFB	-0.67	N/A	-1.09	-0.99
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Mean difference vs placebo	N/A	N/A	-0.42	-0.32
SE	N/A	N/A	NR	NR
95% CI	N/A	N/A	-0.67; -0.17	-0.57; -0.06
Mean difference vs tolterodine	NR	N/A	-0.10	N/A
SE	NR	N/A	NR	N/A
95% CI	NR	N/A	-0.36; 0.15	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=479**	**N=488**
Adjusted mean CFB	N/A	N/A	-1.10	-1.09
SE	N/A	N/A	0.083	0.083
95% CI	N/A	N/A	-1.26; -0.94	-1.25; -0.92
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=479**	**N=488**
Adjusted mean CFB	N/A	N/A	-1.14	-1.36
SE	N/A	N/A	0.094	0.093
95% CI	N/A	N/A	-1.33;-0.96	-1.54; -1.18
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

Table 3: Mean volume voided per micturition

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)	**N=165**	**N=167**	**N=167**	**N=85**
Adjusted mean CFB	7.29	15.32	27.34	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	8.03	20.05	NR
SE	N/A	4.87	4.88	NR
95% CI	N/A	-1.54; 17.60	10.48; 29.63	NR
Adjusted mean CFB	7.05	15.13	27.14	23.86
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	-16.81	-8.73	3.28	N/A
SE	5.97	5.93	5.95	N/A
95% CI	-28.5; -5.09	-20.4; 2.91	-8.40; 14.96	N/A
178-CL-045	**N=211**	**N=209**	**N=208**	**N=0**
Adjusted mean CFB	11.122	23.645	27.326	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Mean difference vs placebo	N/A	12.523	16.204	N/A
SE	N/A	NR	NR	N/A
95% CI	N/A	4.973; 20.073	8.635; 23.774	N/A
178-CL-048	**N=364**	**N=0**	**N=368**	**N=367**
Adjusted mean CFB	9.675	N/A	24.450	28.724
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Mean difference vs placebo	N/A	N/A	14.775	19.049
SE	N/A	N/A	NR	NR
95% CI	N/A	N/A	9.974; 19.576	14.246; 23.852
Mean difference vs tolterodine	NR	N/A	-4.274	N/A
SE	NR	N/A	NR	N/A
95% CI	NR	N/A	-9.066; 0.519	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=789**	**N=791**
Adjusted mean CFB	N/A	N/A	14.8	17.4
SE	N/A	N/A	1.50	1.51
95% CI	N/A	N/A	11.9; 17.8	14.4; 20.3
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=789**	**N=791**
Adjusted mean CFB	N/A	N/A	18.5	18.9
SE	N/A	N/A	1.86	1.86
95% CI	N/A	N/A	14.9; 22.2	15.3; 22.6
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

Table 4: Mean number of urgency episodes (Grade 3/4) per 24 hours

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)	**N=165**	**N=167**	**N=166**	**N=85**
Adjusted mean CFB	-1.07	-1.77	-1.67	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	-0.70	-0.60	NR
SE	N/A	0.35	0.35	NR
95% CI	N/A	-1.38; -0.01	-1.29; 0.08	NR
Adjusted mean CFB	-1.09	-1.77	-1.68	-1.46
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	0.37	-0.31	-0.22	N/A
SE	0.43	0.42	0.43	N/A
95% CI	-0.47; 1.21	-1.14; 0.52	-1.06; 0.62	N/A
178-CL-045[†]	**N=211**	**N=208**	**N=208**	**N=0**
Adjusted mean CFB	−1.87	−2.13	−2.15	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Mean difference vs placebo	N/A	-0.27	-0.29	N/A
SE	N/A	NR	NR	N/A
95% CI	N/A	-0.75; 0.21	-0.77; 0.19	N/A
178-CL-048[†]	N=368	**N=0**	N=369	N=368
Adjusted mean CFB	-1.31	N/A	-1.85	-1.71
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Mean difference vs placebo	N/A	N/A	-0.54	-0.41
SE	N/A	N/A	NR	NR
95% CI	N/A	N/A	-0.90; -0.18	-0.77; -0.05
Mean difference vs tolterodine	NR	N/A	-0.13	N/A
SE	NR	N/A	NR	N/A
95% CI	NR	N/A	-0.49; 0.23	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=738**	**N=733**
Adjusted mean CFB	N/A	N/A	-1.37	-1.55
SE	N/A	N/A	0.103	0.103
95% CI	N/A	N/A	-1.58; -1.17	-1.75; -1.35
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=621**	**N=621**
Adjusted mean CFB	N/A	N/A	-1.81	-1.89
SE	N/A	N/A	0.116	0.116
95% CI	N/A	N/A	-2.04; -1.58	-2.12; -1.66
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

[†] Studies 178-CL-045 and 178-CL-048 recorded episodes of urgency without specifying grades

Mean level of urgency was not an outcome examined in studies 178-CL-045 or 178-CL-048 (Table 5).

Table 5: Mean level of urgency

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)	**N=166**	**N=166**	**N=166**	**N=85**
Adjusted mean CFB	-0.10	-0.21	-0.18	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	-0.12	-0.08	NR
SE	N/A	0.07	0.07	NR
95% CI	N/A	-0.25; 0.02	-0.22; 0.05	NR
Adjusted mean CFB	-0.10	-0.21	-0.18	-0.14
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	0.04	-0.07	-0.04	N/A
SE	0.08	0.08	0.08	N/A
95% CI	-0.12; 0.21	-0.23; 0.10	-0.20; 0.13	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=739**	**N=791**
Adjusted mean CFB	N/A	N/A	-0.21	-0.24
SE	N/A	N/A	0.019	0.019
95% CI	N/A	N/A	-0.25; -0.17	-0.28; -0.20
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=622**	**N=621**
Adjusted mean CFB	N/A	N/A	-0.33	-0.32
SE	N/A	N/A	0.023	0.023
95% CI	N/A	N/A	-0.37; -0.28	-0.37; -0.28
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

Table 6: Mean number urge incontinence episodes per 24 hours

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)	**N=166**	**N=167**	**N=167**	**N=85**
Adjusted mean CFB	-0.44	-1.31	-1.13	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	-0.86	-0.69	NR
SE	N/A	0.26	0.25	NR
95% CI	N/A	-1.38; -0.35	-1.18; -0.19	NR
Adjusted mean CFB	-0.45	-1.31	-1.13	-0.76
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	0.31	-0.55	-0.37	N/A
SE	0.31	0.32	0.31	N/A
95% CI	-0.30; 0.92	-1.18; 0.07	-0.99; 0.24	N/A
178-CL-045	**N=132**	**N=128**	**N=137**	**N=0**
Adjusted mean CFB	−0.80	−1.04	−1.07	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Mean difference vs placebo	N/A	-0.24	-0.27	N/A
SE	N/A	NR	NR	N/A
95% CI	N/A	-0.51; 0.02	-0.53; -0.01	N/A
178-CL-048	**N=258**	**N=0**	**N=254**	**N=230**
Adjusted mean CFB	-0.63	N/A	-0.98	-0.95
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Mean difference vs placebo	N/A	N/A	-0.36	-0.32
SE	N/A	N/A	NR	NR
95% CI	N/A	N/A	-0.59; -0.12	-0.56; -0.08
Mean difference vs tolterodine	NR	N/A	-0.04	N/A
SE	NR	N/A	NR	N/A
95% CI	NR	N/A	-0.28, 0.21	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=441**	**N=440**
Adjusted mean CFB	N/A	N/A	-1.05	-1.06
SE	N/A	N/A	0.077	0.077
95% CI	N/A	N/A	-1.20; -0.90	-1.21; -0.91
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=366**	**N=371**
Adjusted mean CFB	N/A	N/A	-1.17	-1.29
SE	N/A	N/A	0.087	0.086
95% CI	N/A	N/A	-1.34; -1.00	-1.46; -1.12
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

Table 7: Mean number nocturia episodes per 24 hours

Outcome	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine 4 mg
178-CL-044 (DRAGON)	**N=166**	**N=167**	**N=167**	**N=85**
Adjusted mean CFB	-0.38	-0.52	-0.60	NR
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs placebo	N/A	-0.15	-0.22	NR
SE	N/A	0.11	0.11	NR
95% CI	N/A	-0.36; 0.07	-0.44; -0.01	NR
Adjusted mean CFB	-0.38	-0.53	-0.60	-0.59
SE	NR	NR	NR	NR
95% CI	NR	NR	NR	NR
Mean difference vs tolterodine	0.21	0.06	-0.01	N/A
SE	0.13	0.13	0.13	N/A
95% CI	-0.05; 0.47	-0.20; 0.32	-0.27; 0.25	N/A
178-CL-045	**N=168**	**N=179**	**N=176**	**N=0**
Adjusted mean CFB	−0.25	−0.45	−0.41	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Mean difference vs placebo	N/A	-0.20	-0.16	N/A
SE	N/A	NR	NR	N/A
95% CI	N/A	-0.36; -0.04	-0.33; 0.00	N/A
178-CL-048	**N=322**	**N=0**	**N=323**	**N=332**
Adjusted mean CFB	-0.33	N/A	-0.45	-0.43
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Mean difference vs placebo	N/A	N/A	-0.12	-0.10
SE	N/A	N/A	NR	NR
95% CI	N/A	N/A	-0.25; 0.01	-0.23, 0.03
Mean difference vs tolterodine	NR	N/A	-0.02	N/A
SE	NR	N/A	NR	N/A
95% CI	NR	N/A	-0.15; 0.11	N/A
178-CL-049 (TAURUS) 3 months	**N=0**	**N=0**	**N=654**	**N=643**
Adjusted mean CFB	N/A	N/A	-0.41	-0.37
SE	N/A	N/A	0.037	0.037
95% CI	N/A	N/A	-0.48; -0.34	-0.44; -0.30
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A
178-CL-049 (TAURUS) 12 months	**N=0**	**N=0**	**N=554**	**N=550**
Adjusted mean CFB	N/A	N/A	-0.48	-0.46
SE	N/A	N/A	0.042	0.042
95% CI	N/A	N/A	-0.56; -0.40	-0.55; -0.38
Mean difference vs tolterodine	N/A	N/A	NR	N/A
SE	N/A	N/A	NR	N/A
95% CI	N/A	N/A	NR	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

A2 – definitions of incontinence and urge incontinence. Please clarify the definitions used in the submission and each of the trials of incontinence, and urge incontinence.

Incontinence: Any involuntary leakage of urine.

Urge incontinence or urge urinary incontinence: Involuntary leakage accompanied by or immediately preceded by urgency.

A3 – assessment of level of urgency. Please clarify what scale or questionnaire was used to assess level of urgency in each of the 7 trials.

The 5-point categorical Patient Perception of Intensity of Urgency Scale (PPIUS) was used to assess level of urgency *(Footnote on Page 52 and Appendix 15 of manufacturer's submission)*:

0. No urgency, I felt no need to empty my bladder, but did so for other reasons.
1. Mild urgency, I could postpone voiding as long as necessary, without fear of wetting myself.
2. Moderate urgency, I could postpone voiding for a short while, without fear of wetting myself.
3. Severe urgency, I could not postpone voiding, but had to rush to the toilet in order not to wet myself.
4. Urge incontinence, I leaked before arriving to the toilet.

A4 – endpoint and final visit definitions. The ERG is unable to locate definitions for the terms "endpoint" and "final visit" within the manufacturer's submission. Please provide definitions for: (i) endpoint, as presented in Table 21; and (ii) final visit, as presented in Table 22. In addition, please clarify how missing values were handled for the analysis of baseline to endpoint and baseline to final visit analysis.

All analyses within Table 21 and Table 22 of the manufacturer's submission were conducted using the 'final visit'.

In SCORPIO and ARIES, 'final visit' analysis is defined as:

> *In last observation carried forward (LOCF) analyses at the final visit, the Week 12 measurement was used. If no Week 12 measurement was available, the last available earlier postbaseline measurement within the post-dosing window was used.*

In CAPRICORN, 'final visit' analysis is defined as:

> *In last observation carried forward (LOCF) analyses at the final visit, the Week 12 measurement was used. If no Week 12 measurement was available, the last available earlier postbaseline average of the diary data measurements within the post-dosing window was used for efficacy data. For non-diary efficacy data, in LOCF analyses at the final visit, the Week 12 measurement was used. If no Week 12 measurement were available, the last available earlier post-baseline measurement within the post-dosing window was used. For safety data, the last*

available observation within 10 days after the last dose of study drug (7 days for vital signs) was used.

A5 – WinBUGS code. Please provide the working WinBUGS code populated with the appropriate data set for each outcome.

The working WinBUGS codes populated with each appropriate data set for each outcome are presented in Appendix A.

A6 – MTC outcomes in tabular format. Please provide the results from the MTCs for all the outcomes in a tabulated format, as in the example table below.

Table 8: Estimate of the effect of treatment vs mirabegron 50 mg

Micturitions	Mean difference vs mirabegron 50 mg	95% Credible Interval
Micturition		
Tolterodine 4 mg	0.157	-0.0002; 0.3154
Fesoterodine 4 mg	0.137	-0.1613; 0.4345
Fesoterodine 8 mg	-0.048	-0.2489; 0.1524
Oxybutynin 10 mg	0.139	-0.5290; 0.8058
Placebo	0.696	0.5544; 0.8378
Solifenacin 10 mg	-0.583	-0.8324; -0.3326
Solifenacin 5 mg	-0.240	-0.4921; 0.0132
Trospium 60mg	-0.124	-0.5767; 0.3261
Incontinence		
Tolterodine 4 mg	0.082	-0.0649; 0.2286
Fesoterodine 4 mg	0.107	-0.3911; 0.6033
Fesoterodine 8 mg	0.226	-0.2770; 0.7299
Oxybutynin 10 mg	0.137	-0.3986; 0.6752
Placebo	0.497	0.3724; 0.6225
Solifenacin 10 mg	-0.240	-0.4875; 0.0066
Solifenacin 5 mg	-0.237	-0.4824; 0.0073
Urge incontinence		
Tolterodine 4 mg	0.095	-0.1226; 0.3071
Fesoterodine 4 mg	-0.034	-0.3841; 0.3033
Fesoterodine 8 mg	-0.225	-0.5348; 0.0475
Oxybutynin 10 mg	-0.279	-0.9464; 0.3847
Placebo	0.437	0.2553; 0.6244
Solifenacin 10 mg	-0.420	-0.7860; -0.05629
Solifenacin 5 mg	-0.288	-0.6416; 0.0711
Trospium 60mg	-0.112	-0.7071; 0.4853
Dry mouth		
Tolterodine ER 4 mg	4.168	2.733; 6.117
Fesoterodine 4mg	4.436	2.693; 6.974
Fesoterodine 8mg	9.7	6.109; 14.686
Oxybutynin ER 10 mg	6.795	3.894; 11.25

Micturitions	Mean difference vs mirabegron 50 mg	95% Credible Interval
Oxybutynin ER 15 mg	7.864	2.912; 17.48
Oxybutynin ER 5 mg	4.13	1.559; 9.024
Oxybutynin IR 10 mg	14.069	6.565; 26.4
Oxybutynin IR 15 mg	39.208	14.98; 85.64
Oxybutynin IR 9 mg	10.778	5.592; 18.92
Placebo	1.303	0.859; 1.916
Solifenacin 10 mg	10.078	6.027; 15.97
Solifenacin 5 mg	4.229	2.484; 6.825
Tolterodine IR 4 mg	7.042	4.311; 11.03
Trospium 40 mg	5.672	2.955; 9.981
Trospium 60 mg	4.481	1.598; 10.46
Constipation		
Tolterodine ER 4 mg	1.109	0.716; 1.647
Fesoterodine 4mg	1.066	0.576; 1.808
Fesoterodine 8mg	1.926	1.142; 3.059
Oxybutynin ER 10 mg	1.021	0.527; 1.793
Oxybutynin ER 15 mg	2.158	0.27; 8.276
Oxybutynin ER 5 mg	2.459	0.421; 8.71
Oxybutynin IR 15 mg	1.614	0.416; 4.375
Oxybutynin IR 9 mg	0.989	0.412; 1.992
Placebo	0.732	0.483; 1.066
Solifenacin 10 mg	4.369	2.54; 7.071
Solifenacin 5 mg	2.501	1.41; 4.127
Tolterodine IR 4 mg	1.034	0.594; 1.673
Trospium 40 mg	1.692	0.883; 2.979
Trospium 60 mg	7.604	2.08; 22.59
Blurred vision		
Tolterodine ER 4 mg	1.44	0.559; 3.128
Fesoterodine 4mg	0.8	0.041; 3.705
Fesoterodine 8mg	0.727	0.038; 3.402
Oxybutynin ER 10 mg	2.612	0.206; 12.12
Oxybutynin ER 15 mg	7.071	0.021; 41.747
Oxybutynin ER 5 mg	5.117	0.05; 28.873
Oxybutynin IR 15 mg	2.454	0.071; 13.72
Oxybutynin IR 9 mg	0.403	0; 2.577
Placebo	5.271	0.902; 18.47
Solifenacin 10 mg	0.792	0.305; 1.714
Solifenacin 5 mg	1.936	0.669; 4.499
Tolterodine IR 4 mg	1.147	0.382; 2.71
Trospium 40 mg	0.752	0.237; 1.83
Trospium 60 mg	2.437	0.147; 11.93

A7 – additional MTC outcomes. Please provide DIC, residual deviance and number of effective parameters in the MTC, for each of the outcomes assessed.

Table 9: DIC, residual deviance and number of effective parameters in the MTC, for each outcome

	Micturition		Incontinence		Urge incontinence		Dry mouth		Constipation		Blurred vision	
	Fixed effect	Random effect	Fixed effect	Random effect	Fixed effect	Random effect	Fixed effect	Random effect	Fixed effect	Random effect	Fixed effect	Random effect
Residual Deviance	-49.046	-50.935	-29.139	-33.288	-37.888	-52.635	590.207	579.843	437.010	436.933	226.858	227.070
Effective number of parameters	30.999	34.578	21.972	26.707	24.975	34.154	55.918	65.268	51.517	53.523	36.125	37.783
DIC	-18.048	-16.357	-7.166	-6.581	-12.914	-18.481	646.125	645.111	488.527	490.456	262.983	264.853

A8 – subgroup data. Using the example table below, please provide subgroup data of men, women, previously treated, and treatment naive for the following outcomes listed in the final scope:

- ***symptoms of urgency;***
- ***urinary frequency;***
- ***frequency of urge urinary incontinence;***
- ***nocturia;***
- ***health-related quality of life (EQ-5D).***

for the individual trials:

- ***178-CL-044 (DRAGON);***
- ***178-CL-045;***
- ***178-CL-046 (SCORPIO);***
- ***178-CL-047 (ARIES);***
- ***178-CL-048;***

- ***178-CL-049 (TAURUS);***
- ***178-CL-074 (CAPRICORN).***

Available subgroup analyses have been provided as requested (Table 10). Additional requested analyses were not conducted. Post-hoc analyses may be underpowered, given the smaller numbers of events involved, and therefore run the risk of producing spurious differences in treatment effect between different subgroups. This data is not available in the clinical study reports as analyses of these subgroups were not conducted.

Table 10: Overview of subgroup data available

	DRAGON		**178-CL-045**		**SCORPIO**		**ARIES**		**178-CL-048**		**TAURUS**		**CAPRICORN**	
	Gender	Previous treatment	Gender	Previous treatment	Gender	Previous treatment	Gender	Previous treatment	Gender	Previous treatment	Gender	Previous treatment	Gender	Previous treatment
Mean number micturitions/24 hr			✓		✓	✓	✓		✓				✓	✓
Mean number incontinence episodes/24 hr			✓		✓	✓	✓		✓				✓	✓
Mean volume voided per micturition					✓		✓		✓				✓	
Mean number of urgency episodes (Grade 3/4)/24 hr			✓						✓					
Mean level of urgency														
Mean number of incontinence episodes/24 hr														
Mean number of nocturia episodes/24 hr									✓					

Table 11: Subgroup analysis for mean number of micturitions per 24 hours

	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine SR 4 mg
178-CL-045				
Men				
Adjusted mean CFB	-0.39	-1.49	-1.24	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Women				
Adjusted mean CFB	-1.50	-2.02	-2.09	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
SCORPIO				
Men				
Adjusted mean CFB	-0.97	N/A	-1.44	-1.58
SE	0.209	N/A	0.210	0.213
95% CI	-1.38; -0.56	N/A	-1.85; -1.03	-2.00; -1.16
Women				
Adjusted mean CFB	-1.48	N/A	-1.73	-1.59
SE	0.130	N/A	0.131	0.130
95% CI	-1.74; -1.23	N/A	-1.99; -1.48	-1.85; -1.34
Previously treated				
Adjusted mean CFB	-1.06	N/A	-1.74	-1.26
SE	0.156	N/A	0.155	0.158
95% CI	-1.36; -0.75	N/A	-2.05; -1.44	-1.57; -0.95
Treatment-naive				
Adjusted mean CFB	-1.61	N/A	-2.13	-0.29
SE	0.155	N/A	0.220	0.218
95% CI	-1.91; -1.31	N/A	-0.95; -0.09	-0.71; 0.14
ARIES				
Men				
Adjusted mean CFB	-1.02	N/A	-1.40	N/A
SE	0.274	N/A	0.257	N/A
95% CI	-1.56; -0.48	N/A	-1.91; -0.90	N/A
Women				
Adjusted mean CFB	-1.07	N/A	-1.75	N/A
SE	0.151	N/A	0.157	N/A
95% CI	-1.36; -0.77	N/A	-2.06; -1.44	N/A
178-CL-048				
Men				
Mean[†] CFB	-0.74	N/A	-1.03	-0.69
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Women				
Mean[†] CFB	-0.88	N/A	-1.79	-1.66
SE	NR	N/A	NR	NR

95% CI	NR	N/A	NR	NR
CAPRICORN				
Men				
Adjusted mean CFB	-0.78	-1.29	-1.03	N/A
SE	0.225	0.220	0.220	N/A
95% CI	-1.22; -0.34	-1.72; -0.86	-1.47; -0.60	N/A
Women				
Adjusted mean CFB	-1.37	-1.82	-1.86	N/A
SE	0.149	0.153	0.148	N/A
95% CI	-1.66; -1.07	-2.12; -1.52	-2.15; -1.57	N/A
Previously treated				
Adjusted mean CFB	-0.93	-1.47	-1.64	N/A
SE	0.172	0.170	0.176	N/A
95% CI	-1.27; -0.60	-1.81; -1.14	-1.98; -1.29	N/A
Treatment-naïve				
Adjusted mean CFB	-1.46	-1.85	-1.57	N/A
SE	0.179	0.183	0.170	N/A
95% CI	-1.82; -1.11	-2.21; -1.49	-1.91; -1.24	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

†Note: mean (not adjusted mean) for 178-CL-048.

Table 12: Subgroup analysis for mean number of incontinence episodes per 24 hours

	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine SR 4 mg
178-CL-045				
Men				
Adjusted mean CFB	-0.48	-0.70	-0.65	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Women				
Adjusted mean CFB	-0.82	-1.22	-1.24	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
SCORPIO				
Men				
Adjusted mean CFB	-1.43	N/A	-2.02	-1.45
SE	0.282	N/A	0.263	0.281
95% CI	-1.99; -0.88	N/A	-2.54; -1.51	-2.00; -0.90
Women				
Adjusted mean CFB	-1.11	N/A	-1.48	-1.23
SE	0.124	N/A	0.126	0.122
95% CI	-1.36; -0.87	N/A	-1.72; -1.23	-1.47; -1.00
Previously treated				
Adjusted mean CFB	-1.00	N/A	-1.48	-1.10
SE	0.149	N/A	0.152	0.153
95% CI	-1.29; -0.71	N/A	-1.78; -1.18	-1.40; -0.80
Treatment-naive				
Adjusted mean CFB	-1.39	N/A	-1.69	-1.47
SE	0.174	N/A	0.171	0.163
95% CI	-1.74; -1.05	N/A	-2.02; -1.35	-1.79; -1.15
ARIES				
Men				
Adjusted mean CFB	-1.98	N/A	-1.21	N/A
SE	0.271	N/A	0.258	N/A
95% CI	-2.51; -1.45	N/A	-1.72; -0.71	N/A
Women				
Adjusted mean CFB	-0.95	N/A	-1.54	N/A
SE	0.122	N/A	0.127	N/A
95% CI	-1.19; -0.71	N/A	-1.79; -1.29	N/A
178-CL-048				
Men				
Mean† CFB	-0.72	N/A	-0.66	-0.76
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Women				
Mean† CFB	-0.66	N/A	-1.18	-1.01
SE	NR	N/A	NR	NR

95% CI	NR	N/A	NR	NR
CAPRICORN				
Men				
Adjusted mean CFB	-0.79	-1.80	-1.25	N/A
SE	0.278	0.267	0.275	N/A
95% CI	-1.33; -0.24	-2.33; -1.28	-1.79; -0.71	N/A
Women				
Adjusted mean CFB	-1.00	-1.24	-1.41	N/A
SE	0.136	0.140	0.138	N/A
95% CI	-1.26; -0.73	-1.51; -0.96	-1.68; -1.14	N/A
Previously treated				
Adjusted mean CFB	-0.85	-1.19	-1.27	N/A
SE	0.159	0.163	0.161	N/A
95% CI	-1.16; -0.54	-1.51; -0.87	-1.59; -0.95	N/A
Treatment-naive				
Adjusted mean CFB	-1.07	-1.61	-1.54	N/A
SE	0.189	0.191	0.190	N/A
95% CI	-1.44; -0.70	-1.98; -1.23	-1.91; -1.16	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.

†Note: mean (not adjusted mean) for 178-CL-048.

Table 13: Subgroup analysis for mean volume voided per micturition

	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine SR 4 mg
SCORPIO				
Men				
Adjusted mean CFB	7.86	N/A	19.38	N/A
SE	3.917	N/A	3.933	N/A
95% CI	0.17; 15.54	N/A	11.67; 27.10	N/A
Women				
Adjusted mean CFB	13.98	N/A	26.17	N/A
SE	2.550	N/A	2.576	N/A
95% CI	8.98; 18.98	N/A	21.12; 31.23	N/A
ARIES				
Men				
Adjusted mean CFB	6.28	N/A	13.85	N/A
SE	4.513	N/A	4.234	N/A
95% CI	-2.58; 15.14	N/A	5.55; 22.16	N/A
Women				
Adjusted mean CFB	7.32	N/A	19.56	N/A
SE	2.602	N/A	2.702	N/A
95% CI	2.22; 12.43	N/A	14.27; 24.86	N/A
178-CL048				
Men				
Mean† CFB	11.25	N/A	14.34	22.02
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Women				
Mean† CFB	9.42	N/A	26.16	30.27
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
CAPRICORN				
Men				
Adjusted mean CFB	-1.59	N/A	13.09	N/A
SE	4.032	N/A	3.933	N/A
95% CI	-9.51; 6.32	N/A	5.37; 20.80	N/A
Women				
Adjusted mean CFB	13.00	N/A	24.73	N/A
SE	2.795	N/A	2.770	N/A
95% CI	7.52; 18.49	N/A	19.29; 30.16	N/A

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.
†Note: mean (not adjusted mean) for 178-CL-048.

Table 14: Subgroup analysis for mean number of urgency episodes (Grade 3/4) per 24 hours

	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine SR 4 mg
178-CL-045**				
Men				
Adjusted mean CFB	-1.01	-1.12	-1.36	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
Women				
Adjusted mean CFB	-2.09	-2.38	-2.28	N/A
SE	NR	NR	NR	N/A
95% CI	NR	NR	NR	N/A
178-CL048**				
Men				
Mean† CFB	-1.38	N/A	-1.17	-1.10
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Women				
Mean† CFB	-1.37	N/A	-1.97	-1.77
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.
†Note: mean (not adjusted mean) for 178-CL-048.

Table 15: Subgroup analysis for mean number of nocturia episodes per 24 hours

	Placebo	Mirabegron 25 mg	Mirabegron 50 mg	Tolterodine SR 4 mg
178-CL048				
Men				
Mean† CFB	-0.55	N/A	-0.38	-0.40
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR
Women				
Mean† CFB	-0.32	N/A	-0.45	-0.42
SE	NR	N/A	NR	NR
95% CI	NR	N/A	NR	NR

Abbreviations: CFB, change from baseline; CI, confidence interval; N/A, not applicable; NR, not reported; SE, standard error.
†Note: mean (not adjusted mean) for 178-CL-048.

A9 – additional references. Please provide references and full publications for the studies excluded from the MTC based on any of the exclusion criteria listed below (Section 6.7.2):

- ***sub-analysis;***
- ***pooled analysis;***

**Studies 178-CL-045 and 178-CL-048 recorded episodes of urgency without specifying grades

- ***not a major publication;***
- ***not appropriate population for analysis.***

Table 16: Studies excluded from MTC

Author year	Full citation	Exclusion code
Sub-group analysis		
Anderson 2006	Anderson RU, MacDiarmid S, Kell S, Barada JH, Serels S, Goldberg RP. Effectiveness and tolerability of extended-release oxybutynin vs extended-release tolterodine in women with or without prior anticholinergic treatment for overactive bladder. Int Urogynecol J Pelvic Floor Dysfunct. 2006 Sep;17(5):502-11	Sub-group analysis
Armstrong 2005	Armstrong RB, Luber KM, Peters KM. Comparison of dry mouth in women treated with extended-release formulations of oxybutynin or tolterodine for overactive bladder. Int Urol Nephrol. 2005;37(2):247-52	Sub-group analysis
Chapple 2007	Chapple CR, Fianu-Jonsson A, Indig M, Khullar V, Rosa J, Scarpa RM, et al. Treatment outcomes in the STAR study: a subanalysis of solifenacin 5 mg and tolterodine ER 4 mg. Eur Urol. 2007 Oct;52(4):1195-203	Sub-group analysis
Herschorn 2011	Herschorn S, Pommerville P, Stothers L, Egerdie B, Gajewski J, Carlson K, et al. Tolerability of solifenacin and oxybutynin immediate release in older (> 65 years) and younger (</= 65 years) patients with overactive bladder: sub-analysis from a Canadian, randomized, double-blind study. Curr Med Res Opin. 2011 Feb;27(2):375-82	Sub-group analysis
Hsiao 2011	Hsiao SM, Chang TC, Wu WY, Chen CH, Yu HJ, Lin HH. Comparisons of urodynamic effects, therapeutic efficacy and safety of solifenacin versus tolterodine for female overactive bladder syndrome. J Obstet Gynaecol Res. 2011 Aug;37(8):1084-91	Sub-group analysis
Roehrborn 2006	Roehrborn CG, Abrams P, Rovner ES, Kaplan SA, Herschorn S, Guan Z. Efficacy and tolerability of tolterodine extended-release in men with overactive bladder and urgency urinary incontinence. BJU Int. 2006 May;97(5):1003-6	Sub-group analysis
Rovner 2008	Rovner ES, Rackley R, Nitti VW, Wang JT, Guan Z. Tolterodine extended release is efficacious in continent and incontinent subjects with overactive bladder. Urology. 2008 Sep;72(3):488-93	Sub-group analysis
Sand 2004	Sand PK, Miklos J, Ritter H, Appell R. A comparison of extended-release oxybutynin and tolterodine for treatment of overactive bladder in women. Int Urogynecol J Pelvic Floor Dysfunct. 2004 Jul-Aug;15(4):243-8	Sub-group analysis
Sussman 2007	Sussman DO, Kraus SR, Carlsson M, Guan Z. Onset of efficacy of tolterodine extended release in patients with overactive bladder. Curr Med Res Opin. 2007 Apr;23(4):777-81	Sub-group analysis
Swift 2003	Swift S, Garely A, Dimpfl T, Payne C. A new once-daily formulation of tolterodine provides superior efficacy and is well tolerated in women with overactive bladder. Int Urogynecol J Pelvic Floor Dysfunct. 2003 Feb;14(1):50-4; discussion 4-5	Sub-group analysis
Toglia 2010	Toglia MR, Ostergard DR, Appell RA, Andoh M, Fakhoury A, Hussain IF. Solifenacin for overactive bladder: secondary analysis of data from VENUS based on baseline continence status. Int Urogynecol J. 2010 Jul;21(7):847-54	Sub-group analysis
Pooled analysis		
Armstrong 2007	Armstrong RB, Dmochowski RR, Sand PK, Macdiarmid S. Safety and tolerability of extended-release oxybutynin once daily in urinary incontinence: combined results from two phase 4 controlled clinical trials. Int Urol Nephrol. 2007;39(4):1069-77	Combined results of the OPERA and OBJECT studies
Brubaker 2007	Brubaker L, FitzGerald MP. Nocturnal polyuria and nocturia relief in patients treated with solifenacin for overactive bladder symptoms. Int Urogynecol J Pelvic Floor Dysfunct. 2007 Jul;18(7):737-41	Pooled analysis from four 12-week phase III trials. Cardozo 2004 and Chapple 2004 (both in MTC). Also Gittelman 2003 presented as a poster
Dmochowski 2007	Dmochowski R, Abrams P, Marschall-Kehrel D, Wang JT, Guan Z. Efficacy and tolerability of tolterodine extended release in male and female patients with overactive bladder. Eur Urol. 2007	Pooled analysis of Rackley 2006 (in MTC) and Abrams abstract

Author year	Full citation	Exclusion code
	Apr;51(4):1054-64; discussion 64	2005 (to be located)
Dmochowski 2010	Dmochowski RR, Rosenberg MT, Zinner NR, Staskin DR, Sand PK. Extended-release trospium chloride improves quality of life in overactive bladder. Value Health. 2010 Mar-Apr;13(2):251-7	Pooled analysis of Dmochowski 2008 (in MTC) and Staskin 2007 (in MTC)
Kaplan 2006	Kaplan SA, Roehrborn CG, Dmochowski R, Rovner ES, Wang JT, Guan Z. Tolterodine extended release improves overactive bladder symptoms in men with overactive bladder and nocturia. Urology. 2006 Aug;68(2):328-32	Pooled analysis of what is believed to be Rackley 2006 (in MTC) and Abrams abstract 2005
Kraus 2010	Kraus SR, Ruiz-Cerda JL, Martire D, Wang JT, Wagg AS. Efficacy and tolerability of fesoterodine in older and younger subjects with overactive bladder. Urology. 2010 Dec;76(6):1350-7	Pooled analysis of Chapple 2007 (in MTC) and Nitti 2007 (in MTC)
MacDiarmid 2011	MacDiarmid SA, Ellsworth PI, Ginsberg DA, Oefelein MG, Sussman DO. Safety and efficacy of once-daily trospium chloride extended-release in male patients with overactive bladder. Urology. 2011 Jan;77(1):24-9	Pooled analysis of Dmochowski 2008 and Staskin 2007
Millard 2006	Millard RJ, Halaska M. Efficacy of solifenacin in patients with severe symptoms of overactive bladder: a pooled analysis. Curr Med Res Opin. 2006 Jan;22(1):41-8	Pooled analysis of Cardozo 2004 and Chapple 2004 (both in MTC). Data on file from Astellas also included in the pooled analysis
Staskin 2006	Staskin DR, Te AE. Short- and long-term efficacy of solifenacin treatment in patients with symptoms of mixed urinary incontinence. BJU Int. 2006 Jun;97(6):1256-61	Pooled analysis of included studies. Chapple 2004 and Cardozo 2004 (in MTC)
Staskin 2009	Staskin DR, Rosenberg MT, Sand PK, Zinner NR, Dmochowski RR. Trospium chloride once-daily extended release is effective and well tolerated for the treatment of overactive bladder syndrome: an integrated analysis of two randomised, phase III trials. Int J Clin Pract. 2009 Dec;63(12):1715-23	Pooled analysis of Staskin 2007 and Dmochowski 2008 (in MTC)
Zinner 2011	Zinner NR, Dmochowski RR, Staskin DR, Siami PF, Sand PK, Oefelein MG. Once-daily trospium chloride 60 mg extended-release provides effective, long-term relief of overactive bladder syndrome symptoms. Neurourol Urodyn. 2011 Sep;30(7):1214-9	Pooled analysis of Staskin 2007 and Dmochowski 2008 (in MTC)
Not major publication		
Chancellor 2000	Chancellor M, Freedman S, Mitcheson HD, Antoci J, Primus G, Wein A. Tolterodine, an effective and well tolerated treatment for urge incontinence and other overactive bladder symptoms. Clin. Drug Invest. 2000;19(2):83-91	Not the major publication
Chancellor 2000	Chancellor M, Freedman S, Mitcheson HD, Primus G, Wein A. ERRATUM: Tolterodine, an effective and well tolerated treatment for urge incontinence and other overactive bladder symptoms. Clin Drug Investig. 2000;19(5):391.	Erratum (duplicate), Not the major publication
Dmochowski 2008	Dmochowski RR, Sand PK, Zinner NR, Staskin DR. Trospium 60 mg once daily (QD) for overactive bladder syndrome: results from a placebo-controlled interventional study. Urology. 2008 Mar;71(3):449-54	Not the major publication
Wagg 2011	Wagg A, Khullar V, Marschall-Kehrel D, Michel MC, Oelke M, Tincello DG, et al. Assessment of fesoterodine treatment in older people with overactive bladder: Results of SOFIA, a double-blind, placebo-controlled pan European trial. 26th Annual congress of the European Association of Urology, 18-22 March 2011, Vienna, Austria (Abstract)	Not the major publication
Wein 2005	Wein AJ. Treatment of urge-predominant mixed urinary incontinence with tolterodine extended release: a randomized, placebo-controlled trial. J Urol. 2005 Jun;173(6):2056-7	Not the major publication
Not appropriate population for analysis		
Freeman 2003	Freeman R, Hill S, Millard R, Slack M, Sutherst J. Reduced perception of urgency in treatment of overactive bladder with extended-release tolterodine. Obstet Gynecol. 2003 Sep;102(3):605-11	Not a relevant population for analysis
Other reason for exclusion		
Astellas	Astellas Pharma. Data on file: A randomized, double-blind, parallel	Inappropriate study

Author year	Full citation	Exclusion code
2010	group, active controlled, multi-center long-term study to assess the safety and efficiacy of the beta-3 agonist mirabegron (YM178) 50 mg qd and 100 mg qd in subjects with symptoms of overactive bladder. 8 December 2010. 178-CL-049 (TAURUS) clinical study report	duration
Cardozo 2000	Cardozo L, Chapple CR, Toozs-Hobson P, Grosse-Freese M, Bulitta M, Lehmacher W, et al. Efficacy of trospium chloride in patients with detrusor instability: a placebo-controlled, randomized, double-blind, multicentre clinical trial. BJU Int. 2000 Apr;85(6):659-64	Inappropriate study duration
Chapple 2005	Chapple CR, Abrams P. Comparison of darifenacin and oxybutynin in patients with overactive bladder: assessment of ambulatory urodynamics and impact on salivary flow. Eur Urol. 2005 Jul;48(1):102-9	Inappropriate study duration
Halaska 2003	Halaska M, Ralph G, Wiedemann A, Primus G, Ballering-Bruhl B, Hofner K, et al. Controlled, double-blind, multicentre clinical trial to investigate long-term tolerability and efficacy of trospium chloride in patients with detrusor instability. World J Urol. 2003 May;20(6):392-9	Inappropriate study duration
Ulshofer 2001	Ulshofer B, Bihr AM, Bodeker RH, Schwantes U, Jahn HP. Randomised, Double-Blind, Placebo-Controlled Study on the Efficacy and Tolerance of Trospium Chloride in Patients with Motor Urge Incontinence. Clin Drug Investig. 2001;21(8):563-9	Inappropriate study duration
Xia 2001	Xia T, Su RS, Tao XC, Yan JZ, Zhang J, Su BH. Clinical evaluation on the efficacy and safety of tolterodine in the treatment for overactive bladder. Chin J Clin Pharmacol. 2001;17(2):83-6.	Study duration is 6 weeks only
Chancellor 2008	Chancellor MB, Zinner N, Whitmore K, Kobashi K, Snyder JA, Siami P, et al. Efficacy of solifenacin in patients previously treated with tolterodine extended release 4 mg: results of a 12-week, multicenter, open-label, flexible-dose study. Clin Ther. 2008 Oct;30(10):1766-81	Not RCT study design
Chen 2010	Chen YC, Chen CY, Kuo HC. Efficacy and adverse effects of solifenacin in the treatment of lower urinary tract symptoms in patients with overactive bladder. Urological Science. 2010;21(1):38-43	Not RCT study design
Kreder 2002	Kreder K, Mayne C, Jonas U. Long-term safety, tolerability and efficacy of extended-release tolterodine in the treatment of overactive bladder. Eur Urol. 2002 Jun;41(6):588-95	Not RCT study design
Rogers 2009	Rogers RG, Omotosho T, Bachmann G, Sun F, Morrow JD. Continued symptom improvement in sexually active women with overactive bladder and urgency urinary incontinence treated with tolterodine ER for 6 months. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Apr;20(4):381-5	Not RCT study design
Siami 2002	Siami P, Seidman LS, Lama D. A multicenter, prospective, open-label study of tolterodine extended-release 4 mg for overactive bladder: the speed of onset of therapeutic assessment trial (STAT). Clin Ther. 2002 Apr;24(4):616-28	Not RCT study design
Takei 2005	Takei M, Homma Y. Long-term safety, tolerability and efficacy of extended-release tolterodine in the treatment of overactive bladder in Japanese patients. Int J Urol. 2005 May;12(5):456-64	Not RCT study design
Van Kerrebroeck 2010	Van Kerrebroeck PE, Heesakkers J, Berriman S, Padmanabhan Aiyer L, Carlsson M, Guan Z. Long-term safety, tolerability and efficacy of fesoterodine treatment in subjects with overactive bladder symptoms. Int J Clin Pract. 2010 Apr;64(5):584-93	Not RCT study design
Chancellor 2010	Chancellor MB, Oefelein MG, Vasavada S. Obesity is associated with a more severe overactive bladder disease state that is effectively treated with once-daily administration of trospium chloride extended release. Neurourol Urodyn. 2010 Apr;29(4):551-4	Post hoc analysis of Staskin 2007 and Dmochowski 2008 (both in MTC)
Chapple 2008	Chapple CR, Van Kerrebroeck PE, Junemann KP, Wang JT, Brodsky M. Comparison of fesoterodine and tolterodine in patients with overactive bladder. BJU Int. 2008 Nov;102(9):1128-32	Post-hoc analysis in a sub-group that is not of interest
Dmochowski 2007	Dmochowski R, Kreder K, MacDiarmid S, Carlsson M, Guan Z. The clinical efficacy of tolterodine extended-release is maintained for 24 h in patients with overactive bladder. BJU Int. 2007 Jul;100(1):107-10	Post hoc analysis of van Kerrebroeck 2001 (in MTC)
Landis 2004	Landis JR, Kaplan S, Swift S, Versi E. Efficacy of antimuscarinic therapy for overactive bladder with varying degrees of incontinence severity. J Urol. 2004 Feb;171(2 Pt 1):752-6	Post-hoc analysis in a sub-group that is not of interest

Author year	Full citation	Exclusion code
Nitti 2006	Nitti VW, Dmochowski R, Appell RA, Wang JT, Bavendam T, Guan Z. Efficacy and tolerability of tolterodine extended-release in continent patients with overactive bladder and nocturia. BJU Int. 2006 Jun;97(6):1262-6	Post-hoc analysis in a sub-group that is not of interest
Sand 2009	Sand PK, Dmochowski RR, Zinner NR, Staskin DR, Appell RA. Trospium chloride extended release is effective and well tolerated in women with overactive bladder syndrome. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Dec;20(12):1431-8	Post hoc analysis of Dmochowski 2008 and Staskin 2007 (in MTC)
Sand 2009	Sand PK, Morrow JD, Bavendam T, Creanga DL, Nitti VW. Efficacy and tolerability of fesoterodine in women with overactive bladder. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Jul;20(7):827-35	Post hoc analysis of Chapple 2007 and Nitti 2007 (in MTC)
Sand 2011	Sand PK, Johnson Ii TM, Rovner ES, Ellsworth PI, Oefelein MG, Staskin DR. Trospium chloride once-daily extended release is efficacious and tolerated in elderly subjects (aged >/= 75 years) with overactive bladder syndrome. BJU Int. 2011 Feb;107(4):612-20	Post hoc analysis of Dmochowski 2008 and Staskin 2007 (in MTC)
Sand 2011	Sand PK, Rovner ES, Watanabe JH, Oefelein MG. Once-daily trospium chloride 60 mg extended release in subjects with overactive bladder syndrome who use multiple concomitant medications: Post hoc analysis of pooled data from two randomized, placebo-controlled trials. Drugs Aging. 2011 Feb 1;28(2):151-60	Post hoc analysis of Dmochowski 2008 and Staskin 2007 (in MTC)
Scarpero 2011	Scarpero H, Sand PK, Kelleher CJ, Berriman S, Bavendam T, Carlsson M. Long-term safety, tolerability, and efficacy of fesoterodine treatment in men and women with overactive bladder symptoms. Curr Med Res Opin. 2011 May;27(5):921-30	Post hoc analysis of Chapple 2007 and Nitti 2007 (in MTC)
Serels 2010	Serels SR, Toglia MR, Forero-Schwanhaeuser S, He W. Impact of solifenacin on diary-recorded and patient-reported urgency in patients with severe overactive bladder (OAB) symptoms. Curr Med Res Opin. 2010 Oct;26(10):2277-85	Post-hoc analysis in a sub-group that is not of interest
Staskin 2010	Staskin D, Michel MC, Nitti V, Morrow JD, Wang J, Guan Z. Efficacy of fesoterodine over 24 hours in subjects with overactive bladder. Curr Med Res Opin. 2010 Apr;26(4):813-8	Post hoc analysis of Chapple 2007 and Nitti 2007 (in MTC)
Staskin 2011	Staskin D, Khullar V, Michel MC, Morrow JD, Sun F, Guan Z, et al. Effects of voluntary dose escalation in a placebo-controlled, flexible-dose trial of fesoterodine in subjects with overactive bladder. Neurourol Urodyn. 2011 Nov;30(8):1480-5	Post-hoc analysis in a sub-group that is not of interest
Wein 2007	Wein AJ, Khullar V, Wang JT, Guan Z. Achieving continence with antimuscarinic therapy for overactive bladder: effects of baseline incontinence severity and bladder diary duration. BJU Int. 2007 Feb;99(2):360-3	Post hoc analysis of van Kerrebroeck
Weiss 2007	Weiss JP, Blaivas JG, Jones M, Wang JT, Guan Z. Age related pathogenesis of nocturia in patients with overactive bladder. J Urol. 2007 Aug;178(2):548-51; discussion 51	Post hoc analysis of Rackley 2006 (in MTC)
Yokoyama 2011	Yokoyama O, Yamaguchi O, Kakizaki H, Itoh N, Yokota T, Okada H, et al. Efficacy of solifenacin on nocturia in Japanese patients with overactive bladder: impact on sleep evaluated by bladder diary. J Urol. 2011 Jul;186(1):170-4	Post-hoc analysis in a sub-group that is not of interest
Chapple 2005	Chapple CR, Martinez-Garcia R, Selvaggi L, Toozs-Hobson P, Warnack W, Drogendijk T, et al. A comparison of the efficacy and tolerability of solifenacin succinate and extended release tolterodine at treating overactive bladder syndrome: results of the STAR trial. Eur Urol. 2005 Sep;48(3):464-70	No relevant outcome reported
Chu 2005	Chu FM, Dmochowski RR, Lama DJ, Anderson RU, Sand PK. Extended-release formulations of oxybutynin and tolterodine exhibit similar central nervous system tolerability profiles: a subanalysis of data from the OPERA trial. Am J Obstet Gynecol. 2005 Jun;192(6):1849-54; discussion 54-5	No relevant outcome reported (missing the measure of outcome or measure of variability of the outcome [SD or SE or CI])
Junemann 2005	Junemann KP, Halaska M, Rittstein T, Murtz G, Schnabel F, Brunjes R, et al. Propiverine versus tolterodine: efficacy and tolerability in patients with overactive bladder. Eur Urol. 2005 Sep;48(3):478-82	No relevant outcome reported (missing the measure of outcome or measure of variability of the outcome [SD or SE or CI])
Leung	Leung HY, Yip SK, Cheon C, Liu YS, Lau J, Wong HK, et al. A	No relevant outcome

Author year	Full citation	Exclusion code
2002	randomized controlled trial of tolterodine and oxybutynin on tolerability and clinical efficacy for treating Chinese women with an overactive bladder. BJU Int. 2002 Sep;90(4):375-80	reported (missing the measure of outcome or measure of variability of the outcome [SD or SE or CI])
Robinson 2007	Robinson D, Cardozo L, Terpstra G, Bolodeoku J. A randomized double-blind placebo-controlled multicentre study to explore the efficacy and safety of tamsulosin and tolterodine in women with overactive bladder syndrome. BJU Int. 2007 Oct;100(4):840-5	No relevant outcome reported (missing the measure of outcome or measure of variability of the outcome [SD or SE or CI])
Rudy 2006	Rudy D, Cline K, Harris R, Goldberg K, Dmochowski R. Multicenter phase III trial studying trospium chloride in patients with overactive bladder. Urology. 2006 Feb;67(2):275-80	No relevant outcome reported (missing the measure of outcome or measure of variability of the outcome [SD or SE or CI])
Cardozo 2008	Cardozo L, Hessdorfer E, Milani R, Arano P, Dewilde L, Slack M, et al. Solifenacin in the treatment of urgency and other symptoms of overactive bladder: results from a randomized, double-blind, placebo-controlled, rising-dose trial. BJU Int. 2008 Nov;102(9):1120-7	Compares flexible dose with placebo
Dmochowski 2010	Dmochowski RR, Peters KM, Morrow JD, Guan Z, Gong J, Sun F, et al. Randomized, double-blind, placebo-controlled trial of flexible-dose fesoterodine in subjects with overactive bladder. Urology. 2010 Jan;75(1):62-8	Flexible dose fesoterodine. Not flexible treatment
Huang 2012	Huang AJ, Hess R, Arya LA, Richter HE, Subak LL, Bradley CS, et al. Pharmacologic treatment for urgency-predominant urinary incontinence in women diagnosed using a simplified algorithm: a randomized trial. Am J Obstet Gynecol. 2012 May;206(5):444 e1-11	Compares flexible dose with placebo
Karram 2009	Karram MM, Toglia MR, Serels SR, Andoh M, Fakhoury A, Forero-Schwanhaeuser S. Treatment with solifenacin increases warning time and improves symptoms of overactive bladder: results from VENUS, a randomized, double-blind, placebo-controlled trial. Urology. 2009 Jan;73(1):14-8	Compares flexible dose with placebo
Vardy 2009	Vardy MD, Mitcheson HD, Samuels TA, Wegenke JD, Forero-Schwanhaeuser S, Marshall TS, et al. Effects of solifenacin on overactive bladder symptoms, symptom bother and other patient-reported outcomes: results from VIBRANT - a double-blind, placebo-controlled trial. Int J Clin Pract. 2009 Dec;63(12):1702-14	Compares flexible dose with placebo
Malone-Lee 2001	Malone-Lee J, Shaffu B, Anand C, Powell C. Tolterodine: superior tolerability than and comparable efficacy to oxybutynin in individuals 50 years old or older with overactive bladder: a randomized controlled trial. J Urol. 2001 May;165(5):1452-6	Not comparing relevant treatments
Sand 2012	Sand PK, Heesakkers J, Kraus SR, Carlsson M, Guan Z, Berriman S. Long-term safety, tolerability and efficacy of fesoterodine in subjects with overactive bladder symptoms stratified by age: pooled analysis of two open-label extension studies. Drugs Aging. 2012 Feb 1;29(2):119-31	Non-oral formulation of oxybutynin
Zellner 2009	Zellner M, Madersbacher H, Palmtag H, Stohrer M, Bodeker RH. Trospium chloride and oxybutynin hydrochloride in a german study of adults with urinary urge incontinence: results of a 12-week, multicenter, randomized, double-blind, parallel-group, flexible-dose noninferiority trial. Clin Ther. 2009 Nov;31(11):2519-39	Trospium 45 mg not marketed in UK (BNF 62)
Lackner 2011	Lackner TE, Wyman JF, McCarthy TC, Monigold M, Davey C. Efficacy of oral extended-release oxybutynin in cognitively impaired older nursing home residents with urge urinary incontinence: a randomized placebo-controlled trial. J Am Med Dir Assoc. 2011 Nov;12(9):639-47	Results are not presented in a manner that can be used for the MTC
Nitti 2011	Nitti V, Herschorn S, Lee M, Martin NG. Efficacy and tolerability of once-daily mirabegron, a potent and selective B3-adrenoreceptor agonist, in patients with overactive bladder - results from a North American Phase III trial. 41st Annual meeting of the International Continence Society (ICS), 29 Aug - 2 Sept 2011, Glasgow, UK (Abstract).	Same as CSR CL-046 which has been included in the MTC
Sussman	Sussman D, Garely A. Treatment of overactive bladder with once-	Two separate trials

Author year	Full citation	Exclusion code
2002	daily extended-release tolterodine or oxybutynin: the antimuscarinic clinical effectiveness trial (ACET). Curr Med Res Opin. 2002;18(4):177-84	conducted in parallel
Wang 2006	Wang AC, Chih SY, Chen MC. Comparison of electric stimulation and oxybutynin chloride in management of overactive bladder with special reference to urinary urgency: a randomized placebo-controlled trial. Urology. 2006 Nov;68(5):999-1004	No measure of variability

A10 – discrepancies in patient flow. In the patient flow diagrams throughout the submission (Figure 2, 4, 5, and 32) the number of patients assessed for eligibility minus the number of patients who received placebo run-in study drug do not equal the number of patients who discontinued during screening. Please clarify these discrepancies.

Figure 2: this is the clinical SR flow diagram. We have assumed that the query relates to Figure 3 (SCORPIO) as well as the diagrams for ARIES, CAPRICORN and TAURUS.

Patients with a UTI at screening could be rescreened once the UTI had resolved. If rescreened, patients were to be assigned a new screening number. The result of issuing a new screening number increased the total number of patients screened since rescreened patients were counted twice.

Section B: Clarification on cost-effectiveness data

B1 – test of correlation. Please clarify which test (p192) was carried out to investigate potential correlation between the number of micturitions and incontinence episodes per day used to inform the overall severity of OAB. In addition please provide the estimate of correlation (0 or otherwise) obtained from the test.

The potential relationship between the micturition and incontinence variable was assessed with the Pearson correlation coefficient using data from SCORPIO. The correlation between daily numbers of micturitions and incontinence episodes is statistically significant ($p<0.0001$), but low ($r=0.19094$). Similarly, the correlation between changes from baseline in daily numbers of micturitions and incontinence episodes is statistically significant, but low.

Table 17: Pearson correlation coefficient test between micturition and incontinence

Outcomes	Pearson coefficient	P-value
Mean micturition & mean incontinence at final visit	0.19094	<0.0001
CFB micturition & CFB incontinence at final visit	0.17762	<0.0001

Abbreviations: CFB, change from baseline.

B2 – logistic regressions. For the logistic regressions used to obtain the probability of transition between severity levels for each symptom (micturitions and incontinence) please provide the following details:

a) the rationale for using a regression analysis to obtain these probabilities;

We used a regression analysis to obtain the probability (from Astellas trials) of being in a given severity level in the next cycle according to treatment, severity level in current cycle, time of follow-up visit, and adjust on known confounding variables such as gender and age.

There are three advantages of using this regression model rather than simply using proportions of patients moving from one level to another:

1. The probabilities are adjusted on potential confounders, such as age and gender
2. This reduces the number of parameters in the model: the transition matrix for each symptom and each treatment has 25 parameters, or 20 parameters considering that the sum of probabilities in each row must be 1. As transition probabilities are different in the first, second and subsequent months, this would represent 60 parameters for each symptom and treatment. With the regression model, the number of parameters is reduced to four coefficients for each treatment, and 36 parameters not related to treatment. This facilitated the sensitivity analysis on the treatment effect, and most importantly, this made it possible to use a calibration approach to obtain transition probabilities for treatment not included in SCORPIO. It would not be possible to obtain three matrices with 60 independent parameters by calibration.
3. If we had used the matrices based on proportions of patients, patients lost to follow-up would be ignored. Using the regression analysis, accounting for repeated observations, data for patients lost to follow-up are implicitly imputed.

b) the rationale for choosing a multinomial logistic regression model;

Multinomial logistic regression models were used as this is a commonly used type of model for categorical variables. Although the outcome variables (severity levels) are ordered variables, we did not use ordered logistic models because the proportional odds assumption was rejected, based on a statistical test, for each symptom (see paragraph d) below). A multinomial probit could also have been appropriate but it was not tested.

c) the rationale/evidence base for selecting: treatment, symptom severity in previous month, gender and age as explanatory variables;

Treatment was included in the model because the objective was to estimate the effect of treatment. Symptom severity in previous month was also entered in the model because we expected that the severity level in a given month would be dependent on the severity level in the previous month (e.g. patients were more likely to improve than worsen during the trial, thus it would be rather unlikely for a patient at Level 1 to worsen to Level 5 in the next month, whereas patients at Level 5 could stay in the same level). Results confirmed that symptom severity in previous month was a good predictor of severity in current month. Age and gender were also entered as adjustment factors, because we expected that probabilities of improvement or worsening (independent of treatment, i.e. according to natural disease history) might vary with age and gender. The effect of gender was significant, the effect of age was not, but the variable was left in the model nevertheless; removing that variable had little impact on other coefficients.

d) on what basis the null hypothesis of proportional odds was rejected;

The proportional odds assumption was tested based on a multinomial logit model, estimated from SCORPIO for each symptom variable. The hypothesis tested was equality of coefficients associated with different severity levels, for all covariates. This hypothesis was rejected ($p<0.0001$), suggesting that the proportional odds assumptions did not hold for this model.

Table 18: Test of the Proportional Odds Assumption for micturition and incontinence

Outcome	Chi-square	P-value
Micturition	93.3705	<0.0001
Incontinence	122.3068	<0.0001

e) which test (and the p-value obtained) was used to determine the level of interaction between treatment and severity (in the previous month).

A logistic model that contained the interaction between treatment and severity in the previous month showed that this interaction was not significant. The table below presents the result of the Wald chi-square test assessing the interaction.

Table 19: Results the Wald chi-square test for each outcome

Outcome	Wald chi-square	P-value
Interaction "Severity of micturition in the previous month & Treatment"	44.1956	0.6295
Interaction "Severity of incontinence in the previous month & Treatment"	44.1058	0.6331

B3 – linear regression models. For the linear regression models used to estimate utility (based on EQ-5D and OAB-5D data) please provide the following details:

a) the rationale for using regression analyses to obtain these parameters;

A regression model was used to obtain utilities for the following reasons:

- Utilities are known to be dependent on age and gender, as well as symptoms, therefore the regression model was required in order to disentangle effects of age and gender from effects of symptoms on utilities. This is especially important as incontinence severity increases with age (Pearson correlation coefficient between age and incontinence level: $r=0.0647$, $p<0.0001$), and utilities decrease with age, thus differences in average utilities between groups of patients at different severity levels are partly related to age. In other words, if we had not used a regression analysis, the benefit associated with mirabegron in terms of QALYs would have been overestimated.
- The model allowed separating effects of micturitions and incontinence on utilities, and therefore to model variations in micturitions and incontinence separately. This reduced the number of parameters and simplified the model as mentioned below (in B3b).

b) the rationale for choosing a linear regression model;

A linear model was used for simplicity. An advantage of this model is that the utility increments or decrements associated with improvements or symptoms (micturitions and incontinence) can be summed. It is implied that micturitions and incontinence have independent, additive effects on QALYs allowing the model to be run for micturitions and for incontinence separately. Thus, instead of having 1 very complex model, we use 2 simpler models.

c) the rationale/evidence base for selecting: age, gender, and country (as random effect) as explanatory variables;

Utilities and gender were thought to be confounding factors, as mentioned above. Country was also thought to be a potential confounding factor since EQ-5D ratings vary between countries (1). It was kept in the model since the Akaike Information Criterion was improved (reduced) when the country effect was entered.

d) how correlation between changes in the number of micturitions and incontinence episodes in utility estimation was tested (pg 196);

The correlation between changes in daily numbers of micturitions and of incontinence episodes was assessed by the Pearson correlation coefficient, using data from SCORPIO. The correlation was statistically significant ($p<0.0001$), although the correlation coefficient was low (see Table 17).

However, this sentence (p 196 of the submission) was wrongly formulated. We should have written that the *interaction* between the numbers of micturitions and incontinence episodes in the utility model was tested. A variable of interaction between micturitions and incontinence was entered in the model, and the associated Wald test p-value was 0.0566.

e) ***results of the sensitivity test of the two models, which estimated utility changes from baseline to week 12 (pg 209).***

Table 20 presents the results of the analyses of sensitivity of utility estimates to changes in symptoms. Changes in OAB-5D utilities are significantly different between worsening and stable patients, but changes in EQ-5D utilities are not significantly different.

Table 20: Responsiveness of HRQoL and clinical symptoms in the overall population

Clinical symptoms (per 24 hours)	Response in symptoms	N (%)	CFB in utility EQ-5D, adjusted mean (±SD)	P value vs 'Stable'†	CFB in utility OAB-5D, adjusted mean (±SD)	P value vs 'Stable'†
Micturitions	Improvement ≥ 1 level	2286 (56.4%)	0.046 (±0.213)	0.0058	0.076 (±0.092)	<0.0001
	Stable	1260 (31.1%)	0.027 (±0.202)	NA	0.039 (±0.087)	NA
	Worsening ≥ 1 level	506 (12.5%)	0.023 (±0.195)	0.7291	0.021 (±0.085)	0.0001
Incontinence episodes	Improvement ≥ 1 level	1874 (46.3%)	0.053 (±0.223)	0.0002	0.081 (±0.096)	<0.0001
	Stable	1849 (45.6%)	0.028 (±0.206)	NA	0.042 (±0.089)	NA
	Worsening ≥ 1 level	329 (8.1%)	0.007 (±0.197)	0.0662	0.022 (±0.086)	<0.0001

Abbreviations: CFB, change from baseline; EQ-5D, European quality of life – five dimensions; NA, not applicable; OAB-5D, overactive bladder – five dimensions; SD, standard deviation. † to test the null hypothesis that the associated utility change equals the utility change in patients with “Stable” response.

B4 – model rationale. Please clarify the rationale for using a repeated regression model to estimate the disutility associated with AEs.

A regression model was used to predict the disutility associated with AEs for the same reasons as previously mentioned, i.e. primarily to disentangle effects of AEs on utilities from effects of other variables such as age, gender and symptom severity. A repeated observations model was used to account for the dependence between different utility assessments within individuals. Assuming that utilities at different visits are independent would have led to underestimate the variability around estimates of disutilities. The Akaike Information Criteria confirmed that the model accounting for repeated measures was better.

B5 – explanatory variable rationale. Please provide the rationale/evidence base for selecting gender, age and severity of symptoms (incontinence, urgency, micturition), and random effect of geographical region as explanatory variables.

We entered gender, age and geographical regions for the same reason as mentioned in B3. Age in particular was thought to be a potential important confounding factor as EQ-5D utilities are strongly related to age, and adverse events are more frequent amongst the elderly. The proportion of patients experiencing AEs was estimated at 16.00% amongst patients aged 65 years or over, and 13.82% amongst those under 65 years, in the pooled analysis of SCORPIO, ARIES and CAPRICORN (independence chi-square test, p=0.0423).

In addition, we expected symptoms could also be a confounding factor. In the pooled analysis of SCORPIO, ARIES and CAPRICORN, patients experiencing an AE had significantly more episodes of incontinence, compared with patients without an AE (1.24 incontinence episodes per day vs 0.94, respectively, p=0.0004). Thus failing to adjust for incontinence severity would have led to an overestimate of the disutility associated with adverse events.

We entered urgency, as well as micturitions and incontinence, but this had little impact on results: the disutility associated with AEs was estimated at 0.357 with urgency in the model and 0.356 without urgency in the model.

B6 – model of change in symptoms. Regarding the calculation of modelled change in symptoms (carried out as part of the calibration approach; p197), please clarify whether the word "group" in the following sentence "The mean change in frequency of symptom episodes (micturitions or incontinence) was estimated within each *group* ***based on data from the mirabegron 50mg arm of the SCORPIO study." refers to treatment group or each group of the 25 symptom severity groups defined.***

The term 'group' refers to the 25 groups defined according to symptom severity.

B7 – beta coefficients. The beta coefficients informing the regression model used to derive transition probabilities for other antimuscarinic treatments are presented in Table 170, based on optimisation techniques applied to beta

coefficients obtained from the mirabegron 50 mg arm of SCORPIO. Please provide the beta coefficients derived from optimisation using:

a) the coefficients for tolterodine ER 4 mg;
b) the coefficients for solifenacin 5 mg.

The beta coefficients informing the regression model used to derive transition probabilities for other antimuscarinics are presented in Appendix B for each optimisation scenario and for each outcome:

1. the coefficients for mirabegron 50 mg
2. the coefficients for tolterodine ER 4 mg
3. the coefficients for solifenacin 5 mg.

We noted that the coefficients presented in the submission, obtained using the coefficients for mirabegron 50 mg as initial values, were based on a previous model version. The coefficients used in the latest version of the model, submitted to NICE (from which the results presented in the submission were derived) are therefore provided in Appendix B.

In addition, please clarify why the coefficients for solifenacin used in the base case model were derived from optimisation on mirabegron coefficients in the base case, rather than regression analysis of data from study 905-CL-015.

The use of coefficients based on MTC and calibration for solifenacin 5 mg was thought more appropriate than using coefficient estimated from the study 905-CL-015 because all the evidence available about solifenacin was used, rather than a single trial. When using the coefficients estimated from logistic regression based on study 905-CL-015 decreased from £12,493 per QALY gained to £5,991 per QALY gained, i.e. was more favourable to mirabegron than the presented base case.

B8 – Adverse events rates: dry mouth. Table 85 of the submission reports the probabilities of dry mouth at 12 weeks (based on results of SCORPIO) with mirabegron 50 mg and tolterodine 4 mg as 2.5% and 10.1%, respectively. However, the ERG notes that the rate of dry mouth reported for mirabegron 50 mg and tolterodine 4 mg throughout the clinical section of the submission were 1.8% and 9.5%. Please clarify this potential discrepancy.

Two rates for dry mouth AEs are quoted within the clinical section:
- TEAEs: 10.1% (tolterodine) and 2.8% (mirabegron 50 mg) *(Text on page 167 of manufacturer's submission)*
- Treatment-related TEAEs: 9.5% (tolterodine) and 1.8% (mirabegron 50 mg) *(Table 33 of manufacturer's submission)*

For the model, the rates of all TEAEs rather than treatment-related TEAEs was used.

B9 - Adverse events rates: constipation. Please clarify where the rates of constipation recorded in SCORPIO are in the clinical section of the submission.

The rates for constipation were not included in the safety section of the manufacturer's submission, as only common TEAEs (reported in ≥ 2% of patients in any treatment group) were listed for supporting trials.

Rates of TEAEs in SCORPIO are 2.0% (tolterodine) and 1.6% (mirabegron 50 mg).

References

1. Konig HH, Bernert S, Angermeyer MC, Matschinger H, Martinez M, Vilagut G, et al. Comparison of population health status in six european countries: results of a representative survey using the EQ-5D questionnaire. Med Care. 2009 Feb;47(2):255-61.

Appendix

Appendix A: Working WinBUGS code populated with the appropriate data set for each outcome

Micturition: Fixed effect model

```
# Normal likelihood, identity link
# Fixed effects model
model{                          # *** PROGRAM STARTS
for(i in 1:ns){                 #   LOOP THROUGH STUDIES
   mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
   for (k in 1:na[i]) {           #  LOOP THROUGH ARMS
      var[i,k] <- pow(se[i,k],2)   # calculate variances
      prec[i,k] <- 1/var[i,k]      # set precisions
      y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
# model for linear predictor
      theta[i,k] <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
      dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
    }
#  summed residual deviance contribution for this trial
   resdev[i] <- sum(dev[i,1:na[i]])
 }
totresdev <- sum(resdev[])           #Total Residual Deviance
d[1]<-0      # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){  d[k] ~ dnorm(0,.0001) }

#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
     TvMira[c] <- (d[c] - d[2])
 }

}                               # *** PROGRAM ENDS

# Initial Values
#chain 1
list(d=c(NA,-5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -
5.00000E-01))
#chain 2
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00))
#chain 3
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01))


#Data

#for the treatment  we have:
#"Treatment"          "Code"
#"Tolterodine 4 mg"          1
#"Mirabegron 50 mg"          2
#"Fesoterodine 4mg"          3
#"Fesoterodine 8mg"          4
#"Oxybutynin 10 mg"          5
#"Placebo"                   6
#"Solifenacin 10 mg"         7
#"Solifenacin 5 mg"          8
#"Trospium 60 mg"            9


list(ns=23, nt=9.00000E+00, t= structure(.Data= c(1.00000E+00, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,
1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,
NA,    NA, 1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 3.00000E+00,
4.00000E+00, 6.00000E+00,    NA,    NA, 1.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA,    NA,
1.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 5.00000E+00,    NA,    NA,    NA,
NA, 1.00000E+00, 5.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 6.00000E+00, 7.00000E+00,
8.00000E+00,    NA,    NA, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 6.00000E+00,
NA,    NA,    NA,    NA, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 7.00000E+00,
8.00000E+00,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 2.00000E+00,
6.00000E+00,    NA,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 3.00000E+00,
```

4.00000E+00, 6.00000E+00, NA, NA, NA, 3.00000E+00, 4.00000E+00, 6.00000E+00, NA, NA, NA,
6.00000E+00, 7.00000E+00, 8.00000E+00, NA, NA, NA, 6.00000E+00, 7.00000E+00, 8.00000E+00, NA,
NA, NA, 6.00000E+00, 7.00000E+00, NA, NA, NA, NA, 6.00000E+00, 9.00000E+00, NA, NA,
NA, NA), .Dim=c(23, 6)), y= structure(.Data= c(-1.80000E+00, -1.70000E+00, -1.20000E+00, NA, NA, NA,
-1.59000E+00, -1.93000E+00, -1.34000E+00, NA, NA, NA, -2.23000E+00, -2.14000E+00, -1.43000E+00,
NA, NA, NA, -1.40000E+00, -1.67000E+00, -8.60000E-01, NA, NA, NA, -1.73000E+00, -1.76000E+00, -
1.88000E+00, -9.50000E-01, NA, NA, -2.29000E+00, -2.60000E+00, -1.98000E+00, NA, NA, NA, -
2.10000E+00, -2.20000E+00, -1.50000E+00, NA, NA, NA, -2.60000E+00, -1.80000E+00, NA, NA,
NA, NA, -2.90000E+00, -3.68571E+00, NA, NA, NA, NA, -1.88000E+00, -1.20000E+00, -2.61000E+00, -
2.19000E+00, NA, NA, -2.30000E+00, -1.70000E+00, NA, NA, NA, NA, -2.10000E+00, -
1.30000E+00, NA, NA, NA, NA, -2.20000E+00, -1.40000E+00, NA, NA, NA, NA, -2.14000E+00,
-2.47000E+00, -2.18000E+00, NA, NA, NA, -1.66000E+00, -1.05000E+00, NA, NA, NA, NA, -
1.60000E+00, -1.18000E+00, NA, NA, NA, NA, -2.12000E+00, -1.18000E+00, NA, NA, NA, NA,
-1.61000E+00, -2.09000E+00, -1.08000E+00, NA, NA, NA, -1.15000E+00, -1.25000E+00, -5.90000E-01,
NA, NA, NA, -9.40000E-01, -2.19000E+00, -1.93000E+00, NA, NA, NA, -1.66000E+00, -2.88000E+00, -
2.45000E+00, NA, NA, NA, -1.50000E+00, -3.00000E+00, NA, NA, NA, NA, -1.99000E+00, -
2.81000E+00, NA, NA, NA, NA), .Dim=c(23, 6)), se= structure(.Data= c(1.51000E-01, 1.46000E-01,
1.29000E-01, NA, NA, NA, 1.11000E-01, 1.11000E-01, 1.10000E-01, NA, NA, NA, 3.29000E-01,
1.91000E-01, 2.51000E-01, NA, NA, NA, 1.13432E-01, 1.15152E-01, 1.22711E-01, NA, NA, NA,
1.60000E-01, 1.70000E-01, 1.60000E-01, 1.60000E-01, NA, NA, 1.00000E-01, 1.00000E-01, 1.00000E-01,
NA, NA, NA, 1.00000E-01, 1.00000E-01, 1.00000E-01, NA, NA, NA, 2.74000E-01, 3.90000E-01, NA,
NA, NA, NA, 3.04000E-01, 3.47000E-01, NA, NA, NA, NA, 1.90000E-01, 2.05000E-01, 1.99000E-01,
1.76000E-01, NA, NA, 1.00000E-01, 2.00000E-01, NA, NA, NA, NA, 1.01000E-01, 1.36000E-01,
NA, NA, NA, NA, 2.34000E-01, 2.50000E-01, NA, NA, NA, NA, 3.64000E-01, 3.72541E-01,
3.67000E-01, NA, NA, NA, 1.33000E-01, 1.32000E-01, NA, NA, NA, NA, 1.22000E-01, 1.24000E-
01, NA, NA, NA, NA, 1.65000E-01, 1.48000E-01, NA, NA, NA, NA, 1.80000E-01, 1.80000E-01,
1.80000E-01, NA, NA, NA, 2.50000E-01, 2.55102E-01, 2.50000E-01, NA, NA, NA, 1.15000E-01,
1.09000E-01, 1.01000E-01, NA, NA, NA, 1.91493E-01, 1.80864E-01, 1.69115E-01, NA, NA, NA,
2.00000E-01, 2.00000E-01, NA, NA, NA, NA, 1.60000E-01, 1.50000E-01, NA, NA, NA, NA),
.Dim=c(23, 6)), na=c(3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 4.00000E+00, 3.00000E+00,
3.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00,
3.00000E+00, 2.00000E+00, 2.00000E+00))

Micturition: Random effect model

```
# Normal likelihood, identity link
# Random effects model for multi-arm trials
model{                          # *** PROGRAM STARTS
for(i in 1:ns){                 #   LOOP THROUGH STUDIES
   w[i,1] <- 0    # adjustment for multi-arm trials is zero for control arm
   delta[i,1] <- 0            # treatment effect is zero for control arm
   mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
   for (k in 1:na[i]) {            #  LOOP THROUGH ARMS
      var[i,k] <- pow(se[i,k],2)   # calculate variances
      prec[i,k] <- 1/var[i,k]      # set precisions
      y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
      theta[i,k] <- mu[i] + delta[i,k]  # model for linear predictor
#Deviance contribution
      dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
    }
#  summed residual deviance contribution for this trial
   resdev[i] <- sum(dev[i,1:na[i]])
   for (k in 2:na[i]) {            # LOOP THROUGH ARMS
# trial-specific LOR distributions
      delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions, with multi-arm trial correction
      md[i,k] <-  d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
      taud[i,k] <- tau *2*(k-1)/k
# adjustment, multi-arm RCTs
      w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
      sw[i,k] <- sum(w[i,1:k-1])/(k-1)
    }
 }
totresdev <- sum(resdev[])           #Total Residual Deviance
d[1]<-0      # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){  d[k] ~ dnorm(0,.0001) }

sd ~ dunif(0,5)     # vague prior for between-trial SD
```

```
tau <- pow(sd,-2)   # between-trial precision = (1/between-trial variance)


#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}

}

                              # *** PROGRAM ENDS


# Initial Values
#chain 1
list(d=c(NA,-5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -
5.00000E-01))
#chain 2
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00))
#chain 3
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01))


#Data

#for the treatment  we have:
#"Treatment"          "Code"
#"Tolterodine 4 mg"          1
#"Mirabegron 50 mg"          2
#"Fesoterodine 4mg"          3
#"Fesoterodine 8mg"          4
#"Oxybutynin 10 mg"          5
#"Placebo"                   6
#"Solifenacin 10 mg"         7
#"Solifenacin 5 mg"          8
#"Trospium 60 mg"            9


list(ns=23, nt=9.00000E+00, t= structure(.Data= c(1.00000E+00, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,
1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,
NA,    NA, 1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 3.00000E+00,
4.00000E+00, 6.00000E+00,    NA,    NA, 1.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA,    NA,
1.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 5.00000E+00,    NA,    NA,    NA,
NA, 1.00000E+00, 5.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 6.00000E+00, 7.00000E+00,
8.00000E+00,    NA,    NA, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 6.00000E+00,
NA,    NA,    NA,    NA, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 7.00000E+00,
8.00000E+00,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 2.00000E+00,
6.00000E+00,    NA,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 3.00000E+00,
4.00000E+00, 6.00000E+00,    NA,    NA,    NA, 3.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA,    NA,
6.00000E+00, 7.00000E+00, 8.00000E+00,    NA,    NA,    NA, 6.00000E+00, 7.00000E+00, 8.00000E+00,    NA,
NA,    NA, 6.00000E+00, 7.00000E+00,    NA,    NA,    NA,    NA, 6.00000E+00, 9.00000E+00,    NA,    NA,
NA,    NA), .Dim=c(23, 6)), y= structure(.Data= c(-1.80000E+00, -1.70000E+00, -1.20000E+00,    NA,    NA,    NA,
-1.59000E+00, -1.93000E+00, -1.34000E+00,    NA,    NA,    NA, -2.23000E+00, -2.14000E+00, -1.43000E+00,
NA,    NA,    NA, -1.40000E+00, -1.67000E+00, -8.60000E-01,    NA,    NA,    NA, -1.73000E+00, -1.76000E+00, -
1.88000E+00, -9.50000E-01,    NA,    NA, -2.29000E+00, -2.60000E+00, -1.98000E+00,    NA,    NA,    NA, -
2.10000E+00, -2.20000E+00, -1.50000E+00,    NA,    NA,    NA, -2.60000E+00, -1.80000E+00,    NA,    NA,
NA,    NA, -2.90000E+00, -3.68571E+00,    NA,    NA,    NA,    NA, -1.88000E+00, -1.20000E+00, -2.61000E+00, -
2.19000E+00,    NA,    NA, -2.30000E+00, -1.70000E+00,    NA,    NA,    NA,    NA, -2.10000E+00, -
1.30000E+00,    NA,    NA,    NA,    NA, -2.20000E+00, -1.40000E+00,    NA,    NA,    NA,    NA, -2.14000E+00,
-2.47000E+00, -2.18000E+00,    NA,    NA,    NA, -1.66000E+00, -1.05000E+00,    NA,    NA,    NA,    NA, -
1.60000E+00, -1.18000E+00,    NA,    NA,    NA,    NA, -2.12000E+00, -1.18000E+00,    NA,    NA,    NA,    NA,
-1.61000E+00, -2.09000E+00, -1.08000E+00,    NA,    NA,    NA, -1.15000E+00, -1.25000E+00, -5.90000E-01,
NA,    NA,    NA, -9.40000E-01, -2.19000E+00, -1.93000E+00,    NA,    NA,    NA, -1.66000E+00, -2.88000E+00, -
2.45000E+00,    NA,    NA,    NA, -1.50000E+00, -3.00000E+00,    NA,    NA,    NA,    NA, -1.99000E+00, -
2.81000E+00,    NA,    NA,    NA,    NA), .Dim=c(23, 6)), se= structure(.Data= c(1.51000E-01, 1.46000E-01,
1.29000E-01,    NA,    NA,    NA, 1.11000E-01, 1.11000E-01, 1.10000E-01,    NA,    NA,    NA, 3.29000E-01,
1.91000E-01, 2.51000E-01,    NA,    NA,    NA, 1.13432E-01, 1.15152E-01, 1.22711E-01,    NA,    NA,    NA,
1.60000E-01, 1.70000E-01, 1.60000E-01, 1.60000E-01,    NA,    NA, 1.00000E-01, 1.00000E-01, 1.00000E-01,
NA,    NA,    NA, 1.00000E-01, 1.00000E-01, 1.00000E-01,    NA,    NA,    NA, 2.74000E-01, 3.90000E-01,    NA,
NA,    NA,    NA, 3.04000E-01, 3.47000E-01,    NA,    NA,    NA,    NA, 1.90000E-01, 2.05000E-01, 1.99000E-01,
1.76000E-01,    NA,    NA, 1.00000E-01, 2.00000E-01,    NA,    NA,    NA,    NA, 1.01000E-01, 1.36000E-01,
NA,    NA,    NA,    NA, 2.34000E-01, 2.50000E-01,    NA,    NA,    NA,    NA, 3.64000E-01, 3.72541E-01,
```

3.67000E-01, NA, NA, NA, 1.33000E-01, 1.32000E-01, NA, NA, NA, NA, 1.22000E-01, 1.24000E-01, NA, NA, NA, NA, 1.65000E-01, 1.48000E-01, NA, NA, NA, NA, 1.80000E-01, 1.80000E-01, 1.80000E-01, NA, NA, NA, 2.50000E-01, 2.55102E-01, 2.50000E-01, NA, NA, NA, 1.15000E-01, 1.09000E-01, 1.01000E-01, NA, NA, NA, 1.91493E-01, 1.80864E-01, 1.69115E-01, NA, NA, NA, 2.00000E-01, 2.00000E-01, NA, NA, NA, NA, 1.60000E-01, 1.50000E-01, NA, NA, NA, NA), .Dim=c(23, 6)), na=c(3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00))

Incontinence: Fixed effect model

```
# Normal likelihood, identity link
# Fixed effects model
model{                          # *** PROGRAM STARTS
for(i in 1:ns){                 #   LOOP THROUGH STUDIES
   mu[i] ~ dnorm(0,.0001)          # vague priors for all trial baselines
   for (k in 1:na[i]) {           #  LOOP THROUGH ARMS
      var[i,k] <- pow(se[i,k],2)   # calculate variances
      prec[i,k] <- 1/var[i,k]      # set precisions
      y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
# model for linear predictor
      theta[i,k] <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
      dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
    }
#  summed residual deviance contribution for this trial
   resdev[i] <- sum(dev[i,1:na[i]])
  }
totresdev <- sum(resdev[])           #Total Residual Deviance
d[1]<-0      # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){  d[k] ~ dnorm(0,.0001) }

#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])
  }

}                               # *** PROGRAM ENDS

# Initial Values
#chain 1
list(d=c(NA,-5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01))
#chain 2
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00))
#chain 3
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01))


#Data
#For the treatment code
#"Treatment"          "Code"
#"Tolterodine 4 mg"          1
#"Mirabegron 50 mg"          2
#"Fesoterodine 4 mg"         3
#"Fesoterodine 8 mg"         4
#"Oxybutynin 10 mg"          5
#"Placebo"                   6
#"Solifenacin 10 mg"         7
#"Solifenacin 5 mg"          8


list(ns=15, nt=8.00000E+00, t= structure(.Data= c(1.00000E+00, 1.00000E+00, 6.00000E+00, NA, NA, NA, 1.00000E+00, 2.00000E+00, 6.00000E+00, NA, NA, NA, 1.00000E+00, 2.00000E+00, 6.00000E+00, NA, NA, NA, 1.00000E+00, 2.00000E+00, 6.00000E+00, NA, NA, NA, 1.00000E+00, 5.00000E+00, NA, NA, NA, NA, 1.00000E+00, 5.00000E+00, NA, NA, NA, NA, 1.00000E+00, 6.00000E+00, 7.00000E+00, 8.00000E+00, NA, NA, 1.00000E+00, 6.00000E+00, NA, NA, NA, NA, 2.00000E+00, 6.00000E+00, NA, NA, NA, NA, 2.00000E+00, 6.00000E+00, NA, NA, NA, NA, 2.00000E+00, 6.00000E+00, NA, NA, NA, NA, 3.00000E+00, 4.00000E+00, 6.00000E+00, NA, NA, NA, 6.00000E+00, 7.00000E+00, 8.00000E+00, NA, NA, NA, 6.00000E+00, 7.00000E+00, 8.00000E+00, NA, NA, NA, 6.00000E+00, 7.00000E+00, NA, NA, NA, NA), .Dim=c(15, 6)), y= structure(.Data= c(-
```

1.68600E+00, -1.51400E+00, -9.86000E-01, NA, NA, NA, -1.27000E+00, -1.57000E+00, -1.17000E+00, NA, NA, NA, -1.15000E+00, -1.24000E+00, -6.40000E-01, NA, NA, NA, -9.70000E-01, -1.12000E+00, -6.60000E-01, NA, NA, NA, -2.20000E+00, -1.40000E+00, NA, NA, NA, NA, -2.67100E+00, -3.04300E+00, NA, NA, NA, NA, -1.14000E+00, -7.60000E-01, -1.45000E+00, -1.42000E+00, NA, NA, -3.20000E+00, -2.10000E+00, NA, NA, NA, NA, -1.47000E+00, -1.13000E+00, NA, NA, NA, NA, -1.38000E+00, -9.60000E-01, NA, NA, NA, NA, -1.20000E+00, -6.40000E-01, NA, NA, NA, NA, -1.27000E+00, -1.15000E+00, -8.80000E-01, NA, NA, NA, -7.20000E-01, -1.59000E+00, -1.60000E+00, NA, NA, NA, -1.25000E+00, -1.57000E+00, -1.63000E+00, NA, NA, NA, -1.10000E+00, -2.00000E+00, NA, NA, NA, NA), .Dim=c(15, 6)), se= structure(.Data= c(1.13000E-01, 1.06000E-01, 7.60000E-02, NA, NA, NA, 1.12000E-01, 1.13000E-01, 1.13000E-01, NA, NA, NA, 3.72000E-01, 1.92000E-01, 2.47000E-01, NA, NA, NA, 8.40313E-02, 7.67854E-02, 9.70113E-02, NA, NA, NA, 3.39000E-01, 2.78000E-01, NA, NA, NA, NA, 2.38000E-01, 2.31000E-01, NA, NA, NA, NA, 1.72000E-01, 1.83000E-01, 1.78000E-01, 1.53000E-01, NA, NA, 2.52000E-01, 2.77000E-01, NA, NA, NA, NA, 1.14000E-01, 1.12000E-01, NA, NA, NA, NA, 1.23000E-01, 1.22000E-01, NA, NA, NA, NA, 1.21000E-01, 1.15000E-01, NA, NA, NA, NA, 1.73469E-01, 1.78571E-01, 1.73469E-01, NA, NA, NA, 1.16000E-01, 1.29000E-01, 1.09000E-01, NA, NA, NA, 1.92412E-01, 1.81390E-01, 1.61181E-01, NA, NA, NA, 2.00000E-01, 2.00000E-01, NA, NA, NA, NA), .Dim=c(15, 6)), na=c(3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00))

Incontinence: Random effect model

```
# Normal likelihood, identity link
# Random effects model for multi-arm trials
model{                          # *** PROGRAM STARTS
for(i in 1:ns){                 #   LOOP THROUGH STUDIES
   w[i,1] <- 0    # adjustment for multi-arm trials is zero for control arm
   delta[i,1] <- 0            # treatment effect is zero for control arm
   mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
   for (k in 1:na[i]) {            #  LOOP THROUGH ARMS
      var[i,k] <- pow(se[i,k],2)   # calculate variances
      prec[i,k] <- 1/var[i,k]      # set precisions
      y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
      theta[i,k] <- mu[i] + delta[i,k]  # model for linear predictor
#Deviance contribution
      dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
    }
#  summed residual deviance contribution for this trial
   resdev[i] <- sum(dev[i,1:na[i]])
   for (k in 2:na[i]) {            # LOOP THROUGH ARMS
# trial-specific LOR distributions
      delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions, with multi-arm trial correction
      md[i,k] <-  d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
      taud[i,k] <- tau *2*(k-1)/k
# adjustment, multi-arm RCTs
      w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
      sw[i,k] <- sum(w[i,1:k-1])/(k-1)
    }
 }
totresdev <- sum(resdev[])           #Total Residual Deviance
d[1]<-0       # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){  d[k] ~ dnorm(0,.0001) }

sd ~ dunif(0,5)     # vague prior for between-trial SD
tau <- pow(sd,-2)   # between-trial precision = (1/between-trial variance)


#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}

}

                        # *** PROGRAM ENDS

# Initial Values
#chain 1
```

```
list(d=c(NA,-5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -
5.00000E-01))
#chain 2
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00))
#chain 3
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01))


#Data

#For the treatment code
#"Treatment"          "Code"
#"Tolterodine 4 mg"          1
#"Mirabegron 50 mg"          2
#"Fesoterodine 4 mg"         3
#"Fesoterodine 8 mg"         4
#"Oxybutynin 10 mg"          5
#"Placebo"                   6
#"Solifenacin 10 mg"         7
#"Solifenacin 5 mg"          8



list(ns=15, nt=8.00000E+00, t= structure(.Data= c(2.00000E+00, 6.00000E+00, 9.00000E+00,    NA,    NA,    NA,
2.00000E+00, 6.00000E+00, 9.00000E+00,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00, 9.00000E+00,    NA,
NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,
NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 3.00000E+00, 4.00000E+00, 6.00000E+00,
NA,    NA,    NA, 5.00000E+00, 9.00000E+00,    NA,    NA,    NA,    NA, 5.00000E+00, 9.00000E+00,    NA,
NA,    NA,    NA, 6.00000E+00, 7.00000E+00, 8.00000E+00, 9.00000E+00,    NA,    NA, 6.00000E+00,
7.00000E+00, 8.00000E+00,    NA,    NA,    NA, 6.00000E+00, 7.00000E+00, 8.00000E+00,    NA,    NA,    NA,
6.00000E+00, 7.00000E+00,    NA,    NA,    NA,    NA, 6.00000E+00, 9.00000E+00, 9.00000E+00,    NA,    NA,
NA, 6.00000E+00, 9.00000E+00,    NA,    NA,    NA,    NA), .Dim=c(15, 6)), y= structure(.Data= c(-1.57000E+00, -
1.17000E+00, -1.27000E+00,    NA,    NA,    NA, -1.24000E+00, -6.40000E-01, -1.15000E+00,    NA,    NA,    NA,
-1.12000E+00, -6.60000E-01, -9.70000E-01,    NA,    NA,    NA, -1.47000E+00, -1.13000E+00,    NA,    NA,    NA,
NA, -1.38000E+00, -9.60000E-01,    NA,    NA,    NA,    NA, -1.20000E+00, -6.40000E-01,    NA,    NA,    NA,
NA, -1.27000E+00, -1.15000E+00, -8.80000E-01,    NA,    NA,    NA, -1.40000E+00, -2.20000E+00,    NA,    NA,
NA,    NA, -3.04300E+00, -2.67100E+00,    NA,    NA,    NA,    NA, -7.60000E-01, -1.45000E+00, -1.42000E+00, -
1.14000E+00,    NA,    NA, -7.20000E-01, -1.59000E+00, -1.60000E+00,    NA,    NA,    NA, -1.25000E+00, -
1.57000E+00, -1.63000E+00,    NA,    NA,    NA, -1.10000E+00, -2.00000E+00,    NA,    NA,    NA,    NA, -
9.86000E-01, -1.68600E+00, -1.51400E+00,    NA,    NA,    NA, -2.10000E+00, -3.20000E+00,    NA,    NA,    NA,
NA), .Dim=c(15, 6)), se= structure(.Data= c(1.13000E-01, 1.13000E-01, 1.12000E-01,    NA,    NA,    NA,
1.92000E-01, 2.47000E-01, 3.72000E-01,    NA,    NA,    NA, 7.67854E-02, 9.70113E-02, 8.40313E-02,    NA,
NA,    NA, 1.14000E-01, 1.12000E-01,    NA,    NA,    NA,    NA, 1.23000E-01, 1.22000E-01,    NA,    NA,    NA,
NA, 1.21000E-01, 1.15000E-01,    NA,    NA,    NA,    NA, 1.73469E-01, 1.78571E-01, 1.73469E-01,    NA,    NA,
NA, 2.78000E-01, 3.39000E-01,    NA,    NA,    NA,    NA, 2.31000E-01, 2.38000E-01,    NA,    NA,    NA,    NA,
1.83000E-01, 1.78000E-01, 1.53000E-01, 1.72000E-01,    NA,    NA, 1.16000E-01, 1.29000E-01, 1.09000E-01,
NA,    NA,    NA, 1.92412E-01, 1.81390E-01, 1.61181E-01,    NA,    NA,    NA, 2.00000E-01, 2.00000E-01,    NA,
NA,    NA,    NA, 7.60000E-02, 1.13000E-01, 1.06000E-01,    NA,    NA,    NA, 2.77000E-01, 2.52000E-01,    NA,
NA,    NA,    NA), .Dim=c(15, 6)), na=c(3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 3.00000E+00, 2.00000E+00))
```

UUI: Fixed effect model

```
# Normal likelihood, identity link
# Fixed effects model
model{                          # *** PROGRAM STARTS
for(i in 1:ns){                 #   LOOP THROUGH STUDIES
   mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
   for (k in 1:na[i]) {           #  LOOP THROUGH ARMS
      var[i,k] <- pow(se[i,k],2)   # calculate variances
      prec[i,k] <- 1/var[i,k]      # set precisions
      y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
# model for linear predictor
      theta[i,k] <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
      dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
    }
#  summed residual deviance contribution for this trial
   resdev[i] <- sum(dev[i,1:na[i]])
```

```
  }
totresdev <- sum(resdev[])           #Total Residual Deviance
d[1]<-0       # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){  d[k] ~ dnorm(0,.0001) }

#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])
  }

}                              # *** PROGRAM ENDS

# Initial Values
#chain 1
list(d=c(NA,-5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -
5.00000E-01))
#chain 2
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00))
#chain 3
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01))


#Data


#For the treatment code

#"Treatment"          "Code"
#"Tolterodine 4 mg"          1
##"Mirabegron 50 mg"         2
##"Fesoterodine 4 mg"        3
#"Fesoterodine 8 mg"         4
##"Oxybutynin 10 mg"         5
#"Placebo"                   6
#"Solifenacin 10 mg"         7
#"Solifenacin 5 mg"          8
#Trospium 60 mg"             9


list(ns=17, nt=9.00000E+00, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,
1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 2.00000E+00, 6.00000E+00,    NA,
NA,    NA, 1.00000E+00, 3.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA, 1.00000E+00, 4.00000E+00,
6.00000E+00,    NA,    NA,    NA, 1.00000E+00, 5.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00,
6.00000E+00, 7.00000E+00, 8.00000E+00,    NA,    NA, 1.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA,
1.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00, 7.00000E+00, 8.00000E+00,    NA,    NA,
NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,
NA, 2.00000E+00, 6.00000E+00,    NA,    NA,    NA,    NA, 3.00000E+00, 4.00000E+00, 6.00000E+00,    NA,
NA,    NA, 3.00000E+00, 4.00000E+00, 6.00000E+00,    NA,    NA,    NA, 6.00000E+00, 7.00000E+00,
8.00000E+00,    NA,    NA,    NA, 6.00000E+00, 9.00000E+00,    NA,    NA,    NA,    NA), .Dim=c(17, 6)), y=
structure(.Data= c(-1.18000E+00, -1.46000E+00, -1.11000E+00,    NA,    NA,    NA, -1.10000E+00, -1.19000E+00,
-5.00000E-01,    NA,    NA,    NA, -9.50000E-01, -1.01000E+00, -6.00000E-01,    NA,    NA,    NA, -1.74000E+00,
-1.95000E+00, -2.22000E+00, -1.14000E+00,    NA,    NA, -1.74000E+00, -1.95000E+00, -1.62000E+00,    NA,
NA,    NA, -2.40000E+00, -2.77143E+00,    NA,    NA,    NA,    NA, -9.10000E-01, -6.20000E-01, -1.36000E+00, -
1.41000E+00,    NA,    NA, -1.90000E+00, -1.50000E+00,    NA,    NA,    NA,    NA, -1.75714E+00, -
1.14286E+00,    NA,    NA,    NA,    NA, -1.02000E+00, -1.84000E+00, -1.14000E+00,    NA,    NA,    NA, -
1.32000E+00, -8.90000E-01,    NA,    NA,    NA,    NA, -1.31000E+00, -9.50000E-01,    NA,    NA,    NA,    NA, -
1.09000E+00, -6.80000E-01,    NA,    NA,    NA,    NA, -1.65000E+00, -2.28000E+00, -9.60000E-01,    NA,    NA,
NA, -1.35000E+00, -1.40000E+00, -1.01000E+00,    NA,    NA,    NA, -6.90000E-01, -1.52000E+00, -1.45000E+00,
NA,    NA,    NA, -1.93000E+00, -2.48000E+00,    NA,    NA,    NA,    NA), .Dim=c(17, 6)), se= structure(.Data=
c(1.09000E-01, 1.09000E-01, 1.10000E-01,    NA,    NA,    NA, 3.32820E-01, 1.88429E-01, 2.19511E-01,    NA,
NA,    NA, 1.04380E-01, 8.39536E-02, 1.08639E-01,    NA,    NA,    NA, 1.60000E-01, 1.70000E-01, 1.60000E-01,
1.60000E-01,    NA,    NA, 6.00000E-02, 5.00000E-02, 7.00000E-02,    NA,    NA,    NA, 1.96798E-01, 1.88457E-
01,    NA,    NA,    NA,    NA, 1.84256E-01, 1.73922E-01, 1.89007E-01, 1.63685E-01,    NA,    NA, 1.00000E-01,
1.00000E-01,    NA,    NA,    NA,    NA, 8.68388E-02, 1.23547E-01,    NA,    NA,    NA,    NA, 1.79333E-01,
2.99695E-01, 2.55338E-01,    NA,    NA,    NA, 1.04000E-01, 1.00000E-01,    NA,    NA,    NA,    NA, 1.12000E-
01, 1.10000E-01,    NA,    NA,    NA,    NA, 1.14911E-01, 1.18199E-01,    NA,    NA,    NA,    NA, 1.60000E-01,
1.60000E-01, 1.70000E-01,    NA,    NA,    NA, 1.53061E-01, 1.53061E-01, 1.53061E-01,    NA,    NA,    NA,
1.24035E-01, 1.10842E-01, 1.23290E-01,    NA,    NA,    NA, 1.60000E-01, 1.70000E-01,    NA,    NA,    NA,
NA), .Dim=c(17, 6)), na=c(3.00000E+00, 3.00000E+00, 3.00000E+00, 4.00000E+00, 3.00000E+00, 2.00000E+00,
4.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00))
```

UUI: Random effect model

```
# Normal likelihood, identity link
# Random effects model for multi-arm trials
model{                          # *** PROGRAM STARTS
for(i in 1:ns){                 #   LOOP THROUGH STUDIES
    w[i,1] <- 0    # adjustment for multi-arm trials is zero for control arm
    delta[i,1] <- 0            # treatment effect is zero for control arm
    mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
    for (k in 1:na[i]) {            #  LOOP THROUGH ARMS
        var[i,k] <- pow(se[i,k],2)   # calculate variances
        prec[i,k] <- 1/var[i,k]      # set precisions
        y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
        theta[i,k] <- mu[i] + delta[i,k]  # model for linear predictor
#Deviance contribution
        dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
      }
#  summed residual deviance contribution for this trial
    resdev[i] <- sum(dev[i,1:na[i]])
    for (k in 2:na[i]) {            # LOOP THROUGH ARMS
# trial-specific LOR distributions
        delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions, with multi-arm trial correction
        md[i,k] <-  d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
        taud[i,k] <- tau *2*(k-1)/k
# adjustment, multi-arm RCTs
        w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
        sw[i,k] <- sum(w[i,1:k-1])/(k-1)
      }
  }
totresdev <- sum(resdev[])            #Total Residual Deviance
d[1]<-0       # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){  d[k] ~ dnorm(0,.0001) }

sd ~ dunif(0,5)     # vague prior for between-trial SD
tau <- pow(sd,-2)   # between-trial precision = (1/between-trial variance)


#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
       TvMira[c] <- (d[c] - d[2])

}

}

                                # *** PROGRAM ENDS
# Initial Values
#chain 1
list(d=c(NA,-5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -5.00000E-01, -
5.00000E-01))
#chain 2
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00))
#chain 3
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01))


#Data

#For the treatment code

#"Treatment"          "Code"
#"Tolterodine 4 mg"              1
##"Mirabegron 50 mg"             2
##"Fesoterodine 4 mg"            3
#"Fesoterodine 8 mg"             4
##"Oxybutynin 10 mg"             5
#"Placebo"                       6
```

```
#"Solifenacin 10 mg"        7
#"Solifenacin 5 mg"         8
#Trospium 60 mg"            9

list(ns=17, nt=9.00000E+00, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 6.00000E+00,     NA,     NA,     NA,
1.00000E+00, 2.00000E+00, 6.00000E+00,     NA,     NA,     NA, 1.00000E+00, 2.00000E+00, 6.00000E+00,     NA,
NA,     NA, 1.00000E+00, 3.00000E+00, 4.00000E+00, 6.00000E+00,     NA,     NA, 1.00000E+00, 4.00000E+00,
6.00000E+00,     NA,     NA,     NA, 1.00000E+00, 5.00000E+00,     NA,     NA,     NA,     NA, 1.00000E+00,
6.00000E+00, 7.00000E+00, 8.00000E+00,     NA,     NA, 1.00000E+00, 6.00000E+00,     NA,     NA,     NA,     NA,
1.00000E+00, 6.00000E+00,     NA,     NA,     NA,     NA, 1.00000E+00, 7.00000E+00, 8.00000E+00,     NA,     NA,
NA, 2.00000E+00, 6.00000E+00,     NA,     NA,     NA,     NA, 2.00000E+00, 6.00000E+00,     NA,     NA,     NA,
NA, 2.00000E+00, 6.00000E+00,     NA,     NA,     NA,     NA, 3.00000E+00, 4.00000E+00, 6.00000E+00,     NA,
NA,     NA, 3.00000E+00, 4.00000E+00, 6.00000E+00,     NA,     NA,     NA, 6.00000E+00, 7.00000E+00,
8.00000E+00,     NA,     NA,     NA, 6.00000E+00, 9.00000E+00,     NA,     NA,     NA,     NA), .Dim=c(17, 6)), y=
structure(.Data= c(-1.18000E+00, -1.46000E+00, -1.11000E+00,     NA,     NA,     NA, -1.10000E+00, -1.19000E+00,
-5.00000E-01,     NA,     NA,     NA, -9.50000E-01, -1.01000E+00, -6.00000E-01,     NA,     NA,     NA, -1.74000E+00,
-1.95000E+00, -2.22000E+00, -1.14000E+00,     NA,     NA, -1.74000E+00, -1.95000E+00, -1.62000E+00,     NA,
NA,     NA, -2.40000E+00, -2.77143E+00,     NA,     NA,     NA,     NA, -9.10000E-01, -6.20000E-01, -1.36000E+00, -
1.41000E+00,     NA,     NA, -1.90000E+00, -1.50000E+00,     NA,     NA,     NA,     NA, -1.75714E+00, -
1.14286E+00,     NA,     NA,     NA,     NA, -1.02000E+00, -1.84000E+00, -1.14000E+00,     NA,     NA,     NA, -
1.32000E+00, -8.90000E-01,     NA,     NA,     NA,     NA, -1.31000E+00, -9.50000E-01,     NA,     NA,     NA,     NA, -
1.09000E+00, -6.80000E-01,     NA,     NA,     NA,     NA, -1.65000E+00, -2.28000E+00, -9.60000E-01,     NA,     NA,
NA, -1.35000E+00, -1.40000E+00, -1.01000E+00,     NA,     NA,     NA, -6.90000E-01, -1.52000E+00, -1.45000E+00,
NA,     NA,     NA, -1.93000E+00, -2.48000E+00,     NA,     NA,     NA,     NA), .Dim=c(17, 6)), se= structure(.Data=
c(1.09000E-01, 1.09000E-01, 1.10000E-01,     NA,     NA,     NA, 3.32820E-01, 1.88429E-01, 2.19511E-01,     NA,
NA,     NA, 1.04380E-01, 8.39536E-02, 1.08639E-01,     NA,     NA,     NA, 1.60000E-01, 1.70000E-01, 1.60000E-01,
1.60000E-01,     NA,     NA, 6.00000E-02, 5.00000E-02, 7.00000E-02,     NA,     NA,     NA, 1.96798E-01, 1.88457E-
01,     NA,     NA,     NA,     NA, 1.84256E-01, 1.73922E-01, 1.89007E-01, 1.63685E-01,     NA,     NA, 1.00000E-01,
1.00000E-01,     NA,     NA,     NA,     NA, 8.68388E-02, 1.23547E-01,     NA,     NA,     NA,     NA, 1.79333E-01,
2.99695E-01, 2.55338E-01,     NA,     NA,     NA, 1.04000E-01, 1.00000E-01,     NA,     NA,     NA,     NA, 1.12000E-
01, 1.10000E-01,     NA,     NA,     NA,     NA, 1.14911E-01, 1.18199E-01,     NA,     NA,     NA,     NA, 1.60000E-01,
1.60000E-01, 1.70000E-01,     NA,     NA,     NA, 1.53061E-01, 1.53061E-01, 1.53061E-01,     NA,     NA,     NA,
1.24035E-01, 1.10842E-01, 1.23290E-01,     NA,     NA,     NA, 1.60000E-01, 1.70000E-01,     NA,     NA,     NA,
NA), .Dim=c(17, 6)), na=c(3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 4.00000E+00, 3.00000E+00, 2.00000E+00,
4.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00))
```

Dry mouth: Fixed effect model

```
# Binomial likelihood, logit link, MTC
# Fixed effect model
model{                                                  # *** PROGRAM STARTS
for(i in 1:ns){                                          # LOOP THROUGH STUDIES
  mu[i] ~ dnorm(0,.001)                                  # vague priors for all trial baselines
  for (k in 1:na[i]) {                                   # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k])                         # binomial likelihood
    logit(p[i,k]) <- mu[i] + d[t[i,k]]-d[t[i,1]]         # model for linear predictor

   rhat[i,k] <- p[i,k] * n[i,k]                          # expected value of the numerators
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))        #Deviance contribution
       + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
  resdev[i] <- sum(dev[i,1:na[i]])              # summed residual deviance contribution for this trial
}
totresdev <- sum(resdev[])                       #Total Residual Deviance
d[1]<- 0                                        # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.001) }        # vague priors for treatment effects
for (k in 2:nt)  { OR[k] <- exp(d[k])}

#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}
for (k in 1:nt)  { TvMiraOR[k] <- exp(TvMira[k])}

}                                                        # *** PROGRAM ENDS
```

```
# Initial Valu

#chain 1


list(d=c(NA,-1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00), mu=c(-5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00))

#chain 2

list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00), mu=c(0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00))

#chain 3


list(d=c(NA,1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00), mu=c(5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00))


#Data


#	Treatment	Code
#	Tolterodine ER 4 mg	1
#	Mirabegron 50 mg	2
#	Fesoterodine 4mg	3
#	Fesoterodine 8mg	4
#	Oxybutynin ER 10 mg	5
#	Oxybutynin ER 15 mg	6
#	Oxybutynin ER 5 mg	7
#	Oxybutynin IR 10 mg	8
#	Oxybutynin IR 15 mg	9
#	Oxybutynin IR 9 mg	10
#	Placebo	11
#	Solifenacin 10 mg	12
#	Solifenacin 5 mg	13
#	Tolterodine IR 4 mg	14
#	Trospium 40 mg	15
#	Trospium 60 mg	16


list(ns=41, nt=1.60000E+01, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 1.10000E+01,	NA,	NA,	NA,
1.00000E+00, 2.00000E+00, 1.10000E+01,	NA,	NA,	NA, 1.00000E+00, 2.00000E+00, 1.10000E+01,	NA,
NA,	NA, 1.00000E+00, 3.00000E+00, 4.00000E+00, 1.10000E+01,	NA,	NA, 1.00000E+00, 4.00000E+00,
1.10000E+01,	NA,	NA,	NA, 1.00000E+00, 4.00000E+00, 1.10000E+01,	NA,	NA,	NA, 1.00000E+00,
5.00000E+00,	NA,	NA,	NA,	NA, 1.00000E+00, 1.00000E+01, 1.10000E+01,	NA,	NA,	NA,
1.00000E+00, 1.10000E+01, 1.40000E+01,	NA,	NA,	NA, 1.00000E+00, 1.10000E+01,	NA,	NA,	NA,
NA, 1.00000E+00, 1.10000E+01,	NA,	NA,	NA,	NA, 1.00000E+00, 1.10000E+01,	NA,	NA,	NA,
NA, 1.00000E+00, 1.10000E+01,	NA,	NA,	NA,	NA, 1.00000E+00, 1.10000E+01,	NA,	NA,	NA,
NA, 1.00000E+00, 1.10000E+01,	NA,	NA,	NA,	NA, 2.00000E+00, 1.10000E+01,	NA,	NA,	NA,
NA, 2.00000E+00, 1.10000E+01,	NA,	NA,	NA,	NA, 2.00000E+00, 1.10000E+01,	NA,	NA,	NA,
NA, 3.00000E+00, 4.00000E+00, 1.10000E+01,	NA,	NA,	NA, 3.00000E+00, 4.00000E+00, 1.10000E+01,
NA,	NA,	NA, 3.00000E+00, 4.00000E+00, 1.10000E+01,	NA,	NA,	NA, 3.00000E+00, 4.00000E+00,
1.10000E+01,	NA,	NA,	NA, 5.00000E+00, 6.00000E+00, 7.00000E+00,	NA,	NA,	NA, 5.00000E+00,
8.00000E+00,	NA,	NA,	NA,	NA, 5.00000E+00, 1.40000E+01,	NA,	NA,	NA,	NA, 7.00000E+00,
```

1.10000E+01, NA, NA, NA, NA, 8.00000E+00, 1.40000E+01, NA, NA, NA, NA, 9.00000E+00,
1.10000E+01, NA, NA, NA, NA, 9.00000E+00, 1.30000E+01, NA, NA, NA, NA, 1.10000E+01,
1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, 1.40000E+01,
NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, NA, NA, NA, 1.10000E+01, 1.20000E+01,
1.30000E+01, NA, NA, NA, 1.10000E+01, 1.20000E+01, NA, NA, NA, NA, 1.10000E+01,
1.40000E+01, NA, NA, NA, NA, 1.10000E+01, 1.40000E+01, NA, NA, NA, NA, 1.10000E+01,
1.50000E+01, NA, NA, NA, NA, 1.10000E+01, 1.50000E+01, NA, NA, NA, NA, 1.10000E+01,
1.60000E+01, NA, NA, NA, NA, 1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, NA,
1.30000E+01, 1.40000E+01, NA, NA, NA, NA), .Dim=c(41, 6)), n= structure(.Data= c(4.95000E+02,
4.93000E+02, 4.94000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 8.50000E+01, 1.69000E+02,
1.69000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.75000E+02, 3.79000E+02, 3.79000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.90000E+02, 2.72000E+02, 2.87000E+02, 2.83000E+02,
1.00000E+00, 1.00000E+00, 6.84000E+02, 6.79000E+02, 3.34000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 9.73000E+02, 9.60000E+02, 4.78000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
3.99000E+02, 3.91000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.39000E+02,
2.44000E+02, 1.22000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 5.05000E+02, 5.07000E+02,
5.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.23000E+02, 1.17000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01, 6.60000E+01, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.02000E+02, 2.11000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 4.08000E+02, 2.04000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.29000E+02, 4.21000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 5.69000E+02,
2.85000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.42000E+02, 4.53000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.40000E+02, 4.33000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.08000E+02, 2.12000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.80000E+01, 1.90000E+01, 1.90000E+01, 1.00000E+00, 1.00000E+00,
1.00000E+00, 2.50000E+01, 2.80000E+01, 2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
3.20000E+02, 3.13000E+02, 3.18000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.82000E+02,
2.79000E+02, 2.71000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 7.70000E+01, 8.30000E+01,
7.70000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.20000E+01, 6.60000E+01, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.85000E+02, 1.93000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.60000E+01, 2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.15000E+02, 1.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.10000E+01, 2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01,
6.80000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.67000E+02, 2.68000E+02,
2.79000E+02, 2.63000E+02, 1.00000E+00, 1.00000E+00, 3.80000E+01, 3.50000E+01, 3.70000E+01,
3.70000E+01, 1.00000E+00, 1.00000E+00, 4.05000E+02, 3.81000E+02, 3.96000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.81000E+02, 2.90000E+02, 2.86000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 3.32000E+02, 3.40000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
5.10000E+01, 1.03000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.30000E+01,
7.30000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.29000E+02, 3.29000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.61000E+02, 2.62000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.03000E+02, 2.98000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.18000E+02, 1.18000E+02, 1.18000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 3.90000E+01, 3.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00), .Dim=c(41,
6)), r= structure(.Data= c(5.00000E+01, 1.40000E+01, 1.30000E+01, NA, NA, NA, 3.00000E+00,
3.00000E+00, 3.00000E+00, NA, NA, NA, 5.30000E+01, 1.00000E+01, 1.10000E+01, NA, NA, NA,
4.90000E+01, 5.90000E+01, 9.70000E+01, 2.00000E+01, NA, NA, 1.12176E+02, 1.88762E+02, 2.00400E+01,
NA, NA, NA, 1.30000E+02, 2.65000E+02, 2.60000E+01, NA, NA, NA, 8.90000E+01, 1.16000E+02,
NA, NA, NA, NA, 8.00000E+01, 1.31000E+02, 1.20000E+01, NA, NA, NA, 1.18000E+02,
3.90000E+01, 1.56000E+02, NA, NA, NA, 8.97900E+00, 1.98900E+00, NA, NA, NA, NA,
3.00000E+00, 1.00000E+00, NA, NA, NA, NA, 2.60000E+01, 1.90000E+01, NA, NA, NA, NA,
8.90000E+01, 2.10000E+01, NA, NA, NA, NA, 8.58000E+00, 8.42000E+00, NA, NA, NA, NA,
1.12000E+02, 2.30000E+01, NA, NA, NA, NA, 2.00000E+00, 7.00000E+00, NA, NA, NA, NA,
7.00000E+00, 9.00000E+00, NA, NA, NA, NA, 3.00000E+00, 1.00000E+00, NA, NA, NA, NA,
8.00000E+00, 8.00000E+00, 4.00000E+00, NA, NA, NA, 1.10000E+01, 1.70000E+01, 3.00000E+00, NA,
NA, NA, 8.90000E+01, 1.55000E+02, 2.90000E+01, NA, NA, NA, 4.50000E+01, 9.90000E+01,
1.90000E+01, NA, NA, NA, 5.20000E+01, 5.80000E+01, 4.30000E+01, NA, NA, NA, 1.40000E+01,
1.10000E+01, NA, NA, NA, NA, 5.20000E+01, 6.40000E+01, NA, NA, NA, NA, 1.00000E+00,
1.00000E+00, NA, NA, NA, NA, 7.20000E+01, 3.90000E+01, NA, NA, NA, NA, 3.40000E+01,
4.00000E+00, NA, NA, NA, NA, 5.31200E+01, 2.38000E+01, NA, NA, NA, NA, 1.30000E+01,
5.70000E+01, 3.90000E+01, 4.90000E+01, NA, NA, 5.00000E-01, 5.50000E+00, 5.50000E+00, 9.50000E+00,
NA, NA, 2.30000E+01, 1.30000E+02, 6.70000E+01, NA, NA, NA, 7.00000E+00, 7.10000E+01,
2.30000E+01, NA, NA, NA, 1.30000E+01, 9.10000E+01, NA, NA, NA, NA, 3.00000E+00,
3.50000E+01, NA, NA, NA, NA, 3.87000E+00, 3.50400E+01, NA, NA, NA, NA, 1.70000E+01,
6.50000E+01, NA, NA, NA, NA, 1.70000E+01, 5.70000E+01, NA, NA, NA, NA, 9.00000E+00,
2.60000E+01, NA, NA, NA, NA, 2.30000E+01, 9.00000E+00, 2.20000E+01, NA, NA, NA,
7.00000E+00, 3.00000E+00, NA, NA, NA, NA), .Dim=c(41, 6)), na=c(3.00000E+00, 3.00000E+00,
3.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00,
4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 3.00000E+00, 2.00000E+00))

Dry mouth: Random effect model

```
# Binomial likelihood, logit link
# Random effect model, multi-arm trials
model{                                              # *** PROGRAM STARTS
for(i in 1:ns){                                     # LOOP THROUGH STUDIES
  w[i,1] <- 0                                      # adjustment for multi-arm trials is zero for control arm
  delta[i,1] <- 0                                   # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.01)                             # priors for all trial baselines
  for (k in 1:na[i]) {                              # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k])                    # binomial likelihood
    logit(p[i,k]) <- mu[i] + delta[i,k]                # model for linear predictor
     rhat[i,k] <- p[i,k] * n[i,k]                     # expected value of the numerators
     dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))           #Deviance contribution
        + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
 resdev[i] <- sum(dev[i,1:na[i]])                 # summed residual deviance contribution for this trial
  for (k in 2:na[i]) {                            # LOOP THROUGH ARMS
     delta[i,k] ~ dnorm(md[i,k],taud[i,k])              # trial-specific LOR distributions
     md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]         # mean of LOR distributions (with multi-arm correction)
     taud[i,k] <- tau *2*(k-1)/k                       # precision of LOR distributions (with multi-arm correction)
     w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])      # adjustment for multi-arm RCTs
     sw[i,k] <- sum(w[i,1:k-1])/(k-1)                 # cumulative adjustment for multi-arm trials
   }
}
totresdev <- sum(resdev[])                           #Total Residual Deviance
d[1]<- 0                                            # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.01)}                # priors for treatment effects
for (k in 2:nt)  { OR[k] <- exp(d[k])}
sd ~ dunif(0,2)
tau <- pow(sd,-2)


#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}
for (k in 1:nt)  { TvMiraOR[k] <- exp(TvMira[k])}

}                                                   # *** PROGRAM ENDS
```

```
# Initial Valu

#chain 1

list(d=c(NA,-1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00), mu=c(-5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00))

#chain 2

list(d=c(NA,1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01,
1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01),
mu=c(5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-
01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01), sd=1.00000E+00)

#chain 3

list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01),
mu=c(4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
```

4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00), sd=5.00000E-01)

#Data

Treatment Code
Tolterodine ER 4 mg 1
Mirabegron 50 mg 2
Fesoterodine 4mg 3
Fesoterodine 8mg 4
Oxybutynin ER 10 mg 5
Oxybutynin ER 15 mg 6
Oxybutynin ER 5 mg 7
Oxybutynin IR 10 mg 8
Oxybutynin IR 15 mg 9
Oxybutynin IR 9 mg 10
Placebo 11
Solifenacin 10 mg 12
Solifenacin 5 mg 13
Tolterodine IR 4 mg 14
Trospium 40 mg 15
Trospium 60 mg 16

list(ns=41, nt=1.60000E+01, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 1.10000E+01, NA, NA, NA,
1.00000E+00, 2.00000E+00, 1.10000E+01, NA, NA, NA, 1.00000E+00, 2.00000E+00, 1.10000E+01, NA,
NA, NA, 1.00000E+00, 3.00000E+00, 4.00000E+00, 1.10000E+01, NA, NA, 1.00000E+00, 4.00000E+00,
1.10000E+01, NA, NA, NA, 1.00000E+00, 4.00000E+00, 1.10000E+01, NA, NA, NA, 1.00000E+00,
5.00000E+00, NA, NA, NA, NA, 1.00000E+00, 1.00000E+01, 1.10000E+01, NA, NA, NA,
1.00000E+00, 1.10000E+01, 1.40000E+01, NA, NA, NA, 1.00000E+00, 1.10000E+01, NA, NA, NA,
NA, 1.00000E+00, 1.10000E+01, NA, NA, NA, NA, 1.00000E+00, 1.10000E+01, NA, NA, NA,
NA, 1.00000E+00, 1.10000E+01, NA, NA, NA, NA, 1.00000E+00, 1.10000E+01, NA, NA, NA,
NA, 1.00000E+00, 1.10000E+01, NA, NA, NA, NA, 2.00000E+00, 1.10000E+01, NA, NA, NA,
NA, 2.00000E+00, 1.10000E+01, NA, NA, NA, NA, 2.00000E+00, 1.10000E+01, NA, NA, NA,
NA, 3.00000E+00, 4.00000E+00, 1.10000E+01, NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.10000E+01,
NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.10000E+01, NA, NA, NA, 3.00000E+00, 4.00000E+00,
1.10000E+01, NA, NA, NA, 5.00000E+00, 6.00000E+00, 7.00000E+00, NA, NA, NA, 5.00000E+00,
8.00000E+00, NA, NA, NA, NA, 5.00000E+00, 1.40000E+01, NA, NA, NA, NA, 7.00000E+00,
1.10000E+01, NA, NA, NA, NA, 8.00000E+00, 1.40000E+01, NA, NA, NA, NA, 9.00000E+00,
1.10000E+01, NA, NA, NA, NA, 9.00000E+00, 1.30000E+01, NA, NA, NA, NA, 1.10000E+01,
1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, 1.40000E+01,
NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, NA, NA, NA, 1.10000E+01, 1.20000E+01,
1.30000E+01, NA, NA, NA, 1.10000E+01, 1.20000E+01, NA, NA, NA, NA, 1.10000E+01,
1.40000E+01, NA, NA, NA, NA, 1.10000E+01, 1.40000E+01, NA, NA, NA, NA, 1.10000E+01,
1.50000E+01, NA, NA, NA, NA, 1.10000E+01, 1.50000E+01, NA, NA, NA, NA, 1.10000E+01,
1.60000E+01, NA, NA, NA, NA, 1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, NA,
1.30000E+01, 1.40000E+01, NA, NA, NA, NA), .Dim=c(41, 6)), n= structure(.Data= c(4.95000E+02,
4.93000E+02, 4.94000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 8.50000E+01, 1.69000E+02,
1.69000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.75000E+02, 3.79000E+02, 3.79000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.90000E+02, 2.72000E+02, 2.87000E+02, 2.83000E+02,
1.00000E+00, 1.00000E+00, 6.84000E+02, 6.79000E+02, 3.34000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 9.73000E+02, 9.60000E+02, 4.78000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
3.99000E+02, 3.91000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.39000E+02,
2.44000E+02, 1.22000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 5.05000E+02, 5.07000E+02,
5.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.23000E+02, 1.17000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01, 6.60000E+01, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.02000E+02, 2.11000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 4.08000E+02, 2.04000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.29000E+02, 4.21000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 5.69000E+02,
2.85000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.42000E+02, 4.53000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.40000E+02, 4.33000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.08000E+02, 2.12000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.80000E+01, 1.90000E+01, 1.90000E+01, 1.00000E+00, 1.00000E+00,
1.00000E+00, 2.50000E+01, 2.80000E+01, 2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
3.20000E+02, 3.13000E+02, 3.18000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.82000E+02,
2.79000E+02, 2.71000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 7.70000E+01, 8.30000E+01,
7.70000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.20000E+01, 6.60000E+01, 1.00000E+00,
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1.00000E+00, 1.00000E+00, 2.60000E+01, 2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,

```
1.00000E+00, 1.15000E+02, 1.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.10000E+01, 2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01,
6.80000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.67000E+02, 2.68000E+02,
2.79000E+02, 2.63000E+02, 1.00000E+00, 1.00000E+00, 3.80000E+01, 3.50000E+01, 3.70000E+01,
3.70000E+01, 1.00000E+00, 1.00000E+00, 4.05000E+02, 3.81000E+02, 3.96000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.81000E+02, 2.90000E+02, 2.86000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 3.32000E+02, 3.40000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
5.10000E+01, 1.03000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.30000E+01,
7.30000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.29000E+02, 3.29000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.61000E+02, 2.62000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.03000E+02, 2.98000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.18000E+02, 1.18000E+02, 1.18000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 3.90000E+01, 3.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00), .Dim=c(41,
6)), r= structure(.Data= c(5.00000E+01, 1.40000E+01, 1.30000E+01,    NA,    NA,    NA, 3.00000E+00,
3.00000E+00, 3.00000E+00,    NA,    NA,    NA, 5.30000E+01, 1.00000E+01, 1.10000E+01,    NA,    NA,    NA,
4.90000E+01, 5.90000E+01, 9.70000E+01, 2.00000E+01,    NA,    NA, 1.12176E+02, 1.88762E+02, 2.00400E+01,
NA,    NA,    NA, 1.30000E+02, 2.65000E+02, 2.60000E+01,    NA,    NA,    NA, 8.90000E+01, 1.16000E+02,
NA,    NA,    NA,    NA, 8.00000E+01, 1.31000E+02, 1.20000E+01,    NA,    NA,    NA, 1.18000E+02,
3.90000E+01, 1.56000E+02,    NA,    NA,    NA, 8.97900E+00, 1.98900E+00,    NA,    NA,    NA,    NA,
3.00000E+00, 1.00000E+00,    NA,    NA,    NA,    NA, 2.60000E+01, 1.90000E+01,    NA,    NA,    NA,    NA,
8.90000E+01, 2.10000E+01,    NA,    NA,    NA,    NA, 8.58000E+00, 8.42000E+00,    NA,    NA,    NA,    NA,
1.12000E+02, 2.30000E+01,    NA,    NA,    NA,    NA, 2.00000E+00, 7.00000E+00,    NA,    NA,    NA,    NA,
7.00000E+00, 9.00000E+00,    NA,    NA,    NA,    NA, 3.00000E+00, 1.00000E+00,    NA,    NA,    NA,    NA,
8.00000E+00, 8.00000E+00, 4.00000E+00,    NA,    NA,    NA, 1.10000E+01, 1.70000E+01, 3.00000E+00,    NA,
NA,    NA, 8.90000E+01, 1.55000E+02, 2.90000E+01,    NA,    NA,    NA, 4.50000E+01, 9.90000E+01,
1.90000E+01,    NA,    NA,    NA, 5.20000E+01, 5.80000E+01, 4.30000E+01,    NA,    NA,    NA, 1.40000E+01,
1.10000E+01,    NA,    NA,    NA,    NA, 5.20000E+01, 6.40000E+01,    NA,    NA,    NA,    NA, 1.00000E+00,
1.00000E+00,    NA,    NA,    NA,    NA, 7.20000E+01, 3.90000E+01,    NA,    NA,    NA,    NA, 3.40000E+01,
4.00000E+00,    NA,    NA,    NA,    NA, 5.31200E+01, 2.38000E+01,    NA,    NA,    NA,    NA, 1.30000E+01,
5.70000E+01, 3.90000E+01, 4.90000E+01,    NA,    NA, 5.00000E-01, 5.50000E+00, 5.50000E+00, 9.50000E+00,
NA,    NA, 2.30000E+01, 1.30000E+02, 6.70000E+01,    NA,    NA,    NA, 7.00000E+00, 7.10000E+01,
2.30000E+01,    NA,    NA,    NA, 1.30000E+01, 9.10000E+01,    NA,    NA,    NA,    NA, 3.00000E+00,
3.50000E+01,    NA,    NA,    NA,    NA, 3.87000E+00, 3.50400E+01,    NA,    NA,    NA,    NA, 1.70000E+01,
6.50000E+01,    NA,    NA,    NA,    NA, 1.70000E+01, 5.70000E+01,    NA,    NA,    NA,    NA, 9.00000E+00,
2.60000E+01,    NA,    NA,    NA,    NA, 2.30000E+01, 9.00000E+00, 2.20000E+01,    NA,    NA,    NA,
7.00000E+00, 3.00000E+00,    NA,    NA,    NA,    NA), .Dim=c(41, 6)), na=c(3.00000E+00, 3.00000E+00,
3.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00,
4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 3.00000E+00, 2.00000E+00))
```

Constipation: Fixed effect model

```
# Binomial likelihood, logit link, MTC
# Fixed effect model
model{                                                  # *** PROGRAM STARTS
for(i in 1:ns){                                          # LOOP THROUGH STUDIES
  mu[i] ~ dnorm(0,.001)                                  # vague priors for all trial baselines
  for (k in 1:na[i]) {                                   # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k])                         # binomial likelihood
    logit(p[i,k]) <- mu[i] + d[t[i,k]]-d[t[i,1]]          # model for linear predictor

   rhat[i,k] <- p[i,k] * n[i,k]                          # expected value of the numerators
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))        #Deviance contribution
       + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
  resdev[i] <- sum(dev[i,1:na[i]])              # summed residual deviance contribution for this trial
}
totresdev <- sum(resdev[])                       #Total Residual Deviance
d[1]<- 0                                        # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.001) }        # vague priors for treatment effects
for (k in 2:nt)  { OR[k] <- exp(d[k])}

#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}
for (k in 1:nt)  { TvMiraOR[k] <- exp(TvMira[k])}
```

```
}                                                  # *** PROGRAM ENDS

# Initial Values

#chain 1

list(d=c(NA,-1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00), mu=c(-5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00))

#chain 2

list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00),
mu=c(0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00))


#chain 3

list(d=c(NA,1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00),
mu=c(5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00))



#Data

#Treatment Code
#        Treatment           Code
#        Tolterodine ER 4 mg         1
#        Mirabegron 50 mg    2
#        Fesoterodine 4mg    3
#        Fesoterodine 8mg    4
#        Oxybutynin ER 10 mg         5
#        Oxybutynin ER 15 mg         6
#        Oxybutynin ER 5 mg          7
#        Oxybutynin IR 15 mg         8
#        Oxybutynin IR 9 mg 9
#        Placebo    10
#        Solifenacin 10 mg    11
#        Solifenacin 5 mg     12
#        Tolterodine IR 4 mg 13
#        Trospium 40 mg       14
#        Trospium 60 mg       15



list(ns=38, nt=1.50000E+01, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 1.00000E+01,     NA,     NA,     NA,
1.00000E+00, 2.00000E+00, 1.00000E+01,     NA,     NA,     NA, 1.00000E+00, 2.00000E+00, 1.00000E+01,     NA,
NA,     NA, 1.00000E+00, 3.00000E+00, 4.00000E+00, 1.00000E+01,     NA,     NA, 1.00000E+00, 4.00000E+00,
1.00000E+01,     NA,     NA,     NA, 1.00000E+00, 5.00000E+00,     NA,     NA,     NA,     NA, 1.00000E+00,
9.00000E+00, 1.00000E+01,     NA,     NA,     NA, 1.00000E+00, 1.00000E+01, 1.30000E+01,     NA,     NA,     NA,
1.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA, 1.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA,
1.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA, 1.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA,
1.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA, 1.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA,
2.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA, 2.00000E+00, 1.00000E+01,     NA,     NA,     NA,     NA,
```

2.00000E+00, 1.00000E+01, NA, NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.00000E+01, NA, NA,
NA, 3.00000E+00, 4.00000E+00, 1.00000E+01, NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.00000E+01,
NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.00000E+01, NA, NA, NA, 5.00000E+00, 6.00000E+00,
7.00000E+00, NA, NA, NA, 5.00000E+00, 1.30000E+01, NA, NA, NA, NA, 7.00000E+00,
1.00000E+01, NA, NA, NA, NA, 8.00000E+00, 1.00000E+01, NA, NA, NA, NA, 8.00000E+00,
1.20000E+01, NA, NA, NA, NA, 1.00000E+01, 1.10000E+01, 1.20000E+01, 1.30000E+01, NA, NA,
1.00000E+01, 1.10000E+01, 1.20000E+01, 1.30000E+01, NA, NA, 1.00000E+01, 1.10000E+01, 1.20000E+01,
NA, NA, NA, 1.00000E+01, 1.10000E+01, 1.20000E+01, NA, NA, NA, 1.00000E+01, 1.10000E+01,
NA, NA, NA, NA, 1.00000E+01, 1.30000E+01, NA, NA, NA, NA, 1.00000E+01, 1.30000E+01,
NA, NA, NA, NA, 1.00000E+01, 1.40000E+01, NA, NA, NA, NA, 1.00000E+01, 1.40000E+01,
NA, NA, NA, NA, 1.00000E+01, 1.50000E+01, NA, NA, NA, NA, 1.10000E+01, 1.20000E+01,
1.30000E+01, NA, NA, NA, 1.20000E+01, 1.30000E+01, NA, NA, NA, NA), .Dim=c(38, 6)), n=
structure(.Data= c(4.95000E+02, 4.93000E+02, 4.94000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
8.50000E+01, 1.69000E+02, 1.69000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.75000E+02,
3.79000E+02, 3.79000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.90000E+02, 2.72000E+02,
2.87000E+02, 2.83000E+02, 1.00000E+00, 1.00000E+00, 9.73000E+02, 9.60000E+02, 4.78000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.99000E+02, 3.91000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.39000E+02, 2.44000E+02, 1.22000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 5.05000E+02, 5.07000E+02, 5.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.23000E+02, 1.17000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01,
6.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.02000E+02, 2.11000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.08000E+02, 2.04000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 4.29000E+02, 4.21000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 5.69000E+02, 2.85000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 4.42000E+02, 4.53000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.40000E+02, 4.33000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.08000E+02,
2.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.80000E+01, 1.90000E+01,
1.90000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.50000E+01, 2.80000E+01, 2.40000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.20000E+02, 3.13000E+02, 3.18000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.82000E+02, 2.79000E+02, 2.71000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 7.70000E+01, 8.30000E+01, 7.70000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.85000E+02, 1.93000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.60000E+01,
2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.10000E+01, 2.40000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01, 6.80000E+01, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.67000E+02, 2.68000E+02, 2.79000E+02, 2.63000E+02,
1.00000E+00, 1.00000E+00, 3.80000E+01, 3.50000E+01, 3.70000E+01, 3.70000E+01, 1.00000E+00,
1.00000E+00, 4.05000E+02, 3.81000E+02, 3.96000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
2.81000E+02, 2.90000E+02, 2.86000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.32000E+02,
3.40000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 5.10000E+01, 1.03000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.30000E+01, 7.30000E+01, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.29000E+02, 3.29000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.61000E+02, 2.62000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 3.03000E+02, 2.98000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.18000E+02, 1.18000E+02, 1.18000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.90000E+01,
3.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00), .Dim=c(38, 6)), r= structure(.Data=
c(1.00000E+01, 8.00000E+00, 7.00000E+00, NA, NA, NA, 1.00000E+00, 6.00000E+00, 2.00000E+00,
NA, NA, NA, 1.40000E+01, 1.30000E+01, 1.20000E+01, NA, NA, NA, 8.00000E+00, 9.00000E+00,
1.30000E+01, 4.00000E+00, NA, NA, 3.00000E+01, 4.20000E+01, 7.00000E+00, NA, NA, NA,
3.10000E+01, 2.50000E+01, NA, NA, NA, NA, 1.70000E+01, 1.50000E+01, 6.00000E+00, NA, NA,
NA, 3.00000E+01, 2.20000E+01, 3.50000E+01, NA, NA, NA, 7.01100E+00, 3.86100E+00, NA, NA,
NA, NA, 1.50000E+00, 5.00000E-01, NA, NA, NA, NA, 7.00000E+00, 8.00000E+00, NA, NA,
NA, NA, 1.10000E+01, 3.00000E+00, NA, NA, NA, NA, 1.28700E+01, 8.42000E+00, NA, NA,
NA, NA, 9.00000E+00, 2.00000E+00, NA, NA, NA, NA, 6.00000E+00, 8.00000E+00, NA, NA,
NA, NA, 8.00000E+00, 5.00000E+00, NA, NA, NA, NA, 9.00000E+00, 4.00000E+00, NA, NA,
NA, NA, 1.00000E+00, 2.00000E+00, 2.00000E+00, NA, NA, NA, 1.50000E+00, 5.50000E+00, 5.00000E-
01, NA, NA, NA, 1.60000E+01, 3.30000E+01, 1.40000E+01, NA, NA, NA, 1.40000E+01,
2.10000E+01, 7.00000E+00, NA, NA, NA, 3.00000E+00, 4.00000E+00, 4.00000E+00, NA, NA, NA,
1.30000E+01, 1.20000E+01, NA, NA, NA, 2.50000E+00, 5.00000E-01, NA, NA, NA, NA,
4.50000E+00, 5.00000E-01, NA, NA, NA, NA, 3.84000E+00, 8.84000E+00, NA, NA, NA, NA,
5.00000E+00, 2.10000E+01, 2.00000E+01, 7.00000E+00, NA, NA, 5.00000E-01, 2.50000E+00, 5.50000E+00,
1.50000E+00, NA, NA, 1.60000E+01, 7.20000E+01, 4.20000E+01, NA, NA, NA, 6.00000E+00,
2.80000E+01, 1.10000E+01, NA, NA, NA, 1.10000E+01, 5.80000E+01, NA, NA, NA, NA,
2.00000E+00, 2.00000E+00, NA, NA, NA, NA, 1.36000E+00, 5.00000E-01, NA, NA, NA, NA,
1.90000E+01, 3.60000E+01, NA, NA, NA, NA, 1.00000E+01, 2.50000E+01, NA, NA, NA, NA,
4.00000E+00, 2.80000E+01, NA, NA, NA, NA, 1.70000E+01, 8.00000E+00, 3.00000E+00, NA, NA,
NA, 5.00000E+00, 1.00000E+00, NA, NA, NA, NA), .Dim=c(38, 6)), na=c(3.00000E+00, 3.00000E+00,
3.00000E+00, 4.00000E+00, 3.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00,
2.00000E+00))

Constipation: Random effect model

```
# Binomial likelihood, logit link
# Random effect model, multi-arm trials
model{                                                   # *** PROGRAM STARTS
for(i in 1:ns){                                           # LOOP THROUGH STUDIES
  w[i,1] <- 0                                            # adjustment for multi-arm trials is zero for control arm
  delta[i,1] <- 0                                        # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.001)                                   # priors for all trial baselines
  for (k in 1:na[i]) {                                     # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k])                           # binomial likelihood
    logit(p[i,k]) <- mu[i] + delta[i,k]                        # model for linear predictor
     #rhat[i,k] <- p[i,k] * n[i,k]                              # expected value of the numerators
    # dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))            #Deviance contribution
      #   + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
 #resdev[i] <- sum(dev[i,1:na[i]])                   # summed residual deviance contribution for this trial
  for (k in 2:na[i]) {                                  # LOOP THROUGH ARMS
     delta[i,k] ~ dnorm(md[i,k],taud[i,k])                 # trial-specific LOR distributions
     md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]             # mean of LOR distributions (with multi-arm correction)
     taud[i,k] <- tau *2*(k-1)/k                           # precision of LOR distributions (with multi-arm correction)
     w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])          # adjustment for multi-arm RCTs
     sw[i,k] <- sum(w[i,1:k-1])/(k-1)                      # cumulative adjustment for multi-arm trials
   }
}
#totresdev <- sum(resdev[])                                 #Total Residual Deviance
d[1]<- 0                                                 # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.01)}                    # priors for treatment effects
for (k in 2:nt)  { OR[k] <- exp(d[k])}
sd ~ dunif(0,2)
tau <- pow(sd,-2)



#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
       TvMira[c] <- (d[c] - d[2])

}
for (k in 1:nt)  { TvMiraOR[k] <- exp(TvMira[k])}

}                                                        # *** PROGRAM ENDS
```

```
# Initial Values

#chain 1

list(d=c(NA,-1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00), mu=c(-5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00), sd=5.00000E-01)

#chain 2

list(d=c(NA,1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01,
1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01), mu=c(5.00000E-
01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01), sd=1.00000E+00)


#chain 3
```

```
list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01,
5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01),
mu=c(4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00, 4.00000E+00,
4.00000E+00, 4.00000E+00, 4.00000E+00), sd=5.00000E-01)
```

```
#Data

#Treatment Code
#       Treatment       Code
#       Tolterodine ER 4 mg     1
#       Mirabegron 50 mg        2
#       Fesoterodine 4mg        3
#       Fesoterodine 8mg        4
#       Oxybutynin ER 10 mg     5
#       Oxybutynin ER 15 mg     6
#       Oxybutynin ER 5 mg      7
#       Oxybutynin IR 15 mg     8
#       Oxybutynin IR 9 mg 9
#       Placebo 10
#       Solifenacin 10 mg   11
#       Solifenacin 5 mg    12
#       Tolterodine IR 4 mg 13
#       Trospium 40 mg      14
#       Trospium 60 mg      15
```

```
list(ns=38, nt=1.50000E+01, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 1.00000E+01,    NA,    NA,    NA,
1.00000E+00, 2.00000E+00, 1.00000E+01,    NA,    NA,    NA, 1.00000E+00, 2.00000E+00, 1.00000E+01,    NA,
NA,    NA, 1.00000E+00, 3.00000E+00, 4.00000E+00, 1.00000E+01,    NA,    NA, 1.00000E+00, 4.00000E+00,
1.00000E+01,    NA,    NA,    NA, 1.00000E+00, 5.00000E+00,    NA,    NA,    NA,    NA, 1.00000E+00,
9.00000E+00, 1.00000E+01,    NA,    NA,    NA, 1.00000E+00, 1.00000E+01, 1.30000E+01,    NA,    NA,    NA,
1.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA, 1.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA,
1.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA, 1.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA,
1.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA, 1.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA,
2.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA, 2.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA,
2.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA, 3.00000E+00, 4.00000E+00, 1.00000E+01,    NA,    NA,
NA, 3.00000E+00, 4.00000E+00, 1.00000E+01,    NA,    NA,    NA, 3.00000E+00, 4.00000E+00, 1.00000E+01,
NA,    NA,    NA, 3.00000E+00, 4.00000E+00, 1.00000E+01,    NA,    NA,    NA, 5.00000E+00, 6.00000E+00,
7.00000E+00,    NA,    NA,    NA, 5.00000E+00, 1.30000E+01,    NA,    NA,    NA,    NA, 7.00000E+00,
1.00000E+01,    NA,    NA,    NA,    NA, 8.00000E+00, 1.00000E+01,    NA,    NA,    NA,    NA, 8.00000E+00,
1.20000E+01,    NA,    NA,    NA,    NA, 1.00000E+01, 1.10000E+01, 1.20000E+01, 1.30000E+01,    NA,    NA,
1.00000E+01, 1.10000E+01, 1.20000E+01, 1.30000E+01,    NA,    NA, 1.00000E+01, 1.10000E+01, 1.20000E+01,
NA,    NA,    NA, 1.00000E+01, 1.10000E+01, 1.20000E+01,    NA,    NA,    NA, 1.00000E+01, 1.10000E+01,
NA,    NA,    NA,    NA, 1.00000E+01, 1.30000E+01,    NA,    NA,    NA,    NA, 1.00000E+01, 1.30000E+01,
NA,    NA,    NA,    NA, 1.00000E+01, 1.40000E+01,    NA,    NA,    NA,    NA, 1.00000E+01, 1.40000E+01,
NA,    NA,    NA,    NA, 1.00000E+01, 1.50000E+01,    NA,    NA,    NA,    NA, 1.10000E+01, 1.20000E+01,
1.30000E+01,    NA,    NA,    NA, 1.20000E+01, 1.30000E+01,    NA,    NA,    NA,    NA), .Dim=c(38, 6)), n=
structure(.Data= c(4.95000E+02, 4.93000E+02, 4.94000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
8.50000E+01, 1.69000E+02, 1.69000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.75000E+02,
3.79000E+02, 3.79000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.90000E+02, 2.72000E+02,
2.87000E+02, 2.83000E+02, 1.00000E+00, 1.00000E+00, 9.73000E+02, 9.60000E+02, 4.78000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.99000E+02, 3.91000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.39000E+02, 2.44000E+02, 1.22000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 5.05000E+02, 5.07000E+02, 5.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.23000E+02, 1.17000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01,
6.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.02000E+02, 2.11000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.08000E+02, 2.04000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 4.29000E+02, 4.21000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 5.69000E+02, 2.85000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 4.42000E+02, 4.53000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.40000E+02, 4.33000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.08000E+02,
2.12000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.80000E+01, 1.90000E+01,
1.90000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.50000E+01, 2.80000E+01, 2.40000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.20000E+02, 3.13000E+02, 3.18000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.82000E+02, 2.79000E+02, 2.71000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 7.70000E+01, 8.30000E+01, 7.70000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.85000E+02, 1.93000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.60000E+01,
2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.10000E+01, 2.40000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01, 6.80000E+01, 1.00000E+00,
```

1.00000E+00, 1.00000E+00, 1.00000E+00, 2.67000E+02, 2.68000E+02, 2.79000E+02, 2.63000E+02,
1.00000E+00, 1.00000E+00, 3.80000E+01, 3.50000E+01, 3.70000E+01, 3.70000E+01, 1.00000E+00,
1.00000E+00, 4.05000E+02, 3.81000E+02, 3.96000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
2.81000E+02, 2.90000E+02, 2.86000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.32000E+02,
3.40000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 5.10000E+01, 1.03000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.30000E+01, 7.30000E+01, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 3.29000E+02, 3.29000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 2.61000E+02, 2.62000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 3.03000E+02, 2.98000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.18000E+02, 1.18000E+02, 1.18000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.90000E+01,
3.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00), .Dim=c(38, 6)), r= structure(.Data=
c(1.00000E+01, 8.00000E+00, 7.00000E+00, NA, NA, NA, 1.00000E+00, 6.00000E+00, 2.00000E+00,
NA, NA, NA, 1.40000E+01, 1.30000E+01, 1.20000E+01, NA, NA, NA, 8.00000E+00, 9.00000E+00,
1.30000E+01, 4.00000E+00, NA, NA, 3.00000E+01, 4.20000E+01, 7.00000E+00, NA, NA, NA,
3.10000E+01, 2.50000E+01, NA, NA, NA, NA, 1.70000E+01, 1.50000E+01, 6.00000E+00, NA, NA,
NA, 3.00000E+01, 2.20000E+01, 3.50000E+01, NA, NA, NA, 7.01100E+00, 3.86100E+00, NA, NA,
NA, NA, 1.50000E+00, 5.00000E-01, NA, NA, NA, NA, 7.00000E+00, 8.00000E+00, NA, NA,
NA, NA, 1.10000E+01, 3.00000E+00, NA, NA, NA, NA, 1.28700E+01, 8.42000E+00, NA, NA,
NA, NA, 9.00000E+00, 2.00000E+00, NA, NA, NA, NA, 6.00000E+00, 8.00000E+00, NA, NA,
NA, NA, 8.00000E+00, 5.00000E+00, NA, NA, NA, NA, 9.00000E+00, 4.00000E+00, NA, NA,
NA, NA, 1.00000E+00, 2.00000E+00, 2.00000E+00, NA, NA, NA, 1.50000E+00, 5.50000E+00, 5.00000E-
01, NA, NA, NA, 1.60000E+01, 3.30000E+01, 1.40000E+01, NA, NA, NA, 1.40000E+01,
2.10000E+01, 7.00000E+00, NA, NA, NA, 3.00000E+00, 4.00000E+00, 4.00000E+00, NA, NA, NA,
1.30000E+01, 1.20000E+01, NA, NA, NA, NA, 2.50000E+00, 5.00000E-01, NA, NA, NA, NA,
4.50000E+00, 5.00000E-01, NA, NA, NA, NA, 3.84000E+00, 8.84000E+00, NA, NA, NA, NA,
5.00000E+00, 2.10000E+01, 2.00000E+01, 7.00000E+00, NA, NA, 5.00000E-01, 2.50000E+00, 5.50000E+00,
1.50000E+00, NA, NA, 1.60000E+01, 7.20000E+01, 4.20000E+01, NA, NA, NA, 6.00000E+00,
2.80000E+01, 1.10000E+01, NA, NA, NA, 1.10000E+01, 5.80000E+01, NA, NA, NA, NA,
2.00000E+00, 2.00000E+00, NA, NA, NA, NA, 1.36000E+00, 5.00000E-01, NA, NA, NA, NA,
1.90000E+01, 3.60000E+01, NA, NA, NA, NA, 1.00000E+01, 2.50000E+01, NA, NA, NA, NA,
4.00000E+00, 2.80000E+01, NA, NA, NA, NA, 1.70000E+01, 8.00000E+00, 3.00000E+00, NA, NA,
NA, 5.00000E+00, 1.00000E+00, NA, NA, NA, NA), .Dim=c(38, 6)), na=c(3.00000E+00, 3.00000E+00,
3.00000E+00, 4.00000E+00, 3.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 4.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00,
2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00, 3.00000E+00,
2.00000E+00))

Blurred vision: Fixed effect model

```
# Binomial likelihood, logit link, MTC
# Fixed effect model
model{                                                  # *** PROGRAM STARTS
for(i in 1:ns){                                          # LOOP THROUGH STUDIES
  mu[i] ~ dnorm(0,.001)                                  # vague priors for all trial baselines
  for (k in 1:na[i]) {                                   # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k])                         # binomial likelihood
    logit(p[i,k]) <- mu[i] + d[t[i,k]]-d[t[i,1]]          # model for linear predictor

   rhat[i,k] <- p[i,k] * n[i,k]                          # expected value of the numerators
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))        #Deviance contribution
       + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
  resdev[i] <- sum(dev[i,1:na[i]])              # summed residual deviance contribution for this trial
}
totresdev <- sum(resdev[])                       #Total Residual Deviance
d[1]<- 0                                        # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.001) }         # vague priors for treatment effects
for (k in 2:nt)  { OR[k] <- exp(d[k])}


#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}
for (k in 1:nt)  { TvMiraOR[k] <- exp(TvMira[k])}

}                                                       # *** PROGRAM ENDS

# Initial Values
```

#chain 1

```
list(d=c(NA,-1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -
1.00000E+00), mu=c(-5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00, -
5.00000E+00, -5.00000E+00, -5.00000E+00, -5.00000E+00))
```

#chain 2

```
list(d=c(NA,0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00),
mu=c(0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00, 0.00000E+00,
0.00000E+00, 0.00000E+00, 0.00000E+00))
```

#chain 3

```
list(d=c(NA,1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00),
mu=c(5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00, 5.00000E+00,
5.00000E+00, 5.00000E+00, 5.00000E+00))
```

#DATA

```
#	Treatment	Code
#	Tolterodine ER 4 mg	1
#	Mirabegron 50 mg	2
#	Fesoterodine 4mg	3
#	Fesoterodine 8mg	4
#	Oxybutynin ER 10 mg	5
#	Oxybutynin ER 15 mg	6
#	Oxybutynin ER 5 mg	7
#	Oxybutynin IR 10 mg	8
#	Oxybutynin IR 15 mg	9
#	Oxybutynin IR 9 mg	10
#	Placebo	11
#	Solifenacin 10 mg	12
#	Solifenacin 5 mg	13
#	Tolterodine IR 4 mg	14
#	Trospium 60 mg	15
```

```
list(ns=2.40000E+01, nt=15, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 1.10000E+01,     NA,     NA,     NA,
1.00000E+00, 2.00000E+00, 1.10000E+01,     NA,     NA,     NA, 1.00000E+00, 2.00000E+00, 1.10000E+01,     NA,
NA,     NA, 1.00000E+00, 1.00000E+01, 1.10000E+01,     NA,     NA,     NA, 1.00000E+00, 1.10000E+01,
1.40000E+01,     NA,     NA,     NA, 1.00000E+00, 1.10000E+01,     NA,     NA,     NA,     NA, 1.00000E+00,
1.10000E+01,     NA,     NA,     NA,     NA, 2.00000E+00, 1.10000E+01,     NA,     NA,     NA,     NA, 2.00000E+00,
1.10000E+01,     NA,     NA,     NA,     NA, 2.00000E+00, 1.10000E+01,     NA,     NA,     NA,     NA, 3.00000E+00,
4.00000E+00, 1.10000E+01,     NA,     NA,     NA, 3.00000E+00, 4.00000E+00, 1.10000E+01,     NA,     NA,     NA,
5.00000E+00, 6.00000E+00, 7.00000E+00,     NA,     NA,     NA, 5.00000E+00, 8.00000E+00,     NA,     NA,     NA,
NA, 5.00000E+00, 1.40000E+01,     NA,     NA,     NA,     NA, 7.00000E+00, 1.10000E+01,     NA,     NA,     NA,
NA, 9.00000E+00, 1.30000E+01,     NA,     NA,     NA,     NA, 1.10000E+01, 1.20000E+01, 1.30000E+01,
1.40000E+01,     NA,     NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, 1.40000E+01,     NA,     NA, 1.10000E+01,
1.20000E+01, 1.30000E+01,     NA,     NA,     NA, 1.10000E+01, 1.20000E+01, 1.30000E+01,     NA,     NA,     NA,
1.10000E+01, 1.20000E+01,     NA,     NA,     NA,     NA, 1.10000E+01, 1.50000E+01,     NA,     NA,     NA,     NA,
1.20000E+01, 1.30000E+01, 1.40000E+01,     NA,     NA,     NA), .Dim=c(24, 6)), n= structure(.Data=
c(4.95000E+02, 4.93000E+02, 4.94000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 8.50000E+01,
1.69000E+02, 1.69000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.75000E+02, 3.79000E+02,
3.79000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.39000E+02, 2.44000E+02, 1.22000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 5.05000E+02, 5.07000E+02, 5.12000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 6.40000E+01, 6.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 5.69000E+02, 2.85000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.42000E+02, 4.53000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.40000E+02,
```

```
4.33000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.08000E+02, 2.12000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.80000E+01, 1.90000E+01, 1.90000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.50000E+01, 2.80000E+01, 2.40000E+01, 1.00000E+00,
1.00000E+00, 1.00000E+00, 7.70000E+01, 8.30000E+01, 7.70000E+01, 1.00000E+00, 1.00000E+00,
1.00000E+00, 6.20000E+01, 6.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.85000E+02, 1.93000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.60000E+01,
2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01, 6.80000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.67000E+02, 2.68000E+02, 2.79000E+02,
2.63000E+02, 1.00000E+00, 1.00000E+00, 3.80000E+01, 3.50000E+01, 3.70000E+01, 3.70000E+01,
1.00000E+00, 1.00000E+00, 4.05000E+02, 3.81000E+02, 3.96000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 2.81000E+02, 2.90000E+02, 2.86000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
3.32000E+02, 3.40000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.03000E+02,
2.98000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.18000E+02, 1.18000E+02,
1.18000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00), .Dim=c(24, 6)), r= structure(.Data= c(5.00000E-01,
1.50000E+00, 2.50000E+00,    NA,    NA,    NA, 1.00000E+00, 1.00000E+00, 1.00000E+00,    NA,    NA,    NA,
7.00000E+00, 6.00000E+00, 3.00000E+00,    NA,    NA,    NA, 3.50000E+00, 8.50000E+00, 5.00000E-01,    NA,
NA,    NA, 6.00000E+00, 2.00000E+00, 4.00000E+00,    NA,    NA,    NA, 1.50000E+00, 5.00000E-01,    NA,
NA,    NA,    NA, 2.50000E+00, 5.00000E-01,    NA,    NA,    NA,    NA, 5.00000E-01, 1.50000E+00,    NA,    NA,
NA,    NA, 1.50000E+00, 5.00000E-01,    NA,    NA,    NA,    NA, 5.00000E-01, 5.00000E-01,    NA,    NA,    NA,
NA, 5.00000E-01, 1.50000E+00, 1.50000E+00,    NA,    NA,    NA, 1.50000E+00, 5.00000E-01, 1.50000E+00,
NA,    NA,    NA, 1.00000E+00, 1.00000E+00, 1.00000E+00,    NA,    NA,    NA, 4.00000E+00, 3.00000E+00,
NA,    NA,    NA,    NA, 4.00000E+00, 2.00000E+00,    NA,    NA,    NA,    NA, 5.00000E-01, 5.00000E-01,    NA,
NA,    NA,    NA, 5.00000E-01, 2.50000E+00,    NA,    NA,    NA,    NA, 7.00000E+00, 1.50000E+01,
1.00000E+01, 4.00000E+00,    NA,    NA, 2.50000E+00, 5.50000E+00, 1.50000E+00, 5.00000E-01,    NA,    NA,
8.00000E+00, 1.60000E+01, 7.00000E+00,    NA,    NA,    NA, 7.00000E+00, 1.80000E+01, 1.20000E+01,    NA,
NA,    NA, 4.00000E+00, 1.20000E+01,    NA,    NA,    NA,    NA, 2.00000E+00, 3.00000E+00,    NA,    NA,
NA,    NA, 1.90000E+01, 1.60000E+01, 1.20000E+01,    NA,    NA,    NA), .Dim=c(24, 6)), na=c(3.00000E+00,
3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 4.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00,
2.00000E+00, 3.00000E+00))
```

Blurred vision: Random effect model

```
# Binomial likelihood, logit link
# Random effect model, multi-arm trials
model{                                                  # *** PROGRAM STARTS
for(i in 1:ns){                                         # LOOP THROUGH STUDIES
  w[i,1] <- 0                                           # adjustment for multi-arm trials is zero for control arm
  delta[i,1] <- 0                                       # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.001)                                 # priors for all trial baselines
  for (k in 1:na[i]) {                                  # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k])                        # binomial likelihood
    logit(p[i,k]) <- mu[i] + delta[i,k]                 # model for linear predictor
     #rhat[i,k] <- p[i,k] * n[i,k]                     # expected value of the numerators
    # dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))     #Deviance contribution
      #   + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
 #resdev[i] <- sum(dev[i,1:na[i]])                     # summed residual deviance contribution for this trial
  for (k in 2:na[i]) {                                  # LOOP THROUGH ARMS
     delta[i,k] ~ dnorm(md[i,k],taud[i,k])              # trial-specific LOR distributions
     md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]         # mean of LOR distributions (with multi-arm correction)
     taud[i,k] <- tau *2*(k-1)/k                        # precision of LOR distributions (with multi-arm correction)
     w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])     # adjustment for multi-arm RCTs
     sw[i,k] <- sum(w[i,1:k-1])/(k-1)                   # cumulative adjustment for multi-arm trials
   }
}
#totresdev <- sum(resdev[])                             #Total Residual Deviance
d[1]<- 0                                                # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.01)}                 # priors for treatment effects
for (k in 2:nt)  { OR[k] <- exp(d[k])}
sd ~ dunif(0,2)
tau <- pow(sd,-2)



#the effect of treatment Vs trt 2 ."mirabegron 50 mg"
for (c in 1:(nt)) {
      TvMira[c] <- (d[c] - d[2])

}
for (k in 1:nt)  { TvMiraOR[k] <- exp(TvMira[k])}

}                                                       # *** PROGRAM ENDS
```

Initial Values

#chain 1

list(d=c(NA,-1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00, -1.00000E+00), mu=c(-5.00000E+00, -5.00000E+00), sd=5.00000E-01)

#chain 2

list(d=c(NA,1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01, 1.00000E-01), mu=c(5.00000E-01, 5.00000E-01), sd=1.00000E+00)

#chain 3

list(d=c(NA,5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01, 5.00000E-01), mu=c(4.00000E+00, 4.00000E+00), sd=5.00000E-01)

#DATA

#	Treatment	Code
#	Tolterodine ER 4 mg	1
#	Mirabegron 50 mg	2
#	Fesoterodine 4mg	3
#	Fesoterodine 8mg	4
#	Oxybutynin ER 10 mg	5
#	Oxybutynin ER 15 mg	6
#	Oxybutynin ER 5 mg	7
#	Oxybutynin IR 10 mg	8
#	Oxybutynin IR 15 mg	9
#	Oxybutynin IR 9 mg	10
#	Placebo	11
#	Solifenacin 10 mg	12
#	Solifenacin 5 mg	13
#	Tolterodine IR 4 mg	14
#	Trospium 60 mg	15

list(ns=2.40000E+01, nt=15, t= structure(.Data= c(1.00000E+00, 2.00000E+00, 1.10000E+01, NA, NA, NA, 1.00000E+00, 2.00000E+00, 1.10000E+01, NA, NA, NA, 1.00000E+00, 2.00000E+00, 1.10000E+01, NA, NA, NA, 1.00000E+00, 1.00000E+01, 1.10000E+01, NA, NA, NA, 1.00000E+00, 1.10000E+01, 1.40000E+01, NA, NA, NA, 1.00000E+00, 1.10000E+01, NA, NA, NA, NA, 1.00000E+00, 1.10000E+01, NA, NA, NA, NA, 2.00000E+00, 1.10000E+01, NA, NA, NA, NA, 2.00000E+00, 1.10000E+01, NA, NA, NA, NA, 2.00000E+00, 1.10000E+01, NA, NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.10000E+01, NA, NA, NA, 3.00000E+00, 4.00000E+00, 1.10000E+01, NA, NA, NA, 5.00000E+00, 6.00000E+00, 7.00000E+00, NA, NA, NA, 5.00000E+00, 8.00000E+00, NA, NA, NA, NA, 5.00000E+00, 1.40000E+01, NA, NA, NA, NA, 7.00000E+00, 1.10000E+01, NA, NA, NA, NA, 9.00000E+00, 1.30000E+01, NA, NA, NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, NA, NA, NA, 1.10000E+01, 1.20000E+01, 1.30000E+01, NA, NA, NA,

1.10000E+01, 1.20000E+01, NA, NA, NA, NA, 1.10000E+01, 1.50000E+01, NA, NA, NA, NA,
1.20000E+01, 1.30000E+01, 1.40000E+01, NA, NA, NA), .Dim=c(24, 6)), n= structure(.Data=
c(4.95000E+02, 4.93000E+02, 4.94000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 8.50000E+01,
1.69000E+02, 1.69000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.75000E+02, 3.79000E+02,
3.79000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.39000E+02, 2.44000E+02, 1.22000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 5.05000E+02, 5.07000E+02, 5.12000E+02, 1.00000E+00,
1.00000E+00, 1.00000E+00, 6.40000E+01, 6.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.00000E+00, 5.69000E+02, 2.85000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
4.42000E+02, 4.53000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 4.40000E+02,
4.33000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.08000E+02, 2.12000E+02,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.80000E+01, 1.90000E+01, 1.90000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 2.50000E+01, 2.80000E+01, 2.40000E+01, 1.00000E+00,
1.00000E+00, 1.00000E+00, 7.70000E+01, 8.30000E+01, 7.70000E+01, 1.00000E+00, 1.00000E+00,
1.00000E+00, 6.20000E+01, 6.60000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00,
1.85000E+02, 1.93000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.60000E+01,
2.40000E+01, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 6.40000E+01, 6.80000E+01,
1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 2.67000E+02, 2.68000E+02, 2.79000E+02,
2.63000E+02, 1.00000E+00, 1.00000E+00, 3.80000E+01, 3.50000E+01, 3.70000E+01, 3.70000E+01,
1.00000E+00, 1.00000E+00, 4.05000E+02, 3.81000E+02, 3.96000E+02, 1.00000E+00, 1.00000E+00,
1.00000E+00, 2.81000E+02, 2.90000E+02, 2.86000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00,
3.32000E+02, 3.40000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 3.03000E+02,
2.98000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.00000E+00, 1.18000E+02, 1.18000E+02,
1.18000E+02, 1.00000E+00, 1.00000E+00, 1.00000E+00), .Dim=c(24, 6)), r= structure(.Data= c(5.00000E-01,
1.50000E+00, 2.50000E+00, NA, NA, NA, 1.00000E+00, 1.00000E+00, 1.00000E+00, NA, NA, NA,
7.00000E+00, 6.00000E+00, 3.00000E+00, NA, NA, NA, 3.50000E+00, 8.50000E+00, 5.00000E-01, NA,
NA, NA, 6.00000E+00, 2.00000E+00, 4.00000E+00, NA, NA, NA, 1.50000E+00, 5.00000E-01, NA,
NA, NA, NA, 2.50000E+00, 5.00000E-01, NA, NA, NA, NA, 5.00000E-01, 1.50000E+00, NA, NA,
NA, NA, 1.50000E+00, 5.00000E-01, NA, NA, NA, NA, 5.00000E-01, 5.00000E-01, NA, NA, NA,
NA, 5.00000E-01, 1.50000E+00, 1.50000E+00, NA, NA, NA, 1.50000E+00, 5.00000E-01, 1.50000E+00,
NA, NA, NA, 1.00000E+00, 1.00000E+00, 1.00000E+00, NA, NA, NA, 4.00000E+00, 3.00000E+00,
NA, NA, NA, NA, 4.00000E+00, 2.00000E+00, NA, NA, NA, NA, 5.00000E-01, 5.00000E-01, NA,
NA, NA, NA, 5.00000E-01, 2.50000E+00, NA, NA, NA, NA, 7.00000E+00, 1.50000E+01,
1.00000E+01, 4.00000E+00, NA, NA, 2.50000E+00, 5.50000E+00, 1.50000E+00, 5.00000E-01, NA, NA,
8.00000E+00, 1.60000E+01, 7.00000E+00, NA, NA, NA, 7.00000E+00, 1.80000E+01, 1.20000E+01, NA,
NA, NA, 4.00000E+00, 1.20000E+01, NA, NA, NA, NA, 2.00000E+00, 3.00000E+00, NA, NA,
NA, NA, 1.90000E+01, 1.60000E+01, 1.20000E+01, NA, NA, NA), .Dim=c(24, 6)), na=c(3.00000E+00,
3.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 3.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00, 2.00000E+00,
2.00000E+00, 2.00000E+00, 4.00000E+00, 4.00000E+00, 3.00000E+00, 3.00000E+00, 2.00000E+00,
2.00000E+00, 3.00000E+00))

Appendix B: Beta coefficients informing the regression model

Table 21: Beta coefficients for micturition derived from optimisation using the initial beta coefficients for solifenacin 5mg or tolterodine ER 4 mg or mirabegron 50 mg

Initial betas		Mirabegron 50 mg	Tolterodine 4 mg	Fesoterodine 4 mg	Fesoterodine 8 mg	Oxybutynin 10 mg	Placebo	Solifenacin 10 mg	Solifenacin 5 mg	Trospium 60 mg
Solifenacin 5 mg	1.0687	0.8705409	0.8381488	0.875946	0.9209121	0.8720473	0.1884837	1.46458	1.1288648	1.0057509
	0.6566	0.6488051	0.5738913	0.565284	0.6536128	0.5662379	0.5445493	0.7065623	0.6648672	0.6573182
	0.301	0.3112693	0.4828114	0.4972612	0.3038383	0.4956869	0.5346519	0.2044482	0.2858888	0.2992674
	0.2789	0.2926035	0.5181286	0.5373098	0.2826101	0.5352181	0.5858384	0.1472374	0.2588457	0.2765607
	0	0	0	0	0	0	0	0	0	0
Tolterodine 4 mg	0.2683	0.7804671	0.6036642	0.6248522	0.8785082	0.6227023	0.0668459	1.6448588	0.9902683	1.0604196
	0.183	0.2355082	0.3056946	0.3077109	0.4078512	0.3076435	0.167527	-2.9525588	0.3703752	0.5250727
	0.0484	-0.008958	-0.0254884	-0.0275863	-0.0873292	-0.0274639	0.0559453	0.0433259	-0.0842591	-0.1514099
	0.2193	0.0154003	0.0720633	0.0687468	-0.0384601	0.0691174	0.2360527	-0.355984	-0.0802148	-0.1215486
	0	0	0	0	0	0	0	0	0	0
Mirabegron 50 mg	0.6037	0.7712062	0.6192253	0.6386378	0.8179794	0.6367083	0.0298257	1.3642957	0.9977145	0.8892316
	0.3803	0.4192267	0.3838897	0.3883839	0.4296279	0.3879342	0.2832229	0.4148676	0.4933007	0.4508974
	0.1454	0.1042972	0.141603	0.1368493	0.0931167	0.1373248	0.2290496	0.0037059	0.0383556	0.0728419
	0.0665	0.0125956	0.0615523	0.0553335	-0.001556	0.0559679	0.181445	-0.1735636	-0.0728545	-0.0301982
	0.0000	0	0	0	0	0	0	0	0	0

Table 22: Beta coefficients for incontinence derived from optimisation using the initial beta coefficients for solifenacin 5mg or tolterodine ER 4 mg or mirabegron 50 mg

Initial betas		Mirabegron 50 mg	Tolterodine 4 mg	Fesoterodine 4 mg	Fesoterodine 8 mg	Oxybutynin 10 mg	Placebo	Solifenacin 10 mg	Solifenacin 5 mg	Trospium 60 mg
Solifenacin 5 mg	0.9604	0.9081774	0.7545774	0.8245374	-0.2320188	0.3316369	-0.0235821	1.3587263	1.3528821	1.120266
	0.4778	0.4846169	0.4728726	0.3729926	1.0348199	0.7727254	0.353877	0.5364531	0.5355928	0.5010967
	0.8625	0.8556963	0.8677258	0.9684563	0.3010612	0.5810428	0.9421343	0.8034044	0.8042684	0.838922
	0.9816	0.9661372	0.9931987	1.2213599	-0.2888879	0.338933	1.2119896	0.844323	0.8462698	0.9284365
	0	0	0	0	0	0	0	0	0	0
Tolterodine 4 mg	0.1431	0.681784	0.5335206	0.4891803	0.2834052	0.4365229	-0.6018398	1.148042	1.1416982	0.8936735
	0.1768	0.3691849	0.3161592	0.300623	0.2264321	0.2819257	0.5944108	0.5900898	0.5866602	0.4461532
	-0.3271	-0.2868434	-0.2978404	-0.3011007	-0.316662	-0.3050327	-0.2388623	-0.2662257	-0.2653566	-0.2715431
	-0.0298	-0.0785594	-0.0652071	-0.0613521	-0.0423402	-0.0566709	-0.1349218	-0.128158	-0.1277416	-0.0977835
	0	0	0	0	0	0	0	0	0	0
Mirabegron 50 mg	0.3617	0.6533808	0.4966448	0.4494091	0.1503967	0.4924673	-0.9893631	1.1469386	1.1403215	0.8761466
	0.4634	0.579962	0.5297018	0.5148741	0.5981099	0.2143695	0.8044326	0.7364411	0.734266	0.6492994
	-0.0251	0.0284532	0.0263288	0.0257067	0.0292271	0.0130657	0.043188	0.0347324	0.0346597	0.0313464
	0.2040	0.1859377	0.210901	0.2178889	0.1785082	0.3603739	0.0872105	0.1125987	0.1136287	0.1540873
	0.0000	0	0	0	0	0	0	0	0	0