# **1.** Incidence of hepatitis C virus and HIV among new injecting drug users in London: prospective cohort study

## Ali Judd, Matthew Hickman, Steve Jones, et al,

BMJ 2005;330:24-25

Prevalence and incidence of hepatitis C virus and HIV antibody among new injecting drug users in London, 2001-3

Viral antibodies	Baseline		Follow up		
	No positive/total	Prevalence (95% CI)	No of seroconversions/total (mean follow up time)	Incidence rate per 100 person years	
Hepatitis C virus	187/428	43.7 (38.9 to 48.5)	53/151 (372 days)	41.8 (31.9 to 54.7)	
HIV	18/428	4.2 (2.5 to 6.6)	9/273 (360 days)	3.4 (1.8 to 6.6)	

## Questions

In the table above:

1. What does the 95% CI mean in column 3?

2. What is the difference between prevalence (column3) and incidence (column 5)?

# 2. Two-Year Prospective Follow-Up of Children With a Prepubertal and Early Adolescent Bipolar Disorder Phenotype

#### Barbara Geller, M.D., James L. Craney, M.S., M.P.H., Kristine Bolhofner, B.S., Michael J. Nickelsburg, Ph.D., Marlene Williams, R.N., Betsy Zimerman, M.A.

Am J Psychiatry 159:6, June 2002

FIGURE 1. Relation of Rate of Recovery Over 24 Months to Family Intactness for 89 Subjects With a Prepubertal and Early Adolescent Bipolar Disorder Phenotype<sup>a</sup>



<sup>a</sup> Of the 89 subjects, 58 recovered by 24 months. Recovery rates for the subjects who lived with their intact biological families (N=39) and those who resided in other living situations (N=19) were significantly different (Cox proportional hazards model  $\chi^2$ =7.40, df=1, p=0.007). The Kaplan-Meier estimate for recovery was 76.5% in intact families (95% CI=64.8%–88.1%) and 50.0% in other living situations (95% CI=34.1%–65.9%).

#### Questions

- 1) What were the medians for time to recovery for both groups?
- 2) Locate the final Kaplan-Meier estimate for proportion recovered and plot it together with the 95% CI reported in the text.
- 3) Given these 95%CI would you have been able to determine if there was a significant difference in the proportion recovered?

# **3. Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: a randomised controlled trial**

### J H John, S Ziebland, P Yudkin, L S Roe, H A W Neil for the Oxford Fruit and Vegetable Study Group

Lancet, Volume 359 Issue 9322 Page 1969

*Intervention* - a brief negotiation method to increase their consumption of fruit and vegetables to at least five daily portions at the start of the study. *Control* – no intervention.

n	Baseline, mean (SD)	Change at 6-months' follow-up, mean (SD)	Between-group difference in change (95% CI)	Adjusted difference in change* (95% CI)
of fruit and	vegetables (portions)			
329	3.4 (1.7)	1.4 (1.7)	1.3 (1.1 to 1.6)	1-4 (1-2 to 1-6)
326	3.4 (1.5)	0.1 (1.3)		
344	130.2 (19.7)	-2.0 (13.5)	3·4 (1·3 to 5·5)	4-0 (2-0 to 6-0)
346	129.3 (19.6)	1.4 (14.6)		
344	79.2 (11.4)	-1.6 (8.7)	1.4 (0.1 to 2.7)	1.5 (0.2 to 2.7)
346	79.9 (11.9)	-0.3 (8.7)	· ·	
		* /		
344	76·1 (13·8)	0.6 (2.6)	0.0 (-0.3 to 0.5)	0-1 (-0-4 to 0-6)
346	75.6 (14.9)	0.6 (2.6)	• /	· · · · · · · · · · · · · · · · · · ·
	n 5 fruit and 329 326 344 346 344 346 344 346	n Baseline, mean (SD)   of fruit and vegetables (portions)   329 3.4 (1.7)   326 3.4 (1.5)   344 130.2 (19.7)   346 129.3 (19.6)   344 79.2 (11.4)   346 79.9 (11.9)   344 76.1 (13.8)   346 75.6 (14.9)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

l=intervention group. C=controls.\*Adjusted for baseline value and sex.

## Questions

- 1) Does the intervention appear to have an effect on weight? What is the (adjusted) estimated size of this effect?
- 2) Does the intervention appear to have an effect on the Systolic blood pressure? Guess the approximate p-value.
- 3) Why are we confident that the effect shown can be attributed to the intervention?
- 4) Why have the authors used change at 6-month follow-up instead of the actual figures recorded at 6 months for all their outcomes?

#### 4. Insulin resistance and depression: cross sectional study

#### Markku Timonen, et al

#### BMJ 2005;330:17-18

**Figure A** Scatter plot between the Qualitative Insulin Sensitivity Check Index (QUICKI) and Beck's Depression Inventory (BDI)-21 scores in subjects with impaired glucose tolerance (IGT). The solid line shows the fitted 5-knot spline medians. Spearman partial correlation coefficient after adjustment for body mass index, smoking, alcohol consumption, physical inactivity, gender, and basic education. [Figure Legend posted as supplied by author]



### Questions

In the Figure above, what is the:

- 1. Approximate range of Beck Depression Inventory values?
- 2. The approximate median?
- 3. What does the correlation of -0.24 mean?

## 5. Alcohol intake and insulin resistance. A cross-sectional study.

# Villegas R, Salim A, O'Halloran D, Perry IJ.

#### Nutr Metab Cardiovasc Dis. 2004 Oct;14(5):233-40.

**BACKGROUND**: The development of insulin resistance is a critical step in the pathogenesis of type 2 diabetes. The effect of alcohol intake on insulin sensitivity/resistance is not well defined. The aim of this study was to examine the association between alcohol intake and insulin resistance in a sample of middle-aged men and women with data on a wide range of potential confounding factors, including diet.

**METHODS**: We performed a cross sectional study involving a group of 1018 men and women, sampled from 17 general practice lists in the South of Ireland, with a response rate of 69%. Participants completed a detailed health and lifestyle questionnaire and a food frequency questionnaire and provided fasting blood samples for analysis of glucose and insulin. Insulin resistance was estimated on the basis of fasting glucose and insulin, using the glucose homeostasis model (HOMA scores). Insulin resistance was defined as the upper quartile of the HOMA scores.

**RESULTS**: We found evidence of a U-shaped relationship between alcohol intake and insulin resistance fitted as a continuous variable (HOMA scores) with lowest levels in light drinkers (between 0.5 to 0.99 units per day) relative to the other drinking categories. However no significant association between alcohol intake and HOMA score was observed in fully adjusted analyses, including adjustment for dietary saturated fat and fruit and vegetables intake. In logistic regression analysis with insulin resistance (categorical) as the dependent variable, we observed that ex-drinkers were at higher risk of insulin resistance compared to occasional drinkers independently of age, sex, BMI and waist circumference, (OR=2.4, 95% CI, 1.1-5.7, p=0.04). On further adjustment for potential confounders including diet this association was also attenuated and was non-significant.

**CONCLUSIONS**: The reported effects of alcohol intake on insulin resistance may be confounded by other aspects of lifestyle, especially diet.

#### Questions

- 1) What is a "confounding" factor? How can you decrease the impact of confounding factors? What were the measures used by the authors to deal with this problem? How does this affect the findings?
- 2) The 95% CI for the OR obtained in this Logistic regression does not include 1. If a 99% CI were obtained for this OR, do you think it would include 1?

## [Optional]

3) Why are the authors using Logistic regression to calculate the risk that ex-drinkers have to insulin resistance (instead of normal regression)?

# 6. Pain over speed bumps in diagnosis of acute appendicitis: diagnostic accuracy study.

## Ashdown H, D'Souza N, Karim D, et al.

BMJ 2012;345:e8012

Table 1 Pain over speed bumps in relation to appendicitis					
Pain over speed bumps	Арре	Total			
	Positive	Negative	Iotai		
Positive	33	21	54		
Negative	1	9	10		
Total	34	30	64		

## Questions

Based on the Table above:

1. Calculate the Sensitivity of feeling pain over speed bumps as a test for Appendicitis?

2. Calculate the Specificity

3. In the same paper, the Sensitivity and Specificity of "Migratory pain" as a test for Appendicitis is given as 65% and 33% respectively. Which one of the test would you choose to make a diagnosis (one, both, neither)?

# 7. Optimal loading dose of warfarin for the initiation of oral anticoagulation.

## Mahtani K, Heneghan C, Nunan D, et al.

Cochrane Database of Systematic Reviews 2012; DOI: 10.1002/14651858.CD008685.pub2

Background

Warfarin is used as an oral anticoagulant. However, there is wide variation in patient response to warfarin dose. This variation, as well as the necessity of keeping within a narrow therapeutic range, means that selection of the correct warfarin dose at the outset of treatment is not straightforward.

Review: Optimal loading dose of warfarin for the initiation of oral anticoagulation Comparison: 15 mg versus 10 mg Outcome: 1 INR in-range by day 5: 5mg v 10mg

Study or subgroup	10mg n/N	5 m g n/N	Risk Ratio M - H, Random, 95% CI	Weight	Risk Ratio M - H, Random, 95% Cl
Crowther 1999	14/21	27/31	-	25.7 %	0.77 [ 0.55, 1.07 ]
Harrison 1997	20/25	16/24		25.4 %	1.20 [0.85, 1.69]
Kovacs 2003	86/104	45/97		28.0 %	1.78 [1.41, 2.25]
Quiroz 2006	14/25	13/25	-	20.9 %	1.08 [ 0.65, 1.80 ]
<b>Total (95% Cl)</b> Total events: 134 (10mg),	<b>175</b> 101 (5mg)	177	•	100.0 %	117 [ 0.77, 1.77 ]
Heterogeneity: Tau <sup>2</sup> = 0.1 Test for overall effect: Z = Test for subgroup differer	5; Chi <sup>2</sup> = 18.17, df = 3 0.73 (P = 0.46) nces: Not applicable	(P = 0.00041); I <sup>2</sup> =83%			
		0.02	0.1 1 10	50	
		Favours 5 mg	Favours	10 mg	

Analysis 1.1. Comparison 1 5 mg versus 10 mg, Outcome 1 INR in-range by day 5: 5mg v 10mg.

## Questions

Based on the Forest plot above:

1. Which study provides the largest evidence in this comparison? How can you tell?

2. Are the findings for these four papers similar? What is the level of heterogeneity found in this comparison?

3. Based on the pooled estimate of this comparison, determine if there is evidence to support the use of either does to initiate treatment.

## FURTHER READING

You do not need to know much statistics, as you will mostly read rather than do statistics. Some basics books from the reading viewpoint are:

1) Greenhalgh T, How to Read a Paper: The basics of Evidence-Based Medicine, Wiley-Blackwell, 2010.

OR

2) Bowers D, House A, Owens O, Understanding Clinical Papers, Wiley-Blackwell, 2006.

OR

3) Perera R, Heneghan C, Badenoch D, Statistics Toolkit, Wiley-Blackwell, 2008.