

Protecting and improving the nation's health

**Technical Guide** 

# **Confidence Intervals**

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#### Introduction

Confidence intervals are calculated around many different types of statistic used in public health analysis. The background to the use of confidence intervals and the reasons for using them are explained in APHO Technical Briefing 3 – Commonly used public health statistics and their confidence intervals.<sup>1</sup>

Different methods must be used for different types of statistic, reflecting the different statistical distributions underpinning the statistics, particularly where counts or sample sizes are small. Many of the methods are described or implemented in various PHE publications and tools; the purpose of this guide is to act as a directory, linking to appropriate resources. The formulae for most of the methods are set out in appendices to this guide.

#### Software options

Almost all the methods listed or described below can be implemented in a variety of different software environments. It is possible to implement every one of these in *R*, Stata, Excel and other statistical packages. Most can be implemented in SQL. However, some are easier than others. There are three essential types of methodology:

- 1 Byar's method, which is purely arithmetical, and can be implemented easily, anywhere: it is particularly useful for applications in SQL, which does not have statistical lookup tables built in (although it is possible to use *R* scripts from within SQL Server 2016 onwards).
- 2 Simulation (repeated resampling) methods. These can be easily implemented in statistical packages such as Stata and *R*, and also in Excel using VBA scripts, although this tends to be slower to run.
- 3 All other methods, which do not involve simulation, but do involve lookups of statistical distributions, eg normal, *t*, Poisson,  $\chi^2$ . All these methods can easily be implemented in Excel, and several of them are, as referred to below, in the PHE Tool for calculating common public health statistics and their confidence intervals<sup>1</sup> and in the PHEindicatormethods R package.<sup>2</sup> They can also be implemented in Stata, SAS, StatsDirect, or other statistical packages.

# Directory of methods

In the table below, the Excel and R columns indicate respectively whether the method is implemented in the PHE Tool for calculating common public health statistics and their confidence intervals<sup>1</sup> and in the PHE indicatormethods R package.<sup>2</sup>

Type of statistic	Description	Excel	R	Reference
Counts	This section applies to counts that are not constrained to a theoretical maximum, ie they are not numerators of proportions. For the numerator of a proportion, see the Proportions section below.	~	~	Appendix 1 Appendix 2
	Use Byar's method (Appendix 1) when the numerator (count) is at least 10. When the numerator is less than 10, use the exact $\chi^2$ method (Appendix 2). Although Byar's method is an approximation, it is very accurate (except for very small numbers) and it is easy to implement across all software used for the routine production of indicators. For 95% confidence intervals, Byar's method is within 0.2% of the exact value for numerators of 10 or more. For 99.8% confidence intervals it is within 1.5% of the exact value for numerators of at least 10, but it always errs on the conservative side, ie confidence limits are slightly wider than the exact ones.			
Proportions	Use the Wilson Score method.	$\checkmark$	~	Appendix 3
Crude rates	As for Counts (above), use Byar's method when the numerator (count) is at least 10. When the numerator is less than 10, use the exact $\chi^2$ method.	~	~	Appendix 1 Appendix 2
Indirectly standardised rates and ratios	As for Counts (above), use Byar's method when the numerator (count) is at least 10. When the numerator is less than 10, use the exact $\chi^2$ method.	~	~	Appendix 1 Appendix 2

Type of statistic	Description	Excel	R	Reference
Directly standardised rates	There are two methods used within PHE: Dobson's method (with Byar's method) and Tiwari's <sup>3</sup> modified Gamma method. They give extremely similar results. The Dobson method is used in the Health Intelligence Division of PHE and by NHS Digital. The Tiwari method is used by the Cancer Analysis Team in PHE. Work commissioned in 2017 by PHE has shown that there is little to choose between the two methods but for very small numbers (counts between 10 and 25) Dobson's method (with Byar's method) gives very slightly more accurate coverage (ie for 95% confidence intervals, the intervals are slightly closer to the stated 95% coverage). For consistency, it is recommended that Dobson's method is used for any new indicators, and that is implemented in the Excel tool and R package, but the Tiwari method gives confidence intervals that are sufficiently accurate.	✓	✓	Appendix 1 Appendix 4
Odds	Odds are used for excess winter deaths and proportional analysis. Use the Wilson Score method transformed for odds. Odds are directly related to proportions, so the standard method for proportions can be adapted (Appendix 5) and has been shown to give more accurate confidence intervals than alternatives.			Appendix 5
Odds ratio	Use the logit limits.			Appendix 5
Life expectancy	Use Chiang's and Silcocks' method. Implemented in the PHE Life expectancy calculator. <sup>4</sup>			Eayres and Williams⁵
Regression slope	Use the <i>t</i> -distribution method.			Appendix 6

Type of statistic	Description	Excel	R	Reference
Slope index of inequality and relative index of inequality	The method used in PHE is one based on simulation. The confidence intervals for the individual points on which the slope index of inequality (SII) is based are used to estimate the statistical distribution for each one, and then the SII is repeatedly calculated (say 100,000 times) based on random samples from those distributions of the underlying points. This gives a picture of the statistical distribution for the SII, from which confidence intervals can be estimated accurately. The same method is applied to the relative index of inequality (RII).			
	The method is set out step-by-step and implemented by VBA scripts in the PHE Slope index of inequality tool. <sup>6</sup> <i>R</i> scripts are also available in PHE to carry out the calculations.			
	The slope index of inequality (SII) is a regression slope, and before the simulation method was developed the standard published method used for calculating confidence intervals around the SII in PHE publications was the <i>t</i> -distribution method for a regression slope. This method is still applied in the PHE Inequalities Analysis Tool. <sup>7</sup> However, because this method takes no account of the stability of the individual points used to calculate the SII (ie the confidence intervals around the individual points) it is unnecessarily crude: it tends to be overly conservative, but not always: on occasions it gives confidence intervals that are too narrow.			
Concentration index	There is no distributional information about the concentration index, Gini coefficient or other Lorenz-curve based indicators but confidence intervals can be calculated for the by simulation in a similar way to the method used for the slope index of inequality, as set out in the previous section.			Appendix 7

#### Appendix 1 – Byar's method

A rate of events r is given by:

$$r = \frac{0}{n}$$

where:

0 is the numerator number of observed events;

n is the denominator population-years at risk.

The  $100(1 - \alpha)\%$  confidence limits for the rate *r* are given by:

$$r_{lower} = \frac{O_{lower}}{n}$$

$$r_{upper} = \frac{O_{upper}}{n}$$

where:

 $O_{lower}$  and  $O_{upper}$  are the lower and upper confidence limits for the observed number of events.

Using Byar's method<sup>8</sup> the  $100(1 - \alpha)$ % confidence limits for the observed number of events are given by:

$$O_{lower} = O\left(1 - \frac{1}{90} - \frac{z}{3\sqrt{0}}\right)^3$$
$$O_{upper} = (0+1)\left(1 - \frac{1}{9(0+1)} + \frac{z}{3\sqrt{0+1}}\right)^3$$

where:

z is the  $100\left(1-\frac{\alpha}{2}\right)$ th percentile value from the Standard Normal distribution.

For example, for a 95% confidence interval,  $\alpha = 0.05$  and  $z \approx 1.96$  (ie the 97.5th percentile value from the Standard Normal distribution).

For counts, the last pair of formulae are all that are required.

For indirectly standardised ratios, such as standardised mortality ratios (SMRs), the denominator n is not the population-years at risk, but is the expected number of events – otherwise the formulae are the same.

# Appendix $2 - \chi^2$ exact method

Using the link between the Poisson and  $\chi^2$  distributions<sup>9</sup> the  $100(1 - \alpha)\%$  confidence limits for an observed number of events *0* (such as the numerator of a rate – see Appendix 1) are given by:

$$O_{lower} = \frac{\chi^2_{lower}}{2}$$
$$O_{upper} = \frac{\chi^2_{upper}}{2}$$

where:

 $\chi^2_{lower}$  is the  $100\left(1-\frac{\alpha}{2}\right)$ th percentile value from the  $\chi^2$  distribution with 20 degrees of freedom;

 $\chi^2_{upper}$  is the  $100\left(1-\frac{\alpha}{2}\right)$ th percentile value from the  $\chi^2$  distribution with 20 + 2 degrees of freedom.

# Appendix 3 – Wilson Score method

The proportion p is given by:

$$p = \frac{0}{n}$$

where:

*O* is the numerator observed number of individuals in the sample/population having the specified characteristics;

n is the denominator total number of individuals in the sample/population.

Using the Wilson Score method<sup>10,11</sup> the  $100(1 - \alpha)\%$  confidence limits for the proportion *p* are given by:

$$p_{lower} = \frac{20 + z^2 - z\sqrt{z^2 + 40q}}{2(n + z^2)}$$
$$p_{upper} = \frac{20 + z^2 + z\sqrt{z^2 + 40q}}{2(n + z^2)}$$

where:

*q* is 1-*p*;

z is the  $100\left(1-\frac{\alpha}{2}\right)$ th percentile value from the Standard Normal distribution.

For example, for a 95% confidence interval,  $\alpha = 0.05$  and  $z \approx 1.96$  (ie the 97.5th percentile value from the Standard Normal distribution).

#### Appendix 4 – Dobson's method

The directly standardised rate (DSR) is given by:

$$DSR = \frac{1}{\sum_{i} w_i} \sum_{i} \frac{w_i O_i}{n_i}$$

where:

 $O_i$  is the observed number of events in the local or subject population in age group *i*;

 $n_i$  is the number of individuals in the local or subject denominator population in age group *i*, or the population multiplied by the period at risk (eg 'person-years');

 $w_i$  is the number (or proportion) of individuals in the reference or standard population in age group *i*.

The  $100(1 - \alpha)\%$  confidence limits for the directly standardised rate *DSR* are given by:<sup>12</sup>

$$DSR_{lower} = DSR + \sqrt{\frac{Var(DSR)}{Var(O)}} (O_{lower} - O)$$
$$DSR_{upper} = DSR + \sqrt{\frac{Var(DSR)}{Var(O)}} (O_{upper} - O)$$

where:

*O* is the total observed count of events in the local or subject population;

 $O_{lower}$  and  $O_{upper}$  are the lower and upper confidence limits for the observed count of events, given by the formulae for Byar's method in Appendix 1;

Var(0) is the variance of the total observed count 0;

Var(DSR) is the variance of the directly standardised rate.

The variances of the observed count *O* and the *DSR* are estimated by:

$$Var(O) = \sum_{i} O_{i}$$
$$Var(DSR) = \frac{1}{(\sum_{i} w_{i})^{2}} \sum_{i} \frac{w_{i}^{2} O_{i}}{n_{i}^{2}}$$

### Appendix 5 – Wilson Score method transformed for odds

Odds are directly related to proportions: the numerator is the same (the number of cases), but for odds, the denominator is the number of non-cases, whereas for proportions, the denominator is the total number of cases and non-cases.

	Study group		
Cases	а		
Non-cases	С		

In the table above, the proportion of the study group that are cases =  $\frac{a}{a+c}$ 

The equivalent odds =  $\frac{a}{c}$ 

The  $100(1 - \alpha)\%$  confidence interval for odds  $\frac{a}{c}$  can be derived algebraically from the Wilson Score method for proportions:

$$lower \ limit = \frac{2a + z^2 - z\sqrt{z^2 + \frac{4ac}{a+c}}}{2c + z^2 + z\sqrt{z^2 + \frac{4ac}{a+c}}}$$
$$upper \ limit = \frac{2a + z^2 + z\sqrt{z^2 + \frac{4ac}{a+c}}}{2c + z^2 - z\sqrt{z^2 + \frac{4ac}{a+c}}}$$

where z is the  $100\left(1-\frac{\alpha}{2}\right)$ th percentile value from the Standard Normal distribution (for 95% confidence intervals use  $z \approx 1.96$ ).

# Appendix 6 – Logit limits

The logit limits method is used for odds ratios.

	(Local) group of interest	(National) reference group
Cases	а	b
Non-cases	С	d

In the table above, the local odds =  $\frac{a}{c}$  and the reference odds =  $\frac{b}{d}$ 

The odds ratio  $OR = \frac{ad}{bc}$ 

The  $100(1 - \alpha)\%$  confidence limits for the odds ratio are given by the logit limits:<sup>13</sup>

$$OR_{lower} = e^{\ln(OR) - z\sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}}$$
$$OR_{upper} = e^{\ln(OR) + z\sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}}$$

where z is the  $100\left(1-\frac{\alpha}{2}\right)$ th percentile value from the Standard Normal distribution (for 95% confidence intervals use  $z \approx 1.96$ ).

Note that in the case where the odds ratio is used to compare observed and expected odds, we can often assume that the expected odds is fixed, with no variance, as we do for the observed count in an SMR, so the confidence interval is calculated around the observed odds (Appendix 5) and the resulting confidence limits each divided by the expected odds to give the confidence interval for the odds ratio.

#### Appendix 7 - t-distribution method for a regression slope

When calculating a regression slope (gradient), we have n points, each with an x coordinate and a y coordinate.

The regression slope b is calculated as

$$b = \frac{n \sum x_i y_i - \sum x_i \sum y_i}{n \sum x_i^2 - (\sum x_i)^2}$$

A  $100(1 - \alpha)$ % symmetric confidence interval around *b* is given by

$$lower \ limit = b - t_{n-2,\alpha} \sqrt{\frac{n \sum y_i^2 - (\sum y_i)^2 - b^2 (n \sum x_i^2 - (\sum x_i)^2)}{(n-2)(n \sum x_i^2 - (\sum x_i)^2)}}$$
$$upper \ limit = b + t_{n-2,\alpha} \sqrt{\frac{n \sum y_i^2 - (\sum y_i)^2 - b^2 (n \sum x_i^2 - (\sum x_i)^2)}{(n-2)(n \sum x_i^2 - (\sum x_i)^2)}}$$

where  $t_{n-2,\alpha}$  is the  $\alpha$ % quantile of Student's *t*-distribution with n-2 degrees of freedom and all summations are from i = 1 to n.

Note that the method assumes that the points are independent of each other. If they are not independent observations (for example if the points are rolling average time series data – ie the periods overlap) then this method cannot be used to calculate a meaningful confidence interval for the slope.

# Appendix 8 – Simulated confidence intervals for the concentration index

The concentration index is calculated from a Lorenz plot of the cumulative share of health in the population (on the *y*-axis; eg life expectancy) against the cumulative proportion of the population ranked by a socioeconomic variable (on the *x*-axis; eg Indices of Deprivation). If health is distributed perfectly equally across the socioeconomic groups, the Lorenz curve coincides with the diagonal – the equality line illustrated in the figure below. The further the curve is from the diagonal equality line, the greater the degree of inequality. The concentration index is the area between the Lorenz curve and the line of equality, measured and reported as a proportion of the total area beneath (or above) the line of equality.

The concentration index shows how unevenly health is distributed according to population share. It takes a value between zero and 1 (or 100%), where zero indicates perfect equality and 1 indicates 'ultimate inequality' (ie the hypothetical situation where all the 'good health' is in the least deprived group). However, in the context of health the range of observed inequality will usually be much smaller.



Confidence intervals for the concentration index can be calculated using simulation either in an Excel VBA script or using statistical software.

Each value on the *y*-axis is derived from the indicator values for the individual areas. As long as we have some information about the underlying variability of those indicator values, ie from distributional assumptions or calculated variance or confidence intervals, it is possible to simulate other plausible values of the concentration index for each area by

sampling repeatedly from the underlying values' distributions. Randomised values are generated, and concentration index values calculated a large number of times (eg 10,000, 100,000 or more) and the results from each repetition recorded, giving a distribution of plausible values. The 2.5<sup>th</sup> and 97.5<sup>th</sup> centile values from that distribution can be used as estimated 95% confidence intervals for the concentration index. Because the method uses randomly generated repeated samples, running the simulation to generate confidence intervals will not generate precisely the same confidence intervals each time, unless the same software and random number generation algorithm are used, and the seed used for the for generation of random numbers within the software is set to be the same.

#### PHE Technical Guides

This document forms part of a suite of PHE technical guides that are available on the Fingertips website: https://fingertips.phe.org.uk/profile/guidance

#### References

- <sup>1</sup> Eayres D. Technical Briefing 3: Commonly used public health statistics and their confidence intervals. APHO; 2008. Available at https://fingertips.phe.org.uk/documents/APHO Tech Briefing 3 Common PH Stats and CIs.pdf. Tool to accompany briefing available at https://fingertips.phe.org.uk/documents/PHE Tool for common PH Stats and CIs.xlsx
- <sup>2</sup> PHEindicatormethods R package to be released publicly later in 2018. Currently available internally to PHE at https://gitlab.phe.gov.uk/packages/PHEindicatormethods
- <sup>3</sup> Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. *Statistical Methods in Medical Research*, 2006;**15**:547–569.
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- <sup>11</sup> Newcombe RG, Altman DG. Proportions and their differences. In Altman DG et al. (eds). *Statistics with confidence.* 2<sup>nd</sup> edition. London: BMJ Books; 2000: 46–8.
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