

## Sequential Screening

In a recent issue of Down's Screening News[1] there is an article on sequential screening, which we believe is misleading and affects some of the work published from the Wolfson Institute of Preventive Medicine.

1. It is stated that describing the Integrated Test as a single test in Wald et al[2] is an odd statement. It is a single test which is performed in two stages. The same test is performed on everyone and only one screening result is issued. The author of the article does not refute this, but states that "what seems to be meant is that the first trimester component is not used until the end of the process" and adds "which most would regard is a bad thing". Whether it is a good or a bad thing is a separate matter, which does not affect the accuracy of describing the Integrated Test as a single test.

2. Again referring to Wald et al[2], it is stated that the statement that the Integrated Test always provides the best results contradicts modelling in several other papers using exactly the same parameters. This is misleading. The paper[2] shows that if the same markers are used in both tests, the Integrated Test is better. But if more screening markers are used with sequential screening than with the Integrated test, then it can have a better performance if the first trimester false-positive rate is very low (less than about 0.2%). If the same markers are used the Integrated Test performed on all women is always best.

3. The article states that the philosophy of the Integrated Test is to measure each marker only once, in the trimester in which it is most discriminatory. This is incorrect. The principle is that the first trimester markers are not interpreted immediately, but held and interpreted in combination with the second trimester markers. This can include any markers in each trimester, even the same ones.

4. The article repeats the argument presented by Wright et al[3] in response to our paper on CT marker ratios[4] arguing that the repeat measures approach which uses the standard multivariate Gaussian analysis based on all the individual measurements and the CT marker ratio approach, which is a variant to this, in which repeat measures of the same marker are expressed as a ratio are equivalent formulations of the same mathematical approach. No

mention is made of our explanation why this is in practice not the case.[5] The short piece in Down's Screening News is therefore inaccurate, misleading and incomplete.

## References

1. "Sequential Screening". Down's Screening News, 2007:14 (1):31
2. Wald NJ, Rudnicka AR, Bestwick JP. Sequential and contingent prenatal screening for Down syndrome. *Prenat Diagn* 2006;**26**:769-777
3. Wright D, Bradbury I, Benn P, Nix B, Spencer K, Cuckle H. CT ratios: Parameter estimates are inconsistent with SURUSS publications? *Prenat Diagn* 2006;**26**:991-2
4. Wald NJ, Bestwick JP, Morris JK. Cross-trimester marker ratios in prenatal screening Down syndrome. *Prenat Diagn* 2006;**26**:514-23
5. Wald NJ, Bestwick JP, Morris JK. Cross trimester marker ratios: parameter estimates valid with no inconsistency. *Prenat Diagn* 2006;**26**:994

Nicholas Wald, Jon Bestwick, Joan Morris

14 May 2007