

Statistical Appendix for response to question 3 of EMEA Article 31 referral

1.0 Possibly Suicide-Related Events

1.1 Statistical Methods

For each of the defined populations (adult placebo controlled trials, adult active controlled trials and paediatric placebo controlled trials) the effect of the following covariates on the likelihood of a possibly suicide-related event were considered:

- Age
- Gender
- Race (White, Black, Other)
- Severity of Disease (CGI-severity of 1-2, 3-4, 5-6, i.e. normal, mild to moderate, severe)
- Indication (Depression, GAD, OCD, Panic, PMDD, PTSD, SAD)
- CR vs IR vs CRIR (not included for paediatric placebo controlled trials, because none of these trials included a CR formulation)
- Medical history of "suic", "overdos", "over-dos", "over dos"
- Prior psychotropic medication
- Control medication class (Tricyclic, Tetracyclic, SSRI, Benzodiazepine, Other). This only applies to adult active controlled trials.
- Baseline suicidal ideation (i.e. HAMD item 3 \geq 3 or MADRS item 10 \geq 3)
- Baseline agitation (i.e. HAMD item 9 \geq 2).

With the exception of age (which was modelled as a continuous covariate) each covariate was considered as a categorical variable (i.e. not accounting for any specific order). If any covariate did not converge in the model then the categories were collapsed as appropriate.

The covariates were tested in a model building approach using a backwards elimination process at a 5% level of significance (i.e. all covariates were included in the model, then at each step the least significant covariate was removed one at a time until all the remaining covariates were statistically significant at the 5% level). The treatment effect was then added to the model adjusting for the relevant baseline covariates. The final set of covariates included at this stage constituted the "base model".

Treatment by covariate interactions were then assessed by including each in the base model (including treatment) one at a time and determining statistical significance at the 5% level.

Once the base model had been selected, the following treatment-dependent covariates were also considered:

- On-therapy adverse event of agitation (i.e. all events coded to a preferred term of agitation)
- On-therapy adverse event of hyperkinesia (i.e. all events coded to a preferred term of hyperkinesia)
- On-therapy adverse event of hostility (as defined for the analysis of hostility in this response)
- Early emergent agitation, i.e. change from HAMD item 9 of 0 or 1 at baseline to ≥ 2 within the first 28 days of treatment.

For each of these treatment-dependent covariates, only those adverse events occurring prior to the response variable (possibly suicide-related event) were considered.

The model building utilised a forward selection method with a significance level of 5%, i.e. each treatment-dependent covariate was added in turn to the base model (excluding treatment) and at each step, the covariate that gave the most statistically significant result was included in the model. This continued until all statistically significant terms were included in the final model. The treatment effect was then added to the model adjusting for all relevant covariates.

For the fixed dose depression studies, the effect of dose was assessed for the adult placebo controlled trials, including dose in the model as a categorical variable. For the purpose of combining data from CR and IR studies, the CR dose was divided by 1.25 to give an equivalent IR dose (e.g. 25 mg CR is equivalent to 20mg IR). The effect of dose was not modelled for any indications other than depression, because there were too few events for this to be assessed.

1.2 Adult Placebo Controlled Trials

The following baseline covariates were statistically significant at the 5% level for the adult placebo controlled trials population. When treatment was added to the base model, it did not have a significant effect. In the case of age, the odds ratio of 0.95 indicates that, for each additional year of age, the odds of an event are 0.95 times less likely. For other effects the odds are presented for one category of a variable relative to another, e.g. the odds of an event were nearly eight times greater in depression trials than in other trials.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Age		0.95 (0.93, 0.96)	<0.001
Indication	Depression:Other	7.93 (4.82, 13.06)	<0.001
CRvsIRvsCRIR	CR:IR	0.23 (0.10, 0.54)	<0.001
	CRIR:IR	0.28 (0.12, 0.65)	0.003
Medical History	Absent:Present	0.14 (0.04, 0.45)	0.001
Psychotropic Medication	No:Yes	0.27 (0.19, 0.40)	<0.001
Baseline Suicide Ideation	Absent:Present	0.28 (0.18, 0.43)	<0.001
Baseline Agitation	Absent:Present	2.14 (1.15, 3.96)	0.016
Treatment	Paroxetine:Placebo	0.88 (0.61, 1.28)	0.512

* Other includes GAD, OCD, PMDD, PTSD, Panic and SAD

The main effect of baseline agitation was only found to be a significant covariate when indication was also included in the model; this implies an association between indication and baseline agitation, independent of treatment. In depression trials, possibly suicide-related events were reported by 2.1% of patients (88/4133) without agitation at baseline and by 0.8% of patients (11/1405) who were diagnosed with agitation at baseline, i.e. patients who were agitated upon entry to a study appeared to be at a *lower* risk of a possibly suicide-related event. In other indications, possibly suicide-related events were reported by 0.2% (21/8675) of agitation-negative patients and 1.3% (1/76) of agitation-positive patients.

The following baseline covariates and treatment-dependent covariates were statistically significant at the 5% level for the adult placebo controlled trials

population. When treatment was added to the final model below, it did not have a significant effect.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Age		0.95 (0.93, 0.96)	<0.001
Indication	Depression:Other*	8.72 (5.29, 14.37)	<0.001
CRvsIRvsCRIR	CR:IR	0.23 (0.10, 0.53)	<0.001
	CRIR:IR	0.30 (0.13, 0.69)	0.005
Medical History	Absent:Present	0.14 (0.04, 0.47)	0.001
Psychotropic Medication	No:Yes	0.29 (0.19, 0.42)	<0.001
Baseline Suicide Ideation	Absent:Present	0.29 (0.19, 0.44)	<0.001
Baseline Agitation	Absent:Present	2.38 (1.28, 4.41)	0.006
Early Emergent Agitation	Absent:Present	5.45 (1.33, 22.35)	0.019
Treatment	Paroxetine:Placebo	0.88 (0.60, 1.27)	0.486

* Other includes GAD, OCD, PMDD, PTSD, Panic and SAD

There were no statistically significant treatment by covariate interactions, the most significant being treatment with baseline suicidal ideation (P=0.13) and treatment with age (P=0.26).

When assessing the effect of dose alone in the adult placebo controlled fixed-dose depression trials, dose was statistically significant (P<0.001).

Variable	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Dose	5-10mg:Placebo	0.13 (0.04, 0.43)	<0.001
	20mg:Placebo	0.37 (0.18, 0.78)	0.009
	30mg:Placebo	0.10 (0.01, 0.75)	0.025
	40-50mg:Placebo	1.54 (0.91, 2.60)	0.106

The apparently higher incidence of events with the 40mg dose is in fact explained completely by the results of study 057, which compared a dose of paroxetine 40mg against placebo – this study accounted for all 27 events seen with paroxetine 40mg

(see [Tables 3.31](#) and [3.31a](#) for a summary of the results with and without study 057). The results of study 057 itself showed no difference between paroxetine and placebo in the incidence of possibly suicide-related events (see [Table 2.01a](#)). The statistical modelling of the dose effect was repeated without study 057 and showed no statistically association with dose (P=0.08). Taken together with the results in [Table 3.31a](#), this provides strong evidence of no link between possibly suicide-related events and increasing doses of paroxetine.

1.3 Adult Active Controlled Trials

The following baseline covariates were statistically significant at the 5% level for the adult active controlled trials population. When treatment was added to the base model, it was not significant at the 5% level (P=0.075) but the direction of the effect was in favour of paroxetine over active controls.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Age		0.98 (0.97, 0.99)	0.004
Disease Severity	Normal/Missing:Severe	1.14 (0.66, 1.98)	0.633
	Moderate:Severe	0.50 (0.31, 0.81)	0.004
Psychotropic Medication	Absent:Present	0.61 (0.40, 0.91)	0.016
Control Medication Class	Tetracyclic:SSRI	0.35 (0.15, 0.83)	0.018
	Tricyclic:SSRI	0.52 (0.33, 0.82)	0.005
	Other*:SSRI	0.33 (0.15, 0.73)	0.006
Baseline Suicidality	Absent:Present	0.46 (0.30, 0.71)	<0.001
Treatment	Paroxetine:Comparator	0.71 (0.49, 1.03)	0.075

* Other includes Benzodiazepines and a study involving both nortriptyline and fluoxetine

The following baseline covariates and treatment-dependent covariates were statistically significant at the 5% level for the adult active controlled trials population. When treatment was added to the base model, it was not significant at the 5% level (P=0.068) but the direction of the effect was in favour of paroxetine over active controls.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Age		0.98 (0.97, 0.99)	0.005
Disease Severity	Normal/Missing: Severe	1.14 (0.66, 1.97)	0.635
	Moderate:Severe	0.50 (0.31, 0.80)	0.004
Psychotropic Medication	Absent:Present	0.62 (0.42, 0.94)	0.023
Control Medication Class	Tetracyclic:SSRI	0.34 (0.14, 0.82)	0.016
	Tricyclic:SSRI	0.53 (0.33, 0.83)	0.006
	Other:SSRI	0.34 (0.15, 0.75)	0.007
Baseline Suicidality	Absent:Present	0.45 (0.29, 0.70)	<0.001
Emergent Agitation	Absent:Present	0.32 (0.16, 0.61)	<0.001
Treatment	Paroxetine:Comparator	0.71 (0.49, 1.03)	0.068

The most significant treatment by covariate interaction (P=0.08) was with age, and this showed the benefit of treatment with paroxetine compared to active controls was highest among younger patients. Of the remaining covariates the next most significant treatment by covariate interaction was with disease severity (P=0.23).

1.4 Paediatric Placebo Controlled Trials

The following baseline covariates were statistically significant at the 5% level for the paediatric placebo controlled trials population. When treatment was added to the model the effect was not statistically significant at the 5% level (P=0.097) but the direction of the effect showed a higher reporting of these events among paroxetine-treated patients than among placebo-treated patients.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Gender	Female:Male	3.74 (1.26, 11.14)	0.018
Disease Severity	Normal/Missing:Severe	1.24 (0.48, 3.20)	0.663
	Mild/Moderate:Severe	0.28 (0.10, 0.83)	0.021
Baseline Suicidality	Absent:Present	0.15 (0.06, 0.36)	<0.001
Treatment	Paroxetine:Placebo	2.14 (0.87, 5.28)	0.097

None of the treatment-dependent covariates were statistically significant at the 5% level. The most significant treatment by covariate interaction ($P=0.06$) was the treatment by baseline disease severity effect – the greatest difference between paroxetine and placebo was seen in patients where the disease was assessed as severe at baseline, and also where the baseline CGI disease severity was unknown (almost all cases of these patients with unknown severity assessment came from study 329, in which CGI severity was not assessed at baseline). The next most significant interaction was treatment with baseline suicidality ($P=0.50$).

2.0 Self Harm

Self harm was assessed using the same techniques and covariates as described for possibly suicide-related events, and in general produced similar results to those found for possibly suicide-related events. A summary of the findings are provided below.

For adult placebo controlled trials, the base model for self harm included the same covariates as the model for possibly suicide-related events, with the treatment effect not significant. One treatment by covariate interaction was found to be significant, for treatment by baseline suicidal ideation ($P<0.01$). When assessing treatment emergent events, early emergent agitation had a significant effect, consistent with the model for possibly suicide-related events.

For adult active controlled trials, the base model for self harm included the same covariates as the model for possibly suicide-related events, except for control medication, which was not significant at the 5% level ($P=0.086$) for the self harm analysis and therefore was not included in the base model. Treatment effect was not significant and no treatment by covariate interactions were found to be significant, although treatment by age approached significance ($P=0.074$), consistent with the findings for possibly suicide-related events. When assessing treatment emergent events, treatment emergent agitation had a significant effect, consistent with the model for possibly suicide-related events.

For paediatric placebo controlled trials, the base model for self harm included treatment, indication, baseline suicidal ideation and gender, whereas the model for possibly suicide-related events had contained disease severity, baseline suicidal ideation and gender. There was no significant treatment effect and no treatment by

covariate interactions. When considering treatment emergent events, a significant effect was found for the treatment emergent event of hostility (P=0.048).

3.0 Hostility

3.1 Adult Placebo Controlled Trials

Analysis of hostility events was assessed using the same techniques and covariates as described for possibly suicide-related events and self-harm. However, no treatment emergent covariates were considered.

The following baseline covariates were statistically significant at the 5% level for the adult placebo controlled trials population. When treatment was added to the model, it did not have a significant effect.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Indication	OCD:Other*	4.07 (1.86, 8.88)	<0.001
Age	Per year increase	0.97 (0.94, 1.00)	0.022
Treatment	Paroxetine:Placebo	1.01 (0.54, 1.91)	0.970

*Depression, GAD, PMDD, PTSD, Panic, SAD

There were no statistically significant treatment by covariate interactions (P>0.47).

When assessing the effect of dose alone in the adult placebo controlled fixed-dose depression trials, dose did not attain statistical significance at the 5% level (P=0.08).

3.2 Adult Active Controlled Trials

The following baseline covariates were statistically significant at the 5% level of significance for the adult active controlled trials population. When treatment was added to the model, it did not have a significant effect.

Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Disease Severity	Missing/Normal:Severe	0.64 (0.16, 2.59)	0.527
	Mild/Moderate:Severe	2.19 (0.97, 4.96)	0.061
Control Medication	Benzodiazepine/Other: SSRI	1.51 (0.39, 5.87)	0.551
	Tricyclic:SSRI	0.37 (0.16, 0.85)	0.828
	Tetracyclic:SSRI	0.89 (0.32, 2.48)	0.019
Treatment	Paroxetine: Comparator	0.70 (0.36, 1.35)	0.283

There were no statistically significant treatment by covariate interactions ($P>0.49$).

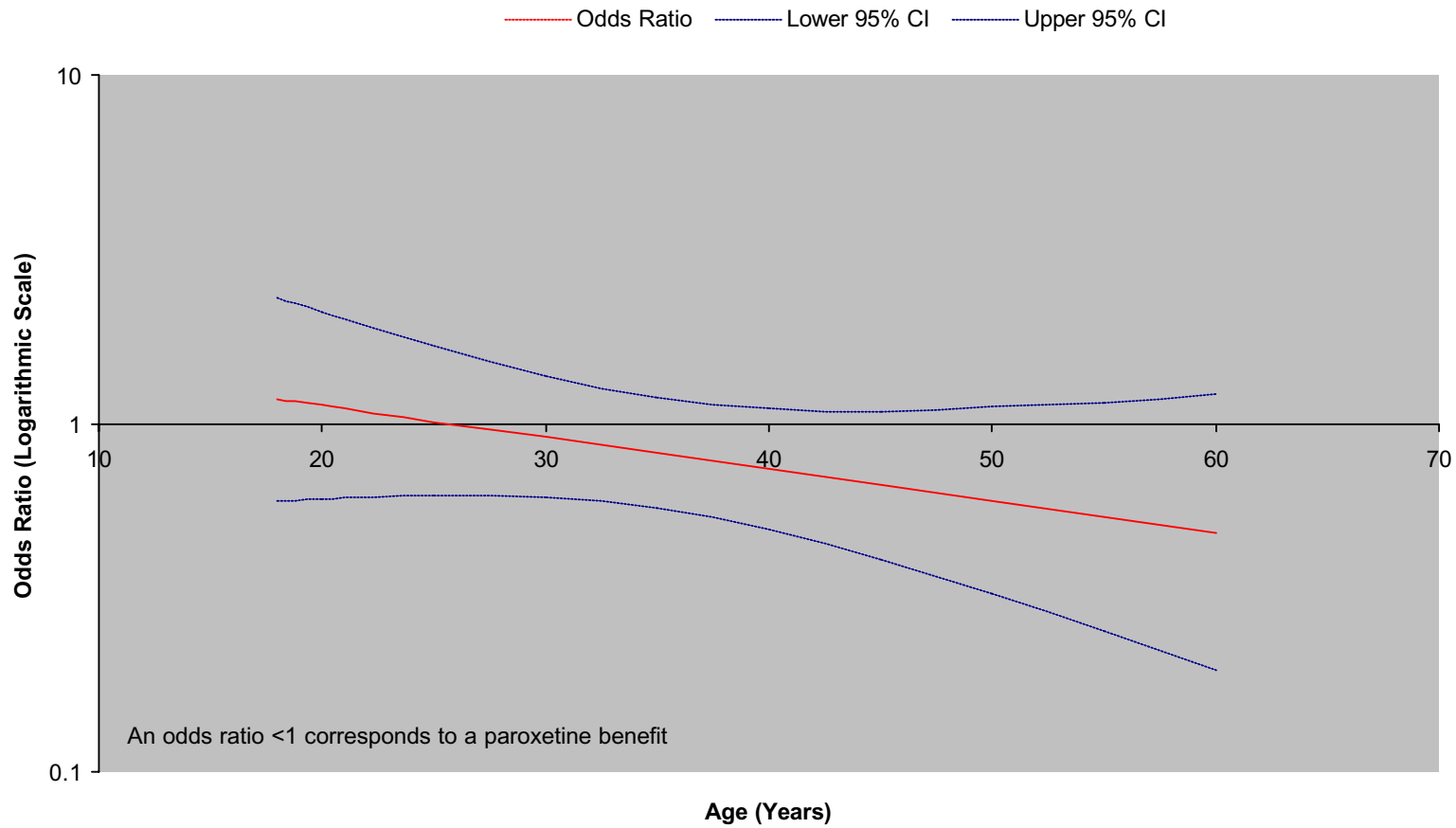
3.3 Paediatric Placebo Controlled Trials

The following baseline covariates were statistically significant at the 5% level of significance for the paediatric placebo controlled trials population. When treatment was added to the model, there was a statistically significant difference between paroxetine and placebo ($P<0.001$) – these events being reported more commonly among paroxetine-treated patients than among placebo-treated patients.

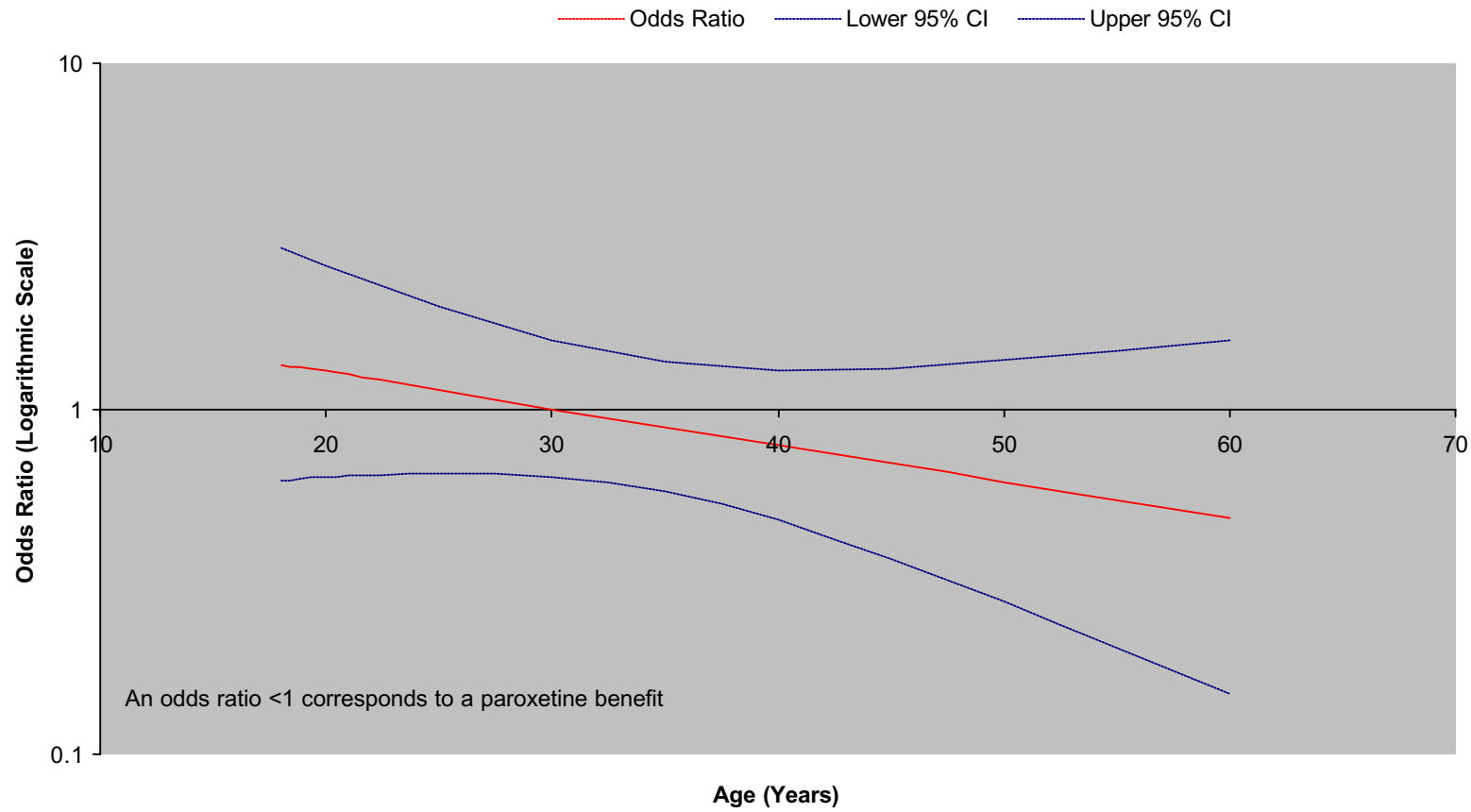
Covariate	Odds Ratio Explanation	Odds Ratio (95% CI)	P-value
Disease Severity	Missing:Severe	5.12 (1.21, 21.70)	0.027
	Normal:Severe	0.45 (0.11, 1.79)	0.256
	Mild/Moderate:Severe	0.41 (0.17, 1.00)	0.051
Indication	Depression:OCD	0.16 (0.04, 0.62)	0.008
	SAD:OCD	0.50 (0.19, 1.36)	0.175
Age	Per Year Increase	0.82 (0.71, 0.95)	0.006
Treatment	Paroxetine: Placebo	7.13 (2.46, 20.69)	<0.001

There were no statistically significant treatment by covariate interactions ($P>0.29$).

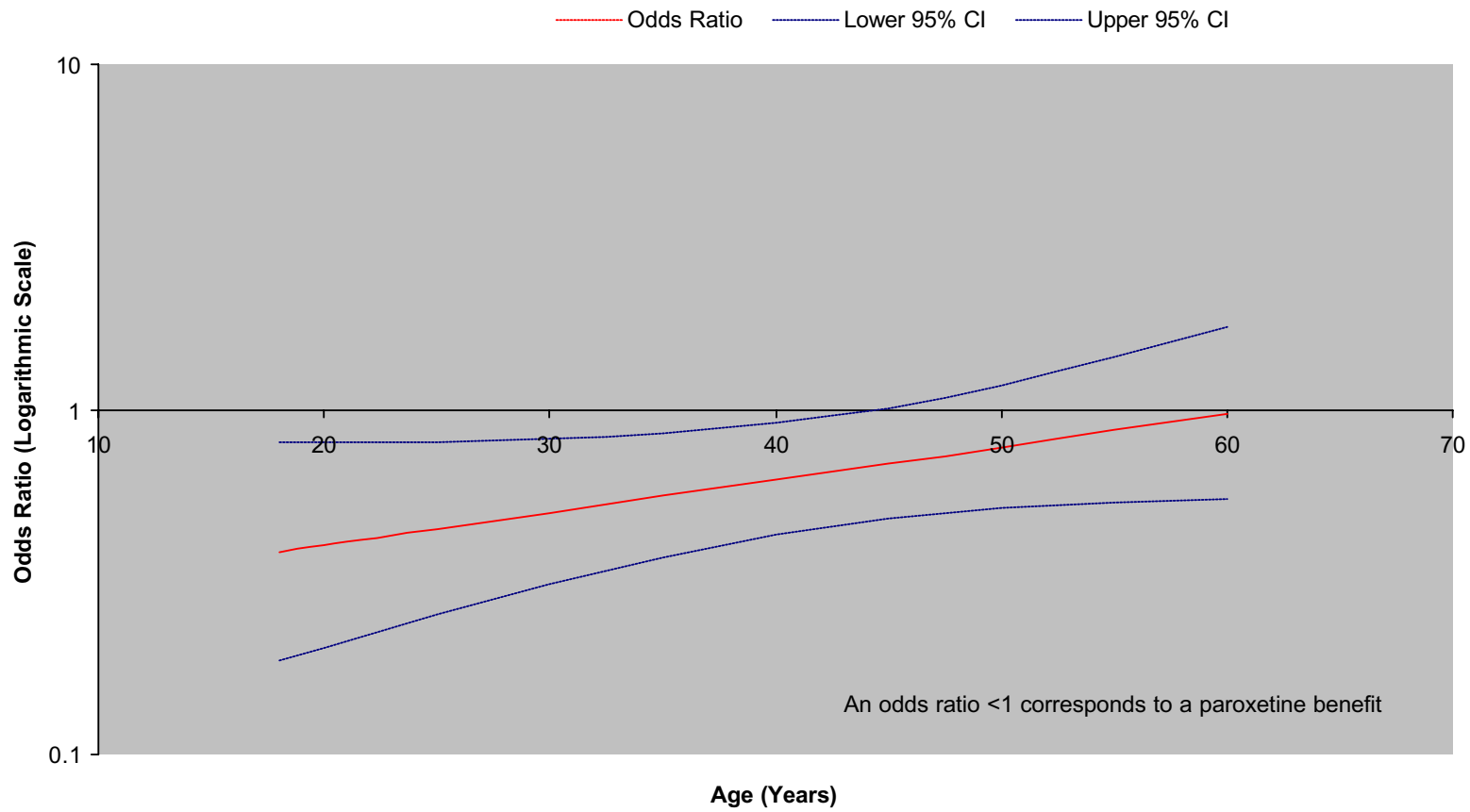
EMA Figure 3.01
Odds Ratio (Paroxetine relative to Placebo) and 95% CI for Possibly Suicide Related AEs by Age
On Therapy, Adult Placebo Controlled Trials



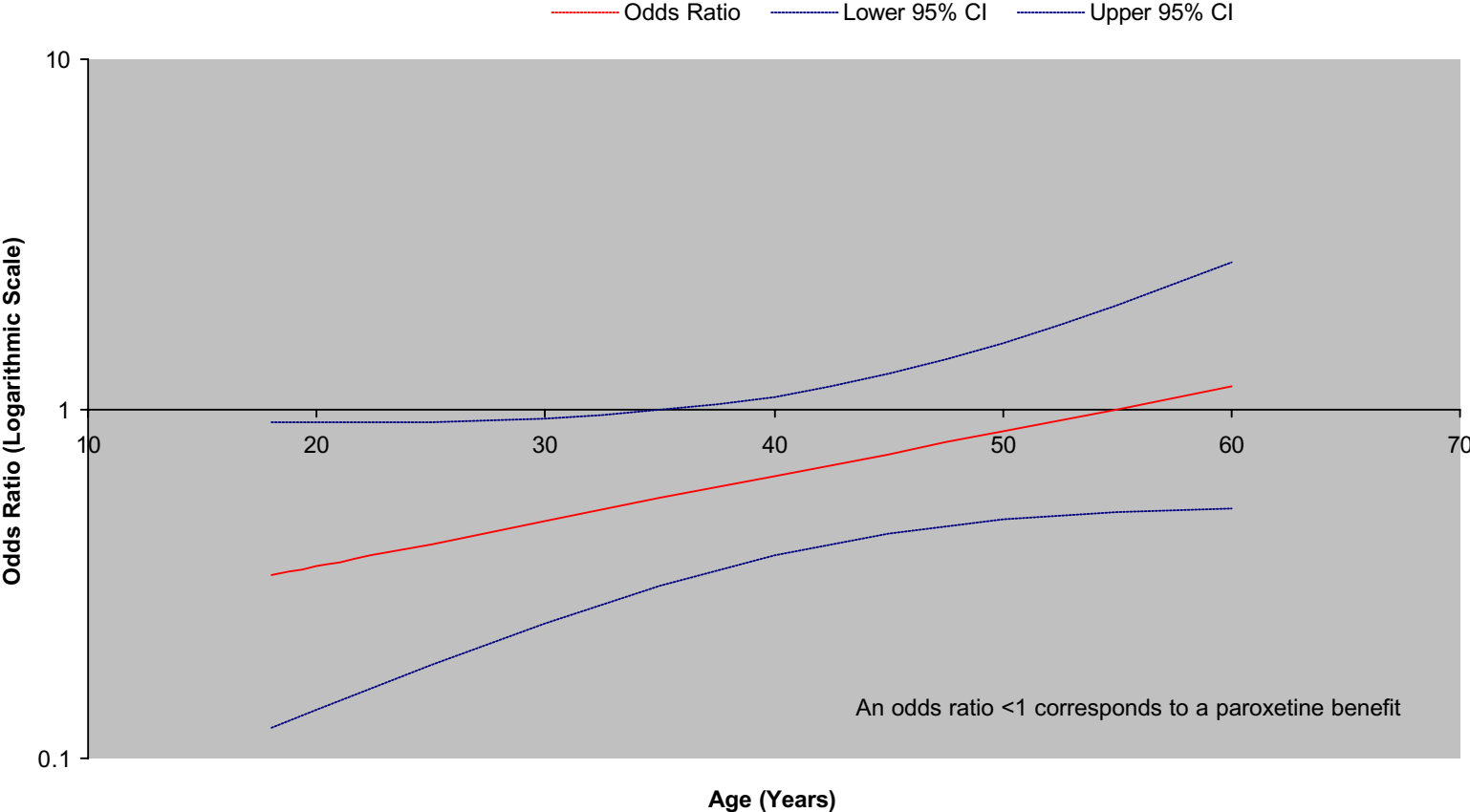
EMA Figure 3.02
Odds Ratio (Paroxetine relative to Placebo) and 95% CI for Self Harm by Age
On Therapy, Adult Placebo Controlled Trials



EMA Figure 3.03
Odds Ratio (Paroxetine relative to Comparator) and 95% CI for Possibly Suicide Related AEs by Age
On Therapy, Adult Active Controlled Trials



EMA Figure 3.04
Odds Ratio (Paroxetine relative to Comparator) and 95% CI for Self Harm by Age
On Therapy, Adult Active Controlled Trials



EMEA Table 3.01
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Age Group
 Adult Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
<18 years	n/N (%)	0/5 (0.0%)	0/1 (0.0%)		
	PYE	2	0		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	31/1727 (1.8%)	17/1204 (1.4%)	1.28 (0.70, 2.32)	0.46
	PYE	363	259		
	n/PYE	0.09	0.07		
30-39 years	n/N (%)	18/2550 (0.7%)	18/1728 (1.0%)	0.68 (0.35, 1.30)	0.24
	PYE	576	390		
	n/PYE	0.03	0.05		
40-49 years	n/N (%)	12/2270 (0.5%)	11/1515 (0.7%)	0.73 (0.32, 1.65)	0.52
	PYE	539	356		
	n/PYE	0.02	0.03		
50-59 years	n/N (%)	3/1152 (0.3%)	9/807 (1.1%)	0.23 (0.06, 0.86)	0.034
	PYE	274	186		
	n/PYE	0.01	0.05		
60-69 years	n/N (%)	0/530 (0.0%)	0/381 (0.0%)		
	PYE	116	87		
	n/PYE	0.00	0.00		
70+ years	n/N (%)	2/247 (0.8%)	0/172 (0.0%)		0.51
	PYE	46	35		
	n/PYE	0.04	0.00		

Includes paroxetine and placebo data from multiple arm trials with active controls

EMEA Table 3.02
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Age Group
 Adult Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	92/8481 (1.1%)	63/5808 (1.1%)	1.00 (0.72, 1.38)	1.00
	PYE	1916	1313		
	n/PYE	0.05	0.05		
<18 years	n/N (%)	0/5 (0.0%)	0/1 (0.0%)		
	PYE	2	0		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	42/1727 (2.4%)	18/1204 (1.5%)	1.64 (0.94, 2.87)	0.085
	PYE	363	259		
	n/PYE	0.12	0.07		
30-39 years	n/N (%)	25/2550 (1.0%)	22/1728 (1.3%)	0.77 (0.43, 1.37)	0.37
	PYE	576	390		
	n/PYE	0.04	0.06		
40-49 years	n/N (%)	20/2270 (0.9%)	14/1515 (0.9%)	0.95 (0.48, 1.89)	1.00
	PYE	539	356		
	n/PYE	0.04	0.04		
50-59 years	n/N (%)	3/1152 (0.3%)	9/807 (1.1%)	0.23 (0.06, 0.86)	0.034
	PYE	274	186		
	n/PYE	0.01	0.05		
60-69 years	n/N (%)	0/530 (0.0%)	0/381 (0.0%)		
	PYE	116	87		
	n/PYE	0.00	0.00		
70+ years	n/N (%)	2/247 (0.8%)	0/172 (0.0%)		0.51
	PYE	46	35		
	n/PYE	0.04	0.00		

Includes paroxetine and placebo data from multiple arm trials with active controls

EMEA Table 3.03
 Incidence and Incidence Density for Self Harm by Treatment Group and Age Group
 Adult Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	51/8481 (0.6%)	38/5808 (0.7%)	0.92 (0.60, 1.40)	0.75
	PYE	1916	1313		
	n/PYE	0.03	0.03		
<18 years	n/N (%)	0/5 (0.0%)	0/1 (0.0%)		
	PYE	2	0		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	27/1727 (1.6%)	12/1204 (1.0%)	1.58 (0.80, 3.13)	0.25
	PYE	363	259		
	n/PYE	0.07	0.05		
30-39 years	n/N (%)	12/2550 (0.5%)	15/1728 (0.9%)	0.54 (0.25, 1.16)	0.12
	PYE	576	390		
	n/PYE	0.02	0.04		
40-49 years	n/N (%)	9/2270 (0.4%)	8/1515 (0.5%)	0.75 (0.29, 1.95)	0.62
	PYE	539	356		
	n/PYE	0.02	0.02		
50-59 years	n/N (%)	2/1152 (0.2%)	3/807 (0.4%)	0.47 (0.08, 2.80)	0.41
	PYE	274	186		
	n/PYE	0.01	0.02		
60-69 years	n/N (%)	0/530 (0.0%)	0/381 (0.0%)		
	PYE	116	87		
	n/PYE	0.00	0.00		
70+ years	n/N (%)	1/247 (0.4%)	0/172 (0.0%)		1.00
	PYE	46	35		
	n/PYE	0.02	0.00		

Includes paroxetine and placebo data from multiple arm trials with active controls

EMEA Table 3.04
 Incidence and Incidence Density for Self Harm by Treatment Group and Age Group
 Adult Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	63/8481 (0.7%)	41/5808 (0.7%)	1.05 (0.71, 1.56)	0.84
	PYE	1916	1313		
	n/PYE	0.03	0.03		
<18 years	n/N (%)	0/5 (0.0%)	0/1 (0.0%)		
	PYE	2	0		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	33/1727 (1.9%)	12/1204 (1.0%)	1.94 (1.00, 3.76)	0.048
	PYE	363	259		
	n/PYE	0.09	0.05		
30-39 years	n/N (%)	15/2550 (0.6%)	17/1728 (1.0%)	0.60 (0.30, 1.20)	0.15
	PYE	576	390		
	n/PYE	0.03	0.04		
40-49 years	n/N (%)	12/2270 (0.5%)	9/1515 (0.6%)	0.89 (0.37, 2.12)	0.83
	PYE	539	356		
	n/PYE	0.02	0.03		
50-59 years	n/N (%)	2/1152 (0.2%)	3/807 (0.4%)	0.47 (0.08, 2.80)	0.41
	PYE	274	186		
	n/PYE	0.01	0.02		
60-69 years	n/N (%)	0/530 (0.0%)	0/381 (0.0%)		
	PYE	116	87		
	n/PYE	0.00	0.00		
70+ years	n/N (%)	1/247 (0.4%)	0/172 (0.0%)		1.00
	PYE	46	35		
	n/PYE	0.02	0.00		

Includes paroxetine and placebo data from multiple arm trials with active controls

EMEA Table 3.05
 Incidence and Incidence Density for Hostility by Treatment Group and Age Group
 Adult Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		
<18 years	n/N (%)	0/5 (0.0%)	0/1 (0.0%)		
	PYE	2	0		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	8/1727 (0.5%)	7/1204 (0.6%)	0.80 (0.29, 2.20)	0.79
	PYE	363	259		
	n/PYE	0.02	0.03		
30-39 years	n/N (%)	7/2550 (0.3%)	4/1728 (0.2%)	1.19 (0.35, 4.06)	1.00
	PYE	576	390		
	n/PYE	0.01	0.01		
40-49 years	n/N (%)	7/2270 (0.3%)	2/1515 (0.1%)	2.34 (0.49, 11.28)	0.33
	PYE	539	356		
	n/PYE	0.01	0.01		
50-59 years	n/N (%)	1/1152 (0.1%)	0/807 (0.0%)		1.00
	PYE	274	186		
	n/PYE	0.00	0.00		
60-69 years	n/N (%)	1/530 (0.2%)	3/381 (0.8%)	0.24 (0.02, 2.30)	0.31
	PYE	116	87		
	n/PYE	0.01	0.03		
70+ years	n/N (%)	0/247 (0.0%)	0/172 (0.0%)		
	PYE	46	35		
	n/PYE	0.00	0.00		

Includes paroxetine and placebo data from multiple arm trials with active controls

EMEA Table 3.06
 Incidence and Incidence Density for Hostility by Treatment Group and Age Group
 Adult Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	32/8481 (0.4%)	16/5808 (0.3%)	1.37 (0.75, 2.50)	0.38
	PYE	1916	1313		
	n/PYE	0.02	0.01		
<18 years	n/N (%)	0/5 (0.0%)	0/1 (0.0%)	1.00 (0.38, 2.62)	1.00
	PYE	2	0		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	10/1727 (0.6%)	7/1204 (0.6%)	1.70 (0.53, 5.42)	0.43
	PYE	363	259		
	n/PYE	0.03	0.03		
30-39 years	n/N (%)	9/2270 (0.4%)	2/1515 (0.1%)	3.01 (0.65, 13.96)	0.22
	PYE	539	356		
	n/PYE	0.02	0.01		
40-49 years	n/N (%)	2/1152 (0.2%)	0/807 (0.0%)	0.24 (0.02, 2.30)	0.31
	PYE	274	186		
	n/PYE	0.01	0.00		
50-59 years	n/N (%)	1/530 (0.2%)	3/381 (0.8%)	0.24 (0.02, 2.30)	0.31
	PYE	116	87		
	n/PYE	0.01	0.03		
60-69 years	n/N (%)	0/247 (0.0%)	0/172 (0.0%)		
	PYE	46	35		
	n/PYE	0.00	0.00		

Includes paroxetine and placebo data from multiple arm trials with active controls

EMEA Table 3.07
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Age Group
 Adult Active Control Trials
 On-Therapy

Age Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
<18 years	n/N (%)	0/4 (0.0%)	0/6 (0.0%)	0.40 (0.18, 0.85)	0.016
	PYE	1	1		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	10/969 (1.0%)	20/779 (2.6%)	0.96 (0.42, 2.21)	1.00
	PYE	170	132		
	n/PYE	0.06	0.15		
30-39 years	n/N (%)	13/1544 (0.8%)	10/1146 (0.9%)	0.66 (0.30, 1.45)	0.31
	PYE	281	214		
	n/PYE	0.05	0.05		
40-49 years	n/N (%)	12/1647 (0.7%)	13/1182 (1.1%)	0.51 (0.22, 1.19)	0.14
	PYE	278	210		
	n/PYE	0.04	0.06		
50-59 years	n/N (%)	9/1038 (0.9%)	14/835 (1.7%)	1.06 (0.33, 3.34)	1.00
	PYE	187	138		
	n/PYE	0.05	0.10		
60-69 years	n/N (%)	7/831 (0.8%)	5/626 (0.8%)	3.43 (0.38, 30.86)	0.38
	PYE	139	92		
	n/PYE	0.05	0.05		
70+ years	n/N (%)	4/457 (0.9%)	1/390 (0.3%)	0.66 (0.30, 1.45)	0.31
	PYE	74	54		
	n/PYE	0.05	0.02		
Unknown	n/N (%)	0/32 (0.0%)	0/5 (0.0%)	0.66 (0.30, 1.45)	0.31
	PYE	4	0		
	n/PYE	0.00	0.00		

Includes paroxetine and active control data from multiple arm trials with placebo

EMEA Table 3.08
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Age Group
 Adult Active Control Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	79/6522 (1.2%)	76/4969 (1.5%)	0.79 (0.57, 1.08)	0.17
	PYE	1135	842		
	n/PYE	0.07	0.09		
<18 years	n/N (%)	0/4 (0.0%)	0/6 (0.0%)		
	PYE	1	1		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	19/969 (2.0%)	22/779 (2.8%)	0.69 (0.37, 1.28)	0.27
	PYE	170	132		
	n/PYE	0.11	0.17		
30-39 years	n/N (%)	19/1544 (1.2%)	15/1146 (1.3%)	0.94 (0.48, 1.86)	0.86
	PYE	281	214		
	n/PYE	0.07	0.07		
40-49 years	n/N (%)	16/1647 (1.0%)	16/1182 (1.4%)	0.71 (0.36, 1.44)	0.37
	PYE	278	210		
	n/PYE	0.06	0.08		
50-59 years	n/N (%)	14/1038 (1.3%)	15/835 (1.8%)	0.75 (0.36, 1.56)	0.46
	PYE	187	138		
	n/PYE	0.07	0.11		
60-69 years	n/N (%)	7/831 (0.8%)	6/626 (1.0%)	0.88 (0.29, 2.63)	1.00
	PYE	139	92		
	n/PYE	0.05	0.07		
70+ years	n/N (%)	4/457 (0.9%)	2/390 (0.5%)	1.71 (0.31, 9.40)	0.69
	PYE	74	54		
	n/PYE	0.05	0.04		
Unknown	n/N (%)	0/32 (0.0%)	0/5 (0.0%)		
	PYE	4	0		
	n/PYE	0.00	0.00		

Includes paroxetine and active control data from multiple arm trials with placebo

EMEA Table 3.09
 Incidence and Incidence Density for Self Harm by Treatment Group and Age Group
 Adult Active Control Trials
 On-Therapy

Age Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	29/6522 (0.4%)	32/4969 (0.6%)	0.69 (0.42, 1.14)	0.16
	PYE	1135	842		
	n/PYE	0.03	0.04		
<18 years	n/N (%)	0/4 (0.0%)	0/6 (0.0%)		
	PYE	1	1		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	6/969 (0.6%)	12/779 (1.5%)	0.40 (0.15, 1.07)	0.092
	PYE	170	132		
	n/PYE	0.04	0.09		
30-39 years	n/N (%)	7/1544 (0.5%)	4/1146 (0.3%)	1.30 (0.38, 4.45)	0.77
	PYE	281	214		
	n/PYE	0.02	0.02		
40-49 years	n/N (%)	5/1647 (0.3%)	6/1182 (0.5%)	0.60 (0.18, 1.96)	0.54
	PYE	278	210		
	n/PYE	0.02	0.03		
50-59 years	n/N (%)	3/1038 (0.3%)	7/835 (0.8%)	0.34 (0.09, 1.33)	0.12
	PYE	187	138		
	n/PYE	0.02	0.05		
60-69 years	n/N (%)	5/831 (0.6%)	3/626 (0.5%)	1.26 (0.30, 5.28)	1.00
	PYE	139	92		
	n/PYE	0.04	0.03		
70+ years	n/N (%)	3/457 (0.7%)	0/390 (0.0%)		0.25
	PYE	74	54		
	n/PYE	0.04	0.00		
Unknown	n/N (%)	0/32 (0.0%)	0/5 (0.0%)		
	PYE	4	0		
	n/PYE	0.00	0.00		

Includes paroxetine and active control data from multiple arm trials with placebo

EMEA Table 3.10
 Incidence and Incidence Density for Self Harm by Treatment Group and Age Group
 Adult Active Control Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	42/6522 (0.6%)	42/4969 (0.8%)	0.76 (0.49, 1.17)	0.22
	PYE	1135	842		
	n/PYE	0.04	0.05		
<18 years	n/N (%)	0/4 (0.0%)	0/6 (0.0%)		
	PYE	1	1		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	11/969 (1.1%)	13/779 (1.7%)	0.68 (0.30, 1.52)	0.41
	PYE	170	132		
	n/PYE	0.06	0.10		
30-39 years	n/N (%)	9/1544 (0.6%)	7/1146 (0.6%)	0.95 (0.35, 2.57)	1.00
	PYE	281	214		
	n/PYE	0.03	0.03		
40-49 years	n/N (%)	7/1647 (0.4%)	9/1182 (0.8%)	0.56 (0.21, 1.50)	0.31
	PYE	278	210		
	n/PYE	0.03	0.04		
50-59 years	n/N (%)	7/1038 (0.7%)	8/835 (1.0%)	0.70 (0.25, 1.94)	0.60
	PYE	187	138		
	n/PYE	0.04	0.06		
60-69 years	n/N (%)	5/831 (0.6%)	4/626 (0.6%)	0.94 (0.25, 3.52)	1.00
	PYE	139	92		
	n/PYE	0.04	0.04		
70+ years	n/N (%)	3/457 (0.7%)	1/390 (0.3%)	2.57 (0.27, 24.81)	0.63
	PYE	74	54		
	n/PYE	0.04	0.02		
Unknown	n/N (%)	0/32 (0.0%)	0/5 (0.0%)		
	PYE	4	0		
	n/PYE	0.00	0.00		

Includes paroxetine and active control data from multiple arm trials with placebo

EMEA Table 3.11
 Incidence and Incidence Density for Hostility by Treatment Group and Age Group
 Adult Active Control Trials
 On-Therapy

Age Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		
<18 years	n/N (%)	0/4 (0.0%)	0/6 (0.0%)	0.60 (0.13, 2.70)	0.71
	PYE	1	1		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	3/969 (0.3%)	4/779 (0.5%)	0.62 (0.19, 2.03)	0.54
	PYE	170	132		
	n/PYE	0.02	0.03		
30-39 years	n/N (%)	4/1647 (0.2%)	7/1182 (0.6%)	0.41 (0.12, 1.40)	0.22
	PYE	278	210		
	n/PYE	0.01	0.03		
40-49 years	n/N (%)	4/1038 (0.4%)	1/835 (0.1%)	3.23 (0.36, 28.92)	0.39
	PYE	187	138		
	n/PYE	0.02	0.01		
50-59 years	n/N (%)	1/831 (0.1%)	0/626 (0.0%)	0.43 (0.04, 4.71)	0.60
	PYE	139	92		
	n/PYE	0.01	0.00		
60-69 years	n/N (%)	1/457 (0.2%)	2/390 (0.5%)	0.43 (0.04, 4.71)	0.60
	PYE	74	54		
	n/PYE	0.01	0.04		
70+ years	n/N (%)	1/457 (0.2%)	2/390 (0.5%)	0.43 (0.04, 4.71)	0.60
	PYE	74	54		
	n/PYE	0.01	0.04		
Unknown	n/N (%)	0/32 (0.0%)	0/5 (0.0%)		
	PYE	4	0		
	n/PYE	0.00	0.00		

Includes paroxetine and active control data from multiple arm trials with placebo

EMEA Table 3.12
 Incidence and Incidence Density for Hostility by Treatment Group and Age Group
 Adult Active Control Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	22/6522 (0.3%)	22/4969 (0.4%)	0.76 (0.42, 1.38)	0.37
	PYE	1135	842		
	n/PYE	0.02	0.03		
<18 years	n/N (%)	0/4 (0.0%)	0/6 (0.0%)		
	PYE	1	1		
	n/PYE	0.00	0.00		
18-29 years	n/N (%)	4/969 (0.4%)	5/779 (0.6%)	0.64 (0.17, 2.40)	0.52
	PYE	170	132		
	n/PYE	0.02	0.04		
30-39 years	n/N (%)	5/1544 (0.3%)	6/1146 (0.5%)	0.62 (0.19, 2.03)	0.54
	PYE	281	214		
	n/PYE	0.02	0.03		
40-49 years	n/N (%)	7/1647 (0.4%)	8/1182 (0.7%)	0.63 (0.23, 1.73)	0.43
	PYE	278	210		
	n/PYE	0.03	0.04		
50-59 years	n/N (%)	4/1038 (0.4%)	1/835 (0.1%)	3.23 (0.36, 28.92)	0.39
	PYE	187	138		
	n/PYE	0.02	0.01		
60-69 years	n/N (%)	1/831 (0.1%)	0/626 (0.0%)		1.00
	PYE	139	92		
	n/PYE	0.01	0.00		
70+ years	n/N (%)	1/457 (0.2%)	2/390 (0.5%)	0.43 (0.04, 4.71)	0.60
	PYE	74	54		
	n/PYE	0.01	0.04		
Unknown	n/N (%)	0/32 (0.0%)	0/5 (0.0%)		
	PYE	4	0		
	n/PYE	0.00	0.00		

Includes paroxetine and active control data from multiple arm trials with placebo

EMEA Table 3.13
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
< 12 years	n/N (%)	0/205 (0.0%)	0/194 (0.0%)		
	PYE	41	40		
	n/PYE	0.00	0.00		
>=12 years	n/N (%)	18/533 (3.4%)	7/453 (1.5%)	2.23 (0.92, 5.38)	0.10
	PYE	135	108		
	n/PYE	0.13	0.06		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.13a
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Modified Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
< 12 years	n/N (%)	0/205 (0.0%)	0/194 (0.0%)		
	PYE	41	40		
	n/PYE	0.00	0.00		
12-15 years	n/N (%)	10/329 (3.0%)	5/269 (1.9%)	1.66 (0.56, 4.90)	0.44
	PYE	82	66		
	n/PYE	0.12	0.08		
≥16 years	n/N (%)	8/204 (3.9%)	2/184 (1.1%)	3.71 (0.78, 17.72)	0.11
	PYE	53	42		
	n/PYE	0.15	0.05		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.14
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	25/738 (3.4%)	8/647 (1.2%)	2.80 (1.25, 6.25)	0.012
	PYE	176	149		
	n/PYE	0.14	0.05		
< 12 years	n/N (%)	1/205 (0.5%)	0/194 (0.0%)		1.00
	PYE	41	40		
	n/PYE	0.02	0.00		
>=12 years	n/N (%)	24/533 (4.5%)	8/453 (1.8%)	2.62 (1.17, 5.90)	0.018
	PYE	135	108		
	n/PYE	0.18	0.07		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.14a
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Modified Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	25/738 (3.4%)	8/647 (1.2%)	2.80 (1.25, 6.25)	0.012
	PYE	176	149		
	n/PYE	0.14	0.05		
< 12 years	n/N (%)	1/205 (0.5%)	0/194 (0.0%)	1.00	1.00
	PYE	41	40		
	n/PYE	0.02	0.00		
12-15 years	n/N (%)	13/329 (4.0%)	6/269 (2.2%)	1.80 (0.68, 4.81)	0.25
	PYE	82	66		
	n/PYE	0.16	0.09		
≥16 years	n/N (%)	11/204 (5.4%)	2/184 (1.1%)	5.19 (1.13, 23.72)	0.022
	PYE	53	42		
	n/PYE	0.21	0.05		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.15
 Incidence and Incidence Density for Self Harm by Treatment Group and Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	15/738 (2.0%)	5/647 (0.8%)	2.66 (0.96, 7.37)	0.069
	PYE	176	149		
	n/PYE	0.09	0.03		
< 12 years	n/N (%)	0/205 (0.0%)	0/194 (0.0%)		
	PYE	41	40		
	n/PYE	0.00	0.00		
>=12 years	n/N (%)	15/533 (2.8%)	5/453 (1.1%)	2.59 (0.94, 7.20)	0.070
	PYE	135	108		
	n/PYE	0.11	0.05		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.15a
 Incidence and Incidence Density for Self Harm by Treatment Group and Modified Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	15/738 (2.0%)	5/647 (0.8%)	2.66 (0.96, 7.37)	0.069
	PYE	176	149		
	n/PYE	0.09	0.03		
< 12 years	n/N (%)	0/205 (0.0%)	0/194 (0.0%)		
	PYE	41	40		
	n/PYE	0.00	0.00		
12-15 years	n/N (%)	7/329 (2.1%)	4/269 (1.5%)	1.44 (0.42, 4.97)	0.76
	PYE	82	66		
	n/PYE	0.09	0.06		
≥16 years	n/N (%)	8/204 (3.9%)	1/184 (0.5%)	7.47 (0.93, 60.31)	0.039
	PYE	53	42		
	n/PYE	0.15	0.02		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.16
 Incidence and Incidence Density for Self Harm by Treatment Group and Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	5/647 (0.8%)	3.21 (1.19, 8.70)	0.019
	PYE	176	149		
	n/PYE	0.10	0.03		
< 12 years	n/N (%)	0/205 (0.0%)	0/194 (0.0%)		
	PYE	41	40		
	n/PYE	0.00	0.00		
>=12 years	n/N (%)	18/533 (3.4%)	5/453 (1.1%)	3.13 (1.15, 8.50)	0.020
	PYE	135	108		
	n/PYE	0.13	0.05		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.16a
 Incidence and Incidence Density for Self Harm by Treatment Group and Modified Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	5/647 (0.8%)	3.21 (1.19, 8.70)	0.019
	PYE	176	149		
	n/PYE	0.10	0.03		
< 12 years	n/N (%)	0/205 (0.0%)	0/194 (0.0%)	1.86 (0.57, 6.12)	0.40
	PYE	41	40		
	n/PYE	0.00	0.00		
12-15 years	n/N (%)	9/329 (2.7%)	4/269 (1.5%)	8.45 (1.06, 67.33)	0.022
	PYE	82	66		
	n/PYE	0.11	0.06		
≥16 years	n/N (%)	9/204 (4.4%)	1/184 (0.5%)		
	PYE	53	42		
	n/PYE	0.17	0.02		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.17
 Incidence and Incidence Density for Hostility by Treatment Group and Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
< 12 years	n/N (%)	15/205 (7.3%)	1/194 (0.5%)	15.24 (1.99, 116.5)	<0.001
	PYE	41	40		
	n/PYE	0.36	0.02		
>=12 years	n/N (%)	12/533 (2.3%)	3/453 (0.7%)	3.45 (0.97, 12.32)	0.064
	PYE	135	108		
	n/PYE	0.09	0.03		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.17a
 Incidence and Incidence Density for Hostility by Treatment Group and Modified Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
< 12 years	n/N (%)	15/205 (7.3%)	1/194 (0.5%)	15.24 (1.99, 116.5)	<0.001
	PYE	41	40		
	n/PYE	0.36	0.02		
12-15 years	n/N (%)	10/329 (3.0%)	3/269 (1.1%)	2.78 (0.76, 10.20)	0.16
	PYE	82	66		
	n/PYE	0.12	0.05		
>=16 years	n/N (%)	2/204 (1.0%)	0/184 (0.0%)		0.50
	PYE	53	42		
	n/PYE	0.04	0.00		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.18
 Incidence and Incidence Density for Hostility by Treatment Group and Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	28/738 (3.8%)	4/647 (0.6%)	6.34 (2.21, 18.17)	<0.001
	PYE	176	149		
	n/PYE	0.16	0.03		
< 12 years	n/N (%)	15/205 (7.3%)	1/194 (0.5%)	15.24 (1.99, 116.5)	<0.001
	PYE	41	40		
	n/PYE	0.36	0.02		
>=12 years	n/N (%)	13/533 (2.4%)	3/453 (0.7%)	3.75 (1.06, 13.24)	0.040
	PYE	135	108		
	n/PYE	0.10	0.03		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.18a
 Incidence and Incidence Density for Hostility by Treatment Group and Modified Age Group
 Paediatric Placebo Controlled Trials
 On-Therapy plus 30 days post-therapy

Age Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	28/738 (3.8%)	4/647 (0.6%)	6.34 (2.21, 18.17)	<0.001
	PYE	176	149		
	n/PYE	0.16	0.03		
< 12 years	n/N (%)	15/205 (7.3%)	1/194 (0.5%)	15.24 (1.99, 116.5)	<0.001
	PYE	41	40		
	n/PYE	0.36	0.02		
12-15 years	n/N (%)	11/329 (3.3%)	3/269 (1.1%)	3.07 (0.85, 11.11)	0.10
	PYE	82	66		
	n/PYE	0.13	0.05		
≥16 years	n/N (%)	2/204 (1.0%)	0/184 (0.0%)		0.50
	PYE	53	42		
	n/PYE	0.04	0.00		

Includes studies 329, 377, 676, 701, 704 and placebo controlled phase of 453

EMEA Table 3.19
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Gender
 Adult Placebo Controlled Trials
 On-Therapy

Gender		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Female	n/N (%)	40/5236 (0.8%)	35/3558 (1.0%)	0.77 (0.49, 1.22)	0.29
	PYE	1234	825		
	n/PYE	0.03	0.04		
Male	n/N (%)	26/3245 (0.8%)	20/2250 (0.9%)	0.90 (0.50, 1.62)	0.76
	PYE	682	487		
	n/PYE	0.04	0.04		

EMA Table 3.20
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Race
 Adult Placebo Controlled Trials
 On-Therapy

Race Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
White	n/N (%)	60/7532 (0.8%)	54/5176 (1.0%)	0.76 (0.53, 1.10)	0.15
	PYE	1755	1191		
	n/PYE	0.03	0.05		
Black	n/N (%)	4/429 (0.9%)	0/257 (0.0%)	1.37 (0.12, 15.14)	1.00
	PYE	72	48		
	n/PYE	0.06	0.00		
Other	n/N (%)	2/460 (0.4%)	1/314 (0.3%)	1.37 (0.12, 15.14)	1.00
	PYE	76	60		
	n/PYE	0.03	0.02		
Unknown	n/N (%)	0/60 (0.0%)	0/61 (0.0%)		
	PYE	13	13		
	n/PYE	0.00	0.00		

EMEA Table 3.21
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Severity of Disease
 Adult Placebo Controlled Trials
 On-Therapy

Disease Severity		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Normal	n/N (%)	6/559 (1.1%)	7/583 (1.2%)	0.89 (0.30, 2.67)	1.00
	PYE	293	245		
	n/PYE	0.02	0.03		
Mild to Moderate	n/N (%)	34/4973 (0.7%)	24/3196 (0.8%)	0.91 (0.54, 1.54)	0.79
	PYE	1016	667		
	n/PYE	0.03	0.04		
Severe	n/N (%)	26/2785 (0.9%)	22/1897 (1.2%)	0.80 (0.45, 1.42)	0.46
	PYE	574	371		
	n/PYE	0.05	0.06		
Unknown	n/N (%)	0/164 (0.0%)	2/132 (1.5%)		0.20
	PYE	32	29		
	n/PYE	0.00	0.07		

EMEA Table 3.22
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and CR vs IR vs CRIR
 Adult Placebo Controlled Trials
 On-Therapy

CR vs IR vs CRIR		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		0.28
CR	n/N (%)	4/2008 (0.2%)	2/1413 (0.1%)	1.41 (0.26, 7.70)	1.00
	PYE	407	279		
	n/PYE	0.01	0.01		0.72
CRIR	n/N (%)	6/649 (0.9%)	0/322 (0.0%)		0.19
	PYE	131	69		
	n/PYE	0.05	0.00		
IR	n/N (%)	56/5824 (1.0%)	53/4073 (1.3%)	0.74 (0.50, 1.07)	0.12
	PYE	1378	965		
	n/PYE	0.04	0.05		0.12

EMEA Table 3.23
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Medical History of Suicide or Overdose
 Adult Placebo Controlled Trials
 On-Therapy

Medical History		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Absent	n/N (%)	64/8446 (0.8%)	53/5775 (0.9%)	0.82 (0.57, 1.19)	0.30
	PYE	1909	1305		
	n/PYE	0.03	0.04		
Present	n/N (%)	2/35 (5.7%)	2/33 (6.1%)	0.94 (0.12, 7.08)	1.00
	PYE	7	8		
	n/PYE	0.28	0.27		

EMEA Table 3.24
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Psychotropic Medication
 Adult Placebo Controlled Trials
 On-Therapy

Psychotropic Medication		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Absent	n/N (%)	38/6578 (0.6%)	25/4308 (0.6%)	1.00 (0.60, 1.65)	1.00
	PYE	1420	933		
	n/PYE	0.03	0.03		
Present	n/N (%)	28/1903 (1.5%)	30/1500 (2.0%)	0.73 (0.44, 1.23)	0.29
	PYE	496	379		
	n/PYE	0.06	0.08		

EMEA Table 3.25
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Baseline Suicide Ideation
 Adult Placebo Controlled Trials
 On-Therapy

Baseline Suicide Ideation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		0.28
Absent	n/N (%)	51/8037 (0.6%)	34/5517 (0.6%)	1.03 (0.67, 1.59)	0.91
	PYE	1840	1262		
	n/PYE	0.03	0.03		0.90
Present	n/N (%)	15/444 (3.4%)	21/291 (7.2%)	0.45 (0.23, 0.89)	0.023
	PYE	76	51		
	n/PYE	0.20	0.41		0.029

EMEA Table 3.26
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Baseline Agitation
 Adult Placebo Controlled Trials
 On-Therapy

Baseline Agitation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Absent	n/N (%)	60/7546 (0.8%)	49/5262 (0.9%)	0.85 (0.58, 1.25)	0.43
	PYE	1766	1230		
	n/PYE	0.03	0.04		
Present	n/N (%)	6/935 (0.6%)	6/546 (1.1%)	0.58 (0.19, 1.81)	0.38
	PYE	150	83		
	n/PYE	0.04	0.07		

EMEA Table 3.27
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Agitation
 Adult Placebo Controlled Trials
 On-Therapy

Treatment Emergent Agitation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Absent	n/N (%)	64/8321 (0.8%)	54/5695 (0.9%)	0.81 (0.56, 1.16)	0.26
	PYE	1879	1289		
	n/PYE	0.03	0.04		
Present	n/N (%)	2/160 (1.3%)	1/113 (0.9%)	1.42 (0.13, 15.83)	1.00
	PYE	37	24		
	n/PYE	0.05	0.04		

EMEA Table 3.28
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Hyperkinesia
 Adult Placebo Controlled Trials
 On-Therapy

Treatment Emergent Hyperkinesia		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%) PYE n/PYE	66/8481 (0.8%) 1916 0.03	55/5808 (0.9%) 1313 0.04	0.82 (0.57, 1.18)	0.31 0.28
Absent	n/N (%) PYE n/PYE	65/8416 (0.8%) 1898 0.03	55/5784 (1.0%) 1307 0.04	0.81 (0.57, 1.16)	0.26 0.26
Present	n/N (%) PYE n/PYE	1/65 (1.5%) 18 0.06	0/24 (0.0%) 5 0.00		1.00

EMEA Table 3.29
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Hostility
 Adult Placebo Controlled Trials
 On-Therapy

Treatment Emergent Hostility		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		0.28
Absent	n/N (%)	66/8469 (0.8%)	55/5796 (0.9%)	0.82 (0.57, 1.17)	0.31
	PYE	1913	1310		
	n/PYE	0.03	0.04		0.28
Present	n/N (%)	0/12 (0.0%)	0/12 (0.0%)		
	PYE	3	3		
	n/PYE	0.00	0.00		

EMEA Table 3.30
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Early Treatment Emergent Agitation
 Adult Placebo Controlled Trials
 On-Therapy

Early Emergent Agitation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	66/8481 (0.8%)	55/5808 (0.9%)	0.82 (0.57, 1.18)	0.31
	PYE	1916	1313		
	n/PYE	0.03	0.04		
Absent	n/N (%)	64/8146 (0.8%)	55/5562 (1.0%)	0.79 (0.55, 1.14)	0.22
	PYE	1855	1271		
	n/PYE	0.03	0.04		
Present	n/N (%)	2/335 (0.6%)	0/246 (0.0%)		0.51
	PYE	61	41		
	n/PYE	0.03	0.00		

EMA Table 3.31
 Incidence and Incidence Density for Possibly suicide-related AEs by Dose and Indication
 Adult Placebo Controlled Trials
 On-Therapy

Dose Group		Depression	Other
Placebo	n/N (%)	35/568 (6.2%)	3/1000 (0.3%)
	PYE	119	228
	n/PYE	0.29	0.01
5 mg	n/N (%)		0/11 (0.0%)
	PYE		1
	n/PYE		0.00
10 mg	n/N (%)	3/355 (0.8%)	0/420 (0.0%)
	PYE	48	118
	n/PYE	0.06	0.00
20 mg	n/N (%)	9/377 (2.4%)	0/1028 (0.0%)
	PYE	51	232
	n/PYE	0.18	0.00
30 mg	n/N (%)	1/150 (0.7%)	
	PYE	17	
	n/PYE	0.06	
40 mg	n/N (%)	27/237 (11.4%)	0/637 (0.0%)
	PYE	72	124
	n/PYE	0.37	0.00
50 mg	n/N (%)	0/57 (0.0%)	
	PYE	10	
	n/PYE	0.00	
60 mg	n/N (%)		0/182 (0.0%)
	PYE		35
	n/PYE		0.00

EMEA Table 3.31a
 Incidence and Incidence Density for Possibly suicide-related AEs by Dose and Indication (Excluding Study 057)
 Adult Placebo Controlled Trials
 On-Therapy

Dose Group		Depression	Other
Placebo	n/N (%)	6/432 (1.4%)	3/1000 (0.3%)
	PYE	57	228
	n/PYE	0.11	0.01
5 mg	n/N (%)		0/11 (0.0%)
	PYE		1
	n/PYE		0.00
10 mg	n/N (%)	3/355 (0.8%)	0/420 (0.0%)
	PYE	48	118
	n/PYE	0.06	0.00
20 mg	n/N (%)	9/377 (2.4%)	0/1028 (0.0%)
	PYE	51	232
	n/PYE	0.18	0.00
30 mg	n/N (%)	1/150 (0.7%)	
	PYE	17	
	n/PYE	0.06	
40 mg	n/N (%)	0/106 (0.0%)	0/637 (0.0%)
	PYE	15	124
	n/PYE	0.00	0.00
50 mg	n/N (%)	0/57 (0.0%)	
	PYE	10	
	n/PYE	0.00	
60 mg	n/N (%)		0/182 (0.0%)
	PYE		35
	n/PYE		0.00

EMEA Table 3.32
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Gender
 Adult Active Control Trials
 On-Therapy

Gender		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
Female	n/N (%)	42/4344 (1.0%)	35/3292 (1.1%)	0.91 (0.58, 1.43)	0.73
	PYE	769	551		
	n/PYE	0.05	0.06		
Male	n/N (%)	13/2174 (0.6%)	28/1677 (1.7%)	0.35 (0.18, 0.69)	0.002
	PYE	366	291		
	n/PYE	0.04	0.10		
Unknown	n/N (%)	0/4 (0.0%)			
	PYE	0			
	n/PYE	0.00			

EMEA Table 3.33
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Race
 Adult Active Control Trials
 On-Therapy

Race Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
White	n/N (%)	32/4124 (0.8%)	49/3951 (1.2%)	0.62 (0.40, 0.97)	0.044
	PYE	770	681		
	n/PYE	0.04	0.07		
Black	n/N (%)	2/117 (1.7%)	1/95 (1.1%)	1.63 (0.15, 18.31)	1.00
	PYE	15	13		
	n/PYE	0.14	0.08		
Other	n/N (%)	2/237 (0.8%)	3/240 (1.3%)	0.67 (0.11, 4.06)	1.00
	PYE	38	30		
	n/PYE	0.05	0.10		
Unknown	n/N (%)	19/2044 (0.9%)	10/683 (1.5%)	0.63 (0.29, 1.36)	0.28
	PYE	312	118		
	n/PYE	0.06	0.09		

EMA Table 3.34
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Severity of Disease
 Adult Active Control Trials
 On-Therapy

Disease Severity		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
Normal	n/N (%)	0/18 (0.0%)	0/16 (0.0%)		
	PYE	3	4		
	n/PYE	0.00	0.00		
Mild to Moderate	n/N (%)	9/2072 (0.4%)	20/2022 (1.0%)	0.44 (0.20, 0.96)	0.040
	PYE	381	358		
	n/PYE	0.02	0.06		
Severe	n/N (%)	23/1898 (1.2%)	31/1771 (1.8%)	0.69 (0.40, 1.19)	0.22
	PYE	378	305		
	n/PYE	0.06	0.10		
Unknown	n/N (%)	23/2534 (0.9%)	12/1160 (1.0%)	0.88 (0.43, 1.77)	0.72
	PYE	373	175		
	n/PYE	0.06	0.07		

EMEA Table 3.35
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and CR vs IR vs CRIR
 Adult Active Control Trials
 On-Therapy

CR vs IR vs CRIR		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		0.019
CR	n/N (%)	1/197 (0.5%)	3/206 (1.5%)	0.35 (0.04, 3.35)	0.62
	PYE	21	22		
	n/PYE	0.05	0.14		0.37
IR	n/N (%)	54/6325 (0.9%)	60/4763 (1.3%)	0.67 (0.47, 0.98)	0.045
	PYE	1114	820		
	n/PYE	0.05	0.07		0.028

No adult active controlled trials contained both CR and IR doses

EMEA Table 3.36
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Medical History of Suicide or Overdose
 Adult Active Control Trials
 On-Therapy

Medical History		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
Absent	n/N (%)	55/6518 (0.8%)	63/4966 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1134	842		
	n/PYE	0.05	0.07		
Present	n/N (%)	0/4 (0.0%)	0/3 (0.0%)		
	PYE	1	0		
	n/PYE	0.00	0.00		

EMEA Table 3.37
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Psychotropic Medication
 Adult Active Control Trials
 On-Therapy

Psychotropic Medication		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
Absent	n/N (%)	38/5051 (0.8%)	38/3678 (1.0%)	0.73 (0.46, 1.14)	0.16
	PYE	847	613		
	n/PYE	0.04	0.06		
Present	n/N (%)	17/1471 (1.2%)	25/1291 (1.9%)	0.59 (0.32, 1.10)	0.12
	PYE	288	229		
	n/PYE	0.06	0.11		

EMEA Table 3.38
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Baseline Suicide Ideation
 Adult Active Control Trials
 On-Therapy

Baseline Suicide Ideation		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		0.019
Absent	n/N (%)	41/5787 (0.7%)	48/4387 (1.1%)	0.65 (0.42, 0.98)	0.041
	PYE	1012	757		
	n/PYE	0.04	0.06		0.035
Present	n/N (%)	14/735 (1.9%)	15/582 (2.6%)	0.73 (0.35, 1.53)	0.45
	PYE	123	85		
	n/PYE	0.11	0.18		0.24

EMEA Table 3.39
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Baseline Agitation
 Adult Active Control Trials
 On-Therapy

Baseline Agitation		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		
Absent	n/N (%)	36/4640 (0.8%)	46/3518 (1.3%)	0.59 (0.38, 0.91)	0.019
	PYE	825	610		
	n/PYE	0.04	0.08		
Present	n/N (%)	19/1882 (1.0%)	17/1451 (1.2%)	0.86 (0.45, 1.66)	0.74
	PYE	310	232		
	n/PYE	0.06	0.07		

EMEA Table 3.40
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Agitation
 Adult Active Control Trials
 On-Therapy

Treatment Emergent Agitation		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		0.019
Absent	n/N (%)	49/6355 (0.8%)	59/4824 (1.2%)	0.63 (0.43, 0.92)	0.019
	PYE	1100	813		
	n/PYE	0.04	0.07		0.011
Present	n/N (%)	6/167 (3.6%)	4/145 (2.8%)	1.31 (0.36, 4.75)	0.76
	PYE	35	29		
	n/PYE	0.17	0.14		0.70

EMEA Table 3.41
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Hyperkinesia
 Adult Active Control Trials
 On-Therapy

Treatment Emergent Hyperkinesia		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		0.019
Absent	n/N (%)	54/6483 (0.8%)	61/4940 (1.2%)	0.67 (0.46, 0.97)	0.037
	PYE	1120	835		
	n/PYE	0.05	0.07		0.026
Present	n/N (%)	1/39 (2.6%)	2/29 (6.9%)	0.36 (0.03, 4.12)	0.57
	PYE	15	8		
	n/PYE	0.07	0.26		0.27

EMEA Table 3.42
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Hostility
 Adult Active Control Trials
 On-Therapy

Treatment Emergent Hostility		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		0.019
Absent	n/N (%)	55/6509 (0.8%)	63/4956 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1133	840		
	n/PYE	0.05	0.08		0.018
Present	n/N (%)	0/13 (0.0%)	0/13 (0.0%)		
	PYE	2	2		
	n/PYE	0.00	0.00		

EMEA Table 3.43
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Early Treatment Emergent Agitation
 Adult Active Control Trials
 On-Therapy

Early Emergent Agitation		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	55/6522 (0.8%)	63/4969 (1.3%)	0.66 (0.46, 0.95)	0.031
	PYE	1135	842		
	n/PYE	0.05	0.07		0.019
Absent	n/N (%)	52/6190 (0.8%)	61/4650 (1.3%)	0.64 (0.44, 0.92)	0.021
	PYE	1067	791		
	n/PYE	0.05	0.08		0.015
Present	n/N (%)	3/332 (0.9%)	2/319 (0.6%)	1.45 (0.24, 8.71)	1.00
	PYE	68	51		
	n/PYE	0.04	0.04		0.89

EMEA Table 3.44
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Gender
 Paediatric Placebo Controlled Trials
 On-Therapy

Gender		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
Female	n/N (%)	15/418 (3.6%)	6/315 (1.9%)	1.92 (0.74, 5.00)	0.26
	PYE	105	73		
	n/PYE	0.14	0.08		
Male	n/N (%)	3/320 (0.9%)	1/332 (0.3%)	3.13 (0.32, 30.27)	0.36
	PYE	71	75		
	n/PYE	0.04	0.01		

EMEA Table 3.45
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Race
 Paediatric Placebo Controlled Trials
 On-Therapy

Race Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
White	n/N (%)	14/596 (2.3%)	4/534 (0.7%)	3.19 (1.04, 9.74)	0.034
	PYE	144	122		
	n/PYE	0.10	0.03		
Black	n/N (%)	1/33 (3.0%)	1/35 (2.9%)	1.06 (0.06, 17.71)	1.00
	PYE	7	7		
	n/PYE	0.14	0.14		
Other	n/N (%)	3/109 (2.8%)	2/78 (2.6%)	1.08 (0.18, 6.59)	1.00
	PYE	25	19		
	n/PYE	0.12	0.11		

EMEA Table 3.46
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Severity of Disease
 Paediatric Placebo Controlled Trials
 On-Therapy

Disease Severity		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
Normal	n/N (%)	0/48 (0.0%)	0/51 (0.0%)		
	PYE	11	10		
	n/PYE	0.00	0.00		
Mild to Moderate	n/N (%)	3/375 (0.8%)	2/298 (0.7%)	1.19 (0.20, 7.19)	1.00
	PYE	85	68		
	n/PYE	0.04	0.03		
Severe	n/N (%)	9/220 (4.1%)	3/207 (1.4%)	2.90 (0.77, 10.87)	0.14
	PYE	51	47		
	n/PYE	0.18	0.06		
Unknown	n/N (%)	6/95 (6.3%)	2/91 (2.2%)	3.00 (0.59, 15.27)	0.28
	PYE	29	23		
	n/PYE	0.21	0.09		

EMEA Table 3.47
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Medical History of Suicide or Overdose
 Paediatric Placebo Controlled Trials
 On-Therapy

Medical History		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
Absent	n/N (%)	18/738 (2.4%)	7/645 (1.1%)	2.28 (0.95, 5.49)	0.069
	PYE	176	148		
	n/PYE	0.10	0.05		
Present	n/N (%)		0/2 (0.0%)		
	PYE		0		
	n/PYE		0.00		

EMEA Table 3.48
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Psychotropic Medication
 Paediatric Placebo Controlled Trials
 On-Therapy

Psychotropic Medication		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		
Absent	n/N (%)	17/627 (2.7%)	7/519 (1.3%)	2.04 (0.84, 4.95)	0.15
	PYE	151	122		
	n/PYE	0.11	0.06		
Present	n/N (%)	1/111 (0.9%)	0/128 (0.0%)		0.46
	PYE	25	27		
	n/PYE	0.04	0.00		

EMEA Table 3.49
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Baseline Suicide Ideation
 Paediatric Placebo Controlled Trials
 On-Therapy

Baseline Suicide Ideation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		0.082
Absent	n/N (%)	12/680 (1.8%)	4/615 (0.7%)	2.74 (0.88, 8.55)	0.081
	PYE	165	141		
	n/PYE	0.07	0.03		0.10
Present	n/N (%)	6/58 (10.3%)	3/32 (9.4%)	1.12 (0.26, 4.80)	1.00
	PYE	11	8		
	n/PYE	0.54	0.38		0.62

EMEA Table 3.50
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Baseline Agitation
 Paediatric Placebo Controlled Trials
 On-Therapy

Baseline Agitation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		0.082
Absent	n/N (%)	14/684 (2.0%)	6/602 (1.0%)	2.08 (0.79, 5.44)	0.18
	PYE	160	138		
	n/PYE	0.09	0.04		0.15
Present	n/N (%)	4/54 (7.4%)	1/45 (2.2%)	3.52 (0.38, 32.69)	0.37
	PYE	16	10		
	n/PYE	0.25	0.10		0.39

EMEA Table 3.51
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Agitation
 Paediatric Placebo Controlled Trials
 On-Therapy

Treatment Emergent Agitation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		0.082
Absent	n/N (%)	17/718 (2.4%)	7/641 (1.1%)	2.20 (0.90, 5.33)	0.098
	PYE	172	148		
	n/PYE	0.10	0.05		0.10
Present	n/N (%)	1/20 (5.0%)	0/6 (0.0%)		1.00
	PYE	5	1		
	n/PYE	0.22	0.00		

EMEA Table 3.52
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Hyperkinesia
 Paediatric Placebo Controlled Trials
 On-Therapy

Treatment Emergent Hyperkinesia		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%) PYE n/PYE	18/738 (2.4%) 176 0.10	7/647 (1.1%) 149 0.05	2.29 (0.95, 5.51)	0.069 0.082
Absent	n/N (%) PYE n/PYE	18/711 (2.5%) 170 0.11	7/638 (1.1%) 147 0.05	2.34 (0.97, 5.64)	0.067 0.074
Present	n/N (%) PYE n/PYE	0/27 (0.0%) 6 0.00	0/9 (0.0%) 2 0.00		

EMEA Table 3.53
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Treatment Emergent Hostility
 Paediatric Placebo Controlled Trials
 On-Therapy

Treatment Emergent Hostility		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		0.082
Absent	n/N (%)	17/711 (2.4%)	7/644 (1.1%)	2.23 (0.92, 5.41)	0.097
	PYE	170	148		
	n/PYE	0.10	0.05		0.097
Present	n/N (%)	1/27 (3.7%)	0/3 (0.0%)		1.00
	PYE	6	1		
	n/PYE	0.17	0.00		

EMEA Table 3.54
 Incidence and Incidence Density for Possibly suicide-related AEs by Treatment Group and Early Treatment Emergent Agitation
 Paediatric Placebo Controlled Trials
 On-Therapy

Early Emergent Agitation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/738 (2.4%)	7/647 (1.1%)	2.29 (0.95, 5.51)	0.069
	PYE	176	149		
	n/PYE	0.10	0.05		0.082
Absent	n/N (%)	17/701 (2.4%)	6/606 (1.0%)	2.49 (0.97, 6.34)	0.058
	PYE	166	138		
	n/PYE	0.10	0.04		0.072
Present	n/N (%)	1/37 (2.7%)	1/41 (2.4%)	1.11 (0.07, 18.42)	1.00
	PYE	10	10		
	n/PYE	0.10	0.10		0.96

EMEA Table 3.55
 Incidence and Incidence Density for Hostility by Treatment Group and Gender
 Adult Placebo Controlled Trials
 On-Therapy

Gender		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		
Female	n/N (%)	12/5236 (0.2%)	11/3558 (0.3%)	0.74 (0.33, 1.68)	0.53
	PYE	1234	825		
	n/PYE	0.01	0.01		
Male	n/N (%)	12/3245 (0.4%)	5/2250 (0.2%)	1.67 (0.59, 4.74)	0.46
	PYE	682	487		
	n/PYE	0.02	0.01		

EMEA Table 3.56
 Incidence and Incidence Density for Hostility by Treatment Group and Race
 Adult Placebo Controlled Trials
 On-Therapy

Race Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		
White	n/N (%)	19/7532 (0.3%)	14/5176 (0.3%)	0.93 (0.47, 1.86)	0.86
	PYE	1755	1191		
	n/PYE	0.01	0.01		
Black	n/N (%)	2/429 (0.5%)	0/257 (0.0%)		0.53
	PYE	72	48		
	n/PYE	0.03	0.00		
Other	n/N (%)	3/460 (0.7%)	1/314 (0.3%)	2.05 (0.21, 19.84)	0.65
	PYE	76	60		
	n/PYE	0.04	0.02		
Unknown	n/N (%)	0/60 (0.0%)	1/61 (1.6%)		1.00
	PYE	13	13		
	n/PYE	0.00	0.08		

EMA Table 3.57
 Incidence and Incidence Density for Hostility by Treatment Group and Severity of Disease
 Adult Placebo Controlled Trials
 On-Therapy

Disease Severity		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		
Normal	n/N (%)	0/559 (0.0%)	3/583 (0.5%)		0.25
	PYE	293	245		
	n/PYE	0.00	0.01		
Mild to Moderate	n/N (%)	16/4973 (0.3%)	8/3196 (0.3%)	1.29 (0.55, 3.01)	0.68
	PYE	1016	667		
	n/PYE	0.02	0.01		
Severe	n/N (%)	6/2785 (0.2%)	5/1897 (0.3%)	0.82 (0.25, 2.68)	0.77
	PYE	574	371		
	n/PYE	0.01	0.01		
Unknown	n/N (%)	2/164 (1.2%)	0/132 (0.0%)		0.50
	PYE	32	29		
	n/PYE	0.06	0.00		

EMEA Table 3.58
 Incidence and Incidence Density for Hostility by Treatment Group and CR vs IR vs CRIR
 Adult Placebo Controlled Trials
 On-Therapy

CR vs IR vs CRIR		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		0.93
CR	n/N (%)	5/2008 (0.2%)	1/1413 (0.1%)	3.52 (0.41, 30.20)	0.41
	PYE	407	279		
	n/PYE	0.01	0.00		0.26
CRIR	n/N (%)	0/649 (0.0%)	0/322 (0.0%)		
	PYE	131	69		
	n/PYE	0.00	0.00		
IR	n/N (%)	19/5824 (0.3%)	15/4073 (0.4%)	0.89 (0.45, 1.74)	0.73
	PYE	1378	965		
	n/PYE	0.01	0.02		0.73

EMEA Table 3.59
 Incidence and Incidence Density for Hostility by Treatment Group and Medical History of Suicide or Overdose
 Adult Placebo Controlled Trials
 On-Therapy

Medical History		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		
Absent	n/N (%)	24/8446 (0.3%)	16/5775 (0.3%)	1.03 (0.54, 1.93)	1.00
	PYE	1909	1305		
	n/PYE	0.01	0.01		
Present	n/N (%)	0/35 (0.0%)	0/33 (0.0%)		
	PYE	7	8		
	n/PYE	0.00	0.00		

EMEA Table 3.60
 Incidence and Incidence Density for Hostility by Treatment Group and Psychotropic Medication
 Adult Placebo Controlled Trials
 On-Therapy

Psychotropic Medication		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	24/8481 (0.3%)	16/5808 (0.3%)	1.03 (0.55, 1.94)	1.00
	PYE	1916	1313		
	n/PYE	0.01	0.01		
Absent	n/N (%)	21/6578 (0.3%)	14/4308 (0.3%)	0.98 (0.50, 1.93)	1.00
	PYE	1420	933		
	n/PYE	0.01	0.02		
Present	n/N (%)	3/1903 (0.2%)	2/1500 (0.1%)	1.18 (0.20, 7.09)	1.00
	PYE	496	379		
	n/PYE	0.01	0.01		

EMEA Table 3.61
 Incidence and Incidence Density for Hostility by Dose and Indication
 Adult Placebo Controlled Trials
 On-Therapy

Dose Group		Depression	Other
Placebo	n/N (%)	5/568 (0.9%)	2/1000 (0.2%)
	PYE	119	228
	n/PYE	0.04	0.01
5 mg	n/N (%)		0/11 (0.0%)
	PYE		1
	n/PYE		0.00
10 mg	n/N (%)	0/355 (0.0%)	0/420 (0.0%)
	PYE	48	118
	n/PYE	0.00	0.00
20 mg	n/N (%)	1/377 (0.3%)	2/1028 (0.2%)
	PYE	51	232
	n/PYE	0.02	0.01
30 mg	n/N (%)	0/150 (0.0%)	
	PYE	17	
	n/PYE	0.00	
40 mg	n/N (%)	3/237 (1.3%)	1/637 (0.2%)
	PYE	72	124
	n/PYE	0.04	0.01
50 mg	n/N (%)	1/57 (1.8%)	
	PYE	10	
	n/PYE	0.10	
60 mg	n/N (%)		1/182 (0.5%)
	PYE		35
	n/PYE		0.03

EMEA Table 3.62
 Incidence and Incidence Density for Hostility by Treatment Group and Gender
 Adult Active Control Trials
 On-Therapy

Gender		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		
Female	n/N (%)	9/4344 (0.2%)	12/3292 (0.4%)	0.57 (0.24, 1.35)	0.27
	PYE	769	551		
	n/PYE	0.01	0.02		
Male	n/N (%)	9/2174 (0.4%)	8/1677 (0.5%)	0.87 (0.33, 2.25)	0.81
	PYE	366	291		
	n/PYE	0.02	0.03		
Unknown	n/N (%)	0/4 (0.0%)			
	PYE	0			
	n/PYE	0.00			

EMEA Table 3.63
 Incidence and Incidence Density for Hostility by Treatment Group and Race
 Adult Active Control Trials
 On-Therapy

Race Group		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		
White	n/N (%)	11/4124 (0.3%)	17/3951 (0.4%)	0.62 (0.29, 1.32)	0.26
	PYE	770	681		
	n/PYE	0.01	0.02		
Black	n/N (%)	1/117 (0.9%)	0/95 (0.0%)	1.00	1.00
	PYE	15	13		
	n/PYE	0.07	0.00		
Other	n/N (%)	1/237 (0.4%)	0/240 (0.0%)	0.50	0.50
	PYE	38	30		
	n/PYE	0.03	0.00		
Unknown	n/N (%)	5/2044 (0.2%)	3/683 (0.4%)	0.56 (0.13, 2.33)	0.42
	PYE	312	118		
	n/PYE	0.02	0.03		

EMEA Table 3.64
 Incidence and Incidence Density for Hostility by Treatment Group and Severity of Disease
 Adult Active Control Trials
 On-Therapy

Disease Severity		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		
Normal	n/N (%)	0/18 (0.0%)	0/16 (0.0%)		
	PYE	3	4		
	n/PYE	0.00	0.00		
Mild to Moderate	n/N (%)	9/2072 (0.4%)	13/2022 (0.6%)	0.67 (0.29, 1.58)	0.40
	PYE	381	358		
	n/PYE	0.02	0.04		
Severe	n/N (%)	4/1898 (0.2%)	4/1771 (0.2%)	0.93 (0.23, 3.74)	1.00
	PYE	378	305		
	n/PYE	0.01	0.01		
Unknown	n/N (%)	5/2534 (0.2%)	3/1160 (0.3%)	0.76 (0.18, 3.20)	0.71
	PYE	373	175		
	n/PYE	0.01	0.02		

EMEA Table 3.65
 Incidence and Incidence Density for Hostility by Treatment Group and CR vs IR vs CRIR
 Adult Active Control Trials
 On-Therapy

CR vs IR vs CRIR		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		0.21
CR	n/N (%)	1/197 (0.5%)	0/206 (0.0%)		0.49
	PYE	21	22		
	n/PYE	0.05	0.00		
IR	n/N (%)	17/6325 (0.3%)	20/4763 (0.4%)	0.64 (0.33, 1.22)	0.19
	PYE	1114	820		
	n/PYE	0.02	0.02		0.16

No adult active controlled trials contained both CR and IR doses

EMEA Table 3.66
 Incidence and Incidence Density for Hostility by Treatment Group and Medical History of Suicide or Overdose
 Adult Active Control Trials
 On-Therapy

Medical History		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		
Absent	n/N (%)	18/6518 (0.3%)	20/4966 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1134	842		
	n/PYE	0.02	0.02		
Present	n/N (%)	0/4 (0.0%)	0/3 (0.0%)		
	PYE	1	0		
	n/PYE	0.00	0.00		

EMEA Table 3.67
 Incidence and Incidence Density for Hostility by Treatment Group and Psychotropic Medication
 Adult Active Control Trials
 On-Therapy

Psychotropic Medication		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	18/6522 (0.3%)	20/4969 (0.4%)	0.68 (0.36, 1.30)	0.25
	PYE	1135	842		
	n/PYE	0.02	0.02		
Absent	n/N (%)	16/5051 (0.3%)	15/3678 (0.4%)	0.78 (0.38, 1.57)	0.47
	PYE	847	613		
	n/PYE	0.02	0.02		
Present	n/N (%)	2/1471 (0.1%)	5/1291 (0.4%)	0.35 (0.07, 1.81)	0.26
	PYE	288	229		
	n/PYE	0.01	0.02		

EMEA Table 3.68
 Incidence and Incidence Density for Hostility by Treatment Group and Gender
 Paediatric Placebo Controlled Trials
 On-Therapy

Gender		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
Female	n/N (%)	11/418 (2.6%)	1/315 (0.3%)	8.49 (1.09, 66.08)	0.016
	PYE	105	73		
	n/PYE	0.10	0.01		
Male	n/N (%)	16/320 (5.0%)	3/332 (0.9%)	5.77 (1.67, 20.00)	0.002
	PYE	71	75		
	n/PYE	0.22	0.04		

EMEA Table 3.69
 Incidence and Incidence Density for Hostility by Treatment Group and Race
 Paediatric Placebo Controlled Trials
 On-Therapy

Race Group		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
White	n/N (%)	24/596 (4.0%)	2/534 (0.4%)	11.16 (2.62, 47.45)	<0.001
	PYE	144	122		
	n/PYE	0.17	0.02		
Black	n/N (%)	0/33 (0.0%)	0/35 (0.0%)		
	PYE	7	7		
	n/PYE	0.00	0.00		
Other	n/N (%)	3/109 (2.8%)	2/78 (2.6%)	1.08 (0.18, 6.59)	1.00
	PYE	25	19		
	n/PYE	0.12	0.11		

EMEA Table 3.70
 Incidence and Incidence Density for Hostility by Treatment Group and Severity of Disease
 Paediatric Placebo Controlled Trials
 On-Therapy

Disease Severity		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
Normal	n/N (%)	3/48 (6.3%)	0/51 (0.0%)		0.11
	PYE	11	10		
	n/PYE	0.28	0.00		
Mild to Moderate	n/N (%)	10/375 (2.7%)	0/298 (0.0%)		0.003
	PYE	85	68		
	n/PYE	0.12	0.00		
Severe	n/N (%)	9/220 (4.1%)	3/207 (1.4%)	2.90 (0.77, 10.87)	0.14
	PYE	51	47		
	n/PYE	0.18	0.06		
Unknown	n/N (%)	5/95 (5.3%)	1/91 (1.1%)	5.00 (0.57, 43.65)	0.21
	PYE	29	23		
	n/PYE	0.17	0.04		

EMEA Table 3.71
 Incidence and Incidence Density for Hostility by Treatment Group and Medical History of Suicide or Overdose
 Paediatric Placebo Controlled Trials
 On-Therapy

Medical History		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
Absent	n/N (%)	27/738 (3.7%)	4/645 (0.6%)	6.09 (2.12, 17.49)	<0.001
	PYE	176	148		
	n/PYE	0.15	0.03		
Present	n/N (%)		0/2 (0.0%)		
	PYE		0		
	n/PYE		0.00		

EMEA Table 3.72
 Incidence and Incidence Density for Hostility by Treatment Group and Psychotropic Medication
 Paediatric Placebo Controlled Trials
 On-Therapy

Psychotropic Medication		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	27/738 (3.7%)	4/647 (0.6%)	6.10 (2.12, 17.54)	<0.001
	PYE	176	149		
	n/PYE	0.15	0.03		
Absent	n/N (%)	23/627 (3.7%)	3/519 (0.6%)	6.55 (1.96, 21.94)	<0.001
	PYE	151	122		
	n/PYE	0.15	0.02		
Present	n/N (%)	4/111 (3.6%)	1/128 (0.8%)	4.75 (0.52, 43.12)	0.19
	PYE	25	27		
	n/PYE	0.16	0.04		

EMEA Table 3.73
 Incidence and Incidence Density for Self Harm by Treatment Group and Baseline Suicide Ideation
 Adult Placebo Controlled Trials
 On-Therapy

Baseline Suicide Ideation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	51/8481 (0.6%)	38/5808 (0.7%)	0.92 (0.60, 1.40)	0.75
	PYE	1916	1313		
	n/PYE	0.03	0.03		0.69
Absent	n/N (%)	40/8037 (0.5%)	20/5517 (0.4%)	1.37 (0.80, 2.35)	0.29
	PYE	1840	1262		
	n/PYE	0.02	0.02		0.25
Present	n/N (%)	11/444 (2.5%)	18/291 (6.2%)	0.39 (0.18, 0.83)	0.019
	PYE	76	51		
	n/PYE	0.15	0.35		0.020

EMEA Table 3.74
 Incidence and Incidence Density for Self Harm by Treatment Group and Baseline Suicide Ideation
 Adult Active Control Trials
 On-Therapy

Baseline Suicide Ideation		Paroxetine	Comparator	Odds Ratio (95% CI)	P value
Overall	n/N (%)	29/6522 (0.4%)	32/4969 (0.6%)	0.69 (0.42, 1.14)	0.16
	PYE	1135	842		
	n/PYE	0.03	0.04		0.12
Absent	n/N (%)	22/5787 (0.4%)	23/4387 (0.5%)	0.72 (0.40, 1.30)	0.29
	PYE	1012	757		
	n/PYE	0.02	0.03		0.26
Present	n/N (%)	7/735 (1.0%)	9/582 (1.5%)	0.61 (0.23, 1.65)	0.45
	PYE	123	85		
	n/PYE	0.06	0.11		0.22

EMEA Table 3.75
 Incidence and Incidence Density for Self Harm by Treatment Group and Baseline Suicide Ideation
 Paediatric Placebo Controlled Trials
 On-Therapy

Baseline Suicide Ideation		Paroxetine	Placebo	Odds Ratio (95% CI)	P value
Overall	n/N (%)	15/738 (2.0%)	5/647 (0.8%)	2.66 (0.96, 7.37)	0.069
	PYE	176	149		
	n/PYE	0.09	0.03		0.072
Absent	n/N (%)	9/680 (1.3%)	3/615 (0.5%)	2.74 (0.74, 10.15)	0.15
	PYE	165	141		
	n/PYE	0.05	0.02		0.16
Present	n/N (%)	6/58 (10.3%)	2/32 (6.3%)	1.73 (0.33, 9.12)	0.71
	PYE	11	8		
	n/PYE	0.54	0.25		0.36