

## Supplemental Material

### 1. Examination of possible effects of Attrition

While the differences between most of the variables employed in the study did not approach significance (see main Table 1) that for PIQ between the analysed and the unanalysed group did so ( $p=.089$ ) For that reason it was decided to carry out a further analysis to test the sensitivity of the effect of reducing (by selection) the mean value of PIQ in the analysed group to 99.0, which is that of the value for PIQ in the unanalysed group. An analysis similar to that used to produce Table 2 in the main results section was carried out and is presented here as Supplement Table 1. The results are for the whole samples, not split according to the sex of the subjects as in main Table 2, so as not to complicate the presentation. It is seen from this comparison that the results from both samples are substantially the same with the exception of those for the relation between stunting and disorganisation in path c .

**Supplement Table 1** Regression beta weights for paths relating Stunting, Anemia at age 3 to Verbal and Performance IQ at age 11 and to Schizotypy measures at age 23 in the analysed sample and in a sample with subjects selected to have a mean PIQ of 99.00 similar to that of the unanalysed sample The groups of results are for separate paths in the SEM analyses ( see text)

	Analysed sample			Sample with mean PIQ =99.00		
	beta	SE	<i>p</i>	beta	SE	<i>p</i>
<b>Path a</b>						
Stunting - Verbal IQ	<b>-3.4</b>	<b>.41</b>	<b>&lt;.001</b>	<b>-3.0</b>	<b>.41</b>	<b>&lt;.001</b>
Stunting – Performance IQ	<b>-4.2</b>	<b>.40</b>	<b>&lt;.001</b>	<b>-3.7</b>	<b>.39</b>	<b>&lt;.001</b>
Anemia – Verbal IQ	<b>-1.5</b>	<b>.31</b>	<b>&lt;.001</b>	<b>-1.3</b>	<b>.31</b>	<b>&lt;.001</b>
Anemia – Performance IQ	<b>-1.7</b>	<b>.30</b>	<b>&lt;.001</b>	<b>-1.4</b>	<b>.28</b>	<b>&lt;.001</b>
Adversity-Stunting	<b>.20</b>	<b>.02</b>	<b>&lt;.001</b>	<b>.19</b>	<b>.02</b>	<b>&lt;.001</b>
Adversity-Anemia	<b>.19</b>	<b>.03</b>	<b>&lt;.001</b>	<b>.17</b>	<b>.03</b>	<b>&lt;.001</b>
<b>Path b</b>						
Verbal IQ-Cognitive perceptual	.01	.01	.313	.02	.01	.281
Perf IQ Cognitive perceptual	.01	.01	.359	.02	.02	.254

Verbal IQ-Interpersonal	-.01	.02	.721	-.01	.02	.567
Perf IQ - Interpersonal	<b>-.06</b>	<b>.02</b>	<b>&lt;.001</b>	<b>-.06</b>	<b>.02</b>	<b>&lt;.001</b>
Verbal IQ-Disorganisation	-.01	.01	.251	-.01	.01	.114
Perf IQ- Disorganisation	<b>-.03</b>	<b>.01</b>	<b>&lt;.001</b>	<b>-.03</b>	<b>.01</b>	<b>.002</b>

**Path c**

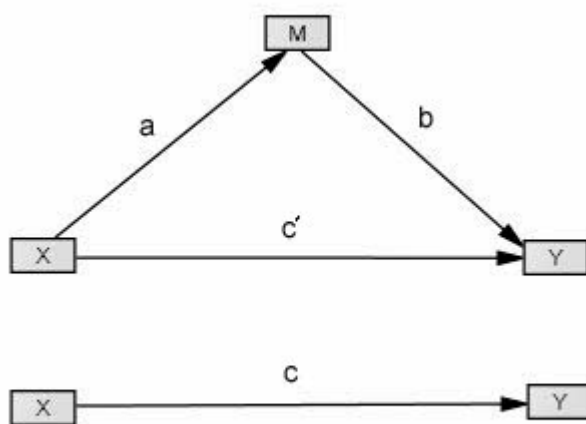
Stunting-Cognitive perceptual	.11	.19	.579	.09	.22	.663
Stunting-Interpersonal	.06	.21	.783	-.02	.23	.925
Stunting-Disorganisation	.06	.12	.624	.04	.14	.766
Anemia-Cognitive-perceptual	.08	.14	.575	.07	.16	.676
Anemia-Interpersonal	.27	.15	.080	.25	.17	.139
Anemia-Disorganisation	.10	.09	.255	.08	.10	.430

**Path c**

Stunting-Cognitive perceptual	.04	.18	.812	.02	.20	.930
Stunting-Interpersonal	.37	.20	.056	.26	.22	.238
Stunting-Disorganisation	<b>.23</b>	<b>.11</b>	<b>.039</b>	.21	.13	.109
Anemia-Cognitive-perceptual	.02	.14	.864	.02	.15	.891
Anemia-Interpersonal	<b>.35</b>	<b>.15</b>	<b>.017</b>	<b>.33</b>	<b>.17</b>	<b>.047</b>
Anemia-Disorganisation	.15	.09	.077	.13	.10	.182

**2. Discussion concerning the mediation analyses used in this paper.**

The original definitive paper on mediation analysis was that of Baron and Kenny (1). These authors set three criteria for the presence of mediation. (see figure); (1) that the direct path **c**



relating X (the independent variable) and Y (the dependent variable) which they call the “effect to be mediated” should be significant, (2) that the path **a** relating X and M (the mediator) should be significant and (3) that the path **b** relating M and Y, taking account of path **a** should also be

significant. If the path **a x b** is significant and the path **c** (where **c** is the path between X and Y taking account of the indirect path **a x b**) is not, then the mediation is said to be full,

On the other hand if both paths  $a \times b$  and  $c$  are significant the mediation is partial. The Baron and Kenny criteria have been questioned by Zhao (2) who state that there should be only one requirement to establish mediation that is that the indirect effect  $a \times b$  should be significant. These authors also recommend that the bootstrap method of Preacher and Hayes (3) should be used in determining the significance of this indirect effect as it is independent of the type of distribution of the variables. In addition Iacobucci et al (4) show that where there are multiple  $a$  and  $b$  paths, as in the present study it is better to use structural equation modelling (SEM) than regressions. These are the methods which are used in the main analyses in the paper.

However, the position is further complicated by developments recommended by VanderWeele (5) and Hafeman (6) who have proposed an approach to the analysis of mediation which necessitates taking into account the influence of variables other than those directly concerned in the earlier versions of mediation analysis above, that is the independent variable X, the mediator M and the dependent variable Y. They identify variables of type A which may influence X, variables of type K which may influence M at the time when A and X are present, variables of type B which may influence M at the time when M operates, variables of type C which influence the role of X at the time when M operates, variables of type F which operate on the joint effect of X and M and variables of type L which operate on Y directly.

Their proposals on how their structure operates are made in the context where all the variables are binary. Hafemen (6) states (p719) that “ the MSC ( minimal sufficient cause) based model and response type framework apply most readily to dichotomous variables, further work might extend these methods to polytomous or continuous variables”. As all the variables in the present study are continuous it was thought appropriate use the SEM

modelling approach but to attempt to apply the VanderWeele and Hafeman logic in identification of variables which might influence the mediation analysis.

In the present instance the use of additional variables is of necessity confined to those which are available because they are present in the database of this cohort study (7) and which in addition have been shown in other studies, or may be thought on other grounds, to be relevant intervening variables.

### **3 Application of the VanderWeele and Hafeman approach to the present data.**

The following variables are thought to be representative of those identified by capital letters in the VanderWeele and Hafeman approach.

A. (1) Adversity measured at age 3, (2) birthweight

B. Adversity at age 11 see (8) for details of measurement

K (1) Stimulus seeking measured at the time of testing at age 3 see reference (9) for details of the construction of a measure of stimulus seeking. This study found a strong correlation between stimulus seeking and intelligence. (2) Pregnancy and delivery complications. There is good evidence that prenatal and perinatal events influence risk for schizophrenia see for instance (10). Details of the measures used here are given in (11)

L Adversity measured at age 23. This index was calculated by adding a score of 1 for each of the following variables, poor housing, problems in the area, overcrowding, poor education, unhappiness at work, unemployment, low income, and inability to get on with mother or father.

The analysis involved a model including these variables and the X, M and Y variables used previously.

The results are presented in Supplement Table 2. All the paths involving measures of adversity at each of the three ages are significant as expected but even when effectively

taking account of these relations, the path X-M (equivalent to path **a** in the main analysis) and path M-Y (equivalent to path **b** in the main analysis), the findings substantially replicate those presented in Table 2 in the main part of the paper. The path K-M is highly significant as expected as it replicates the findings in (9). The paths K-Y examining the effects of birth complications on schizotypy factors are complex and involve sex differences. However, even taking account of the role of these variables, as shown above, the main mediation findings are basically unchanged. It is perhaps surprising that the measure of birthweight was unrelated to that of stunting or to Performance IQ, however as the measure of birthweight available was not corrected for gestational age it is perhaps not reliable. It may be noted that adversity measured at age 23 is related (Path M-Y) not only to the interpersonal and disorganisation aspects of schizotypy but also to the cognitive perceptual aspect thus confirm the suggestion made earlier (12) that a the form of schizotypy termed “pseudoschizotypy” measured in this instance by the cognitive-perceptual features of SPD has its origins in social adversity.

In summary, even when taking into account all the available and relevant variables which might influence the mediation findings presented in the main section of the paper it is shown that the main findings are substantially replicated.

**Supplement Table 2** Regression beta weights for paths following VanderWeele’s 2009 model N=815 (significant results in Bold type)

	Males			Females		
	beta	SE	<i>p</i>	beta	SE	<i>p</i>
<b>Path A-X</b>						
Adversity3-Stunting	<b>.19</b>	<b>.03</b>	<b>&lt;.001</b>	<b>.20</b>	<b>.03</b>	<b>&lt;.001</b>
Adversity3-Anemia	<b>.17</b>	<b>.04</b>	<b>&lt;.001</b>	<b>.21</b>	<b>.04</b>	<b>&lt;.001</b>
Birth weight-Stunting	.00	.00	.795	.00	.00	.422
<b>Path A-M</b>						
Birth weight-Performance IQ	.00	.00	.802	.00	.00	.396
<b>Path X-M</b>						
Stunting - Performance IQ	<b>-3.6</b>	<b>.56</b>	<b>&lt;.001</b>	<b>-1.9</b>	<b>.54</b>	<b>&lt;.001</b>
Anemia – Performance IQ	-.61	.43	.16	<b>-1.1</b>	<b>.40</b>	<b>.004</b>

<b>Path K-M</b>						
Stimulus seek-Perf IQ	<b>2.0</b>	<b>.58</b>	<b>&lt;.001</b>	<b>3.0</b>	<b>.58</b>	<b>&lt;.001</b>
<b>Path B-M</b>						
Adversity11-Performance IQ	<b>-1.3</b>	<b>.38</b>	<b>&lt;.001</b>	<b>-2.1</b>	<b>.36</b>	<b>&lt;.001</b>
<b>Path M-Y</b>						
Perf IQ Cognitive perceptual	.02	.02	.365	.04	.02	.074
Perf IQ - Interpersonal	<b>-.05</b>	<b>.02</b>	<b>.012</b>	<b>-.04</b>	<b>.02</b>	<b>.043</b>
Perf IQ- Disorganisation	<b>-.03</b>	<b>.01</b>	<b>.009</b>	<b>-.03</b>	<b>.01</b>	<b>.033</b>
<b>Path K-Y</b>						
Preg Comps- Cog Perceptual	<b>1.75</b>	<b>.77</b>	<b>.024</b>	.43	.70	.535
Preg Comps-Interpersonal	.96	.87	.267	<b>1.8</b>	<b>.72</b>	<b>.014</b>
Preg Comps-Disorganisation	<b>1.2</b>	<b>.50</b>	<b>.022</b>	.25	.44	.578
Del Comps-Cog Perceptual	.55	.36	.125	-.17	.40	.667
Del Comps-Interpersonal	.55	.40	.164	-.44	.40	.280
Del Comps-Disorganisation	1.1	.49	.022	-.21	.25	.407
<b>Path L-Y</b>						
Adversity23-Cog perceptual	.94	.19	<.001	.33	.17	.048
Adversity23-Intepersonal	1.08	.21	<.001	.66	.17	<.001
Adversity23-Disorganisation	.51	.12	<.001	.53	.10	<.001

#### **(4) Analyses with those subjects taking part in intervention study(13) excluded.**

The analyses presented in the paper are on all available subjects, however some of these subjects took part in an intervention study in which 100 of the subjects were placed in special nursery schools and among other things were given an enhanced diet. This regime was shown to have beneficial effects on those who previously showed signs of malnutrition. The inclusion of these subjects in the analyses may therefore have had distorting effects on the findings presented.

Further analyses were therefore carried out with these subjects omitted. The Table 3 below show results which are parallel to those in Table 2 in the paper and show that the main findings are not distorted by the inclusion of the enriched subjects.

**Supplemental Table 3.** Regression beta weights for paths relating Stunting, Anemia and Adversity at age 3 to Verbal and Performance IQ at age 11 and to Schizotypy measures at age 23 in separate samples of males and females. The groups of results are for separate paths in the SEM analyses N=796, sample with subjects in intervention study removed. (significant results in Bold type)

	Males			Females		
	beta	SE	p	beta	SE	P
<b>Path a</b>						
Stunting-Verbal IQ	<b>-3.4</b>	<b>.63</b>	<b>&lt;.001</b>	<b>-1.9</b>	<b>.60</b>	<b>&lt;.001</b>
Stunting-Performance IQ	<b>-4.2</b>	<b>.59</b>	<b>&lt;.001</b>	<b>-3.2</b>	<b>.60</b>	<b>&lt;.001</b>
Anemia-Verbal IQ	<b>-1.1</b>	<b>.50</b>	<b>.021</b>	<b>-1.5</b>	<b>.44</b>	<b>&lt;.001</b>
Anemia-Performance IQ	<b>-.93</b>	<b>.46</b>	<b>.045</b>	<b>-2.0</b>	<b>.43</b>	<b>&lt;.001</b>
<b>Path b</b>						
Verbal IQ- Cognitive perceptual	-.005	.019	.789	.034	.022	.118
Verbal IQ- Interpersonal	-.014	.021	.494	-.002	.023	.992
Verbal IQ-Disorganisation	-.005	.012	.687	-.015	.014	.277
Performance IQ - Cognitive perceptual	.021	.020	.289	.008	.022	.730
<b>Performance IQ - Interpersonal</b>	<b>-.058</b>	<b>.022</b>	<b>.010</b>	<b>-.066</b>	<b>.023</b>	<b>.004</b>
<b>Performance IQ- Disorganisation</b>	<b>-.031</b>	<b>.013</b>	<b>.014</b>	<b>-.036</b>	<b>.014</b>	<b>.009</b>

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