

**Eat2beNICE****Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing Behaviours
H2020 - 728018**

D 2.5 – Manuscript: Predictors of clinical response to nutritional interventions

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Executive Summary

In this report, we compare predictors and mediators of response to nutritional interventions within WP2. The main finding that stands out from both studies, is that higher levels of impulsivity predict poorer adherence to nutritional intervention programs. In adults, poorer adherence mediates the relation between the intervention and response. In contrast, in children, higher impulsivity was also associated with better response after 5 weeks and 1 year. This may seem counterintuitive at first sight, but can be explained by the degree to which parents are able to restrict / prevent the child from impulsive eating and violating dietary restrictions. As this is easier for younger children than older children, and easier for parents without mental health problems than for parents with mental health problems, the other relevant predictors of response may support the hypothesis that those that are able to benefit most from nutritional interventions are the ones that have the most difficulties to adhere to the dietary restrictions. Nutritional intervention programs should therefore consider co-interventions (mindfulness, pharmacotherapy) targeting impulsivity to improve adherence and response to the intervention.

Abbreviations

ADHD	Attention deficit / hyperactivity disorder
RCT	Randomized Controlled Trial
ED	Elimination diet
HD	Healthy diet
CAU	Care as usual
ITT	Intention-to-treat
BMI	Body mass index
HbA1c	Glycated haemoglobin
MedDiet	Mediterranean Diet
T2D	Type 2 diabetes



1. Deliverable report

Study 1

Study design

In this study we assessed the short- and long-term effects of an elimination diet (ED) versus a healthy diet (HD) according to WHO health guidelines on reducing impulsive, compulsive, and aggressive behaviour. A total of N=165 children (5-12 years) with ADHD were randomized by means of minimization (1:1) to either ED (N=84) or HD (N=81) within two Dutch child and adolescent psychiatry centers.

Ordinal logistic regression ITT analyses were run to determine which child or parental factors could predict adherence and respondership taking into account type of dietary treatment.

Predictors of adherence after 5 weeks

The majority of participants showed good to excellent adherence (91.9% of ED participants and 87.5% of HD participants). Chi-square tests revealed no differences between the two dietary treatment groups in adherence rated by parents ($\chi^2(2, N = 147) = 1.33, p = .515$) and dietician ($\chi^2(2, N = 147) = 0.41, p = .813$). A trend significant difference showed that almost three times as many ED participants (N = 9; 10.7%) quit the diet (but did not quit the study) before T1 compared to HD participants (N = 3; 3.7%), $\chi^2(1, N = 165) = 3.01, p = .083$. These participants also showed more often insufficient adherence to treatment (until they quitted the diet) compared to participants who followed the diet until T1. Factors that predicted better adherence to the diet were: younger age, less severe emotion regulation problems at baseline rated by teachers, higher educational level of mothers, fathers' country of birth the Netherlands, not often using the parenting style 'punishment', and higher parental prior believes about success of treatment.

Predictors of response after 5 weeks

Results showed a significant difference in adherence between ED participants who followed the diet until T1 and ED participants who quit the diet before T1. The latter group showed more often insufficient adherence to treatment before quitting $\chi^2(2, N = 147) = 8.06, p = 0.018$. For HD participants, a trend was found $\chi^2(2, N = 147) = 5.29, p = 0.071$. Therefore, proportions of adherence were compared in the HD group using a z-test with Bonferroni corrections. Results showed a difference of 26.2% (95% CI [3.87, 48.61]) in the category insufficient adherence: more HD participants who quit the diet before T1 were categorized in the insufficient adherence group compared to participants who followed the diet until T1.

Logistic regression analyses using the backward step method were run to determine which factors predicted good to excellent adherence to the dietary treatments. Analyses including child characteristics as predictors showed that older children were less likely to show good or excellent adherence to the diets, rated by parents (OR: 0.57, 95% CI [0.34, 0.95], $p = 0.030$). The interaction term with treatment was significant (OR: 0.19, 95% CI [0.04, 0.99], $p = 0.037$) indicating that specifically older children following the HD were less likely to show good or excellent adherence to the HD. Adherence rated by dieticians showed the same trend for age and adherence (OR: 0.69, 95% CI [0.47, 1.01], $p = 0.059$). In addition, children with higher severity of emotion regulation problems at baseline rated by teachers were less likely to show good or excellent adherence to the diets, rated by dieticians (OR: 0.78, 95% CI [0.64, 0.94], $p = 0.009$). The interaction term with treatment was not significant (OR: 1.18, 95% CI [0.49, 2.86], $p = 0.714$).

Analyses including parental characteristics as predictors showed that children of parents with higher prior believes about success of treatment were more likely to show good or excellent adherence, rated



by parents (OR: 9.65, 95% CI [1.62, 57.62], $p = 0.013$). Children of mothers with secondary level of education (see Table 1) were more likely to show good or excellent adherence, rated by parents (OR: 0.78, 95% CI [0.64, 0.94], $p = 0.017$). Moreover, children of fathers with another country of birth than the Netherlands were less likely to show good or excellent adherence, rated by parents (OR: 0.10, 95% CI [0.01, 0.60], $p = 0.012$). Adherence rated by dieticians showed the same result for country of birth of father and adherence (OR: 0.10, 95% CI [0.01, 0.32], $p = 0.001$). Interaction terms with treatment were not significant for these predictors (OR: 0.10, 95% CI [0.01, 11.62], $p = 0.343$), (OR: 3.57, 95% CI [0.05, 254.99], $p = 0.559$), (OR: 24.07, 95% CI [0.14, 4141.82], $p = 0.226$), (OR: >100, 95% CI [n.a.], $p = .997$), respectively. Finally, when parents more often used the parenting style 'punishment', a trend significant results showed that children were less likely to show good or excellent adherence, rated by dieticians (OR: 0.33, 95% CI [0.11, 0.97], $p = 0.051$). The interaction term with treatment was not significant (OR: 1.57, 95% CI [0.11, 23.42], $p = 0.742$).

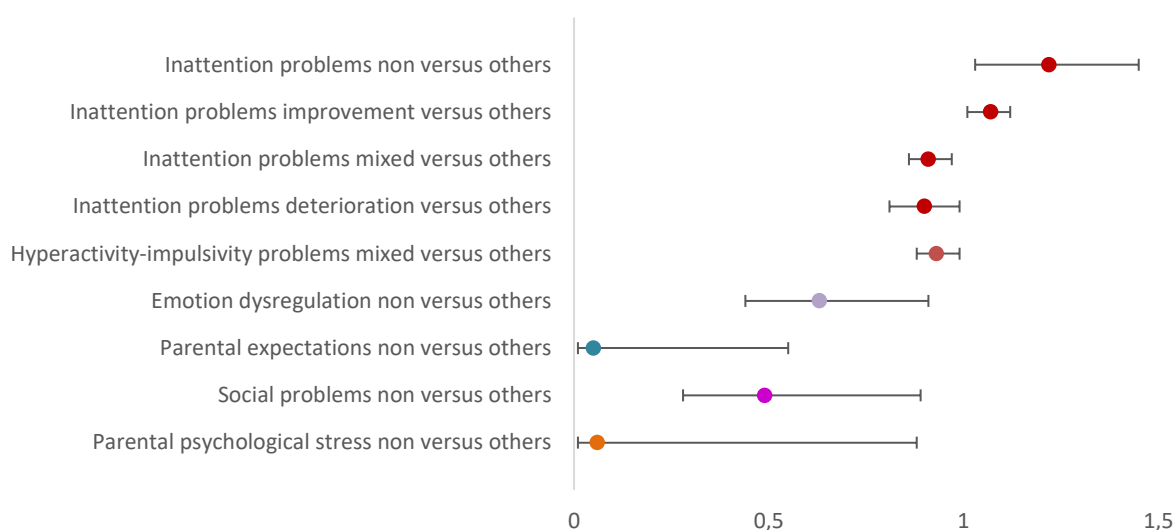
Predictors of adherence after 1 year

Participants who complied with the HD until T4, showed better adherence during the first five weeks compared to the time after five weeks until the one-year follow-up, according to both parents ($p < .05$) and dieticians ($p < .05$). Also, participants who complied with the ED combined with CAU until T4, showed better adherence during the first five weeks compared to the time after five weeks until the one-year follow-up, according to both parents ($p < .05$) and dieticians ($p < .05$).

Children who showed insufficient adherence to the dietary treatment scored significantly higher on emotional problems (based on the SDQ) at T0 compared to children who showed good to excellent adherence, rated by dieticians ($t=2.18$, $p=0.037$). Families of children who showed good to excellent adherence to the dietary treatment scored significantly higher on family resilience (e.g. parents are confident about their parenting skills and receive support from family or friends) at T0 compared to families of children who showed insufficient adherence, rated by dieticians ($t=2.48$, $p=0.019$). Moreover, parents of children who showed good to excellent adherence scored lower (trend significance) on parental stress at T0 compared to parents of children who showed insufficient adherence, rated by parents ($t=1.82$, $p=0.052$). Finally, more parents of children (20.0%) who showed insufficient adherence to treatment had a lower education level compared to parents of children who showed good to excellent adherence to treatment (0.0%), rated by dieticians $\chi^2 (2, N = 33) = 7.58$, $p = .023$.

Predictors of response after 1 year

Figure 1 displays the results of binary Logistic Regression Analyses using Baseline Measurements to predict specific Improvement Categories versus all other Improvement Categories for Dietary Treatments. Results demonstrate that more inattention problems at baseline rated by teachers predicted higher chances of improvement and lower chances of mixed improvement or deterioration. Rated by parents this predicted higher chances of non-improvement. More hyperactivity-impulsivity problems at baseline rated by parents predicted lower chances of mixed improvement. More emotion regulation problems and social problems (both rated by teachers) at baseline predicted lower odds of non-improvement. In addition, higher parental believes about success of treatment at baseline and higher levels of parental clinical psychological stress predicted lower odds of non-improvement.



Note. Values represent odds ratios and corresponding 95% confidence intervals; improvement, partial improvement, mixed improvement, non-improvement and deterioration is coded as 1 and category others is coded as 0; parental psychological stress is based on the GHQ-12 using the cut-off score ≥ 3 is coded as 1 and scores below the cut-off are coded as 0.

Study 2

Study design

A 3-year prospective cohort analysis within the PREDIMED-Plus-Cognition study conducted in 4 PRED-IMED-Plus study centers was performed. The PREDIMED-Plus study aimed to test the beneficial effect of a lifestyle intervention on the primary prevention of cardiovascular disease. The participants with overweight or obesity and metabolic syndrome included in the present study ($n=462$; mean age of 65.3 years; 51.5% female) completed both the UPPS-P Impulsive Behavior Scale (range: 0–236 points) and the 143-item Food Frequency Questionnaire at base-line, 1-year and 3-years of follow-up. Ten diet scores assessing healthy and unhealthy dietary patterns were evaluated. Linear mixed models were performed adjusting by several confounders to study the longitudinal associations between impulsivity trait and adherence to dietary pattern scores over 3 years of follow-up (also assessing interactions by sex, age, and intervention group).

Predictors of adherence

Impulsivity was negatively associated with adherence to the Healthy Plant-Based [$\beta = -0.92$ (95%CI -1.67, -0.16)], Mediterranean [$\beta = -0.43$ (95%CI -0.79, -0.07)], Energy-Restricted Mediterranean [$\beta = -0.76$ (95%CI -1.16, -0.37)], Alternative Healthy Eating Index [$\beta = -0.88$ (95%CI -1.52, -0.23)], Portfolio [$\beta = -0.57$ (95%CI -0.91, -0.22)], and DASH [$\beta = -0.50$ (95%CI -0.79, -0.22)] diet scores over 3 years of follow-up, whereas impulsivity was positively related with adherence to the unhealthy Western diet [$\beta = 1.59$ (95%CI 0.59, 2.58)] over time. An interaction by intervention group was found, with those participants in the intervention group with high impulsivity levels having lower adherence to several healthy dietary patterns.

Predictors of response

Higher levels of impulsivity (sensation seeking) were associated with poorer response after 3 years (changes in BMI: $\beta = -.26$, $p = .002$; changes in weight: $\beta = -.31$, $p < .001$)



Comparison of predictors of adherence and response

The main finding that stands out from both studies, is that higher levels of impulsivity predict poorer adherence to nutritional intervention programs. In adults, poorer adherence mediates the relation between the intervention and response. In contrast, in children, higher impulsivity was also associated with better response after 5 weeks and 1 year. This may seem counterintuitive at first sight, but can be explained by the degree to which parents are able to restrict / prevent the child from impulsive eating and violating dietary restrictions. As this is easier for younger children than older children, and easier for parents without mental health problems than for parents with mental health problems, the other relevant predictors of response may support the hypothesis that those that are able to benefit most from nutritional interventions are the ones that have the most difficulties to adhere to the dietary restrictions. Nutritional intervention programs should therefore consider co-interventions (mindfulness, pharmacotherapy) targeting impulsivity to improve adherence and response to the intervention.

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