**Reviewer's report**

**Title:** A IGF-I promoter polymorphism modifies the relationship between birth weight and risk factors for cardiovascular disease and diabetes at age 36

**Version:** 1 **Date:** 13 March 2005

**Reviewer:** johan eriksson

**Reviewer's report:**

General
IGF-I is involved in fetal growth, cell differentiation and well as in the regulation of metabolic function. An identified polymorphism in the IGF-I gene promoter region is thought to influence the transcription rate of IGF-I. The authors of the present manuscript have focused upon the role of IGF-I genotypes in relation to cardiovascular risk factors and fetal growth.

The research questions are clearly stated and relevant. The manuscript is well-written. The blood pressure finding is interesting although the overall findings are otherwise fairly modest.

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**Major Compulsory Revisions** (that the author must respond to before a decision on publication can be reached)

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**Minor Essential Revisions** (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

There are some points that need further clarification

1) The authors state that the Dutch population described in this study was selected from participants in the AGAHLS. The obvious question is based upon what criteria were people selected? What was the original size of the AGAHLS? Selection bias? Please provide more information on this aspect.

2) Twins and prematurely born individuals were excluded. How were siblings treated in the analyses? Would it have influenced the results if those born prematurely had been included?

3) The AGAHLS study is a longitudinal follow-up of children meaning that some childhood growth data should be available? Is this the case? Were there interactions between childhood growth and the IGF-I genotypes studied? Were there any other birth information available than birth weight (e.g. birth length).

4) One aim of the study was to assess risk factors for type 2 diabetes (T2DM – please use this in the text instead of DM-2 if abbreviations are needed) but no glucose measurements were available. HbA1c was used – please provide the reference value for the method applied. Based on only HbA1c values the presence or absence of T2DM cannot be confirmed/ruled out.

5) The association between birth weight and FFM is interesting and something that has been observed previously. The authors state that this association lost significance after adjustment for adult body weight. The FFM could perhaps be studied in various adult BMI groups separately for the sexes.

6) In the discussion the rather small study population should be commented upon.

7) Page 9, para 2 states that the results concerning risk factors for CVD and T2DM did not show an increased risk in the VC group while the authors state that subjects in the VC group had significantly higher LDL concentrations on page 7. Please correct/clarify.

8) Page 9 para 2 the authors are discussing disease incidence – however the risk factor profile was
assessed.
9) Page 3 para 2 Please delete the word “three” in relation to studies on gene-environment interactions published.
10) Table 2 is “heavy”, please make is more reader friendly since most information is not that exciting

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests