Reviewer’s report

**Title:** Age-of-onset-dependent Influence of NOD2/CARD15 gene variants on Disease behaviour and treatment in Crohn’s disease

**Version:** 2 **Date:** 22 January 2013

**Reviewer:** Maria Francisca Gonzalez-Escribano

**Reviewer’s report:**

I have reviewed the revised version of the manuscript entitled “Age of onset dependent influence of NOD2/CARD15 gene variants on disease behaviour and treatment in Crohn’s disease” by Posovszky et al. I have also read the response of the authors to reviewers.

The authors have made a big effort to meet the different questions raised and to improve the original manuscript. Unfortunately, in my opinion, the main problems persist. Thus, the most original point of the manuscript (BMD variants / osteoporosis and NOD2) is lost among other results and comparisons.

Other questions:

1. Taking into account the sample size, it is difficult to extract conclusions with the type of analysis performed and the number of variables included. Likely some of the variables are not independent why authors did not performed an multivariate analysis?

2. In the section “Pediatric-onset CD patients…..” of the Results (page 10) the numbers of the Figures seem to be erroneous

3. Authors suggest a trend of patients with variants of NOD2 towards low BMD but the frequency of patients with two variants is the same among patients with low BMD as among patients with normal BMD

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests