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- Kelly B.
- Pharmaceutical rep
- In her brief case: BRAINEX®, the new treatment for AD
- On her way to Dr G.



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- Kelly B.
- Pharmaceutical rep
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- At Dr G's clinic she demonstrates drug effects



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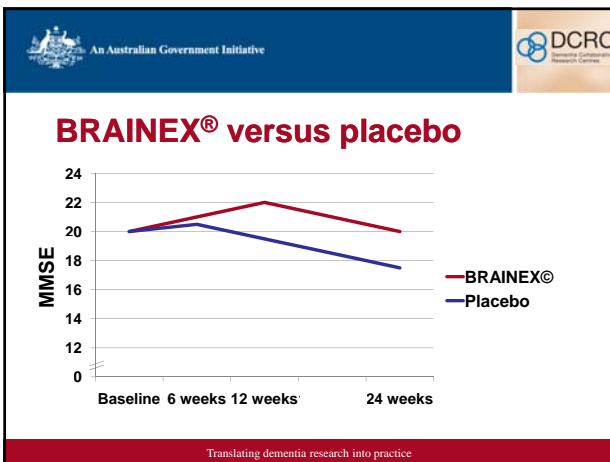
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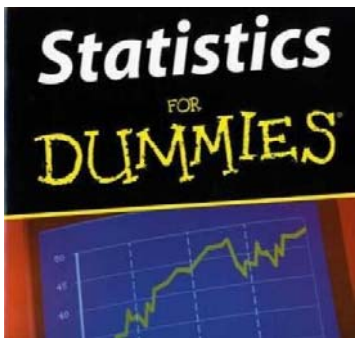
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# Statistics FOR DUMMIES



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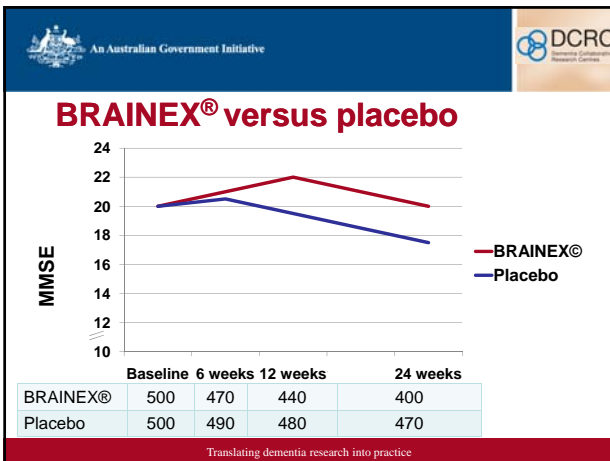
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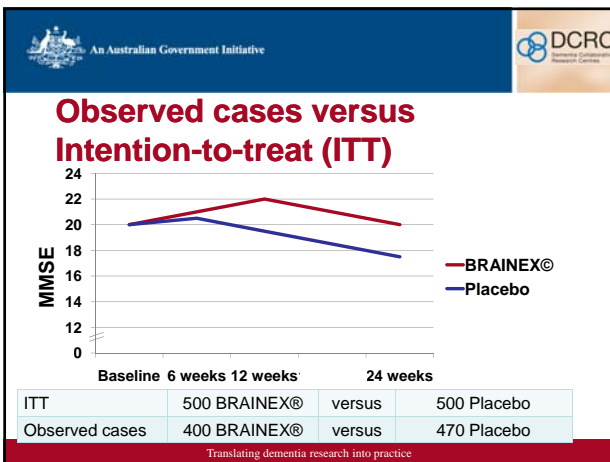
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### Compare completers versus Drop-outs

	BRAINEX®		Placebo	
	Complete	Drop-out	Complete	Drop-out
n	400	100	470	30
B/L MMSE	20	20	20	20
Last MMSE	20	17	18	18
Mean	18.5	Not significant	18.0	

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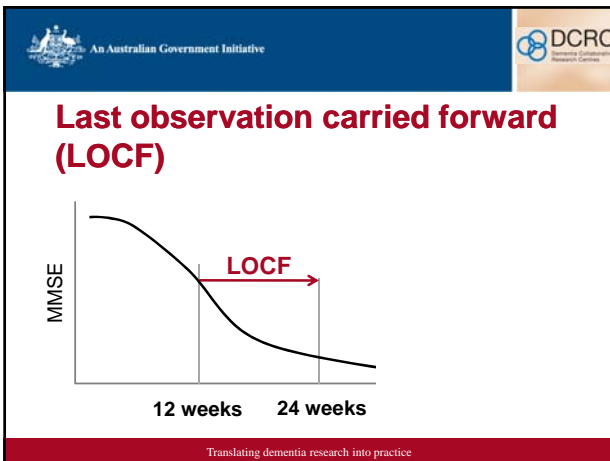
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### OK...it's statistically significant but is it clinically useful?

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### OK...it's statistically significant but is it clinically useful?

...Number needed to treat

And is it safe?

.... Number needed to harm

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**The number needed to treat (NNT)**

= number of patients who need to be treated with the treatment (BRAINEX®) compared to another treatment (e.g. placebo) for one patient to gain a specified benefit (here 4 points improvement on ADAS-cog)

Cook and Sackett (1995). Br Med K. 310, 452-454

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**The number needed to treat (NNT)**

= defined as the reciprocal of the absolute risk reduction (ARR)

**NNT = 1/ARR**

Cook and Sackett (1995). Br Med J. 310, 452-454

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**NNT and Relative Risk Reduction for BRAINEX® compared to placebo**

- Positive outcome = 4-point improvement on ADAS-cog

	4-point improvement	No improvement	
Placebo (N=500)	135	365	} = 73%
BRAINEX®(N=500)	265	235	

*→ NNT 26% (ARR)*

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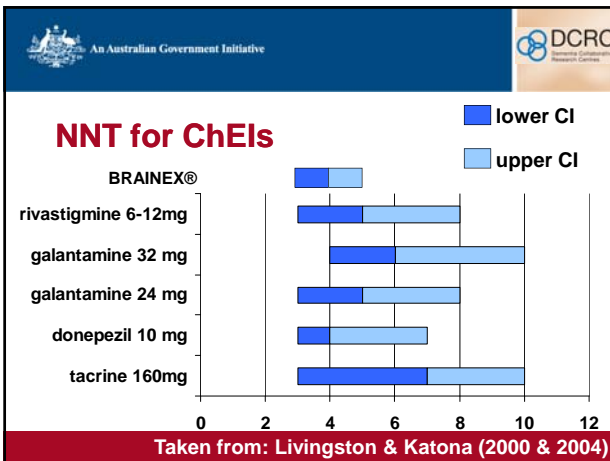
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**What factors might determine NNT?**

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**An NNT example for pts with hypertension**

	Outcome: Stroke in 5 years				
Hypertension	Controls	Active Rx	RRR	Absolute RR	NNT
<b>Moderate (diastolic &gt;115mmHg)</b>					
Event rate (p)	0.20	0.12	0.4	0.08	13
Total N	16778	16898			
<b>Mild (diastolic &gt; 110mmHg)</b>					
Event rate (p)	0.015	0.009	0.4	0.006	167
Total N	15165	15238			

Taken from: Cook and Sackett (1995). Br Med K. 310, 452-454

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### Calculation of risk reduction and NNT for patients with hypertension

Stroke in 5 years in persons with moderate high BP (diastolic >115 mm Hg)

Total No of patients 16 778 & 16 898

Stroke rate: Control 20% Treatment 12%

Relative risk reduction is 8%

NNT =  $1/0.08 = 12.5 = \text{rounded up} = 13$

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### Calculation of risk reduction and NNT for pts with mild hypertension, diastolic > 110

Stroke rate Placebo = 1.5% Treatment = 0.9%

Total No of patients 15 165 15 238

Relative risk reduction is 0.6%

NNT =  $1/0.006 = 167$

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### Different definitions of response in dementia lead to different NNTs

- You can define response as
  - Global improvement
  - Cognitive improvement
  - Or functional improvement

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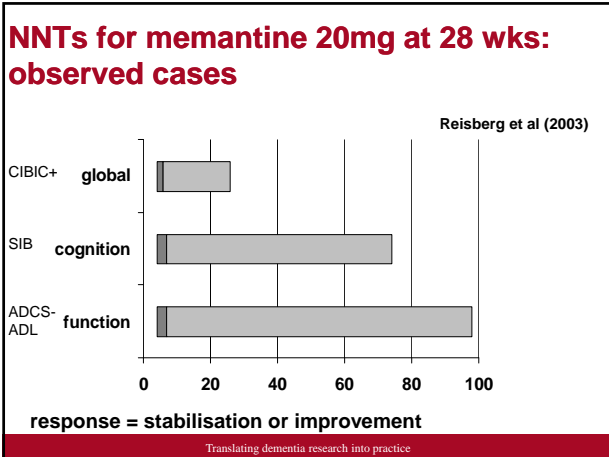
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### Different definitions of response lead to different NNTs

- You can also define response as a combination of
  - Global rating
  - Cognition
  - Function

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### NNTs for BRAINEX® vs placebo by different definitions of response (1)

Definition of response	BRAINEX®		Placebo	
	N=500		N=500	
Improvement OR stabilisation			ARR=19%	
			ARR=5%	
			ARR=15%	
Improvement			ARR=9%	

G = global, C = cognition, F = function

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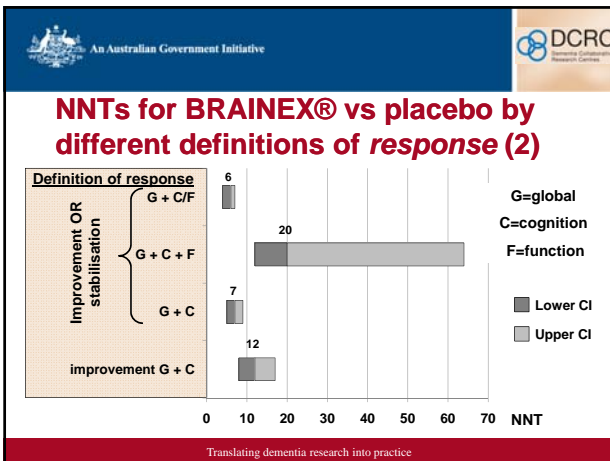
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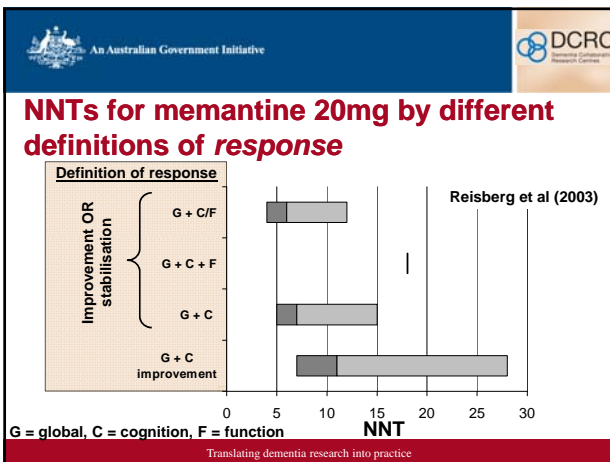
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### The number needed to harm (NNH)

- As NNT but to compare adverse effects (e.g. any adverse event or withdrawal from study)
- eg NNH = 7 → This means that about one in every 7 patients will experience this negative outcome

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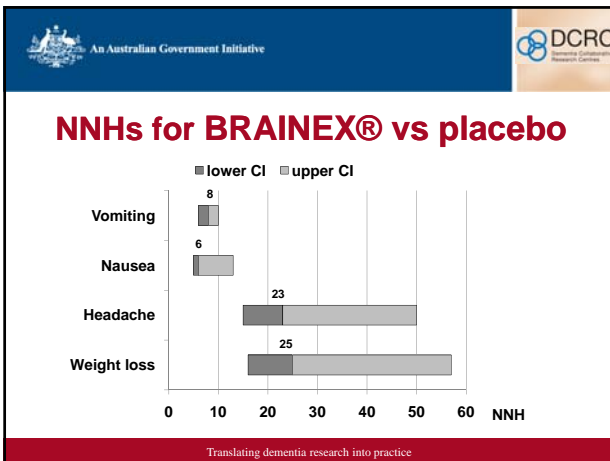
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**The meaning of statistically significant results**

- If sample size is just big enough it becomes “easy” to detect statistically significant differences
- → difference/improvement might not be clinically meaningful
- → calculate effect size

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**Effect size**

= standardised mean difference  
 i.e. difference between two means divided by SD of the mean

- 0.20 = small effect
- 0.5 = medium effect
- 0.8 = large effect

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**What do you think ES is for ...**

- Antidepressant Rx for depression?
- Caregiver interventions?

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**what do you think IS ES for Antidepressants for depression (all ages)?...**

antidepressants vs active placebos (Moncrieff et al, 2004. Cochrane review):  
Mood improvement: **ES = 0.39 (0.24-0.54)**

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**what do you think IS ES for interventions for caregivers of PWD...**

**ES = 0.3**

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## Conclusions

- Researchers want to be published
- Drug companies want to sell
- Caveat emptor
- Read past abstract if you are interested
- Has it been replicated?

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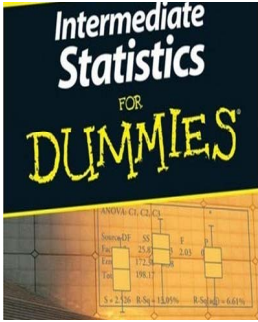
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## Thank you

[www.dementia.unsw.edu.au](http://www.dementia.unsw.edu.au)

Thanks to Katrin Seeher



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