

Prevention of cardiometabolic risk in European children and adolescents: extended post-intervention follow-up of the IDEFICS/I.Family cohort

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The present study investigates the long-term impact of the Identification and Prevention of Dietary- and Lifestyle-induced Health Effects in Children and Infants (IDEFICS) controlled intervention designed to prevent overweight, while promoting cardiometabolic health in a cohort of children in eight European countries.¹ Over the years, systematic reviews of controlled interventions to prevent obesity in children have been published, based on randomized and non-randomized studies (e.g. Waters *et al.*² and Brown *et al.*³). The results have been inconsistent, with small effect sizes for body mass index (BMI), which varied by age, sex, and type of intervention. Few studies have monitored other cardiometabolic indicators or conducted a long-term follow-up. The purpose of this communication is to report an extended analysis of the IDEFICS intervention impact after 6 years on cardiometabolic indicators and BMI.

At the IDEFICS baseline examination in academic year 2007–08, 16 229 children aged 2–9 years participated in health examinations. A community-oriented health promotion intervention was designed based on a standardized intervention mapping protocol, including three thematic areas, diet, physical activity, and stress control.⁴ The intervention was community-oriented and non-randomized. Within each survey country, around half of the children lived in intervention communities, the remainder in socioeconomically matched control areas. Post-intervention examinations including BMI and cardiometabolic risk markers were conducted 2 years after recruitment. In the subsequent I.Family study, the same children from intervention and control communities were re-examined 6 years after their original

recruitment. The cohort study was registered in the ISRCTN, <https://doi.org/10.1186/ISRCTN62310987>.

This communication compares 6-year cardiometabolic trajectories of intervention vs. control groups. The primary study outcome is a four-component metabolic syndrome risk score (MetS-RS), developed for children by Eisenmann.⁵ Age- and sex-specific z-scores were internally calculated for all components of the MetS-RS.⁶ International-Obesity-Task-Force standards were used for the other study outcome, BMI z-score. The present analysis includes a sub-sample of intervention and control children who provided fasting blood samples at baseline and again at 6-year follow-up. Some of the survey centres did not measure all laboratory components of the MetS-RS or require fasting, resulting in the final analytic sample of 1159 participants from Belgium, Estonia, Germany, Hungary, Italy, and Sweden. The intervention impact was assessed with a difference-in-difference (DID) approach,⁷ using mixed models for repeated measures with unstructured covariance pattern and robust (empirical) standard errors, controlling for age, sex, and survey country. The model for MetS-RS was also further adjusted for z-BMI and parental education. Sensitivity analyses adjusted for correlations of outcome variables within communities by adding random intercepts. Sex-stratified analyses were conducted based on earlier evidence of an intervention impact on BMI in girls but not boys.⁸

Changes in MetS-RS indicated a modest advantage in the intervention group, compared with controls, independent of age, sex, survey country, z-BMI, and parental education (*Table 1*) as well as pubertal

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Table 1 Sample characteristics at baseline and at 6-year follow-up examination ($n = 1159$ children) as well as differences (95% confidence intervals) in longitudinal changes in metabolic syndrome risk score, its four components, and body mass index z-score between intervention and control group

Sample characteristics	Intervention group ($n = 685$)		Control group ($n = 474$)	
	Baseline	6-year follow-up	Baseline	6-year follow-up
	Mean (SD)			
MetS-RS ^a	0.35 (2.67)	0.72 (3.07)	0.01 (2.71)	0.77 (2.97)
z-HOMA	0.08 (1.05)	0.20 (1.28)	0.08 (1.12)	0.24 (1.08)
(z-TG—z-HDL)/2	−0.00 (0.74)	0.03 (0.85)	0.01 (0.72)	0.06 (0.87)
z-WC	0.16 (1.39)	0.46 (1.52)	0.08 (1.42)	0.29 (1.50)
(z-SBP + z-DBP)/2	0.11 (0.90)	0.03 (0.90)	−0.15 (0.89)	0.18 (0.90)
z-BMI	0.37 (1.18)	0.55 (1.14)	0.25 (1.15)	0.44 (1.10)
Age	6.4 (1.7)	12.2 (1.7)	6.3 (1.7)	12.1 (1.7)
	n (%)			
Female sex	331 (48)	—	239 (50)	—
ISCED ^b				
Low	47 (6.9)	—	21 (4.5)	—
Medium	328 (48.2)	—	199 (42.5)	—
High	306 (44.9)	—	248 (53.0)	—
Analyses in the entire sample				
Outcome		n	DID^c (95% CI)	
MetS-RS ^a		1159	−0.39 (−0.70, −0.07)	
MetS-RS, further adjusted for z-BMI			−0.36 (−0.64, −0.07)	
MetS, further adjusted for z-BMI and parental education ^b		1149	−0.37 (−0.65, −0.08)	
Components of MetS-RS				
z-HOMA		1159	−0.04 (−0.21, 0.12)	
(z-TG—z-HDL)/2			−0.02 (−0.12, 0.08)	
z-waist WC			0.09 (−0.04, 0.22)	
(z-SBP + z-DBP)/2			−0.41 (−0.52, −0.29)	
z-score for BMI				
z-BMI			−0.02 (−0.12, 0.08)	
Stratified analyses				
Outcome	Sample	n	DID^c (95% CI)	
MetS-RS ^a	Boys	589	−0.57 (−1.02, −0.12)^d	
z-BMI			0.01 (−0.12, 0.15) ^e	
MetS-RS ^a	Girls	570	−0.19 (−0.63, 0.25) ^d	
z-BMI			−0.05 (−0.20, 0.10) ^e	

HOMA, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL, HDL-cholesterol; WC, waist circumference; BMI, body mass index; parental education according to ISCED (International Standard Classification of Education).

^aMetS risk score = z-waist circumference + z-HOMA + (z-SBP + z-DBP)/2 + (z-TG − z-HDL)/2.

^bReduced number of subjects due to missing data on parental education.

^cDifference-in-difference (DID), adjusted for sex, country, age at baseline; statistically significant results are indicated in bold.

^dP-value for interaction by sex = 0.2.

^eP-value for interaction by sex = 0.5.

status (not shown). Mean blood pressure z-score was the MetS-RS component contributing most to improvement in the overall metabolic score, and this association was individually observed for z-systolic blood pressure, DID = −0.34 (−0.46, −0.22), and z-diastolic blood pressure, DID = −0.47 (−0.60, −0.35). The BMI z-scores, which are not part of the metabolic score, remained unaffected by the intervention after 6

years. Despite non-significance of sex-intervention interaction, stratified analyses showed a significant intervention effect on MetS-RS in boys, which had not been observed for either sex in the 2-year follow-up.⁹ Moreover, despite the earlier short-term effect on z-BMI in girls,⁸ no significant advantage remained after 6 years (Table 1). Earlier evidence of 2-year BMI benefits limited to children with overweight at baseline¹⁰

could not be observed after 6 years, DID = 0.03 (−0.19, 0.25). Further accounting for correlations of outcome variables between children from the same community did not affect the results (not shown). A figure illustrating the DID results is available upon request.

In summary, our results suggest beneficial outcomes of the IDEFICS intervention on the overall metabolic syndrome score, particularly on blood pressure. The intervention had a protective effect on MetS-RS in boys, but no long-term effect on z-BMI in either sex.

The extended follow-up examinations in the IDEFICS/I.Family cohort provided a unique opportunity to determine whether any benefits to cardiometabolic health could be observed during the cohort's transition to adolescence. A major strength of the IDEFICS intervention and cohort follow-up lies in the diversity of environments and lifestyles and the standardized protocols applied in all European survey centres. In particular, the program to promote healthier lifestyles was harmonized across countries with only minimal country-specific adaptations. However, due to design factors, the study has limitations. For instance, intervention and control areas were matched in each country to be similar in terms of socio-economic characteristics, but for logistical reasons, the intervention was community-based and non-randomized. Additionally, in the follow-up study, metabolic scores were only available in a reduced sub-sample, due to natural cohort attrition after 6 years combined with protocol differences among survey centres in measuring MetS-RS components. Participation rates among eligible children were found to be higher in the intervention than control areas (19.6% vs. 14.5%, respectively), and moreover, children's initial BMI and parental education were previously found to be associated with non-participation.¹ However, the observed intervention effects on MetS-RS are independent of these two factors, reducing the likelihood of selection bias, although residual confounding on individual, family or community level cannot be excluded.

Our findings add to the limited evidence on sustainability of early-life interventions, suggesting that multi-faceted behavioural programmes have the potential to improve cardiometabolic risk trajectories into adolescence. However, the apparent lack of association between the intervention and improved weight status is discouraging and underscores the difficulties that are often experienced in community-based obesity prevention initiatives. The IDEFICS intervention aimed to change structural and environmental factors in the community, but was *de facto* heavily oriented towards individual children, families and schools. Nevertheless, it is important to document the observation that childhood interventions may offer modest cardiovascular benefits, without improvements in anthropometric outcomes. Finally, the sex-stratified results are suggestive of a need for gender-sensitive cardiometabolic interventions in children.

Consent to participate

Participant inclusion required that parents give written informed consent for their children, and young children also gave verbal consent. From the age of 12 years onwards, children gave their own written informed consent in plain language. We followed the general data protection regulation. Data are stored on a secure central server with password encryption, and samples are stored in secure biobanks.

Author contributions

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Conflict of interest: none declared.

Ethical approval

The IDEFICS and I.Family study protocols adhered to the Declaration of Helsinki ethics principles for research that includes human subjects. The study was coordinated by the Leibniz Institute for Prevention Research and Epidemiology—BIPS (Germany), and survey centres obtained ethics approval from respective local institutions in each country. The cohort study is registered at the ISRCTN registry: <https://doi.org/10.1186/ISRCTN62310987>.

Data availability

The data that support the findings of this study are available from IDEFICS (<http://www.idefics.eu>) and the I.Family Study (<http://www.ifamilystudy.eu/>) but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the IDEFICS consortium.

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