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12th November 2010

Dear Ms. Moore:

RE: GOLIMUMAB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS ("RA") AFTER THE FAILURE OF PREVIOUS DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS ("DMARDS") – COMMENTS ON THE APPRAISAL CONSULTATION DOCUMENT ("ACD")

Schering-Plough Limited, which is now part of MSD ("MSD"), welcomes the opportunity to comment on the ACD, which sets out the Appraisal Committee's ("the Committee") recommendations on golimumab for the treatment of RA.

We are disappointed that the Committee, having reviewed all of the evidence as well as hearing from stakeholders, has not felt able to recommend golimumab for the treatment of patients suffering from RA in a DMARD experienced or TNFα inhibitor experienced population.

There is a role for golimumab, based on significantly reduced injection frequency and fewer injection site reactions, reducing pain and discomfort for the patient that translates into a better quality of life. In addition, it provides physicians with a further treatment option to enable the more effective management of RA. This was clearly articulated by the patient representatives and the clinical experts in both submissions to, and depositions at the Committee meeting.

MSD believes that the original submission with the addition of the analyses provided below demonstrates that golimumab is both clinically efficacious and cost-effective for use in the treatment of DMARD experienced and TNFα inhibitor experienced patients with RA.

The response to the Committee request for additional analyses in section 1.4, MSD follows:

1. 'incorporation of ACR70 data in the economic model'

MSD has incorporated the ACR70 data into the 'methotrexate experienced patients' model as requested.

The addition of the ACR70 data increases all of the ICERs and reverses the relative positions of certolizumab and infliximab (Tables 1 and 2 below).

Table 1: Original base case analysis

	Total Costs (£)	Total QALYs	ICER (£) vs. baseline (methotrexate)
Methotrexate	35,869	4.569	-
Infliximab	69,899	5.651	31,451
Certolizumab	73,571	5.768	31,445
Adalimumab	66,875	5.792	25,352
Golimumab	67,747	5.827	25,340
Etanercept	74,208	6.133	24,513

Table 2: Revised base case analysis incorporating ACR70 data

	Total Costs (£)	Total QALYs	ICER (£) vs. baseline (methotrexate)
Methotrexate	38,175	5.261	-
Certolizumab	77,348	6.252	39,529
Infliximab	78,527	6.447	34,024
Adalimumab	70,514	6.323	30,451
Golimumab	74,201	6.554	27,862
Etanercept	83,472	6.900	26,795

The addition of the ACR70 data *and* changing the HAQ progression rate from 0.09 to 0.06 is also presented for completeness (Table 3 below).

Table 3: Revised base case analysis with the inclusion of ACR70 data *and* HAQ progression changed to 0.06

	Total Costs (£)	Total QALYs	ICER (£) vs. baseline (methotrexate)
Methotrexate	38,175	6.050	-
Certolizumab	77,,348	6.946	43,721
Infliximab	78,527	7.070	39,564
Golimumab	70,514	6.930	36,728
Etanercept	83,472	7.387	33,884
Adalimumab	74,201	7.143	32,955

This revised analysis places **all** interventions comfortably above an ICER threshold of £30,000 and leaves the relative positioning as for Table 2.

The comment in the ERG regarding the base case results presented by the manufacturer (p.121):

> *"…shows that infliximab and certolizumab are both dominated by golimumab, because golimumab is more effective and less costly. The remaining strategies all have very similar ICERs when compared to methotrexate, at around £25,000. The incremental analysis shows that adalimumab and golimumab are both extendedly dominated by etanercept. Etanercept generates the most QALYs of any strategy, but at a lower cost per QALY ratio. The full incremental analysis shows that etanercept is the optimal strategy, with an ICER of £21,000 compared to golimumab. The analysis also shows that golimumab is a cost-effective strategy when compared to infliximab and certolizumab, which are already recommended by NICE*."

From the point of view of relative efficacy the text essentially still applies to the revised analysis; as does the concluding comment regarding *"golimumab being a cost-effective strategy when compared to infliximab and certolizumab, which are already recommended by NICE."*

2. 'provision of SF-36 data from the GO-FORWARD and GO-AFTER trials…'

MSD has obtained the SF-36 data for weeks 14 and 24 from the GO-FORWARD study (see Appendix 1).

MSD is unable to provide SF-36 data from the GO-AFTER study given that it did not form part of the study protocol and was therefore not collected.

3. '...and a sensitivity analysis in which these data are included in the economic model using SF-6D and/or mapping approaches to EQ-5D'

MSD has now been able to obtain individual patient level data to inform our response to the ACD.

Individual patient level data has been mapped to SF-6D using the algorithm developed by Sheffield University (**http://www.shef.ac.uk/scharr/sections/heds/mvh/sf-6d/revisions.html**). We present both the parametric and posterior estimates. ACR70 data was not available within the provided dataset and therefore the ACR 70 values are assumed to be the same as for ACR50 (this is likely to be conservative). We have provided the estimates in appendix 2.

The sensitivity analysis was run in the model after it was updated with the ACR70 results for all other TNFα Inhibitors. Please note that although this analysis may (with considerable caution) be compared against Tables 1 and 2 it should not be compared with the results in Table 3. The results are presented below in Tables 4 and 5.

Table 4: Total costs and QALYs for golimumab and methotrexate in one way sensitivity analysis SF-36 to SF-6D (parametric)

	Total Costs (£)	Total QALYs	ICER (£) versus baseline (Methotrexate)
methotrexate	36,485	7.214	-
Golimumab	68,824	8.085	37,129

Table 5: Total costs and QALYs for golimumab and methotrexate in one way sensitivity analysis SF-36 to SF-6D (posterior)

	Total Costs (£)	Total QALYs	ICER (£) versus baseline (Methotrexate)
methotrexate	36,716	7.196	-
Golimumab	69,054	8.066	37,170

There are a number of caveats attached to this analysis:

- Inputting the mapped SF-6D data not only modifies the golimumab total costs and QALYs gained but also modifies those for methotrexate as can be seen when comparing against the comparable values in Table 2.
- We have not been able to perform the same mapping for the other TNFα Inhibitors
- There is significant concern regarding the ability of SF-36 and therefore SF-6D to accurately capture/reflect the utility associated with patient reported outcomes in patients with rheumatoid arthritis (Adams et al, 2010; Bansback et al, 2007; Hurst et al, 1997; Ruta et al, 1998; Scott, D., & Garrood, T., 2000).
- SF-6D is consistently seen to underestimate utility in relation to EQ-5D (Marra et al, 2004).

Given the caveats the estimates do provide face validity to the derived values used in the original submission as evidenced in Table 6 below.

Table 6: ICERs derived from Sheffield algorithm SF-6D mapped estimates.

	Total Costs (£)	Total QALYs	ICER (£) vs. baseline (methotrexate)
Methotrexate	36,327	7.227	-
Certolizumab	75,499	8.062	46,913
Infliximab	76,678	8.207	41,174
Golimumab	68,666	8.086	37,647
Etanercept	81,627	8.501	35,557
Adalimumab	72,352	8.278	34,277

3. 'data including the proportion of people who will receive 100 mg golimumab (that is, people who weigh more than 100 kg and whose disease has not responded after three or four doses) and inclusion of this proportion in the economic model.'

The Committee may or may not be aware that Committee C, their counterpart reviewing golimumab for use in patients with Psoriatic Arthritis (PsA), had expressed concerns regarding potential dose escalation to 100mg and the subsequent effect on cost-effectiveness.

MSD took the decision to propose a patient access scheme to address the concerns of Committee C.

MSD does not believe that dose-escalation will occur for any of the three indications for which golimumab is currently licensed. This view is supported by the clinical experts however the scheme (outline details below) has been put in place to ensure that the NHS will not bear any additional cost should dose escalation occur, and in such a way as to essentially remove any associated administrative burden from the NHS.

Patient Access Scheme

MSD has submitted a request to the Department of Health for consideration of a Patient Access Scheme for golimumab that will apply across all three licensed indications (PsA, RA and ankylosing spondylitis (AS)). This will have the effect of 'flat pricing' golimumab irrespective of whether the patient is prescribed 50mg pcm (1 x 50mg auto injector) or 100mg pcm (2 x 50mg auto injector). I.e. irrespective of whether a patient weighing >100kg is treated with 50mg pcm or 100mg pcm, the cost to the NHS will be as for a dose of 50mg pcm.

The scheme has been designed to minimise any impact on the NHS by placing the administrative burden on the wholesaler (Medco) when patients are prescribed golimumab at a total dose of 100mg pcm outside of the hospital setting. This means that patients who are prescribed the 100mg dose will receive it at the price of the 50mg dose, with the only action required being to request the appropriate dose on the prescription request. For the small number of patients who may be treated from hospital stocks (unlikely to occur in reality), MSD will work with the wholesaler to simplify any audit/reconciliation required.

It should also be noted that prescribing a dose of 100mg (2 x 50mg auto injector) can only occur for patients who weigh more than 100kg and are described as inadequately responding to a 50mg dose given the prescribing metrics between the provider and Medco.

We have not re-run the cost-effectiveness analyses, given that we believe there will be only rare use of a total dose of 100mg pcm. The PAS would absorb any additional cost should dose escalation occur.

We would also note that we are aware that the respective timelines of NICE and PASLU militate against presenting the Committee with an approved scheme for the November 25th meeting.

It is possible that the Committee conclude in its final guidance that there is no compelling evidence to support dose escalation to a total of 100mg pcm and therefore does not recommend clinicians to do so from the perspective of cost-effectiveness. Given that there is no direct clinical data supporting dose escalation for patients weighing >100kg, MSD will not be advocating dose escalation and would thus not be marketing golimumab at odds with such a recommendation were it to be included in the final guidance.

4. 'a sensitivity analysis in which disease progression on palliative treatment is reflected as an increase in HAQ score of 0.06 per year'

We have re-run the analysis after modifying the HAQ progression for palliative treatment to 0.06 per year (Table 7 below).

Table 7: Original base case analysis with palliative treatment HAQ progression of 0.06 pa

	Total Costs (£)	Total QALYs	ICER (£) vs. baseline (methotrexate)
Methotrexate	39,161	5.472	-
Infliximab	76,659	6.430	39,142
Certolizumab	77,296	6.538	35,774
Adalimumab	71,467	6.550	29,968
Golimumab	73,082	6.608	29,860
Etanercept	79,759	6.863	29,057

This has the effect of increasing the ICERs for all five TNFα Inhibitors and does not modify their original relative relationship. An analysis incorporating this change plus the addition of ACR70 has been provided above (Table 3, p.2).

5. 'cost-effectiveness results for the population in 1.3 for golimumab compared with adalimumab, etanercept, infliximab, abatacept and tocilizumab.'

Given the (lack of) availability of comparator data MSD has conducted an analysis comparing golimumab to only tocilizumab. The results are presented below in table 8.

Table 8: Golimumab compared with tocilizumab in TNFα Inhibitor experienced patients.

Technologies	Total Costs (£)	Total QALYs	ICER (£) versus baseline (Methotrexate)	Incremental analysis
methotrexate	37,134	3.849	-	-
Tocilizumab	51,207	4.210	38,983	38,983
Golimumab	53,519	4.361	32,002	17,927
Rituximab	53,530	4.514	24,656	72

CONCLUSION

MSD is confident that the analyses provided in this response, in addition to our original submission, provide the Committee with the required information to modify provisional recommendations 1.1 and 1.3 to recommend golimumab for use in line with TNFα Inhibitor guidance in TA130 and TA195 respectively.

The decision to do so will result in an enhancement to the physician's armamentarium as well as providing a valuable option for patients who need flexibility in their treatment regimen to maintain a reasonable quality of life.

MSD would also argue that the additional analysis provided above comparing the use of golimumab versus tocilizumab in patients who have received a previous TNFα Inhibitor should lead to a re-consideration of point 1.2 of the provisional recommendation.

MSD will cooperate in the provision of any other information or analyses that the Committee might wish to review.

Sincerely,

[redacted]

MSD

Appendix 1

Summary of SF-36 physical and mental component summary scores at baseline; randomized subjects

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Subjects randomized	133	133	89	89	178
Physical component summary					
n	132	131	89	88	177
Mean ± SD	31.63 ± 8.298	30.93 ± 8.462	30.45 ± 8.373	29.93 ± 8.036	30.19 ± 8.188
Median	31.45	30.30	28.60	29.05	28.70
IQ range	(25.80, 37.10)	(24.20, 36.40)	(24.20, 36.10)	(24.65, 35.40)	(24.30, 35.90)
Range	(8.6, 53.6)	(15.1, 53.7)	(15.9, 50.6)	(12.4, 51.8)	(12.4, 51.8)
Mental component summary					
n	132	131	89	88	177
Mean ± SD	43.93 ± 10.322	43.93 ± 11.218	44.14 ± 10.579	43.15 ± 11.785	43.65 ± 11.174
Median	43.25	43.20	43.60	42.10	42.70
IQ range	(35.25, 53.40)	(36.00, 52.30)	(35.20, 53.10)	(33.55, 50.60)	(34.50, 53.00)
Range	(22.5, 66.0)	(18.6, 72.9)	(20.7, 63.9)	(16.8, 68.6)	(16.8, 68.6)

Summary of norm-based scores of SF-36 scales at baseline; randomized subjects

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Subjects randomized	133	133	89	89	178
Physical functioning					
n	132	132	89	89	178
Mean ± SD	32.58 ± 10.276	30.85 ± 9.746	30.50 ± 10.535	29.62 ± 10.184	30.06 ± 10.342
Median	32.74	30.55	28.37	28.37	28.37
IQ range	(24.00, 41.47)	(24.00, 37.10)	(21.82, 37.10)	(21.82, 37.10)	(21.82, 37.10)
Range	(13.1, 54.6)	(13.1, 54.6)	(13.1, 54.6)	(13.1, 56.8)	(13.1, 56.8)
Role-physical					
n	132	132	89	89	178
Mean ± SD	33.15 ± 9.968	33.93 ± 11.328	32.87 ± 10.024	32.13 ± 9.412	32.50 ± 9.702
Median	25.97	25.97	25.97	25.97	25.97
IQ range	(25.97, 40.77)	(25.97, 40.77)	(25.97, 40.77)	(25.97, 33.37)	(25.97, 33.37)
Range	(26.0, 55.6)	(26.0, 55.6)	(26.0, 55.6)	(26.0, 55.6)	(26.0, 55.6)
Bodily pain					
n	132	132	89	89	178
Mean ± SD	34.12 ± 8.223	33.65 ± 8.046	33.19 ± 7.907	32.45 ± 7.125	32.82 ± 7.514
Median	35.36	35.36	31.54	31.54	31.54
IQ range	(27.29, 39.60)	(27.29, 39.60)	(27.29, 39.60)	(27.29, 35.36)	(27.29, 35.78)
Range	(18.0, 60.4)	(18.0, 53.6)	(18.0, 53.6)	(18.0, 49.4)	(18.0, 53.6)
General health					
n	132	131	89	89	178
Mean ± SD	35.64 ± 9.160	35.40 ± 10.044	36.18 ± 10.435	34.73 ± 9.861	35.45 ± 10.150
Median	35.02	34.03	35.02	34.03	34.03
IQ range	(29.07, 41.47)	(29.07, 41.47)	(29.07, 44.94)	(29.07, 39.98)	(29.07, 42.46)
Range	(16.7, 63.8)	(16.7, 63.8)	(14.2, 59.8)	(16.7, 61.3)	(14.2, 61.3)
Vitality					
n	132	132	89	89	178
Mean ± SD	39.62 ± 8.326	40.00 ± 8.922	38.70 ± 9.322	39.37 ± 9.057	39.04 ± 9.171
Median	39.91	39.91	37.52	39.91	39.91
IQ range	(35.12, 44.70)	(32.72, 44.70)	(32.72, 44.70)	(32.72, 44.70)	(32.72, 44.70)
Range	(20.7, 63.9)	(20.7, 68.7)	(20.7, 63.9)	(20.7, 61.5)	(20.7, 63.9)

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Social functioning					
n	132	132	89	89	178
Mean ± SD	38.58 ± 10.147	37.91 ± 11.288	37.75 ± 11.208	36.87 ± 11.878	37.31 ± 11.524
Median	40.57	34.99	40.57	34.99	37.78
IQ range	(32.19, 46.16)	(34.99, 46.16)	(29.40, 46.16)	(29.40, 46.16)	(29.40, 46.16)
Range	(12.6, 57.3)	(12.6, 57.3)	(12.6, 57.3)	(12.6, 57.3)	(12.6, 57.3)
Role-emotional					
n	132	132	89	88	177
Mean ± SD	39.76 ± 13.782	40.75 ± 13.226	40.69 ± 13.188	38.69 ± 12.945	39.70 ± 13.069
Median	35.47	35.47	35.47	35.47	35.47
IQ range	(25.39, 55.66)	(25.39, 55.66)	(25.39, 55.66)	(25.39, 55.66)	(25.39, 55.66)
Range	(25.4, 55.7)	(25.4, 55.7)	(25.4, 55.7)	(25.4, 55.7)	(25.4, 55.7)
Mental health					
n	132	132	89	89	178
Mean ± SD	41.83 ± 10.123	40.41 ± 10.820	41.11 ± 10.145	40.36 ± 11.652	40.74 ± 10.900
Median	39.54	39.54	39.54	39.54	39.54
IQ range	(35.10, 50.64)	(32.88, 46.20)	(35.10, 48.42)	(32.88, 48.42)	(35.10, 48.42)
Range	(12.9, 61.7)	(12.9, 64.0)	(19.6, 64.0)	(8.4, 64.0)	(8.4, 64.0)

Summary of change from baseline in SF-36 physical component summary scores at Week 14 and Week 24; randomized subjects

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Subjects randomized	133	133	89	89	178
Change from baseline					
Week 14					
n	127	127	85	85	170
Mean ± SD	2.39 ± 7.798	4.72 ± 8.782	8.02 ± 7.170	7.41 ± 8.044	7.71 ± 7.603
Median	1.90	3.80	7.70	6.60	7.00
IQ range	(-3.30, 6.10)	(-1.70, 10.30)	(3.80, 12.60)	(1.90, 13.20)	(2.10, 12.90)
Range	(-16.9, 31.7)	(-14.5, 28.4)	(-8.7, 28.4)	(-15.7, 25.7)	(-15.7, 28.4)
p-value		0.033	< 0.001	< 0.001	< 0.001
Week 24					
n	125	125	88	86	174
Mean ± SD	2.54 ± 8.055	4.74 ± 8.844	8.28 ± 8.327	7.01 ± 7.796	7.65 ± 8.071
Median	2.40	3.00	8.10	6.65	7.55
IQ range	(-1.70, 6.00)	(-0.90, 10.60)	(2.50, 13.70)	(1.50, 12.50)	(2.00, 12.70)
Range	(-17.2, 31.2)	(-12.6, 30.5)	(-8.7, 31.7)	(-11.1, 27.2)	(-11.1, 31.7)
p-value		0.070	< 0.001	< 0.001	< 0.001

Summary of change from baseline in norm-based scores of SF-36 scales at Week 14 and Week 24; randomized subjects

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Subjects randomized	133	133	89	89	178
Physical functioning					
Week 14					
n	128	128	87	86	173
Mean ± SD	1.78 ± 7.845	3.60 ± 9.547	6.45 ± 8.665	7.44 ± 9.454	6.94 ± 9.053
Median	2.18	2.18	4.37	6.55	4.37
IQ range	(-2.18, 6.55)	(-2.18, 8.74)	(0.00, 13.10)	(2.18, 13.10)	(2.18, 13.10)
Range	(-21.8, 30.6)	(-24.0, 39.3)	(-13.1, 28.4)	(-19.7, 30.6)	(-19.7, 30.6)
p-value		0.099	< 0.001	< 0.001	< 0.001
Week 24					
n	126	126	88	87	175
Mean ± SD	1.73 ± 8.442	4.01 ± 9.768	6.78 ± 9.062	7.48 ± 8.771	7.13 ± 8.900
Median	2.18	2.18	4.37	6.55	6.55
IQ range	(-2.18, 6.55)	(-2.18, 8.74)	(0.00, 13.10)	(2.18, 10.92)	(0.00, 13.10)
Range	(-21.8, 32.8)	(-24.0, 41.5)	(-13.1, 30.6)	(-21.8, 30.6)	(-21.8, 30.6)
p-value		0.045	< 0.001	< 0.001	< 0.001
Role-physical					
Week 14					
n	128	128	87	86	173
Mean ± SD	3.35 ± 12.027	6.30 ± 12.560	6.89 ± 12.086	8.00 ± 12.747	7.44 ± 12.396
Median	0.00	0.00	0.00	7.40	7.40
IQ range	(0.00, 7.40)	(0.00, 14.79)	(0.00, 14.79)	(0.00, 14.79)	(0.00, 14.79)
Range	(-29.6, 29.6)	(-29.6, 29.6)	(-29.6, 29.6)	(-29.6, 29.6)	(-29.6, 29.6)
p-value		0.110	0.022	0.007	0.003
Week 24					
n	126	126	88	87	175
Mean ± SD	2.99 ± 11.618	5.75 ± 12.231	8.07 ± 13.014	6.63 ± 12.099	7.35 ± 12.552
Median	0.00	0.00	7.40	0.00	0.00
IQ range	(0.00, 7.40)	(0.00, 14.79)	(0.00, 22.19)	(0.00, 14.79)	(0.00, 14.79)
Range	(-29.6, 29.6)	(-29.6, 29.6)	(-29.6, 29.6)	(-29.6, 29.6)	(-29.6, 29.6)
p-value		0.088	0.004	0.030	0.003

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Bodily pain					
Week 14					
n	128	128	87	86	173
Mean ± SD	3.01 ± 9.758	5.24 ± 8.064	8.68 ± 8.131	7.79 ± 7.806	8.24 ± 7.960
Median	0.00	4.24	8.06	8.28	8.06
IQ range	(-1.91, 8.06)	(0.00, 9.34)	(4.24, 14.01)	(3.82, 13.16)	(3.82, 13.58)
Range	(-17.8, 38.2)	(-12.3, 37.4)	(-8.1, 33.1)	(-12.7, 29.3)	(-12.7, 33.1)
p-value		0.025	< 0.001	< 0.001	< 0.001
Week 24					
n	126	126	88	87	175
Mean ± SD	2.67 ± 9.542	4.96 ± 8.805	8.61 ± 8.920	8.06 ± 7.972	8.33 ± 8.442
Median	0.21	4.46	8.49	8.06	8.06
IQ range	(-0.42, 8.06)	(0.00, 9.76)	(0.00, 14.01)	(3.82, 14.01)	(0.00, 14.01)
Range	(-24.6, 38.2)	(-13.6, 29.3)	(-8.1, 33.1)	(-8.5, 26.3)	(-8.5, 33.1)
p-value		0.038	< 0.001	< 0.001	< 0.001
General health					
Week 14					
n	128	127	85	86	171
Mean ± SD	0.84 ± 7.458	2.17 ± 8.642	4.13 ± 7.004	3.91 ± 7.900	4.02 ± 7.447
Median	0.00	2.48	4.96	2.97	3.97
IQ range	(-3.47, 4.96)	(-2.48, 7.44)	(0.00, 7.44)	(-2.48, 8.43)	(0.00, 8.43)
Range	(-19.8, 19.8)	(-23.3, 30.7)	(-9.9, 24.8)	(-13.4, 28.3)	(-13.4, 28.3)
p-value		0.194	0.001	0.005	< 0.001
Week 24					
n	125	125	88	87	175
Mean ± SD	1.19 ± 8.340	2.65 ± 8.836	4.03 ± 7.566	4.08 ± 8.163	4.05 ± 7.846
Median	0.00	2.48	3.47	2.48	3.47
IQ range	(-3.47, 5.95)	(-2.48, 7.44)	(0.00, 8.43)	(-2.48, 9.92)	(0.00, 9.92)
Range	(-19.8, 25.8)	(-23.3, 30.7)	(-10.9, 28.3)	(-12.4, 27.3)	(-12.4, 28.3)
p-value		0.159	0.010	0.011	0.002
Vitality					
Week 14					
n	127	128	86	86	172
Mean ± SD	2.62 ± 8.340	5.13 ± 9.275	6.07 ± 8.305	5.35 ± 8.132	5.71 ± 8.203
Median	0.00	2.40	4.79	4.79	4.79
IQ range	(-2.40, 7.19)	(0.00, 11.98)	(0.00, 11.98)	(0.00, 11.98)	(0.00, 11.98)
Range	(-16.8, 28.8)	(-19.2, 28.8)	(-16.8, 31.1)	(-14.4, 21.6)	(-16.8, 31.1)
p-value		0.017	0.002	0.016	0.001
Week 24					
n	126	126	88	87	175
Mean ± SD	2.14 ± 8.450	5.08 ± 9.245	5.66 ± 8.651	5.35 ± 7.682	5.51 ± 8.161
Median	2.40	4.79	4.79	4.79	4.79
IQ range	(-2.40, 7.19)	(-2.40, 9.58)	(0.00, 9.58)	(0.00, 9.58)	(0.00, 9.58)
Range	(-24.0, 26.4)	(-19.2, 28.8)	(-16.8, 28.8)	(-12.0, 28.8)	(-16.8, 28.8)
p-value		0.011	0.003	0.004	< 0.001

Social functioning					
Week 14					
n	128	128	87	86	173
Mean ± SD	1.88 ± 11.222	4.89 ± 11.476	3.85 ± 11.502	7.60 ± 11.932	5.72 ± 11.834
Median	0.00	5.59	0.00	5.59	5.59
IQ range	(-5.59, 5.59)	(0.00, 11.17)	(0.00, 11.17)	(0.00, 16.76)	(0.00, 11.17)
Range	(-27.9, 27.9)	(-27.9, 33.5)	(-22.3, 33.5)	(-22.3, 33.5)	(-22.3, 33.5)
p-value		0.023	0.240	< 0.001	0.005
Week 24					
n	126	126	88	87	175
Mean ± SD	1.24 ± 11.215	4.70 ± 10.933	3.94 ± 11.893	6.04 ± 10.052	4.98 ± 11.035
Median	0.00	5.59	2.79	5.59	5.59
IQ range	(-5.59, 5.59)	(0.00, 11.17)	(-2.79, 11.17)	(0.00, 11.17)	(0.00, 11.17)
Range	(-27.9, 39.1)	(-27.9, 27.9)	(-22.3, 33.5)	(-16.8, 33.5)	(-22.3, 33.5)
p-value		0.007	0.111	< 0.001	0.004
Role-emotional					
Week 14					
n	128	128	87	85	172
Mean ± SD	2.37 ± 15.119	2.84 ± 15.196	1.63 ± 13.928	6.06 ± 14.875	3.81 ± 14.532
Median	0.00	0.00	0.00	0.00	0.00
IQ range	(0.00, 10.08)	(0.00, 10.08)	(0.00, 10.08)	(0.00, 20.20)	(0.00, 10.10)
Range	(-30.3, 30.3)	(-30.3, 30.3)	(-30.3, 30.3)	(-30.3, 30.3)	(-30.3, 30.3)
p-value		0.672	0.755	0.064	0.350
Week 24					
n	126	126	88	86	174
Mean ± SD	1.36 ± 14.180	3.20 ± 14.024	3.33 ± 14.657	5.16 ± 14.667	4.23 ± 14.649
Median	0.00	0.00	0.00	0.00	0.00
IQ range	(0.00, 10.08)	(0.00, 10.08)	(0.00, 10.11)	(0.00, 10.08)	(0.00, 10.11)
Range	(-30.3, 30.3)	(-30.3, 30.3)	(-30.3, 30.3)	(-30.3, 30.3)	(-30.3, 30.3)
p-value		0.266	0.284	0.060	0.080

Mental health					
Week 14					
n	127	128	86	86	172
Mean ± SD	1.28 ± 8.160	3.80 ± 10.417	3.00 ± 9.088	4.29 ± 10.252	3.64 ± 9.681
Median	0.00	2.22	3.33	4.44	4.44
IQ range	(-2.22, 6.66)	(-2.22, 11.10)	(0.00, 8.88)	(-2.22, 11.10)	(-2.22, 8.88)
Range	(-24.4, 26.6)	(-37.8, 31.1)	(-35.5, 22.2)	(-17.8, 31.1)	(-35.5, 31.1)
p-value		0.031	0.085	0.017	0.015
Week 24					
n	126	126	88	87	175
Mean ± SD	0.74 ± 8.394	3.38 ± 9.607	2.98 ± 9.343	5.11 ± 10.239	4.04 ± 9.828
Median	0.00	2.22	3.33	4.44	4.44
IQ range	(-4.44, 4.44)	(-2.22, 8.88)	(-2.22, 8.88)	(-2.22, 11.10)	(-2.22, 8.88)
Range	(-22.2, 28.9)	(-22.2, 31.1)	(-26.6, 22.2)	(-26.6, 37.8)	(-26.6, 37.8)
p-value		0.026	0.041	< 0.001	0.001

Appendix 2

Utilities - Final.xls

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