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To the Editor:

In the July issue (*Contraception* 2003;68:11–17), you published a meta-analysis by Dr. Khader et al. on the risk of myocardial infarction associated with the use of oral contraception [1]. The article has a nearly one-page long description of the methods, i.e., how articles were identified by several approaches, how two reviewers independently reviewed studies and how the data from 19 studies were extracted by no less than three investigators using a standard protocol.

Among these 19 studies I find, listed with their study characteristics in Table 1, one study by “Frits et al.” and one study by “Tanis et al.” In the table, these two studies have different reference numbers and, indeed, in the reference list, we find one by “Tanis et al.” and one by “Frits R.” Interestingly, the first one has only two authors, the second one being “Rosendaal FR.” Both references cite the same article title and the same journal and source (N Engl J Med 2001;345:1887–1793) [2].

Nevertheless, in the table the article by Frits and the article by Tanis appear to have different characteristics: one included women aged 18–49, and the other women aged 24–49. Under the column that gives details about adjustment, it says Frits et al. adjusted, “but factors are unknown,” while Tanis et al. adjusted for smoking, diabetes, hypercholesterolemia, hypertension, obesity, family history of CVD, education and alcohol intake. The studies apparently also had different locations, since one (Tanis) was conducted in the Netherlands, whereas Frits et al. performed his study in “Nationwide.” Closer inspection of the article yields more inaccuracies, e.g., a US article is cited to include data on prothrombin 20210A mutation, while it only relied on interviews, and the information is not consistent over the tables.

Readers of meta-analyses rely on the integrity and accuracy of those who performed and reported the study. In theory, it is easier to spot unreliable analyses in meta-analyses than in original research, since one only needs a library to repeat the exercise. This article shows that it may not be so easy after all, since the independent reviewers and abstractors did not notice that they included the same article twice and abstracted it incorrectly, nor did the editors and reviewers of *Contraception*. It is needless to say that this particular article is completely invalidated by the inclusion of nonexistent data, but there are also wider lessons to be

learned; first, that a meta-analysis or systematic review should be viewed as seriously as an original study, e.g., when performed by junior researchers they should be adequately supervised and second, that even when a label of Ia Level of Evidence is attached to a study, readers should not believe all they read.

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References

- [1] Khader YS, Rice J, John L, Abueita O. Oral contraceptives use and the risk of myocardial infarction: a meta-analysis. *Contraception* 2003;68: 11–7.
- [2] Tanis BC, van den Bosch MA, Kemmeren JM, Manger Cats V, Helmerhorst FM, Algra A, van der Graaf Y, Rosendaal FR. Oral contraceptives and the risk of myocardial infarction. *N Engl J Med* 2001;345:1787–93.

Response to Letter to the Editor

Dear Editor:

We agree with Frits R. Rosendaal that we described the study by Tanis et al. [1] twice using different author names and somewhat different characteristics and references. The correct reference is reference [21], in our study that refers to the study by Tanis et al. (the correct age group is 18–49). However, this study was used once in our data analyses and not repeated at all. Also, it is clear from graphs (Forest plots) that nonexistent data were not included in our data analysis. It is obvious in our study that the incorrect reference (i.e., reference [19]) was neither shown in the main analysis nor in the subgroup analysis.

The mistakes that happened in: (a) enumerating the study