**Confidence Intervals for Directly Age-Standardised Rates: Modified Gamma Methodology**

***Paper for Discussion at UKIACR Analysis Group Meeting on 12th February 2014***

**Recommendation:**

Confidence intervals for directly standardised rates should be calculated using the modified gamma methodology, rather than the gamma methodology.

***Current methodology used in UK-CIS (and by at least some UK cancer analysis teams):***

Confidence intervals for directly standardized rates are based on the gamma distribution, as proposed by Fay and Feuer (1997).

***Proposed methodology change:***

The Tiwari, Clegg and Zou (2006) paper proposed a modification of the formula for the upper confidence limit, although still based on the gamma distribution.

***Methodology used by former PHO teams and HSCIC:***

As detailed in the APHO Technical Briefing 3 (2008) and a SOP discussed recently by the PHE KIT Technical Group, the Poisson based confidence intervals proposed by Dobson et al (1991) are frequently used for many other public health analyses. Additionally, these are often calculated using Byar’s approximation.

***Brief discussion:***

All three methods are more appropriate for rates than intervals based on the normal distribution. They are particularly useful for rarer diseases, with low cell counts, since they result in non-symmetrical intervals, which cannot contain inappropriate negative values.

However, direct standardisation is known to be unreliable when based on small numbers, producing unstable rates. Some concerns have also been noted about the calculation of rates where the count is zero in one or more of the specific age and sex strata. Future work is likely to investigate these issues in more detail. It could also consider which of these various confidence interval methodologies is most appropriate.

The Tiwari paper demonstrates, by simulation, that the modified gamma methodology provides better coverage than the existing Fay and Feuer gamma methodology, which had a tendency to be overly conservative. Without providing detailed results, the paper also briefly discusses the Dobson confidence intervals; it reports that, although they did not retain the nominal coverage, their coverage was closer to the nominal level than for any of the alternative intervals considered.

The confidence interval methodology used is unlikely to be fully standardised across all areas of public health, at least at the current time. While Dobson limits will continue to be recommended and used by some, there are some reasons to recommend the use of the modified gamma methodology for the UK-CIS’s replacement system, as well as for the other cancer analyses where the gamma methodology would currently be used.

***Examples of the recommended use of the modified gamma methodology:***

1. Stata’s -distrate- function has been updated to implement this modified gamma methodology, reporting that the updated function provides improved confidence intervals. Although the current version (1.1.5) does provide options to additionally report the gamma and/or Dobson limits.
2. The modified gamma methodology is recommended and used by SEER.

For example, the statistical methods section of recent paper by Edward et al references the Tiwari paper when saying:

“Corresponding 95% confidence intervals were calculated as modified gamma intervals.”

***Effect of a change from gamma methodology to modified gamma methodology:***

* This would not have a large impact, since the confidence interval changes are generally small.
* The modified gamma methodology results in upper confidence limits which are slightly lower than those obtained using the Fay and Feuer gamma methodology.
* The lower confidence limit is unchanged.

***Example:*** Uterine cancer (ICD10 C54-C55) incidence in 2009 by cancer network in England:

Largest difference: For Dorset (N27), with a rate of 19.26 per 100,000 women. The 95% confidence interval changes from (15.69, 23.76) to (15.69, 23.52). That is, the upper confidence limit decreases by 0.24 per 100,000 women.

Smallest difference: For East Midlands CN (N39), with a rate of 22.75 per 100,000. The 95% confidence interval changes from (20.89, 24.76) to (20.89, 24.74). That is, the upper confidence limit decreases by 0.02 per 100,000 women.

***References:***

Fay and Feuer (1997); Confidence intervals for directly standardized rates: A method based on the gamma distribution; Statistics in Medicine 16: 791-801

Tiwari, Clegg and Zou (2006); Efficient interval estimation for age-adjusted cancer rates; Statistical Methods in Medical Research 15: 547–569

Association of Public Health Observatories (APHO, 2008). Technical Briefing 3: Commonly Used Public Health Statistics and their Confidence Intervals.

[www.apho.org.uk/resource/item.aspx?RID=48457](http://www.apho.org.uk/resource/item.aspx?RID=48457)

Dobson, Kuulasmaa, Eberle and Scherer (1991); Confidence intervals for weighted sums of poisson parameters. Statistics in Medicine 10: 457-462

Edwards et al (2013); Annual Report to the Nation on the Status of Cancer,1975-2010, Featuring Prevalence of Comorbidity and Impact on Survival Among Persons With Lung, Colorectal, Breast, or Prostate Cancer; Cancer, DOI: 10.1002/cncr.28509

*Excel note:*

Excel isn't a formal statistical package and so has some limitations for statistical analyses. Confidence interval results produced in Excel will differ slightly from those obtained using other statistical software (eg. Stata).

In particular, Excel’s inverse Chi-squared function truncates fractional degrees of freedom. This means that gamma confidence intervals calculated in Excel will differ to those calculated using other software. However, this issue affects the calculation of confidence intervals using both the Fay and Feuer gamma methodology and the Tiwari modified gamma methodology. Other than this issue with fractional degrees of freedom, the modified gamma methodology can be implemented in Excel.

***Formulae:***

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