Interpretation of graphs and effect estimates in meta-analysis

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- For each trial or study
  - estimate (square)
  - 95% confidence interval (CI) (line)
  - size (square) indicates weight allocated
- Solid vertical line of 'no effect'
  - if CI crosses line then effect not significant (p>0.05)
- Horizontal axis
  - arithmetic: RD, MD, SMD
  - Iogarithmic: OR, RR
- Diamond represents combined estimate and 95% CI
- Dashed line plotted vertically through combined estimate



# What are dichotomous outcomes?

- when the outcome for every participant is one of two possibilities or events
  - alive or dead
  - healed or not healed
  - pregnant or not pregnant

# What were the chances of that?

- Risk and odds
- express chance in numbers
- for dichotomous outcomes, express the chance within a group of being in one of two states
- particular statistical meanings, calculated differently

## Risk

- 24 people drank coffee
  6 developed a headache
- risk of a headache
  - = 6 headaches / 24 people who could have had one
  - $= 6/24 = \frac{1}{4} = 0.25 = 25\%$

risk =<u>no. participants with event of interest</u> total no. participants

# Odds

- 24 people drank coffee
  6 developed a headache
- odds of a headache
  - = 6 headaches/18 without headaches

= 6/18 = 1/3 = 0.33 = 1:3 (not usually as %)

odds = <u>no. participants with event of interest</u> no. participants without event of interest

# Do risks and odds differ much?

Two examples from caffeine trials

- 5 people with 'headaches' out of 65
- chance of having a headache
   risk = 5/65 = 0.077 odds = 5/60 = 0.083
- 130 people 'still awake' out of 165
- chance of still being awake

risk = 130/165 = 0.79 odds = 130/35 = 3.71

# Comparing two groups

	Headache	No headache	Total	
Caffeine	17	51	68	
Decaf	9	55	64	
Total	26	106	132	

## Comparing two groups

effect measures

- risk ratio (RR) (relative risk)
- odds ratio (OR)
- risk difference (RD) (absolute risk reduction)

all estimates are uncertain, and should be presented with a confidence interval

# **Risk ratio**

- risk of event with intervention
   = 17/68=0.25
- risk of event with control
   = 9/64=0.14
- risk ratio = intervention risk
- control risk
- **=17/68** = 0.25 = 1.79
- **9/64** 0.14

	Headache	No headache	Total
Caffeine	17	51	68
Decaf	9	55	64
Total	26	106	132

Where risk ratio = 1, there is no difference between the groups

## Expressing it in words

#### □ Risk ratio 1.79

- the risk of having a headache with treatment was 179% of the risk in the control group
- intervention increased the risk of headache by 79%

#### or for a reduction in risk:

- Risk ratio 0.56
  - the risk of having a headache with Decaf was 56% of the risk in the caffein group
  - intervention reduced the risk of headache by 44%

# Odds ratio

- odds of event with intervention
   = 17/51
- odds of event with control
   = 9/55
- odds ratio = intervention odds
   control odds

**9/55** 0.16

	Headache	No headache	Total
Caffeine	17	51	68
Decaf	9	55	64
Total	26	106	132

Where odds ratio = 1, there, is no difference between the groups

## Expressing it in words

□ Odds ratio 2.06

- intervention doubled the odds of headache
- intervention increased the odds to 206% of the odds in the control group
- Intervention increased the odds of headache by 106%

#### or for a reduction in odds:

- Odds ratio 0.48
  - Decaff reduced the odds of headache to 48% of the odds in the caffein group
  - Decaf reduced the odds of headache by 52%



## Expressing it in words

Risk difference 0.11

- intervention increased the risk of headache by 11 percentage points
- 14 out of 100 people experienced a headache in the control group. 11 more people experienced a headache with caffeine.

#### or for a reduction in risk:

- □ Risk difference -0.11
  - intervention reduced the risk of headache by 11 percentage points
  - 14 out of 100 people experienced a headache in the control group. 11 fewer people experienced a headache with caffeine.

## Now it's your turn!

	Event	No Event	Total
Intervention	2	8	10
Control	5	5	10
Total	7	13	20

#### 1. calculate:

risk ratio for the effect of treatment on chance of event
 odds ratio for the effect of treatment on chance of event

2. express the results in words

### The answers

Risk ratio 
$$=\frac{2/10}{5/10}=\frac{0.2}{0.5}=0.4$$

$$=\frac{2/8}{5/5}=\frac{0.25}{1}=0.25$$

Odds ratio

# Communication

- OR is hard to understand, often misinterpreted
- RR is easier, but relative
  - can mean a very big or very small change
- □ RD is easiest
  - absolute measure of actual change in risk
  - easily converted to natural frequencies or NNT





1.1. Comparison 1 Incidence of death over all time periods, Outcome 1 Heparin vs placebo or untreated control.

Andrade-Castellanos CA, Colunga-Lozano LE, Delgado-Figueroa N, Magee K. Heparin versus placebo for non-ST elevation acute coronary syndromes. Cochrane Database of Systematic Reviews 2014, 6. Art. No.: CD003462. DOI: http://dx.doi.org/10.1002/14651858.CD003462.pub3

Comparison: Sub Outcome: Lur	ogroup: Qu nbar BMD	ality of Blinding					
	Expt	Expt	Ctrl	Ctrl	WMD	Weight	WMD
Study	П	mean(sd)	Π	mean(sd)	(95%Cl Fixed)	%	(95%Cl Fixed)
Blinding = 0							
Evans 1993	15	2.40 (9.10)	11	-4.70 (4.40)	$  \longrightarrow$	1.7	7.100 [1.811,12.389]
Gurlek 1997	10	4.54 (17.96)	10	0.14 (3.42)		0.4	4.400 [-6.932,15.732]
Montessori 1997	40	6.28 (5.02)	34	-0.03 (9.20)		3.9	6.310 [2.848,9.772]
Wimalawansa 95	14	4.22 (3.93)	14	-2.25 (3.55)		6.0	6.470 [3.696,9.244]
Wimalawansa 98	16	4.30 (2.80)	16	-0.90 (2.40)	_ <b>_</b>	14.1	5.200 [3.393,7.007]
Subtotal (95%Cl)	95		85			26.0	5.767 [4.435,7.100]
Chi-square 1.02 (df=	=4) Z=8.48						
Blinding = 1							
Herd 1997	64	2.14 (3.76)	71	-1.72 (3.45)	-	30.9	3.860 [2.638,5.082]
Meunier 1997	25	0.58 (4.15)	24	-2.34 (4.02)	<b>_</b> _	8.8	2.920 [0.632,5.208]
Pouilles 1997	43	0.06 (5.90)	43	-2.46 (4.44)	<b>_</b>	9.5	2.520 [0.313,4.727]
Storm 1990	22	4.80 (7.79)	21	-4.50 (7.97)		2.1	9.300 [4.587,14.013]
Watts 1990	92	4.20 (7.67)	90	1.38 (7.98)	<b>_</b> _	8.9	2.820 [0.545,5.095]
Watts B 1990	93	5.20 (6.75)	88	1.47 (5.83)	_ <b>_</b>	13.7	3.730 [1.895,5.565]
Subtotal (95%Cl)	339		337		•	74.0	3.579 [2.789,4.370]
Chi-square 7.52 (df=	=5) Z=8.88						
Total (95%Cl)	434		422		•	100.0	4.148 [3.469,4.828]
Chi-square 16.20 (df	f=10) Z=11.	.96					

utcome: 02 Leav	ing the study early risperidone	clozapine	) RR	Weight	RR	
tudy	n/N	DAN	(95%Cl Fixed)	%	(95%Cl Fixed)	
Clozapine 1996	22 / 39	6/20	- 9	- 13.2	1.88[0.91,3.88]	
Clozapine 1998a	9/43	9/43	<b>a</b>	15.0	1.00[0.44,2.27]	
Clozapine 1998b	34 / 135	38/138		62.7	0.91[0.61,1.36]	
Clozapine 1999	0/15	0/14	<b>–</b>	0.0	Not Estimable	
Clozapine 2000	1/9	6/11 ←		9.0	0.20[0.03,1.40]	
otal(95%Cl)	66 / 241	59 / 226	<b></b>	100.0	0.99[0.73,1.35]	
est for heterogeneity chi-so	quare=5.76 df=3 p=0.12					
est for overall effect z=-0.	06 p=1					

Comparison: 01 RISP Outcome: 02 Leav	PERIDONE versus CL ving the study early	.OZAPINE					
Study	risperidone n/N	clozapine n/N	R (95%Cl	R   Fixed)	Weight %	RR (95%Cl Fixed)	
Clozapine 1996	22 / 39	6/20	-	<b>6</b>	13.2	1.88[0.91,3.88]	
Clozapine 1998a	9/43	9/43		<b>9</b>	15.0	1.00[0.44,2.27]	
Clozapine 1998b	34 / 135	38/138		<b></b>	62.7	0.91[0.61,1.36]	
x Clozapine 1999	0/15	0/14	_	Ţ	0.0	Not Estimable	
Clozapine 2000	1/9	6/11			9.0	0.20[0.03,1.40]	
Total(95%CI)	66 / 241	59 / 226	•	-	100.0	0.99[0.73,1.35]	
Test for heterogeneity chi-s	quare=5.76 df=3 p=0.12	2					
Test for overall effect z=-0	).06 p=1						
			.1 .2	1 5 10			
			Favours risperidone	Favours clozapine			

Commonland, 0/			OZADINE			
Comparison: 0		IDONE VEISUS CL	LUZAPINE			
Outcome: 02	2 Leaving	j the study early	1			
		risperidone	clozapine	RR	Weight	RR
Study		n/N	- AN	(95%Cl Fixed)	. %	(95%Cl Fixed)
Clozapine 1996	/	22/39	6 / 20		13.2	1.88[0.91,3.88]
Clozapine 1998a		9/43	9/43	∖	- 15.0	1.00[0.44,2.27]
Clozapine 1998b	(	34/135	38/138		62.7	0.91[0.61,1.36]
x Clozapine 1999		0/15	0/14		0.0	Not Estimable
Clozapine 2000		1/9	6/11 ←	/	9.0	0.20[0.03,1.40]
			/	/		
Total(95%Cl)		66 / 241	59/226	-	100.0	0.99[0.73,1.35]
Test for heterogene	ity chi-squar	re=5.76 d <del>f=3 p=0.12</del>	2			
Test for overall effe	ct z=-0.06	p=1				
			.1	.2 1	5 10	
			Fav	ours risperidone Fa	ivours clozapine	

Comparison: 01 RISE Outcome: 02 Leav	PERIDONE versus CL ving the study early	OZAPINE			$\cap$		
Study	risperidone n/N	clozapine n/N	RI (95%Cl	R Fixed)	Weight %	RR (95%Cl Fixed)	
Clozapine 1996	22 / 39	6/20	-		13.2	1.88[0.91,3.88]	
Clozapine 1998a	9/43	9/43		<b>—</b> —	15.0	1.00[0.44,2.27]	
Clozapine 1998b	34 / 135	38/138		<b>—</b>	62.7	0.91[0.61,1.36]	
x Clozapine 1999	0/15	0/14			0.0	Not Estimable	
Clozapine 2000	1/9	6/11	< <b>•</b>		9.0	0.20[0.03,1.40]	
Total(95%Cl)	66 / 241	59 / 226	-	•	100.0	0.99[0.73,1.35]	
Test for heterogeneity chi-s	square=5.76 df=3 p=0.12	2					
Test for overall effect z=-0	0.06 p=1						
			.1 .2 1	5 10	$\uparrow /$		
			Favours risperidone	Favours clozapine	$\cup$		

Outcome: 02 Leav	ing the study early risperidone	y clozapine		RR	ined	Weight	RR (95% CL Sing d)	
study	N/N	D/N		(35%CLL	ixea)	70	(ao%Ci Fixed)	
Clozapine 1996	22/39	6/20		+		13.2	1.88[0.91,3.88]	
Clozapine 1998a	9/43	9/43				15.0	1.00[0.44,2.27]	
Clozapine 1998b	34/135	38/138			_	62.7	0.91[0.61,1.36]	
Clozapine 1999	0/15	0/14				0.0	Not Estimable	
Clozapine 2000	1/9	6/11	<b>← •</b>		_	9.0	0.20[0.03,1.40]	
otal(95%Cl)	66 / 241	59 / 226		-	-	100.0	0.99[0.73,1.35]	
est for heterogeneity chi-si	quare=5.76 df=3 p=0.1	12						
est for overall effect z=-0.	06 p=1				/			
			.1 .2 Favours ri:	spenidone 1	Favours o	5 10 Iozapine		

Study         n/N         n/N         (95%CTFixed)         %         (95%CTFixed)         % <t< th=""></t<>
Clozapine 1996         22/39         6/20         13.2         1.88[0.91           Clozapine 1998a         9/43         9/43         15.0         1.00[0.44           Clozapine 1998b         34/135         38/138         62.7         0.91[0.61           Clozapine 1999         0/15         0/14         0.0         Not Estim           Clozapine 2000         1/9         6/11         9.0         0.20[0.03
Clozapine 1998a         9 / 43         9 / 43         15.0         1.00[0.44           Clozapine 1998b         34 / 135         38 / 138         62.7         0.91[0.61           Clozapine 1999         0 / 15         0 / 14         0.0         Not Estim           Clozapine 2000         1 / 9         6 / 11         9.0         0.20[0.03
Clozapine 1998b         34 / 135         38 / 138         62.7         0.91[0.61           Clozapine 1999         0 / 15         0 / 14         0.0         Not Estim           Clozapine 2000         1 / 9         6 / 11         9.0         0.20[0.03
Clozapine 1999 0/15 0/14 0.0 Not Estim Clozapine 2000 1/9 6/11 ← 9.0 0.20[0.03
Clozapine 2000 1 / 9 6 / 11 ← ■ 9.0 0.20[0.03
rotal(95%Cl) 66 / 241 59 / 226 📥 100.0 0.99[0.73
est for heterogeneity chi-square=5.76 df=3 p=0.12
est for overall effect_z=-0.06_p=1
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itudy	risperidone n/N	clozapine n/N	RR (95%Cl Fixed)	Weight %	RR (95%Cl Fixed)	
Clozapine 1996	22/39	6/20		13.2	1 880 91 3 881	
Clozapine 1998a	9/43	9/43		15.0	1.00[0.44.2.27]	
Clozapine 1998b	34 / 135	38/138		62.7	0.91[0.61,1.36]	
Clozapine 1999	0/15	0/14	1000	0.0	Not Estimable	
Clozapine 2000	1/9	6/11	•	9.0	0.20[0.03,1.40]	
ʻotal(95%Cl)	66 / 241	59 / 226	-	100.0	0.99[0.73,1.35]	
est for heterogeneity chi-so	quare=5.76 df=3 p=0.13	2				
est for overall effect z=-0.	06 p=1					

Comparison: 01	<b>RISPERIDONE versus CLO</b>	DZAPINE				
Outcome: 02	Leaving the study early					$\frown$
Study	risperidone n/N	clozapine n/N	RI (95%CI	₹ Fixed)	Weight %	RR (95%Cl Fixed)
Clozapine 1996	22/39	6/20	-	<b>B</b>	13.2	1.88[0.91,3.88]
Clozapine 1998a	9/43	9/43			15.0	1.00[0.44,2.27]
Clozapine 1998b	34 / 135	38/138		_	62.7	0.91[0.61,1.36]
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Clozapine 2000	1/9	6/11	~ <b>-</b>	_	9.0	0.20[0.03,1.40]
Total(95%Cl)	66 / 241	59 / 226	-	•	100.0	0.99[0.73,1.35]
Test for heterogeneit	/chi-square=5.76 df=3 p=0.12					
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			1 2 1	5	10	
			Favours risperidone	Favours cloz	apine	

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Clozapine 1999	0/15	0/14	500-	0.0	Not Estimable	
Clozapine 2000	1/9	6/11	← <b>□</b>	9.0	0.20[0.03,1.40]	
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est for overall effect_z=-0.0	06 p=1					

Clozapine 1996     22 / 39     6 / 20       Clozapine 1998a     9 / 43     9 / 43       Clozapine 1998b     34 / 135     38 / 138       X     Clozapine 1999     0 / 15       X     Clozapine 2000     1 / 9	- 13.2 15.0 62.7 0.0	1.88[0.91,3.88] 1.00[0.44,2.27] 0.91[0.61,1.36]		
Clozapine 1998a     9 / 43     9 / 43       Clozapine 1998b     34 / 135     38 / 138       < Clozapine 1999	15.0 62.7 0.0	1.00[0.44,2.27] 0.91[0.61,1.36]		
Clozapine 1998b 34 / 135 38 / 138 < Clozapine 1999 0 / 15 0 / 14 Clozapine 2000 1 / 9 6 / 11 / •	62.7 0.0	0.91[0.61,1.36]		
x Clozapine 1999 0/15 0/14	0.0			
		Not Estimable		
	9.0	0.20[0.03,1.40]		
Total(95%Cl) 66 / 241 59 / 226	100/0	0.99[0.73,1.35]	$\sum$	
Test for heterogeneity chi-square=5.76 df=3 p=0.12				
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itudy	risperidone n/N	clozapine n/N	RR (95%Cl Fixed)	Weight %	RR (95%Cl Fixed)	
Clozapine 1996	22/39	6/20		13.2	1.88[0.91,3.88]	
Clozapine 1998a	9/43	9/43	<b>e</b>	15.0	1.00[0.44,2.27]	
Clozapine 1998b	34 / 135	38/138		62.7	0.91[0.61,1.36]	
Clozapine 1999	0/15	0/14		0.0	Not Estimable	
Clozapine 2000	1/9	6/11 ←		9.0	0.20[0.03,1.40]	
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