positive and false-negative findings rapidly increases as multiple subgroups are evaluated.[2] Subgroups should only be evaluated for the direction of effect: in our study there was an increased risk of fractures in women with diabetes who received either pioglitazone or rosiglitazone.

In addition, in implementing a random-effects model, Toulis and colleagues not only reduced the power of the meta-analysis[3] but also shifted the weight of the analysis toward smaller, short-term studies that recorded relatively few events. When one is dealing with a rare adverse event that occurs only with prolonged therapy, it is only with adequately powered trials of longer duration that one will be able to discern these effects, as seen with the thiazolidinediones and fracture risk. Indeed, use of the random-effects model has been shown to lead to biased results in the analysis of rare events.[3]

Finally, the manufacturers of pioglitazone have released results confirming the increase in fracture risk seen with pioglitazone (1.9 fractures per 100 patient-years in the pioglitazone group and 1.1 fractures per 100 patient-years in the comparator group in 19 company-conducted trials).[4] Hence, the available biologic, clinical and epidemiologic evidence confirms that fractures are a class effect of both of the thiazolidinediones: rosiglitazone and pioglitazone.

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Correction

A recent News article[1] mistakenly identified Derek Jones as an ex-officio member of the Inter-Agency Advisory Panel on Research Ethics. In fact, Jones is the former executive director of the panel, who was interviewed for the article but was not present at the launch of the Tri-Council Guidelines. *CMAJ* apologizes for any inconvenience this information may have caused.

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