

Appendix 15 Numbers Needed To Treat Anxiety Disorders using Medication

What does Number Needed to Treat or Number Needed to Harm Mean?

The NNT is an estimate of the number of patients that would need to be given a treatment for one of them to achieve a desired outcome. The NNT is derived from evidence from randomised placebo controlled studies and calculated relative to exposure to a placebo. For example, consider a trial of a medication such as 'extract of hens teeth' for treating Obsessive Compulsive Disorder.

If we decide that 50% symptom relief is considered to be 'benefit' from treatment, the NNT may be calculated very simply as: $NNT = 1 / (\text{the proportion of patients not benefiting from the placebo} - \text{the proportion of patients not benefiting from the treatment})$

Taking a hypothetical example from a randomised placebo controlled trial of 'extract of hens teeth': 50 patients were given 'extract of hens teeth' at a dose of 200 mg per day for 12 weeks, and 10 of them had less than 50% symptom relief at 12 week assessment. Fifty patients were given placebo, and 27 of them had less than 50% symptom relief at 12 week assessment.

$$\begin{aligned} \text{The NNT is therefore } & 1 / ((27/50) - (10/50)) \\ & = 1 / (0.54 - 0.20) \\ & = 1 / 0.34 \\ & = 2.9 \end{aligned}$$

This means that a clinician would expect to treat about three patients with 'extract of hens teeth' in order for one of them to achieve the specified degree of benefit from treatment.

The best NNT would, of course, be 1, which would mean every patient with treatment benefited, but no patient given placebo control benefited. Generally NNTs between 2 and 5 are indicative of effective treatments. (However, it does depend on the intervention and the consequences: NNTs of 20, 50 or 100 may be useful for prophylactic treatments, like interventions to reduce death after heart attack).

Harm

For adverse effects, we can calculate a number needed to harm (NNH), in exactly the same way as an NNT. For an NNH, large numbers are obviously better than small numbers, because this means that the adverse effect occurs with less frequency. The NNH is usually compared with the NNT as a way of comparing benefits of treatment with significant hazards of treatment. In other areas of medicine this is usually calculated for severe adverse events (such as death or a major complication of treatment). Caution is needed in interpreting the data described in this guideline, as the research has generally reported only mild adverse events such as nausea, dry mouth, sweating. There is no consistent format or rating scale for describing side effects of medications. Some studies report a general measure of harm, while others provide measures of specific side effects.

Procedure and methods

Studies were sampled using electronic searching of the Medline, PsycLit, and Cochrane Collaboration databases, and by manual searching with reference to published reviews and authoritative texts. In some instances, recommendations made in this guideline reflect evidence from studies in which NNTs cannot be calculated (e.g. comparison of two active drugs but no inert placebo). All Randomised Placebo Controlled Trials were included in an initial pool of 125 studies. Fifty three studies which reported data that permitted the calculation of NNT or NNH were included in the analyses.

NNT Estimates were calculated using intention to treat analyses. Confidence intervals were calculated using the Pukka method and verified using Arcus Biostat software.

Outcome measures, doses and duration of treatment varied across the sampled studies. Pooled analyses were undertaken wherever this was possible given the heterogeneity of outcome measures.

A Pooled NNT was used to summarise the findings of individual studies wherever there are three or more randomised controlled trials.

Panic Disorder						
STUDY	DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	POOLED SAMPLE SIZE
3,117,77,137	Imipramine	5	3.0-11	35-225	8.0-12	239
3,688,128,119 117,65,137	Alprazolam	3	2.0-4	2.0-6.1	4.0-15	769
84,34,69	Clomipramine	4	3.0-8	50-150	6.0-12	268
69,25	Paroxetine	4	3.0-7	10.0-60	10.0-12	368
Obsessive-Compulsive Disorder						
STUDY	DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	POOLED SAMPLE SIZE
148,130,56, 132,78,58	Clomipramine	2	2.0-3	100-300	5.0-12	1057
133,86	Fluoxetine	4	3.0-6	20-60	7.0-8	267
Social Phobia						
STUDY	DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	POOLED SAMPLE SIZE
131,143, 92,116	Moclobemide	9	5.0-24	580-900	8.0-16	681
73,143,43	Phenelzine	2	2.0-3	55-76	8.0-12	131
Post Traumatic Stress Disorder						
STUDY	DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	POOLED SAMPLE SIZE
41,66	Imipramine	2	2.0-6	225-240	8	64
41,66	Phenelzine	3	2.0-7	68-71	5.0-8	59
Generalised Anxiety Disorder						
STUDY	DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	POOLED SAMPLE SIZE
98,107,105	Diazepam	3	2.0-6	19-26	4.0-8	234

KEY TO ABBREVIATIONS USED IN TABLES	
%IMP	Percent improvement
%PF	Percent Panic free
CGI	Clinicians Global Improvement
CRS	Clinician Rating Scale
GAS	Global Assessment Scale
GPS	Global Phobia Scale
HAM-A	Hamilton Anxiety Scale
IES	Impact of Events Scale
ISPI	Index of Social Phobia Improvement Scale
NIMH	NIMH Obsessive Compulsive Scale
PGI	Patient Global Impression Scale
PHYGIS	Physicians Global Impression of functioning Scale
SAS	Social Anxiety Scale
SCL90-OCL	Symptom CheckList-90 Obsessive Compulsive Scale
SI-PTSD	Severity index of PTSD
SPS	Social Phobia Scale
Y-BOCS	Yale-Brown Obsessive Compulsive Scale
NNT	Number needed to treat
NNH	Number needed to harm
NS	Not significant
ARR	Absolute risk reduction
RRR	Relative risk reduction
NR	Not reported
General	Side effects of medication not reported individually
INF	Infinity

Panic Disorder

STUDY	TREATMENT	DOSE (mg)	DURATION (wks)	SAMPLE	MEASURE	RRR	95% CI	ARR	95% CI	NNT	95% CI	NNH	95% CI	NNH	95% CI	95% CI
3	Imipramine	150	8	123	PHYGIS %PF	0.413	0.130-0.621	0.292	0.077-0.482	3	2.0-13					
3	Alprazolam	6.1	8	123	PHYGIS %PF	0.517	0.250-0.705	0.366	0.151-0.548	3	2.0-7					
6	Alprazolam	4.9	4	479	%PF	0.629	0.503-0.723	0.343	0.243-0.439	3	2.0-4					
140	Brofaromine	150	12	30	SCL-90 %PF	0.736	0.373-0.908	0.598	0.245-0.815	2	1.0-4	1 (insomnia)	1.0-2	2 (nausea)	1.0-4	
88	Alprazolam	3.62	5	55	%PF	0.556	-0.020-0.817	0.313	-0.012-0.584	3	2.0-INF					
88	Propranolol	185	5	55	%PF	NS		NS		NS						
128	Alprazolam	5.39	6	71	%PF	0.368	0.067-0.600	0.315	0.044-0.544	3	2.0-23	5 (General)	2.0-INF			
12	Clonazepam	2.5	6	71	%PF	0.416	0.127-0.634	0.357	0.087-0.576	3	2.0-12	15 (General)	4.0-INF			
119	Alprazolam	5.2	8	85	CGI %IMP	0.684	0.468-0.828	0.589	0.359-0.752	2	1.0-3	2 (sedation)	1.0-4			3.0-27
119	Buspirone	61	8	85	CGI %IMP	0.042	-0.233-0.286	0.036	-0.168-0.259	28	4.0-INF					
119	Alprazolam	5.2	8	85	PGI %IMP	0.78	0.571-0.897	0.646	0.417-0.797	2	1.0-2					
119	Buspirone	61	8	85	PGI %IMP	0.054	-0.253-0.316	0.045	-0.173-0.278	22	4.0-INF					
119	Alprazolam	5.2	8	85	%PF	0.385	0.031-0.623	0.265	0.015-0.483	4	2.0-66					
119	Buspirone	61	8	85	%PF	NS		NS		NS						
117	Alprazolam	5.7	8	106	%PF	0.395	0.09-0.614	0.281	0.052-0.483	4	2.0-19	3 (sedation)	2.0-6			
117	Imipramine	175	8	106	%PF	0.218	-0.121-0.471	0.155	-0.073-0.37	6	3.0-INF	7 (insomnia)	3.0-INF			
77	Imipramine	35	8	63	Composite	NS		NS		NS						
77	Imipramine	99	8	63	Composite	0.433	0.136-0.672	0.404	0.098-0.647	2	2.0-10					
77	Imipramine	200	8	63	Composite	0.464	0.154-0.716	0.464	0.117-0.689	2	1.0-9					
84	Clomipramine	109	12	57	%PF	1	0.603-1.0	0.4	0.166-0.691	2	1.0-6	3 (sweat)	2.0-89			
84	Imipramine	124	12	57	%PF	NS		NS		NS				4 (insomnia)	2.0-INF	
65	Cognitive Therapy		15	57	%PF	0.79	0.302-0.944	0.503	0.128-0.763	2	1.0-8					
65	Alprazolam	4.6	15	57	%PF	NS		NS		NS						
34	Clomipramine	100	6	66	%PF	0.429	-0.122-0.737	0.25	-0.059-0.512	4	2.0-INF					
34	Lofepramine	140	6	66	%PF	0.429	-0.072-0.712	0.25	0.035	4	2.0-INF					
74	Desimipramine	177	12	56		NS		NS		NS						
137	Alprazolam	2	8	63	%PF	0.093	-0.350-0.38	0.079	-0.222-0.349	13	3.0-INF					
137	Alprazolam	6	8	63	%PF	0.592	0.265-0.794	0.507	0.173-0.730	2	1.0-6					
137	Imipramine	225	8	63	%PF	0.364	-0.066-0.681	0.312	-0.051-0.623	3	2.0-INF					
144	Clomipramine	60-90	8	475	PHYGIS %PF	0.179	0.051-0.303	0.227	0.070-0.366	6	3.0-20	8 (sweat)	5.0-33	8 (dizzy)	5.0-30	
144	Citalopram	20-30	8	475	PHYGIS %PF	0.242	0.085-0.382	0.192	0.062-0.317	5	3.0-16					

144	Citalopram	40-60	8	475	PHYSIS %PF	0.163	0.001-0.308	0.129	0.000-0.256	8	4.0-3136		
13	Fluoxetine	230	8	75	%PF	0.736	0.394-0.897	0.532	0.223-0.745	2	1.0-4		
13	Cognitive Therapy		8	50	%PF	0.2	-0.141-0.462	0.16	0.093-0.397	6	3.0-INF		
69	Paroxetine	20-60	12	367	%PF	0.282	0.104-0.432	0.193	0.065-0.315	5	3.0-15	(general)	
69	Clomipramine	50-150	12	367	%PF	0.074	-0.117-0.238	0.0507	-0.073-0.174	20	6.0-INF	5 (general)	3.0-9
25	Paroxetine	10	10	278	%PF	NS		NS		NS			
25	Paroxetine	20	10	278	%PF	NS		NS		NS			
25	Paroxetine	40	10	278	%PF	0.582	0.347-0.74	0.329	0.170-0.473	3	2.0-6		
7	Cognitive Therapy		8	67	%PF	0.789	0.546-0.910	0.549	0.326-0.716	2	1.0-3		
127	Cognitive Therapy		12	32	%PF	0.75	0.155-0.934	0.375	0.0514-0.634	3	2.0-18		

STUDY		DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	SAMPLE SIZE
"3,117,77,137"		Imipramine	5	3.0-11	35-225	8.0-12	239
"3,6,88,128,119,117,65,137"		Alprazolam	3	2.0-4	2.0-6.1	4.0-15	769
"84,34,69"		Clomipramine	4	3.0-8	50-150	6.0-12	268
"69,25"		Paroxetine	4	3.0-7	10.0-60	10.0-12	368
"65,13,7,127"		Cognitive Therapy	2	2.0-4		8.0-15	175

Obsessive-compulsive disorder

STUDY	DRUG	DOSE (mg)	DURATION (wks)	SAMPLE	MEASURE	RRR	95% CI	ARR	95% CI	NINT	95% CI	NNH	95% CI	NNH	95% CI
133	Fluoxetine	20-60	7	355	Y-BOCS %IMP	0.29	0.164-0.417	0.265	0.142-0.389	4	3.0-7				
148	Paroxetine	37.5	12	391	Y-BOCS %IMP	0.305	0.135-0.436	0.197	0.077-0.309	5	3.0-13				
148	Clomipramine	113.1	12	391	Y-BOCS %IMP	0.319	0.118-0.484	0.209	0.069-0.342	5	3.0-14				
130	Clomipramine	218-234	10	501	NIMH CUT-OFF	0.475	0.410-0.539	0.46	0.394-0.525	2	2.0-3				
86	Fluoxetine	20	8	108	Y-BOCS/CGI	0.133	-0.122-0.343	0.098	-0.078-0.270	10	4.0-INF				
86	Fluoxetine	40	8	108	Y-BOCS/CGI	0.29	0.048-0.488	0.213	0.023-0.384	5	3.0-33				
86	Fluoxetine	60	8	110	Y-BOCS/CGI	0.266	0.023-0.463	0.195	0.014-0.365	5	3.0-69				
21	Sertraline	200	8	87	CGI %IMP	0.352	0.055-0.571	0.24	0.03-0.43	4	2.0-33				
56	Clomipramine	100	6	40	CGI %IMP	0.5	0.266-0.694	0.5	0.297-0.703	2	1.0-3				
132	Clomipramine	150	5	48	CPRS % IMP	0.364	0.121-0.581	0.333	0.093-0.530	3	2.0-11				
78	Clomipramine	230	12	12	CRS (Ciba-Geigy)	0.571	0.269-1.34	0.423	-0.117-0.759	2	1.09-INF				
100	Fluoxetine	150	20	32	OCL/SCL-90 %IMP	0.769	0.436-0.920	0.625	0.288-0.824	2	1.0-3				
46	Sertraline	50-200	12	224	CGI %IMP	0.128	-0.079-0.289	0.09	-0.048-0.215	11	5-INF	7 (General)	4.0-15		
45	Fluoxetine	255	8	42	Y-BOCS %IMP										
21	Sertraline				CGI %IMP			0.24		4					
147	Paroxetine	60			Y-BOCS %IMP			0.2		5					
58	Clomipramine	250-300	10	263	NIMH CUT-OFF	0.488	0.397-0.575	0.469	0.376-0.557	2	2.0-3	5 Nausea	4.0-10	5 (sweat)	4.0-8
STUDY		DRUG	DOSE RANGE	POOLED NINT	95% CI	DURATION	SAMPLE	DURATION		DURATION		DURATION		DURATION	
					mg	wks	SIZE	wks		wks		wks		wks	
"148,130,56,132,78,58"		Clomipramine	100-300	2	2.0-3	5.0-12	1057	5.0-12		5.0-12		5.0-12		5.0-12	
"133,86"		Fluoxetine	20-60	4	3.0-6	7.0-8	267	7.0-8		7.0-8		7.0-8		7.0-8	

Social Phobia

STUDY	TREATMENT	DOSE av (mg)	DURATION (wks)	SAMPLE	MEASURE	RRR	95% CI	ARR	95% CI	NNT	95% CI	NNH	95% CI	NNH	95% CI
142	Bupirone	30	12	30	SPS 50% IMP	NS		NS		NS					
24	Clonazepam	2.4	10	72	CGI % IMP	0.73	0.517-0.860	0.583	0.367-0.740	2	1.0-3				
73	Phenelzine	76	8	74	CGI CUT-OFF	0.532	0.218-0.744	0.409	0.138-0.625	2	2.0-7				
131	Moclobemide	300	12	382	CIC-SP	NS		NS		NS					
131	Moclobemide	600	12	384	CIC-SP	0.199	0.054-0.325	0.131	0.033-0.227	8	4.0-30				
135	Atenolol	100	12	41	ISPI %IMP	0.116	0.402-0.45	0.081	-0.211-0.358	12	3.0-INF				
135	Flooding		12	41	ISPI %IMP	0.456	0.025-0.717	0.319	0.009-0.572	3	2.0-101				
59	Sertraline	50-200	10	12	L-SAS	0.273	-0.125-0.580	0.25	-0.649	4	2.0-INF				
143	Moclobemide	580	16	78	CGI % IMP	0.478	0.229-0.680	0.423	0.175-0.627	2	2.0-6	NS			
143	Phenelzine	67.5	16	78	CGI % IMP	0.696	0.366-0.784	0.615	0.366-0.784	2	1.0-3	2 (General)	1.0-4		
43	Phenelzine	55	12	57	SPS 50% IMP	0.616	0.200-0.846	0.492	0.121-0.745	2	1.0-8				
43	Alprazolam	4.2	12	57	SPS 50% IMP	0.271	0.121-0.745	0.217	-0.135-0.537	5	2.0-INF				
43	Cognitive Therapy		12	57	SPS 50% IMP	0.044	-0.463-0.369	0.035	-0.269-0.324	28	3.0-INF				
141	Fluvoxamine	150	12	28	SAS % IMP	0.422	0.084-0.678	0.389	0.054-0.650	3	2.0-19	2 (nausea)	1.0-7	4 (insomnia)	2.0-INF
92	Moclobemide	900	12	506	CGI % IMP	NS		NS		NS					
116	Moclobemide	728	8	77	CGI % IMP	NS		NS		NS		NS		NS	
33	Brofaromine	150	12	76	CGI% IMP	0.713	0.491-0.851	0.553	0.340-0.712	2	1.0-3				

STUDY	DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	SAMPLE SIZE
"131,143,92,116"	Moclobemide	9	5.0-24	580-900	8.0-16	681
"73,143,43"	Phenelzine	2	2.0-3	55-76	8.0-12	131

Post-traumatic Stress Disorder

STUDY	DRUG	DOSE (mg)	DURATION (wks)	SAMPLE	MEASURE	RRR	95% CI	ARR	95% CI	NNT	95% CI	NNH	95% CI	NNH	95% CI	NNH	95% CI
41	Imipramine	240	8	33	GAS % IMP	0.656	0.133 to 0.883	0.477	0.060-0.753	2	1.0-17						
41	Phenelzine	71	8	33	GAS % IMP	0.5	-0.103 to 0.677	0.364	0.061-0.677	3	1-inf						
139	Fluoxetine	40	5	59		NR		NR		NR		4 (Diarrhoea)	2.0-INF	3 (sweating)	2.0-33	5 (headache)	2.0-505
66	Imipramine	225	8	60	CGI %IMP	0.518	0.121-0.751	0.374	0.063-0.617	3	2.0-16						
66	Phenelzine	68	8	60	CGI %IMP	0.562	0.152-0.796	0.406	0.081-0.653	2	2.0-12						
66	Imipramine	225	8	60	IES % IMP	0.217	-0.043-0.439	0.205	-0.037-0.425	5	2.0-INF						
66	Phenelzine	68	8	60	IES % IMP	0.54	0.299-0.731	0.51	0.241-0.707	2	1.0-4						
23	Amitryptiline	175	8	66	SI-PTSD	NS		NS		NS		NS					
120	Phenelzine	30-90	5		CGI %IMP/IOES	NS		NS		NS							

STUDY/DRUG	POOLED NNT	95% CI	DOSE RANGE mg	DURATION wks	SAMPLE SIZE
"41,66" Imipramine	2	2.0-6	225-240	8	64
"41,66" Phenelzine	3	2.0-7	68-71	5.0-8	59

