Risk

Study 1

In 1988 the results of the Physicians' Health Study Research Group study were reported in the *New England Journal of Medicine*. In this study 22 071 male physicians (aged from 40 to 84) were randomly assigned to two groups. One group took an aspirin every second day and the other group took a placebo, a pill with no active ingredient which looked just like an aspirin. The participants did not know whether they were taking aspirin or the placebo.

After five years the number of participants in each group who had had a heart attack was recorded. The results are shown in the table below.

Treatment	Heart attack	No heart attack	**Total**
Aspirin	104	10 933	11 037
Placebo	189	10 845	11 034
Total	293	21 778	22 071

1. All parts of this question apply to Study 1.

   (a) For those in the aspirin group:

   (i) The proportion who had a heart attack $= \frac{104}{11037}$

   $= 0.00942$

   (ii) The probability that a randomly selected participant had a heart attack

   $= 0.00942$

   (iii) The percentage who had a heart attack = 0.942%

   (iv) The risk of having a heart attack = 0.00942

   (v) Write this risk as a rate per 1000 participants 9.42 per 1000

   (vi) Write this risk as a rate per 10 000 participants 94.2 per 10 000

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(b) (i) For those in the placebo group, the risk of having a heart attack

$= \frac{189}{11034}$

$= 0.01713$

(ii) Write this risk as a rate per 1000 participants 17.13 per 1000

(iii) Write this risk as a rate per 10 000 participants 171.3 per 10 000

(c) (i) Calculate the relative risk of having a heart attack using the risk for the placebo group as the denominator (i.e., as the baseline risk).

Relative risk $= \frac{0.00942}{0.01713}$

$= 0.55$

(ii) Interpret this relative risk.

For male physicians aged 40 to 84, the risk of having a heart attack for those taking aspirin every second day is 0.55 the risk for those taking a placebo.

(iii) Calculate the relative risk of having a heart attack using the risk for the aspirin group as the baseline risk.

Relative risk $= \frac{0.01713}{0.00942}$

$= 1.82$

(iv) Interpret this relative risk.

For male physicians aged 40 to 84, the risk of having a heart attack for those taking a placebo is about 1.8 times the risk for those taking aspirin every second day.

(v) Which group is more appropriate as the baseline group? Briefly explain.

Placebo. It makes more sense to compare the risk for a treatment group to that for a non-treatment (control) group.

(d) (i) Do male physicians aged 40 to 84 who take aspirin every second day have an **increased** or **decreased** risk of having a heart attack compared to those who take a placebo?

Circle one: **increased** **decreased**

(ii) Calculate the percentage change in risk relative to the baseline (placebo group) risk.

$$\text{Percentage change in risk} = \frac{0.00942 - 0.01713}{0.01713} \times 100\%$$

$$= -45\%$$

(iii) Interpret this percentage change in risk.

For male physicians aged 40 to 84 there is a 45% decrease in the chances of having a heart attack for those taking aspirin every second day (compared to those taking a placebo).

Study 2

In 2006 the results of a study carried out among 132 271 Jewish children born in Israel during 6 consecutive years in the 1980s were published in the *Archives of General Psychiatry*. The objective of the study was to examine the relationship between father's age at birth of child (offspring) and their risk of autism.

The offspring were assessed for autism at age 17 years. The results are shown in the table below.

Father's Age Group	Autism	No autism	**Total**
15 – 29	34	60 654	60 688
30 – 39	62	67 211	67 273
≥ 40	14	4 296	4 310
Total	110	132 161	132 271

2. All parts of this question apply to Study 2.

(a) For offspring from fathers aged 15 to 29 at the birth of their child:

(i) The proportion who had autism $= \frac{34}{60688}$

$= 0.00056$

(ii) The probability that a randomly selected offspring had autism

$= 0.00056$

(iii) The percentage who had autism $= 0.056\%$

(iv) The risk of having autism $= 0.00056$

(v) Write this risk as a rate per 10 000 offspring **5.6 per 10 000**

(b) (i) For offspring from fathers aged 30 to 39 at the birth of their child, the risk of having autism

$= \frac{62}{67273}$

$= 0.00092$

(ii) Write this risk as a rate per 10 000 offspring **9.2 per 10 000**

(c) (i) For offspring from fathers aged 40 or more at the birth of their child, the risk of having autism

$$= \frac{14}{4310}$$

$$= 0.00325$$

(ii) Write this risk as a rate per 10 000 offspring **32.5 per 10 000**

(d) Using the risk for fathers in the 15 – 29 year age group as the baseline:

(i) Calculate the relative risk for fathers in the 30 – 39 year age group of having autistic offspring.

$$\text{Relative risk} = \frac{0.00092}{0.00056}$$

$$= 1.64$$

(ii) Interpret this relative risk.

Men aged 30 to 39 are about 1.6 times more likely to father an autistic child than those aged 15 to 29.

(iii) Calculate the relative risk for fathers in the 40 or more year age group of having autistic offspring.

$$\text{Relative risk} = \frac{0.00325}{0.00056}$$

$$= 5.8$$

(iv) Interpret this relative risk.

Men aged 40 or over are about 6 times more likely to father an autistic child than those aged 15 to 29.

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In parts (e) and (f), use the 15 – 29 year age group as the baseline group.

(e) (i) Do fathers aged 30 to 39 have an **increased** or **decreased** risk of having autistic offspring compared to those aged 15 to 29?

Circle one: **(increased)** **decreased**

(ii) Calculate the percentage change in risk relative to the baseline risk.

$$\text{Percentage change in risk} = \frac{0.00092 - 0.00056}{0.00056} \times 100\%$$

$$= 64\%$$

(iii) Interpret this percentage change in risk.

There is a 64% increase in the chances of fathering an autistic child for men aged 30 to 39 compared to those for men aged 15 to 29.

(f) (i) Do fathers aged 40 or more have an **increased** or **decreased** risk of having autistic offspring compared to those aged 15 to 29?

Circle one: **(increased)** **decreased**

(ii) Calculate the percentage change in risk relative to the baseline risk.

$$\text{Percentage change in risk} = \frac{0.00325 - 0.00056}{0.00056} \times 100\%$$

$$= 480\%$$

(iii) Interpret this percentage change in risk.

There is a 480% increase in the chances of fathering an autistic child for men aged 40 or more compared to those for men aged 15 to 29.

Study 3

Reports on autism and parental age have yielded conflicting results on whether mothers, fathers, or both, contribute to increased risk. A study carried out by researchers from the University of California aimed to examine the effect of one parent's increasing age within a narrow interval of the other parent's age. One of the main differences between this study and the study quoted above was the proportion of older mothers. The Israeli cohort had 588 mothers over the age of 40, while the Californian cohort had 113,080 mothers over the age of 40. The objective of the study was to examine the relationship between mothers' and father's age at birth of child (offspring) and their risk of autism.

The results of the Californian study, carried out among almost 5 million children born between 1990 and 1999 were published in the *Autism Research*.

Cases (i.e. children with autism) were diagnosed prior to the age of 6. Some results are shown in the table below.

Mother's Age Group	Autism	No autism	**Total**
< 25	2 689	1 713 971	1 716 660
25 – 29	3 304	1 406 234	1 409 538
30 – 34	3 576	1 161 890	1 165 466
35 – 39	2 089	541 102	543 191
≥ 40	501	112 579	113 080
Total	12 159	4 935 776	4 947 935

3. All parts of this question apply to Study 3.

(a) For offspring from mothers aged under 25 at the birth of their child:

(i) The proportion who had autism = $\frac{2689}{1716660} = 0.00157$

ii) The probability that a randomly selected offspring had autism

= **0.00157**

(iii) The percentage who had autism = **0.157%**

(iv) The risk of having autism = **0.00157**

(v) Write this risk as a rate per 10 000 offspring **15.7 per 10 000**

(b) (i) For offspring from mothers aged 25 to 29 at the birth of their child, the risk of having autism = $\frac{3304}{1409538} = 0.002344$

(ii) Write this risk as a rate per 10 000 offspring **23.44 per 10 000**

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(c) (i) For offspring from mothers aged 40 or more at the birth of their child, the risk of having autism = $\frac{501}{113080} = 0.00443$

(ii) Write this risk as a rate per 10 000 offspring **44.3 per 10 000**

(d) Using the risk for mothers in the 25 – 29 year age group as the baseline:

(i) Calculate the relative risk for mothers in the under 25 year age group of having autistic offspring.

Relative risk = $\frac{0.00157}{0.002344}$

= **0.67**

(ii) Interpret this relative risk.

Mothers aged under 25 are about 0.67 times as likely (i.e. less likely) to give birth to an autistic child as those aged 25 to 29

(iii) Calculate the relative risk for mothers in the 40 or more year age group of having autistic offspring.

Relative risk = $\frac{0.00443}{0.002344}$

= **1.89**

(iv) Interpret this relative risk.

Mothers aged over 40 are about 1.89 times more likely (or almost twice as likely) to give birth to an autistic child as those aged 25 to 29

In parts (e) and (f), use the 25 – 29 year age group as the baseline group.

(e) (i) Do mothers aged less than 25 have an **increased** or **decreased** risk of having autistic offspring compared to those aged 25 to 29?

Circle one: **increased** **decreased**

(ii) Calculate the percentage change in risk relative to the baseline risk.

$$\text{Percentage change in risk} = \frac{0.00157 - 0.002344}{0.002344} \times 100\%$$

$$= -33\%$$

(iii) Interpret this percentage change in risk.

There is a 33% decrease in the chances of giving birth to an autistic child for women aged less than 25 compared to those for women aged 25 to 29

(f) (i) Do mothers aged 40 or more have an **increased** or **decreased** risk of having autistic offspring compared to those aged 25 to 29?

Circle one: **increased** **decreased**

(ii) Calculate the percentage change in risk relative to the baseline risk.

$$\text{Percentage change in risk} = \frac{0.00443 - 0.002344}{0.002344} \times 100\%$$

$$= 89\%$$

(iii) Interpret this percentage change in risk.

There is an 89% increase in the chances of giving birth to an autistic child for women aged over 40 compared to those for women aged 25 to 29

Note:
Another way of calculating increased or decreased risk is to use the following formula:

Change in risk = (Relative Risk – 1) x 100%

So, when comparing mothers under 25 with mothers between 25 and 29, the relative risk is 0.67 (from above).
Change in Risk = (Relative Risk – 1) x 100% = (0.67 – 1) x 100% = -33%, thus a decreased risk.
And comparing mothers over 40 with mothers between 25 and 29, the relative risk is 1.89 (from above).
Change in Risk = (Relative Risk – 1) x 100% = (1.89 – 1) x 100% = 89%, thus an increased risk.