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Cross-sectional and longitudinal associations between psychosocial well-being and cardio-metabolic markers in European children and adolescents

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ABSTRACT

Objective: Research examining aspects of positive mental health as potential determinants of cardio-metabolic health in young populations is scarce. We investigated associations between psychosocial well-being and waist circumference (WAIST), blood pressure (BP), the homeostasis model assessment (HOMA) for insulin resistance, triglycerides (TRG) and high-density lipoprotein cholesterol (HDL-C) considering lifestyle factors as mediators.

Methods: Data of European children and adolescents participating in the baseline (2007/2008), first follow-up (FU1, 2009/2010) and second follow-up (FU2, 2013/2014) examinations of the IDEFICS/I.Family study were used ($N_{cross\text{-}sectional}$=6,519; $N_{longitudinal}$=1,393). A psychosocial well-being score was calculated from 16 items on emotional well-being, self-esteem and social relationships (0-48 points). Cardio-metabolic markers were transformed to age- and sex-specific and in case of BP also height-specific z-scores. Lifestyle factors included diet, physical activity, sleep and electronic media use. Applying path analysis, unstandardized estimates of direct and indirect effects of well-being on cardio-metabolic markers were obtained.

Results: Cross-sectionally, well-being score showed a negative direct and a negative indirect effect through lifestyle factors on WAIST z-score (estimate per 4-point increase -0.051 p=0.001 and -0.014, p<0.001, respectively). Longitudinally, positive changes in well-being score between baseline and FU1 and between FU1 and FU2, respectively, demonstrated negative indirect effects through lifestyle $factors_{FU2}$ on WAIST $z\text{-}score_{FU2}$. Both cross-sectionally and longitudinally, higher levels of well-being showed lowering indirect effects on HOMA, BP and TRG z-scores and an increasing indirect effect on HDL-C z-score through both lifestyle factors and WAIST z-score.

Conclusions: Our results supported our hypothesis that a healthier lifestyle may be one mechanism through which higher well-being is linked with lower abdominal obesity and fewer other cardio-metabolic disorders in young populations.

Clinical trial registry information: Pan-European IDEFICS/I.Family children cohort, ISRCTN registry number: ISRCTN62310987 (http://www.isrctn.com/ISRCTN62310987)

Keywords obesity, overweight, blood lipids, metabolic syndrome

Abbreviations BMI = body mass index, BP = blood pressure, FU1 = first follow-up, FU2 = second follow-up, HDL-C = high-density lipoprotein cholesterol, HOMA-IR = homeostasis model assessment for insulin resistance, IDEFICS = Identification and prevention of Dietary- and lifestyle-induced health EFfects In Children and infantS, TRG = triglycerides, WAIST = waist circumference

INTRODUCTION

Cardio-metabolic disturbances such as overweight, elevated blood pressure, insulin resistance and abnormal blood lipid levels in childhood and adolescence have been shown to precede adverse cardio-metabolic outcomes in adulthood (1,2). An unhealthy diet and lack of physical activity are widely accepted as risk factors for cardio-metabolic disturbances (3). Further, the influence of mental health on cardio-metabolic markers is increasingly recognized. For instance, aspects of mental ill-health such as depression were found to predict the metabolic syndrome in adults (4). In children and adolescents, depressive symptoms were found to be associated with higher insulin resistance (5-7). However, mental health is more than the absence of mental disorders (8). More recently, the potential influence of positive mental health, the second dimension of mental health next to mental ill-health (8), on cardio-metabolic health has gained attention. Positive mental health focusses on resources such as self-esteem, optimism and satisfying personal relationships and is a huge domain including many theories and concepts such as health-related quality of life (8). In adults, for instance, positive emotions were found to be associated with a lower allostatic load, i.e. a sum of twelve inflammatory, cardiovascular and metabolic markers (9). In another study in adults, a composite measure of well-being including items on positive relations with others, purpose in life and self-acceptance has been shown to be longitudinally associated with a lower metabolic syndrome risk (10). Although the transition from childhood to adolescence is an important developmental period during which well-being has been found to gradually decrease (11,12), there are only a few cross-sectional studies that investigated the association between aspects of positive mental health and cardio-metabolic markers in young populations and to our knowledge no longitudinal study has ever investigated this question. As one example, Midei et al. (13) found positive attributes, i.e. a measure comprising optimism, positive affect, self-esteem and subjective social standing, to be cross-sectionally associated with a lower metabolic syndrome composite score.

Both biological and behavioral mechanisms may explain the link between positive mental health and cardio-metabolic health. First, positive mental health may have beneficial effects on the hypothalamic-pituitary-adrenal axis and the pattern of cortisol release which in turn can be advantageous

for cardio-metabolic health (14,15). Another biological possibility is that positive mental health reduces levels of inflammatory markers such as C-reactive protein and interleukin 6 which are known to play a role in cardiovascular disease (14,15). As a behavioral mechanism, positive mental health may result in a healthier lifestyle such as increased physical activity, a healthier diet and better sleep and may thereby positively influence cardio-metabolic health (14,15). This latter pathway may be particularly relevant among adolescents who are more independent with respect to their lifestyle in contrast to very young children in whom lifestyle factors such as diet and sleep are more strongly regulated by parents.

In order to improve our understanding of the potential influence of positive mental health on cardio-metabolic markers, this study aims to investigate associations between psychosocial well-being - which in the present study should be understood as one aspect belonging to the overarching framework of positive mental health comprising aspects of emotional well-being, self-esteem and social relationships - and cardio-metabolic markers in 6 to 15 year children and adolescents. Both direct (and thus potentially psychophysiological) and indirect behavioral pathways were investigated. Furthermore, next to lifestyle factors, waist circumference was considered as another mediator in associations between well-being and blood pressure, insulin resistance and blood lipids because increased visceral adipose tissue is a risk factor for insulin resistance and other cardio-metabolic disorders (16), i.e. well-being might first act on waist circumference which subsequently may influence other cardio-metabolic markers (see Fig. 1 for details on hypothesized associations).

Considering that well-being may fluctuate during childhood (as it also does in adulthood) and therefore measurement of well-being on a single occasion may be a poor predictor of cardio-metabolic markers several years later (11,14,15), we applied two different analytical approaches. First, to investigate the potential effect of well-being on cardio-metabolic markers within short time intervals we conducted a cross-sectional analysis. Second, to study the potential influence of long-term improvement in well-being on cardio-metabolic health we conducted a longitudinal analysis where we used changes in well-being over several years as the exposures.

METHODS

Study sample

For the IDEFICS (Identification and prevention of Dietary- and lifestyle-induced health EFfects In Children and infantS)/I.Family cohort study, children and adolescents from eight European countries (Belgium, Cyprus, Estonia, Germany, Hungary, Italy, Spain and Sweden) were recruited using a setting-based approach in kindergartens and primary schools in two regions in each country. The baseline examination (2007/2008) took place in the framework of the IDEFICS study when children were 2-9 years old (N=16,229). A first follow-up examination (FU1) was conducted in 2009/2010 after an intervention aiming to prevent childhood overweight was completed (N=11,043 plus 2,543 newcomers). A second follow-up examination (FU2) was carried out in 2013/2014 in the framework of the I.Family study (17). At FU2, 7,117 children who already participated in IDEFICS and 2,501 newly recruited siblings were examined. A detailed description of the study design is provided in Text S1 (Supplemental Digital Content 1).

Apart from the cardio-metabolic markers, all measures used in the present investigation were collected by questionnaires. All instruments used in the IDEFICS/I.Family study and their development are described in detail in Bammann et al. (18). Parents filled in all questionnaires if their children were younger than 12 years old while older children reported for themselves. Before children entered the study, parents provided informed written consent. Moreover, children 12 years and older provided simplified written consent. Younger children gave oral consent for examinations and sample collection. Ethical approval was obtained by the appropriate Ethics Committees by each of the eight study centers conducting fieldwork.

Cardio-metabolic markers

Cardio-metabolic markers comprised (i) waist circumference, (ii) the average of systolic and diastolic blood pressure, (iii) the homeostasis model assessment for insulin resistance (HOMA-IR) calculated by insulin [µU/ml]*glucose [mg/dl]/405, (iv) triglycerides and (v) high-density lipoprotein cholesterol (HDL-

C). The markers were transformed to age- and sex-specific and in case of blood pressure also height-specific z-scores (waist circumference: WAIST z-score, blood pressure: BP z-score, HOMA-IR: HOMA z-score, triglycerides: TRG z-score, HDL-C: HDL-C z-score). This was done using reference values that were obtained from participants of the IDEFICS and I.Family studies according to previously described methods (19-23). As the assessment method changed for insulin, glucose, triglycerides and HDL-C over time, separate reference curves were estimated for HOMA-IR, triglycerides and HDL-C depending on the assessment method used (for a detailed description of measurement methods see Text S2, Supplemental Digital Content 1).

Psychosocial well-being

Psychosocial well-being was assessed with questions on emotional well-being, self-esteem, family life and relations to friends based on four subscales of the "KINDL^R questionnaire", an instrument for measuring health-related quality of life in children and adolescents (24). According to the responses to the 16 items asking about the frequency of feelings and experiences during the past week, a well-being score was calculated ranging from 0-48 points where a higher score indicates higher psychosocial well-being (for a detailed description of the questions on psychosocial well-being and scoring of items see Text S3 and Table S1, Supplemental Digital Content 1). Cronbach's alpha for this set of items was 0.74 in the present cross-sectional analysis sample indicating satisfactory internal consistency.

For the cross-sectional analysis, we report changes in the outcomes for every 4-point increase in well-being score which equals approximately the interquartile range of well-being score in our study sample. For the longitudinal analysis, we calculated the changes in well-being score between baseline and FU1 and between FU1 and FU2 expressed in annual change to account for differing follow-up times among participants:

$\Delta\text{well-being score}_{FU1\text{-}baseline}=(\text{well-being score}_{FU1}-\text{well-being score}_{baseline})/(\text{age}_{FU1}-\text{age}_{baseline})$

$\Delta\text{well-being score}_{FU2\text{-}FU1}=(\text{well-being score}_{FU2}-\text{well-being score}_{FU1})/(\text{age}_{FU2}-\text{age}_{FU1})$

Lifestyle factors

The consumption frequencies of snacks and salty foods (includes e.g. hamburger, kebab and fritters) (times/week) and of fruit and vegetables (times/week) were obtained from a Food Frequency Questionnaire developed in the framework of the IDEFICS/I.Family study and used as indicators for unhealthy and healthy dietary intake, respectively (25-27). The time spent doing physical activity in a sports club (hours/week) served as a measure for physical activity. The weighted average of habitual sleep duration (hours/night) during weekdays and weekend days was calculated ([sleep duration on weekdays*5 + sleep duration on weekend days*2] / 7) and transformed to an age-specific z-score. Analogously, the weighted average of computer and television consumption on weekdays and weekend days was calculated and used as an indicator for electronic media use (hours/week).

Covariates

Information on age (years), sex and highest level of parental education defined according to the "International Standard Classification of Education" (levels 0-2=low, 3-5=medium and 6-8=high) as a proxy for socio-economic status was collected (28). Pubertal status was self-reported by children 8 years and older at FU2. Girls were classified as pubertal when they reported that their menarche had already occurred and boys when they reported that their voice mutation had already started or was completed. Further, information on country of recruitment and residence in the intervention vs. control region during the IDEFICS intervention was recorded.

Analysis dataset

For the cross-sectional analysis, we used data collected at FU2. From the sample of children with plausible values (N=9,490), we excluded those with missing values on well-being score, covariates and/or waist circumference (N=2,554) to ensure that we have information on a minimum set of variables for all participants. Lastly, the dataset was restricted to 6-15 year old children to allow a meaningful analysis by age group (N=6,519) (Fig. 2). For the longitudinal analysis, those children of the cross-sectional analysis

sample were eligible who also participated both at baseline and at FU1 and who had complete information on change in well-being score$_{FU1\text{-}baseline}$, change in well-being score$_{FU2\text{-}FU1}$, baseline cardio-metabolic markers and baseline covariates (N=1,393) (Fig. 2).

Statistical analysis

Descriptive analyses were conducted with SAS 9.3 (Statistical Analysis System, SAS Institute Inc., Cary, NC, USA). To investigate the associations of interest, we conducted a path analysis with Mplus 7.11. With a path model several related regression relationships are modelled simultaneously and it can be investigated whether the effect of one variable on another is mediated through one or more intervening variables. Such mediated effects are called indirect effects whereas unmediated effects represent direct effects (29). The terms "direct effect" and "indirect effect" are standard terminology in path analysis but this does not necessarily imply causality of associations. For parameter estimation we used maximum likelihood estimation with robust standard errors together with the "TYPE=COMPLEX" command and the "CLUSTER" option to account for non-independence of data (inclusion of siblings in the sample) (30). This estimator can also handle missing values of dependent (including mediating) variables in the model under a missing at random assumption, i.e. the inclusion of participants with incomplete information on lifestyle factors, blood pressure, HOMA-IR, triglycerides and HDL-C was possible (30).

Guided by our conceptual framework (Fig. 1), we set up one cross-sectional path model to estimate the direct effect of the well-being score on the WAIST z-score and the sum of indirect effects through all lifestyle factors. Further, direct effects of the well-being score on BP, HOMA, TRG and HDL-C z-scores were estimated and indirect effects through (i) lifestyle factors, (ii) WAIST z-score and (iii) both lifestyle factors and WAIST z-score. Age, sex, country, parental education, pubertal status and place of residence (intervention vs. control region) were included in all regressions of the path model. Further, we fitted a longitudinal path model to investigate whether change in well-being score$_{FU1\text{-}baseline}$ and change in well-being score$_{FU2\text{-}FU1}$ were associated with the five cardio-metabolic markers measured at FU2 under consideration of potential mediators (for a schematic presentation of this model see Fig. S1, Supplemental

Digital Content 2). Again, all regressions within the path model were adjusted for baseline covariates, baseline well-being score and the baseline value of the respective cardio-metabolic marker. Further details on the statistical analysis are provided in Text S4, Table S2 and Table S3 (Supplemental Digital Content 2). Both the cross-sectional and longitudinal model was also stratified by age group. Multiple testing was accounted for by using the adjustment method of Benjamini et al. (31) to control for the false discovery rate at the 0.05 level of significance resulting in an adjusted alpha level of 0.013.

RESULTS

The characteristics of the cross-sectional and longitudinal analysis groups are displayed in Table 1. Both samples were almost equally balanced with regard to sex. Key variables like well-being score and cardio-metabolic markers were similarly distributed in both the cross-sectional and longitudinal analysis group. On average, well-being score was slightly decreasing over time although changes varied largely among individuals (change in well-being $score_{FU1\text{-}baseline}$: median [interquartile range] -0.5 [-1.9 to 1]; change in well-being $score_{FU2\text{-}FU1}$: median [interquartile range] 0.0 [-1.0 to 0.9]).

Cross-sectional analysis

All direct and indirect effects obtained from the cross-sectional path model are reported in Table 2. Well-being score showed a negative direct effect on WAIST z-score (effect estimate per 4-point increase in well-being score -0.051; 95% confidence interval [-0.081; -0.021]; p=0.001). In absolute values this means, for instance, that when comparing a 14-year old girl with average waist circumference who has a well-being score of 40 with a girl of the same age who has a well-being score of 44, we would expect this girl to have a 0.26 cm lower waist circumference. Additionally, well-being score exerted a negative indirect effect on WAIST z-score through lifestyle factors (-0.014; [-0.019; -0.008]; p<0.001), i.e. for every 4-point increase in well-being score WAIST z-score further decreases on average by 0.014 units due to the association of a higher well-being with a healthier lifestyle.

Concerning the other cardio-metabolic markers, well-being score showed a negative direct effect only on HOMA z-score (-0.039; [-0.067; -0.011]; p=0.007). For all of them (HOMA, BP, TRG and HDL-C z-scores), only indirect effects through WAIST z-score and thus also through both lifestyle factors and WAIST z-score were observed. A negative indirect effect exclusively through lifestyle factors on TRG z-score was also shown.

Effect estimates were slightly larger in children compared to adolescents (Tables S4 and S5, Supplemental Digital Content 2).

Longitudinal analysis

Table 3 displays all direct and indirect effects obtained from the longitudinal path model. We observed a negative direct effect of change in well-being score$_{FU2\text{-}FU1}$ on WAIST z-score$_{FU2}$ (effect estimate per 1-point annual increase in well-being score$_{FU2\text{-}FU1}$ -0.060; [-0.102; -0.017]; p=0.006), i.e. a 4 point increase in well-being score over 4 years of follow-up was associated with a -0.060 unit decrease in WAIST z-score at FU2. The effect estimate of change in well-being score$_{FU1\text{-}baseline}$ on this cardio-metabolic marker did not reach statistical significance but pointed in the same direction. Both well-being change scores showed negative indirect effects on WAIST z-score$_{FU2}$ through the lifestyle factors$_{FU2}$.

Concerning the other cardio-metabolic markers, change in well-being score$_{FU2\text{-}FU1}$ showed a positive direct effect only on HDL-C z-score$_{FU2}$ (0.058; [0.016; 0.099]; p=0.007). Furthermore, similar to the cross-sectional analysis, change in well-being score$_{FU2\text{-}FU1}$ was indirectly associated with lower BP, lower HOMA, lower TRG and higher HDL-C z-scores through its negative direct effect on WAIST z-score$_{FU2}$. Further, small indirect effects were observed for both well-being change scores on BP, HOMA, TRG and HDL-C z-scores$_{FU2}$ following the path via both lifestyle factors$_{FU2}$ and WAIST z-score$_{FU2}$.

The results of the age-stratified analysis revealed that direct effects of change in well-being score$_{FU2\text{-}FU1}$ on cardio-metabolic markers pointed to the same directions, except for HOMA z-score$_{FU2}$. Also no major differences in indirect effects between the age groups became apparent (Tables S6 and S7, Supplemental Digital Content 2).

Sensitivity analyses

Results of several sensitivity analyses (complete case analysis, analysis stratified by sex, additional adjustment for self- vs. proxy- report, alternative longitudinal models) are described in Text S5 and Tables S8-S17 (Supplemental Digital Content 3).

DISCUSSION

To our knowledge, this is one of the first studies in children and adolescents testing the hypothesis of two potential pathways from psychosocial well-being to cardio-metabolic markers, namely a direct (and thus potentially psychophysiological) pathway and an indirect behavioral pathway. The results support our hypothesis that higher well-being may be connected with lower abdominal obesity and other cardio-metabolic disturbances partially through a healthier lifestyle. Furthermore, the findings are in line with the hypothesis of a direct pathway linking higher well-being with lower waist circumference, lower HOMA-IR and higher HDL-C z-score.

To date, there are only few studies that investigated associations between aspects of positive mental health and cardio-metabolic markers in young populations. Although positive mental health and mental ill-health can be regarded as two distinct continua, they are still correlated (32). For instance, low scorings on the KINDL^{R} questionnaire were found to be associated with symptoms of depression and anxiety as well as with mental health difficulties in other studies (33,34). Because of the scarcity of research on positive mental health, we will in the following also refer to studies focusing on mental ill-health.

Both our cross-sectional and longitudinal analysis showed an association between higher psychosocial well-being and lower waist circumference, partially dependent but also independent of lifestyle factors. A cross-sectional study in 364 Australian adolescents also reported an association between higher general well-being (including items on optimism and perceived support) and lower waist circumference, but the potential influence of lifestyle factors was not considered (35). Existing longitudinal studies focusing on mental ill-health did not find evidence for an association. For instance, Van Jaarsveld et al. (36) found neither perceived stress to predict increases in waist circumference 1 to 4 years later nor persistent stress over a period of 5 years to lead to greater gain in waist circumference in British adolescents. In 5-12 year old Belgian children, a composite stress score consisting of negative events, negative emotions and behavioral problems was only associated with waist-to-height ratio two years later when cortisol and lifestyle factors were considered as moderators (37).

In our cross-sectional analysis, higher psychosocial well-being was directly associated with lower HOMA-IR independent of waist circumference and lifestyle factors. Also several previous studies reported cross-sectional associations between mental ill-health measures and HOMA-IR independent of adiposity measures (5-7) and lifestyle factors (5). Louise et al. (5) showed that 14-year-old Australian girls with higher levels of anxiety and/or depressive symptoms had higher HOMA-IR. In studies conducted in the United States Shomaker et al. (6) found depressive symptoms to be associated with decreased insulin sensitivity in adolescents and depressive symptoms in childhood (at the age of 5-13 years) to predict HOMA-IR approximately 6 years later (7).

Our study suggests that higher psychosocial well-being may only be indirectly associated with lower blood pressure through a healthier lifestyle and lower waist circumference. Louise et al. (5) found higher depressive symptoms to be associated with lower systolic blood pressure adjusting for body mass index (BMI) in 14-year old Australian boys (but not in girls). Furthermore, boys with continuously high anxious-depressed scores over time had a lower systolic blood pressure trajectory (5). Similar results were reported by studies in adults (38,39). Interestingly, our cross-sectional and longitudinal sensitivity analyses stratified by sex also suggested a direct association between higher well-being and higher blood pressure in boys (Text S5, Tables S10-S13, Supplemental Digital Content 3). Researchers who have previously observed the counterintuitive association between poor mental health and low blood pressure have tried to find explanations (5,38,39) but the mechanisms remain unclear.

In our longitudinal analysis, increases in psychosocial well-being were directly associated with higher HDL-C. This finding is in line with a study conducted in the United States of America that found higher optimism to be associated with higher HDL-C and lower triglycerides adjusting for BMI in black adolescents (40). Louise et al. (5) found no association between anxious and/or depressive symptoms and triglycerides adjusting for physical activity and BMI.

Strengths of our study include the investigation of longitudinal associations and the standardized data collection from a large sample of European children and adolescents. Furthermore, using path analysis allowed us to consider all cardio-metabolic markers within one model (i.e. less multiple testing)

and to quantify not only direct but also indirect effects. However, any causal interpretation of our results relies on the assumption of no unmeasured confounding (e.g. by genetic factors) and on the correctness of the hypothesized direction of the associations. Our models are partially based on data that preclude determining the temporal sequence of exposure, mediators and outcomes thereby impairing causal inferences. A detailed discussion on the directionality of associations is provided in Text S6 (Supplemental Digital Content 4). However, although the association between well-being and abdominal obesity may indeed be bidirectional, we consider reverse causation less likely for the association with other cardio-metabolic markers in our young study sample since most of the children were not aware of these more subtle physiological changes. Furthermore, although lifestyle factors might also impact on well-being, our assumption that well-being acts on lifestyle factors is supported by studies that have shown lower stress and higher well-being to be determinants of a healthier lifestyle in children (41,42). Further, part of the children in our cross-sectional (39%) and longitudinal (55%) study sample participated in an intervention for the prevention of childhood obesity between baseline and first follow-up. The intervention did not have measurable effects on cardio-metabolic markers (43) and lifestyle factors (44). We therefore consider the inclusion of children from both groups as justified but we nevertheless adjusted our analyses for residence in the intervention vs. control region. Further limitations exist with respect to our measurement instruments. First, psychosocial well-being was reported by parents for younger children. It has been found that parents generally tend to overestimate the health-related quality of life of their children (45). In addition, the lifestyle factors might have been measured with some error. For example, underreporting of dietary intake is common in children with overweight (46) and although sports club physical activity has previously been found to be associated with accelerometer-derived moderate-to-vigorous physical activity in the IDEFICS study (47), it does not cover the full physical activity spectrum. We also used a rather crude measure of pubertal status based on menarche and voice mutation which has however been found to be strongly associated with self-reported breast development (girls) and pubic hair development (boys) in a large subgroup of children who also completed the more detailed questionnaire with pictograms of Tanner stages (data not shown). We therefore consider that those two indicators of

pubertal status are sufficient for the purpose of adjustment. Another limitation of our study is that a high proportion of children did not participate in all three waves and those children with poor psychosocial well-being and children with overweight were found to be more likely to drop out at follow-up (48). Furthermore, biological markers had a high proportion of missing data (mainly due to refusal of a venous blood draw). Nevertheless, it is one of the big advantages of the applied analysis method that participants with missing values on these dependent variables could be included in the models thus allowing us to efficiently use the existing data.

Clinical and public health implications

Most indirect effect estimates were of very small size and may therefore not be clinically relevant when considering each single effect in isolation. Nevertheless, the accumulation of single indirect effects may result in a relevant effect size. Further, from a preventive perspective, even a small effect may be meaningful as it indicates a pathway (49), i.e. higher well-being may lead to a healthier lifestyle and subsequently to fewer cardio-metabolic disorders. Well-being can be enhanced by training resilience and emotion regulation as this will then influence both psychophysiological responses (such as cortisol) and lifestyle changes (such as diet, physical activity and sleep) on the pathway to metabolic health as already investigated in several intervention studies in adults (50). A meta-analysis showed that resilience training trials successfully changed four out of seven mental health outcomes in school children (51).

Conclusions

Our cross-sectional and longitudinal study in children and adolescents supported our hypothesis that higher psychosocial well-being may be connected with lower waist circumference through a behavioral pathway. Further, higher psychosocial well-being may be linked to lower blood pressure, lower HOMA-IR, lower triglycerides and higher HDL-C through both lifestyle factors and waist circumference. Also direct associations were observed between higher psychosocial well-being and lower waist circumference, lower HOMA-IR and higher HDL-C, although associations were less consistent across analyses. As

literature is mainly focused on mental ill-health, further longitudinal studies investigating aspects of positive mental health as potential determinants of cardio-metabolic health in young populations are needed.

Supplemental Digital Content

Supplemental_Digital_Content_1.docx

Supplemental_Digital_Content_2.docx

Supplemental_Digital_Content_3.docx

Supplemental_Digital_Content_4.docx

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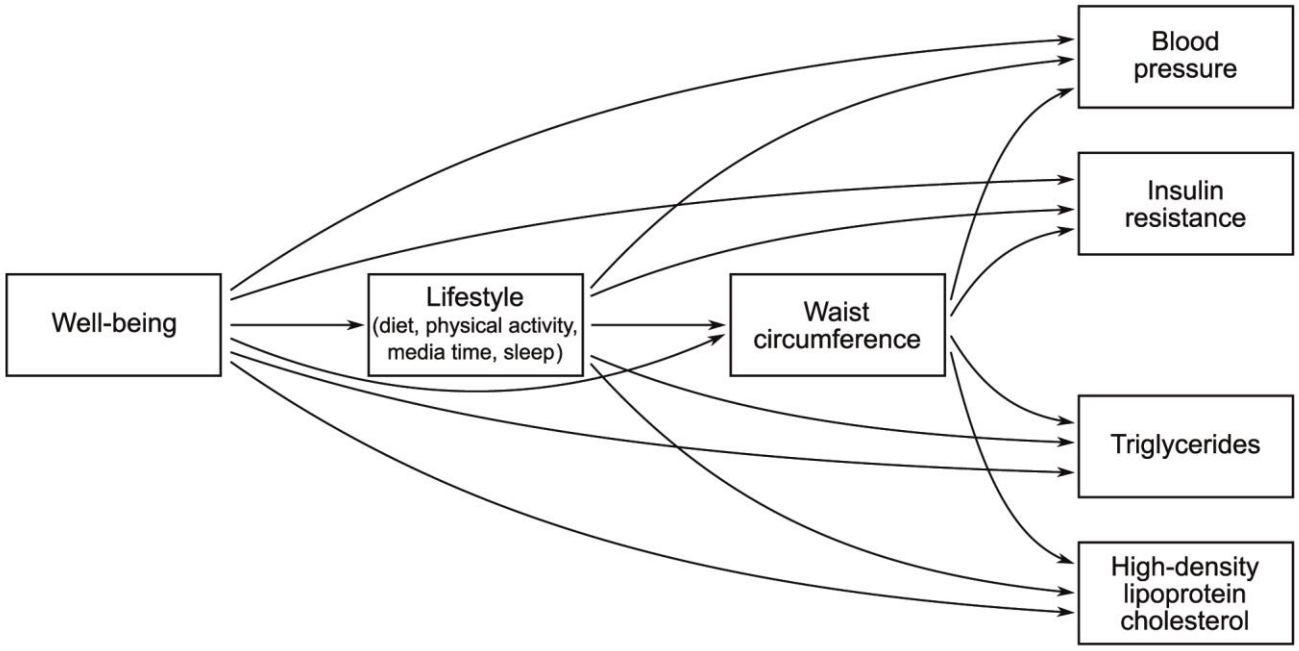

Fig. 1: Conceptual framework of the associations between psychosocial well-being and cardio-metabolic markers. The framework was developed based on the following hypotheses: (1) Higher psychosocial well-being is directly linked with all five cardio-metabolic markers; (2) Lifestyle factors partially mediate the association between psychosocial well-being and waist circumference; (3) Both lifestyle factors and waist circumference mediate the associations between psychosocial well-being and blood pressure, insulin resistance, triglycerides and high-density lipoprotein cholesterol, respectively.

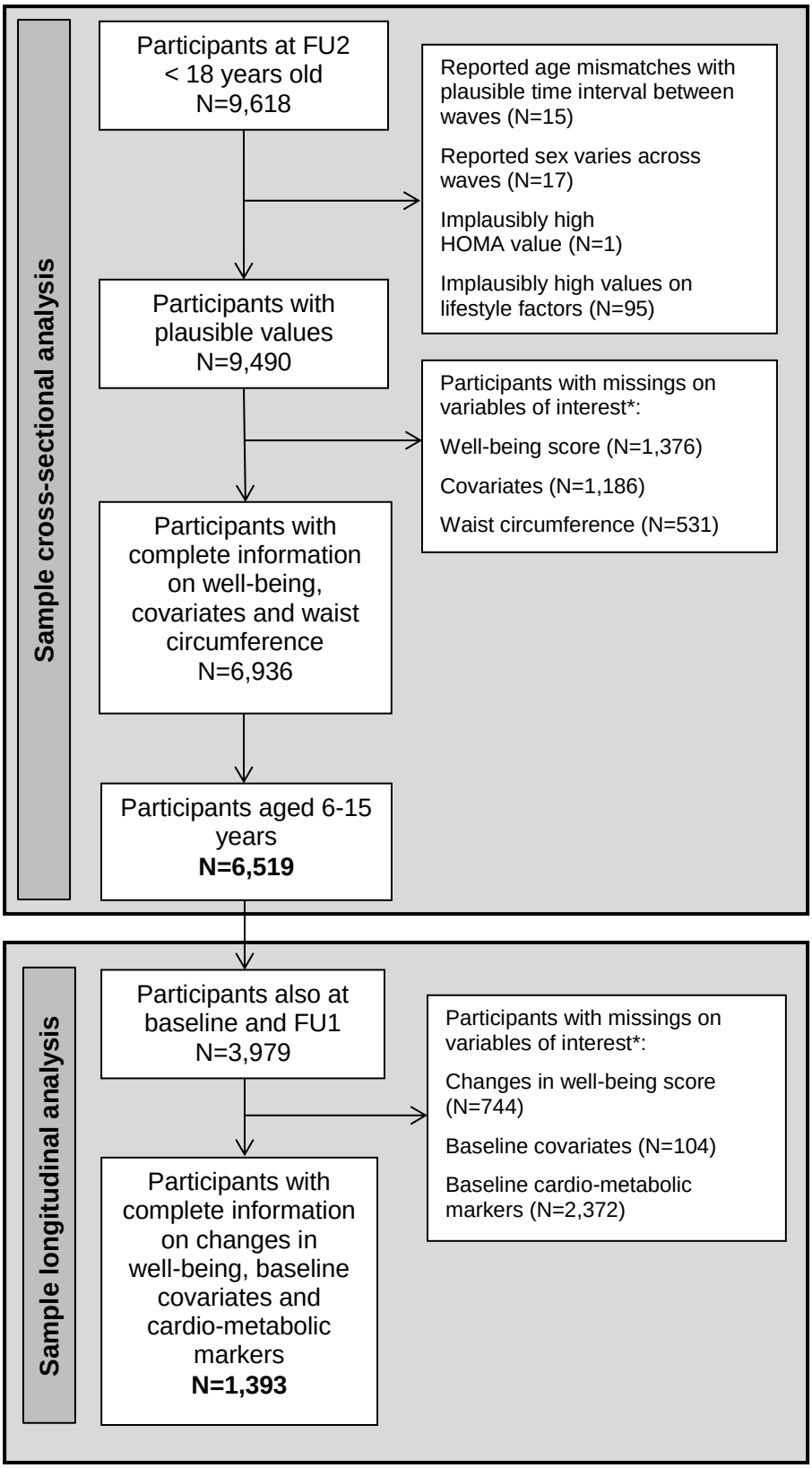

Fig. 2: Flowchart of participants in the samples for the cross-sectional analysis and the longitudinal analysis; FU1: first follow-up; FU2: second follow-up; * missings on multiple variables possible

Table 1 Characteristics of the study sample measured at second follow-up in 2013/14

	Missing N (%)	Cross-sectional analysis sample N=6,519	Missing N (%)	Longitudinal analysis sample N=1,393
Age, mean (SD)		11.3 (2.3)		12.0 (1.8)
Girls, N (%)		3,290 (50.5)		689 (49.5)
Pubertal status (pubertal), N (%)		2,456 (37.7)		593 (42.6)
Country, N (%)				
Italy		1,175 (18.0)		224 (16.1)
Estonia		1,081 (16.6)		237 (17.0)
Cyprus		1,348 (20.7)		--
Belgium		277 (4.3)		61 (4.4)
Sweden		603 (9.3)		243 (17.4)
Germany		809 (12.4)		239 (17.2)
Hungary		887 (13.6)		234 (16.8)
Spain		339 (5.2)		155 (11.1)
Highest level of parental education, N (%)				
Low		310 (4.8)		52 (3.7)

	Missing N (%)	Cross-sectional analysis sample N=6,519	Missing N (%)	Longitudinal analysis sample N=1,393
Medium		2,869 (44.0)		588 (42.2)
High		3,340 (51.2)		753 (54.1)
Snack/salty foods intake (times/week), median (IQR)	347 (5.3)	5 (2-7)	56 (4.0)	5 (2-7)
Fruit and vegetables intake (times/week), median (IQR)	564 (8.7)	16 (11-25)	103 (7.4)	18 (11-25)
Sports club physical activity (hours/week), median (IQR)	155 (2.4)	2 (0-4)	25 (1.8)	2.5 (0-4.5)
Electronic media time (hours/week), median (IQR)	263 (4.0)	14.3 (9.0-21.8)	52 (3.7)	14.3 (9.0-22.0)
Nocturnal sleep duration (hours), mean (SD)	277 (4.2)	9.18 (0.94)	42 (3.0)	9.16 (0.97)
Well-being score, median (IQR)		40 (37-43)		40 (36-43)
Waist circumference (cm), median (IQR)		64.2 (58.2-71.8)		65.0 (60.0-72.0)
Waist circumference $\geq 90^{th}$ percentile*, N (%)		1,951 (29.9)		363 (26.1)

	Missing	Cross-sectional analysis sample	Missing	Longitudinal analysis sample
	N (%)	**N=6,519**	**N (%)**	**N=1,393**
Systolic blood pressure (mmHg), mean (SD)	147 (2.3)	106.4 (9.9)	36 (2.6)	107.8 (9.2)
Diastolic blood pressure (mmHg), mean (SD)	147 (2.3)	64.0 (6.6)	36 (2.6)	65.2 (6.3)
Systolic or diastolic blood pressure ≥ 90th percentile*, N (%)	147 (2.3)	1,039 (16.3)	36 (2.6)	248 (18.3)
HOMA-IR, median (IQR)	3,528 (54.1)	1.27 (0.82-1.95)	597 (42.9)	1.23 (0.83-1.89)
HOMA-IR ≥ 90th percentile*, N (%)	3,528 (54.1)	545 (18.2)	597 (42.9)	128 (16.1)
HDL-C (mg/dl), median (IQR)	2,387 (36.6)	58 (50-68)	472 (33.9)	60 (50-69)
HDL-C ≤10th percentile*, N (%)	2,387 (36.6)	470 (11.4)	472 (33.9)	82 (8.9)
Triglycerides (mg/dl), median (IQR)	2,387 (36.6)	57 (45-75)	472 (33.9)	56 (44-74)
Triglycerides ≥ 90th percentile*, N (%)	2,387 (36.6)	435 (10.5)	472 (33.9)	89 (9.7)

N: number, IQR: interquartile range, SD: standard deviation, HOMA-IR: homeostasis model assessment for insulin resistance, HDL-C: high-density lipoprotein cholesterol; *according to reference values based on the IDEFICS/I.Family cohort that were derived according to previously described methods (19-23)

Table 2 Results of the path model investigating cross-sectional associations between well-being score and cardio-metabolic markers at second follow-up

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Whole group N=6,519		
	Unst. estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	**-0.051**	-0.081; -0.021	0.001
Well-being score→BP z-score	0.007	-0.011; 0.025	0.468
Well-being score→HOMA z-score	**-0.039**	-0.067; -0.011	0.007
Well-being score→HDL-C z-score	0.018	-0.007; 0.043	0.156
Well-being score→TRG z-score	-0.002	-0.027; 0.024	0.895
Indirect effects*			
Well-being score→LIF→WAIST z-score	**-0.014**	-0.019; -0.008	<0.001
Well-being score→WAIST z-score→BP z-score	**-0.006**	-0.010; -0.003	0.001
Well-being score→LIF→BP z-score	-0.004	-0.006; -0.001	0.015
Well-being score→LIF→WAIST z-score→BP z-score	**-0.002**	-0.002; -0.001	<0.001
Well-being score→WAIST z-score→HOMA z-score	**-0.015**	-0.024; -0.006	0.001
Well-being score→LIF→HOMA z-score	-0.006	-0.011; -0.001	0.022
Well-being score→LIF→WAIST z-score→HOMA z-score	**-0.004**	-0.006; -0.002	<0.001
Well-being score→WAIST z-score→HDL-C z-score	**0.010**	0.004; 0.016	0.001
Well-being score→LIF→HDL-C z-score	0.004	0.000; 0.008	0.028
Well-being score→LIF→WAIST z-score→HDL-C z-score	**0.003**	0.002; 0.004	<0.001
Well-being score→WAIST z-score→TRG z-score	**-0.008**	-0.012; -0.003	0.001

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Whole group N=6,519		
	Unst. estimate	*95% CI*	*p-value*
Well-being score→LIF→TRG z-score	**-0.006**	-0.010; -0.002	0.007
Well-being score→LIF→WAIST z-score→TRG z-score	**-0.002**	-0.003; -0.001	<0.001

Unst.: Unstandardized, CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region. Bold figures indicate a false discovery rate <0.05; a false discovery rate adjusted significance value corresponds to α_{adj}=0.013. *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table 3 Results of the path model investigating longitudinal associations between changes in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=1,393		
	Unst. estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.019	-0.051; 0.013	0.250
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	**-0.060**	-0.102; -0.017	0.006
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	0.017	-0.009; 0.044	0.193
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	0.025	-0.011; 0.060	0.173
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	-0.022	-0.061; 0.017	0.274
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	-0.008	-0.058; 0.042	0.763
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.031	-0.001; 0.063	0.059
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	**0.058**	0.016; 0.099	0.007
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	-0.005	-0.039; 0.029	0.775
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.025	-0.077; 0.028	0.358
Indirect effects*			

Longitudinal analysis	Whole group		
(ΔWell-being score: 1 unit ≙ 1 point per year)	N=1,393		
	Unst. estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$	**-0.011**	-0.018; -0.004	0.001
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$	**-0.013**	-0.021; -0.005	0.002
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→BP z-score$_{FU2}$	-0.002	-0.007; 0.002	0.255
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→BP z-score$_{FU2}$	**-0.008**	-0.016; -0.002	0.012
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→BP z-score$_{FU2}$	-0.004	-0.009; 0.000	0.061
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→BP z-score$_{FU2}$	-0.004	-0.010; 0.001	0.132
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→BP z-score$_{FU2}$	**-0.001**	-0.002; 0.000	0.005
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→BP z-score$_{FU2}$	**-0.002**	-0.003; 0.000	0.008
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.004	-0.012; 0.003	0.258
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	**-0.014**	-0.024; -0.003	0.010
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.006	-0.015; 0.003	0.197
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.005	-0.017; 0.006	0.355
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	**-0.003**	-0.004; -0.001	0.002
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	**-0.003**	-0.005; -0.001	0.004
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	-0.003; 0.009	0.255

Longitudinal analysis	Whole group		
(ΔWell-being score: 1 unit ≙ 1 point per year)	N=1,393		
	Unst. estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	**0.011**	0.003; 0.019	0.009
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	-0.002; 0.008	0.272
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	0.003	-0.003; 0.010	0.274
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	**0.002**	0.001; 0.003	0.002
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	**0.002**	0.001; 0.004	0.004
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.004	-0.010; 0.003	0.261
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	**-0.011**	-0.020; -0.003	0.011
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.008; 0.004	0.517
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.001	-0.009; 0.006	0.697
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	**-0.002**	-0.003; -0.001	0.002
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	**-0.002**	-0.004; -0.001	0.005

Unst.: Unstandardized, CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education, well-being score (all at baseline), baseline value of the respective cardio-metabolic marker, pubertal status (at FU2) and included an indicator for residence in intervention vs. control region. Bold figures indicate a false discovery rate <0.05; a false discovery rate adjusted significance value corresponds to α_{adj}=0.013. *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Text S1: Detailed description of study design

Of the two regions selected in each country for the IDEFICS study one region was defined as the intervention region, where an intervention for the prevention of childhood obesity was implemented, and the other served as the control region with no intervention (1). The regions were selected by convenience, i.e. it was not feasible to obtain nationally representative samples (2). The study followed a population-based approach and study regions were selected as to represent the socio-demographic profile of their geographic areas (3). The setting-based intervention targeting nutrition, physical activity and stress coping was implemented between baseline (2007/2008) and the first follow-up examination (2009/10) (4).

References

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Text S2: Detailed description of measurement methods of the cardio-metabolic markers

Anthropometric measurements. As an indicator of abdominal obesity, waist circumference (cm) of participants was measured in all three waves with an inelastic tape (Seca 200, seca GmbH & Co. KG, Hamburg, Germany) in upright position with relaxed abdomen and feet together, midway between the lowest rib margin and the iliac crest to the nearest 0.1 cm.

Blood pressure. Systolic and diastolic blood pressure (mmHg) was measured in all three examination waves with an automated oscillometric device (Welch Allyn 4200B-E2, Welch Allyn Inc., Skaneateles Falls, NY, USA). The cuff length was chosen according to the child's arm circumference. After participants had rested for at least 5 minutes, two measurements were taken with 2 minutes interval in between them. In case the first and second measurement differed by more than 5%, a third one was taken. Subsequently, first the average of the two measurements (in case of three measurements: the two measurements most closely together) of systolic and diastolic blood pressure, respectively, was calculated to obtain one value for systolic and one value for diastolic blood pressure. Second, the average of systolic and diastolic blood pressure was calculated.

Blood collection. Children's venous blood was collected in a fasting state. At baseline and FU1, children refusing venipuncture were offered to give fasting capillary blood by finger-prick. In the first two examination waves, insulin was analyzed using a luminescence immunoassay (AUTO-GA Immulite 2000, Siemens, Eschborn, Germany) and blood glucose, HDL-C and triglycerides were assessed with a point-of-care analyzer (Cholestech LDX, Cholestech Corp., Hayward, CA, USA). The laboratory intra- and inter-assay coefficients of variation were at most 5.5% and 7.3% for insulin, 6.2% and 5.0% for glucose, 3.6% and 3.2% for triglycerides and 4.8% and 6.3% for HDL-C. At FU2, insulin was determined by electrochemiluminescence technology (MULTI-SPOT® Assay System - Human Leptin, Insulin Assay Kit, Meso Scale Diagnostics, LLC., Rockville, MD, USA), glucose with an enzymatic UV test (Cobas c701, Roche Diagnostics GmbH, Mannheim, Germany), HDL-C and triglycerides with an enzymatic colorimetric test (Cobas c701, Roche Diagnostics GmbH, Mannheim, Germany). The laboratory intra- and inter-assay coefficients of variation were at most 15% and 18% for insulin, 0.8% and 1.3% for glucose, 0.9% and 2.0% for triglycerides and 0.8% and 1.5% for HDL-C. As a measure of insulin resistance the homeostasis model assessment (HOMA-IR) was calculated by: insulin [µU/ml]*glucose [mg/dl]/405.

Text S3: Detailed description of the questions on psychosocial well-being and scoring of items

In all three examination waves of the IDEFICS/I.Family study 16 items from four subscales of the KINDL^R Questionnaire („**R**evidierter Fragebogen für **KIND**er und Jugendliche zur Erfassung der gesundheitsbezogenen **L**ebensqualität") (Table S1) were implemented as part of a comprehensive questionnaire covering also several other topics such as socio-demographic background and lifestyle of the children/adolescents. To keep the questionnaire at a reasonable length, it was not feasible to implement the full version of the KINDL^R questionnaire which contains 24 items from six subscales. Furthermore, the response scales of the items differed across examination waves. At baseline and FU1, a 4-point response scale (never, seldom, sometimes, often/all the time) was used because the midpoint of an uneven Likert scale might be chosen by participants to reduce cognitive burden of answering questions rather than expressing the true meaning of the midpoint (1). At FU2, however, a 5-point response scale (never, seldom, sometimes, often, all the time) was implemented to allow comparison with an increasing number of studies using the KINDL^R questionnaire. As we used data from all three examination waves in the present investigation, we assigned 0 points for "never", 1 point for "seldom", 2 points for "sometimes" and 3 points for "often/all the time" (baseline and FU1), "often" (FU2) and "all the time" (FU2), respectively. Six negatively worded items (e.g. "… my child felt alone") were coded inversely. The points of all items were summed which resulted in a well-being score theoretically ranging from 0-48 points.

Although our psychosocial well-being measure is not directly comparable with the original KINDL^R questionnaire because of the described differences (fewer items, differences in response scales), some of its psychometric properties may be transferable to our measure. The parent- and self-report versions of the KINDL^R questionnaire have been tested for their reliability and validity in 3-17 year old children with good results (2,3). Cronbach's alpha, a measure of a scale's internal consistency, was reported to be 0.82 for the total health-related quality of life score obtained from self-reports of 11-17 year olds (3). Using our longitudinal study sample, we obtained Cronbach's alpha values of 0.68 (well-being score$_{baseline}$), 0.73 (well-being score$_{FU1}$) and 0.74 (well-being score$_{FU2}$) which can be regarded as satisfactory. Discriminant validity of the KINDL^R questionnaire was determined by showing that the total health-related quality of life score was lower among chronically ill children in comparison to healthy children (3). Similarly, we observed that children from the IDEFICS cohort with a diagnosis of attention deficit hyperactivity disorder were more likely to have a low well-being score (unpublished data).

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Table S1 Item list KINDL^{R} Health-Related Quality of Life Questionnaire (excluding "Physical Well-being" and "Everyday Functioning" subscales)

Kid- & Kiddo-KINDL^{R} parents version for 7-17 year old children/adolescents[*]	**Kiddo-KINDL^{R} self-report version for 14-17 year old adolescents**
During the past week…	During the past week…
Emotional Well-being	**Emotional Well-being**
…my child had fun and laughed a lot	... I had fun and laughed a lot
... my child didn't feel much like doing anything	... I was bored
... my child felt alone	... I felt alone
... my child felt scared or unsure of him-/herself	... I felt scared or unsure of myself
Self-esteem	**Self-esteem**
... my child was proud of him-/herself	... I was proud of myself
... my child felt on top of the world	... I felt on top of the world
... my child felt pleased with him-/herself	... I felt pleased with myself
... my child had lots of good ideas	... I had lots of good ideas
Family	**Family**
... my child got on well with us as parents	... I got on well with my parents
... my child felt fine at home	... I felt fine at home
... we quarrelled at home	... we quarrelled at home
... my child felt that I was bossing him/her around	... I felt restricted by my parents
Friends	**Friends**
... my child did things together with friends	... I did things together with my friends
... my child was liked by other kids	... I was a "success" with my friends
... my child got along well with his/her friends	... I got along well with my friends
... my child felt different from other children	... I felt different from other people
Response categories and scoring:	
never, seldom, sometimes, often, all the time	

Source: **Ravens-Sieberer U and Bullinger M** (2000) *KINDL-R. Questionnaire for Measuring Health-Related Quality of Life in Children and Adolescents - Revised Version - Manual* [Online]. Available at http://www.kindl.org/english/manual/. Accessed 6th August 2018.

[*]The wording of the "Kiddy KINDL^{R} parents version for 3-6 year old children" is the same except that in the "Friends" subscale the item "…my child did things together with friends" is replaced by "…my child played with friends"

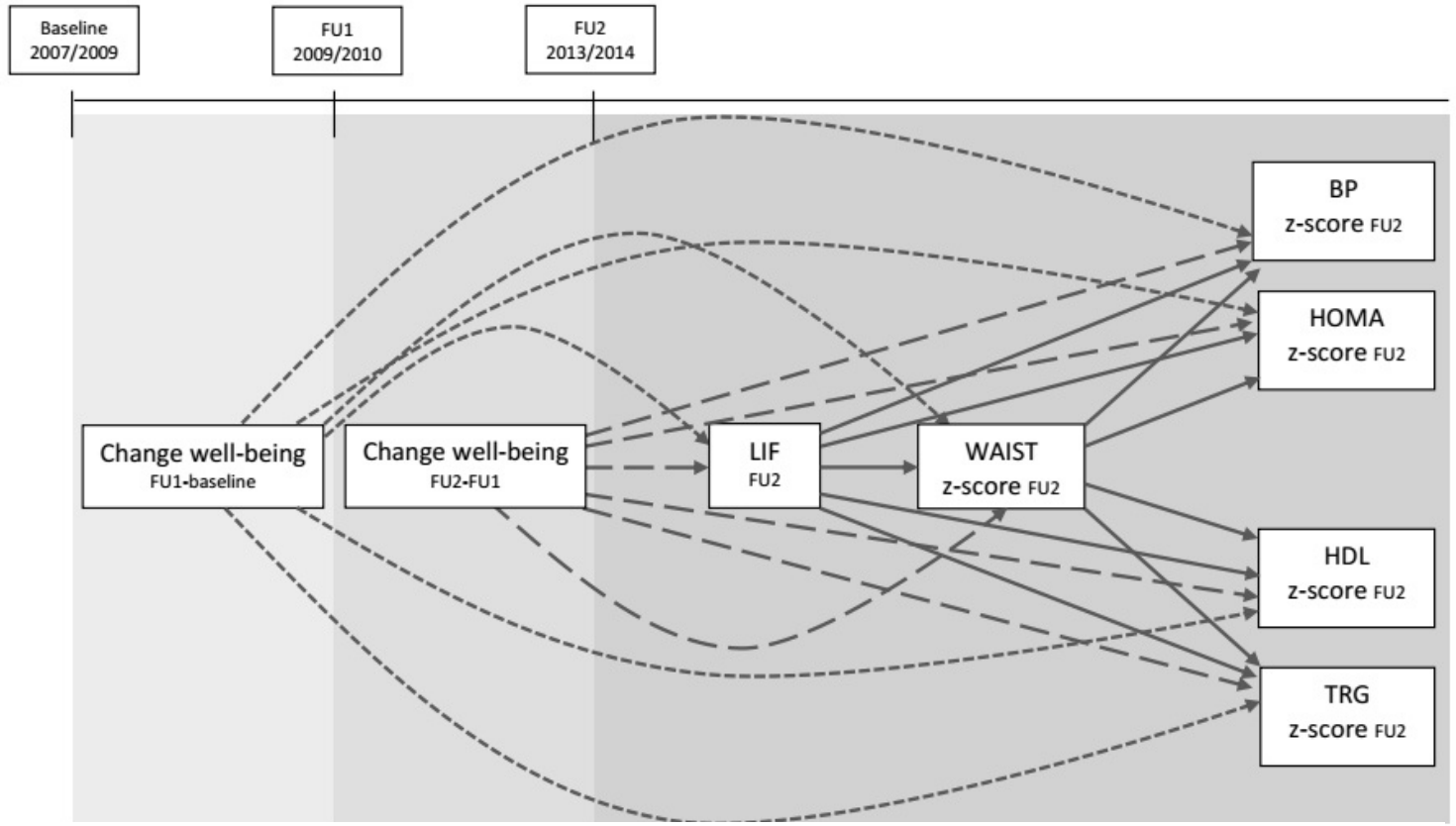

Figure S1 Schematic presentation of the longitudinal path model on the association between changes in well-being score and cardio-metabolic markers. FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors

Text S4 Details on statistical analysis

To improve model fit of the *a priori* defined cross-sectional and longitudinal path model, residuals of some of the lifestyle factors were permitted to covary based on both modification indices and theoretical considerations. Additionally, in the longitudinal path model WAIST z-score measured at baseline was added as a covariate to the regression models with BP z-score and TRG z-score, respectively, as the outcomes. An overview of variables and permitted residual covariances included in the final model in comparison to the *a priori* defined path models is displayed in Table S2.

Adequate model fit was achieved for both models as indicated by values close to 0.95 for the Comparative Fit Index and the Tucker-Lewis Index and a value close to 0.06 for the Root Mean Square Error of Approximation (for exact values see Table S3) (1). Standard errors of indirect effects for assessing statistical significance were estimated with the delta method (2,3).

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Table S2 Dependent and independent variables, covariates and residual covariances included in the *a priori* defined and final cross-sectional and longitudinal path models

Dependent variables	**Independent variables and covariates in *a priori* defined path model**	**Independent variables and covariates in final path model based on whole group**	**Independent variables and covariates in final age-stratified path models**
	CROSS-SECTIONAL PATH MODEL		
BP z-score	Well-being score WAIST z-score age, sex, country, parental education, pubertal status, intervention vs. control region nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake	*same as a priori defined path model*	*same as a priori defined path model*
WAIST z-score	Well-being score age, sex, country, parental education, pubertal status, intervention vs. control region nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake	*same as a priori defined path model*	*same as a priori defined path model*
HOMA z-score	Well-being score WAIST z-score age, sex, country, parental education, pubertal status, intervention vs. control region nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake	*same as a priori defined path model*	*same as a priori defined path model*
HDL-C z-score	Well-being score WAIST z-score age, sex, country, parental education, pubertal status, intervention vs. control region nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake	*same as a priori defined path model*	*same as a priori defined path model*
TRG z-score	Well-being score WAIST z-score age, sex, country, parental education, pubertal status, intervention vs. control region nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake	*same as a priori defined path model*	*same as a priori defined path model*
Nocturnal sleep duration	Well-being score age, sex, country, parental education, pubertal status, intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
Sports club-PA	Well-being score age, sex, country, parental education, pubertal status, intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*

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Media time	Well-being score age, sex, country, parental education, pubertal status, intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
Snack/salty foods intake	Well-being score age, sex, country, parental education, pubertal status, intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
F+V intake	Well-being score age, sex, country, parental education, pubertal status, intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
Residual covariances	---	*added to a priori defined path model:* media time – nocturnal sleep duration media time – sports club-PA snack/salty foods intake – media time F+V intake – sports club-PA F+V intake – media time F+V intake – snack/salty foods intake	*added to a priori defined path model:* media time – nocturnal sleep duration media time – sports club-PA snack/salty foods intake – media time F+V intake – sports club-PA F+V intake – media time F+V intake – snack/salty foods intake
	LONGITUDINAL PATH MODEL		
BP z-score$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ Well-being score$_{baseline}$ WAIST z-score$_{FU2}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region BP z-score$_{baseline}$ nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake (all FU2)	*added to a priori defined path model:* WAIST z-score$_{baseline}$	*added to a priori defined path model:* WAIST z-score $_{baseline}$
WAIST z-score$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ Well-being score$_{baseline}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region WAIST z-score$_{baseline}$ nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake (all FU2)	*same as a priori defined path model*	*same as a priori defined path model*
HOMA z-score$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ Well-being score$_{baseline}$ WAIST z-score$_{FU2}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region HOMA z-score$_{baseline}$ nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake(all FU2)	*same as a priori defined path model*	*same as a priori defined path model*

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HDL-C z-score$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ Well-being score$_{baseline}$ WAIST z-score$_{FU2}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region HDL-C z-score$_{baseline}$ nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake (all FU2)	*same as a priori defined path model*	*same as a priori defined path model*
TRG z-score$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ Well-being score$_{baseline}$ WAIST z-score$_{FU2}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region TRG z-score$_{baseline}$ nocturnal sleep duration, sports club-PA, media time, snack/salty foods intake, F+V intake (all FU2)	*added to a priori defined path model:* WAIST z-score$_{baseline}$	*added to a priori defined path model:* WAIST z-score$_{baseline}$
Nocturnal sleep duration$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
Sports club-PA$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
Media time$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
Snack/salty foods intake $_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control vs. control region	*same as a priori defined path model*	*same as a priori defined path model*
F+V intake$_{FU2}$	ΔWell-being score$_{FU1\text{-}baseline}$ ΔWell-being score$_{FU2\text{-}FU1}$ age, sex, country, parental education (all baseline), pubertal status (FU2), intervention vs. control region	*same as a priori defined path model*	*same as a priori defined path model*

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Residual covariances	---	*added to a priori defined path model:* media time – nocturnal sleep duration media time – sports club-PA snack/salty foods intake – media time F+V intake – media time F+V intake – snack/salty foods intake	*added to a priori defined path model:* media time – nocturnal sleep duration media time – sports club-PA snack/salty foods intake – media time F+V intake – media time F+V intake – snack/salty foods intake sports club-PA – nocturnal sleep duration F+V intake – sports club-PA

WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides; F+V intake: fruit and vegetables intake; sports club-PA: time spent doing physical activity in a sports club

Table S3 Fit indices cross-sectional and longitudinal path models

CROSS-SECTIONAL PATH MODEL			
	Whole sample N=6,519	Children 6-11 years N=3,706	Adolescents 12-15 years N=2,813
Chi-Square Test of Model Fit*			
Degrees of freedom	4	4	4
P-Value	0.46	0.26	0.92
Comparative Fit Index	1.00	1.00	1.00
Tucker-Lewis Index	1.00	0.99	1.05
Root Mean Square Error of Approximation	<0.001	0.009	<0.001
LONGITUDINAL PATH MODEL			
	Whole sample N=1,393	Children 6-11 years at FU2 N=663	Adolescents 12-15 years at FU2 N=730
Chi-Square Test of Model Fit*			
Degrees of freedom	48	46	46
P-Value	0.001	0.001	0.014
Comparative Fit Index	0.99	0.97	0.99
Tucker-Lewis Index	0.94	0.86	0.93
Root Mean Square Error of Approximation	0.024	0.034	0.027

FU2: second follow-up

*The chi-square test of model fit is shown for completeness but was not used for assessing model fit because of its sensitivity to large sample sizes (Fan X, Thompson B, Wang L. Effects of sample size, estimation methods, and model specification on structural equation modeling fit indexes. Struct Equ Modeling. 1999;6(1):56-83. doi:10.1080/10705519909540119)

Table S4 Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of cross-sectional associations between well-being score and cardio-metabolic markers at second follow-up – age-stratified analysis – children

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Children (6-11 years) N=3,706		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	**-0.067**	-0.108; -0.025	0.002
Well-being score→BP z-score	0.019	-0.005; 0.043	0.120
Well-being score→HOMA z-score	-0.045	-0.087; -0.003	0.038
Well-being score→HDL-C z-score	0.020	-0.015; 0.055	0.273
Well-being score→TRG z-score	0.008	-0.027; 0.042	0.666
Indirect effects*			
Well-being score→LIF→WAIST z-score	**-0.019**	-0.028; -0.010	<0.001
Well-being score→WAIST z-score→BP z-score	**-0.008**	-0.014; -0.003	0.002
Well-being score→LIF→BP z-score	-0.002	-0.006; 0.002	0.393
Well-being score→LIF→WAIST z-score→BP z-score	**-0.002**	-0.004; -0.001	<0.001
Well-being score→WAIST z-score→HOMA z-score	**-0.022**	-0.036; -0.008	0.002
Well-being score→LIF→HOMA z-score	-0.001	-0.009; 0.006	0.714
Well-being score→LIF→WAIST z-score→HOMA z-score	**-0.006**	-0.009; -0.003	<0.001
Well-being score→WAIST z-score→HDL-C z-score	**0.013**	0.004; 0.021	0.003
Well-being score→LIF→HDL-C z-score	0.005	-0.001; 0.011	0.113
Well-being score→LIF→WAIST z-score→HDL-C z-score	**0.004**	0.002; 0.005	<0.001
Well-being score→WAIST z-score→TRG z-score	**-0.010**	-0.017; -0.003	0.003
Well-being score→LIF→TRG z-score	-0.005	-0.011; 0.001	0.083
Well-being score→LIF→WAIST z-score→TRG z-score	**-0.003**	-0.004; -0.001	<0.001

CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region. Bold figures indicate a false discovery rate <0.05; a false discovery rate adjusted significance value corresponds to α_{adj}=0.013. *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S5 Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of cross-sectional associations between well-being score and cardio-metabolic markers at second follow-up – age-stratified analysis – adolescents

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Adolescents (12-15 years) N=2,813		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	-0.051	-0.092; -0.010	0.014
Well-being score→BP z-score	-0.008	-0.035; 0.019	0.558
Well-being score→HOMA z-score	-0.040	-0.078; -0.001	0.045
Well-being score→HDL-C z-score	0.013	-0.021; 0.048	0.458
Well-being score→TRG z-score	-0.017	-0.054; 0.020	0.358
Indirect effects*			
Well-being score→LIF→WAIST z-score	-0.010	-0.018; 0.002	0.016
Well-being score→WAIST z-score→BP z-score	-0.007	-0.012; -0.001	0.018
Well-being score→LIF→BP z-score	-0.005	-0.009; 0.000	0.044
Well-being score→LIF→WAIST z-score→BP z-score	-0.001	-0.002; 0.000	0.019
Well-being score→WAIST z-score→HOMA z-score	-0.013	-0.023; -0.002	0.017
Well-being score→LIF→HOMA z-score	**-0.011**	-0.019, -0.003	0.006
Well-being score→LIF→WAIST z-score→HOMA z-score	-0.003	-0.005; 0.000	0.017
Well-being score→WAIST z-score→HDL-C z-score	0.011	0.002; 0.019	0.016
Well-being score→LIF→HDL-C z-score	0.004	-0.002; 0.010	0.157
Well-being score→LIF→WAIST z-score→HDL-C z-score	0.002	0.000; 0.004	0.017
Well-being score→WAIST z-score→TRG z-score	-0.007	-0.013; -0.001	0.019
Well-being score→LIF→TRG z-score	-0.006	-0.012; 0.001	0.086
Well-being score→LIF→WAIST z-score→TRG z-score	-0.001	-0.003; 0.000	0.018

CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region. Bold figures indicate a false discovery rate <0.05; a false discovery rate adjusted significance value corresponds to α_{adj}=0.013. *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S6 Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between changes in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up – age-stratified analysis – children

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Children (6-11 years at FU2) N=663		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.033	-0.083; 0.017	0.194
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	-0.073	-0.146; 0.000	0.050
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	-0.011	-0.048; 0.027	0.585
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	0.006	-0.053; 0.064	0.849
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	-0.039	-0.106; 0.027	0.243
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	-0.108	-0.198; -0.019	0.018
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.045	-0.004; 0.094	0.074
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	0.054	-0.014; 0.122	0.121
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	0.006	-0.049; 0.061	0.822
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.062	-0.145; 0.021	0.141
Indirect effects*			
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	-0.013	-0.028; 0.002	0.079
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.019	-0.041; 0.003	0.093
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.005	-0.013; 0.003	0.205
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.011	-0.023; 0.001	0.066
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.011; 0.007	0.705
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.004	-0.018; 0.009	0.509
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.004; 0.000	0.098
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.003	-0.006; 0.001	0.113
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.009	-0.023; 0.005	0.205
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.020	-0.042; 0.001	0.063

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Children (6-11 years at FU2) N=663		
	Estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	0.007	-0.011; 0.024	0.450
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	0.009	-0.018; 0.036	0.502
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.004	-0.008; 0.000	0.081
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	-0.005	-0.011; 0.001	0.095
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.006	-0.004; 0.016	0.205
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.014	-0.001; 0.029	0.062
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	-0.005	-0.017; 0.006	0.358
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	-0.008	-0.024; 0.009	0.356
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	0.000; 0.006	0.087
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.004	-0.001; 0.008	0.097
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.006	-0.016; 0.004	0.218
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.014	-0.028; 0.001	0.070
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	0.008	-0.006; 0.022	0.266
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	0.012	-0.009; 0.033	0.257
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.005; 0.000	0.086
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.003	-0.008; 0.001	0.097

CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country (Belgium and Germany were collapsed into one category because low participant numbers for Belgium resulted in estimation problems), parental education, well-being score (all at baseline), baseline value of the respective cardio-metabolic marker, pubertal status (at FU2) and included an indicator for residence in intervention vs. control region. Bold figures indicate a false discovery rate <0.05; a false discovery rate adjusted significance value corresponds to α_{adj}=0.013. [*]indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S7 Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between changes in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up – age-stratified analysis – adolescents

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Adolescents (12-15 years at FU2) N=730		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.006	-0.046; 0.034	0.781
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	-0.053	-0.106, -0.001	0.047
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	0.036	-0.001; 0.073	0.054
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	0.030	-0.017; 0.077	0.212
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	0.000	-0.051; 0.051	0.998
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	0.061	-0.005; 0.126	0.068
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.033	-0.010; 0.075	0.137
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	**0.077**	0.023; 0.131	0.005
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	-0.015	-0.059; 0.029	0.517
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.007	-0.075; 0.061	0.836
Indirect effects*			
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	**-0.010**	-0.017; -0.002	0.012
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.008	-0.017; 0.001	0.072
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.005; 0.004	0.781
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.006	-0.013; 0.001	0.090
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.005	-0.011; 0.001	0.128
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.004	-0.011; 0.003	0.289
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.054
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.121
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.001	-0.009; 0.006	0.782
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.010	-0.021; 0.001	0.072

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Adolescents (12-15 years at FU2) N=730		
	Estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.012	-0.024; 0.001	0.066
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.013	-0.026; 0.001	0.074
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.002	-0.003; 0.000	0.028
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	-0.002	-0.003; 0.000	0.090
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.001	-0.006; 0.008	0.781
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.009	0.000; 0.018	0.061
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	0.005	-0.002; 0.011	0.144
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	0.004	-0.003; 0.012	0.258
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.002	0.000; 0.003	0.021
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.001	0.000; 0.003	0.086
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.001	-0.009; 0.007	0.782
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.010	-0.021; 0.001	0.070
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.006	-0.013; 0.002	0.142
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.005	-0.014; 0.003	0.241
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.003; 0.000	0.026
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.003; 0.000	0.093

CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country (Belgium and Germany were collapsed into one category because low participant numbers for Belgium resulted in estimation problems), parental education, well-being score (all at baseline), baseline value of the respective cardio-metabolic marker, pubertal status (at FU2) and included an indicator for residence in intervention vs. control region. Bold figures indicate a false discovery rate <0.05; a false discovery rate adjusted significance value corresponds to α_{adj}=0.013. [*]indirect effects via LIF are the sum of indirect effects via the five single LIF.

Text S5: Results of sensitivity analyses

As sensitivity analyses, we conducted a complete case analysis ($N_{cross\text{-}sectinal}$=2,441, $N_{longitudinal}$=658) and ran all models stratified by sex because cardio-metabolic markers are influenced by pubertal stage with girls generally maturing faster. Furthermore, because reporting mode of well-being and lifestyle factors differed among participants (information was parent-reported for children younger than 12 years old and self-reported by older children), we additionally adjusted our models with an indicator for self- vs. proxy-report. Lastly, we fitted two alternative models, i.e. (i) a longitudinal model using change in well-being score between baseline and FU2 instead of two well-being change scores and (ii) a longitudinal model using baseline well-being score and well-being score at FU1 as predictors instead of the two well-being change scores.

Results of the complete case analysis were largely similar to the main analysis (Tables S8 and S9), although p-values were generally larger. Both the cross-sectional and longitudinal analysis stratified by sex revealed differences between girls and boys regarding the direct effect of well-being score on BP z-score (no association in girls, positive association in boys) (Tables S10-S13). Adding an indicator for self- vs. proxy-report only marginally affected some effect estimates (Tables S14 and S15). Change in well-beings $score_{FU2\text{-}baseline}$ showed a negative direct effect on WAIST z-$score_{FU2}$ and a positive direct effect on HDL z-$score_{FU2}$, i.e. these direct effects and also the indirect effects were similar to those observed for change in well-being $score_{FU2\text{-}FU1}$ on cardio-metabolic markers at FU2 (Table S16). Neither well-being $score_{baseline}$ nor well-being $score_{FU1}$ showed direct effects on cardio-metabolic markers at FU2 (Table S17).

Table S8 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of cross-sectional associations between well-being and cardio-metabolic markers at second follow-up – complete case analysis

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Whole group N=2,441		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	-0.058	-0.106; -0.010	0.018
Well-being score→BP z-score	-0.006	-0.035; 0.024	0.692
Well-being score→HOMA z-score	-0.048	-0.079; -0.016	0.003
Well-being score→HDL-C z-score	-0.003	-0.033; 0.027	0.844
Well-being score→TRG z-score	-0.019	-0.051; 0.013	0.254
Indirect effects*			
Well-being score→LIF→WAIST z-score	-0.013	-0.021; -0.005	0.002
Well-being score→WAIST z-score→BP z-score	-0.008	-0.015; -0.001	0.021
Well-being score→LIF→BP z-score	-0.004	-0.008; 0.001	0.088
Well-being score→LIF→WAIST z-score→BP z-score	-0.002	-0.003; -0.001	0.003
Well-being score→WAIST z-score→HOMA z-score	-0.017	-0.031; -0.003	0.019
Well-being score→LIF→HOMA z-score	-0.003	-0.009; 0.002	0.231
Well-being score→LIF→WAIST z-score→HOMA z-score	-0.004	-0.006; -0.001	0.002
Well-being score→WAIST z-score→HDL-C z-score	0.012	0.002; 0.023	0.019
Well-being score→LIF→HDL-C z-score	0.003	-0.001; 0.008	0.156
Well-being score→LIF→WAIST z-score→HDL-C z-score	0.003	0.001; 0.004	0.002
Well-being score→WAIST z-score→TRG z-score	-0.010	-0.018; -0.002	0.020
Well-being score→LIF→TRG z-score	-0.004	-0.009; 0.001	0.100
Well-being score→LIF→WAIST z-score→TRG z-score	-0.002	-0.003; -0.001	0.002

CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region; *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S9 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between change in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up – complete case analysis

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=658		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	0.003	-0.046; 0.052	0.902
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	-0.076	-0.140; -0.013	0.018
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	0.019	-0.021; 0.058	0.355
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	0.015	-0.039; 0.070	0.576
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	-0.027	-0.070; 0.016	0.219
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	-0.009	-0.068; 0.050	0.753
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.015	-0.023; 0.053	0.429
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	0.064	0.015; 0.114	0.011
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	0.008	-0.034; 0.050	0.711
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.071	-0.134; -0.007	0.029
Indirect effects*			
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	-0.010	-0.018; -0.001	0.026
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.009	-0.021; 0.003	0.148
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	0.000	-0.005; 0.005	0.902
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.008	-0.016; 0.000	0.056
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.004	-0.011; 0.003	0.213
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.002	-0.011; 0.008	0.745
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.081
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.198
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	0.001	-0.011; 0.012	0.902
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.018	-0.033; -0.002	0.026
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.005	-0.015; 0.004	0.295

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=658		
	Estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.003	-0.016; 0.010	0.652
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.002	-0.004; 0.000	0.034
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	-0.002	-0.005; 0.001	0.154
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	-0.001	-0.009; 0.008	0.902
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.013	0.001; 0.024	0.028
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	0.001	-0.004; 0.007	0.630
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	0.003	-0.005; 0.010	0.500
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.002	0.000; 0.003	0.035
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.001	-0.001; 0.004	0.158
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	0.001	-0.008; 0.009	0.902
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.013	-0.026; -0.001	0.029
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.001	-0.008; 0.006	0.766
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	0.002	-0.007; 0.011	0.732
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.003; 0.000	0.040
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.004; 0.001	0.164

CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education (all at baseline), pubertal status (at FU2) and included an indicator for residence in intervention vs. control region; [*]indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S10 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of cross-sectional associations between well-being and cardio-metabolic markers at second follow-up – analysis by sex – boys

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Whole group N=3,229		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	-0.065	-0.109; -0.020	0.004
Well-being score→BP z-score	0.032	0.005; 0.058	0.021
Well-being score→HOMA z-score	-0.040	-0.081; 0.001	0.056
Well-being score→HDL-C z-score	0.004	-0.035; 0.042	0.854
Well-being score→TRG z-score	0.018	-0.020; 0.055	0.350
Indirect effects*			
Well-being score→LIF→WAIST z-score	-0.012	-0.019; -0.004	0.002
Well-being score→WAIST z-score→BP z-score	-0.008	-0.013; -0.002	0.006
Well-being score→LIF→BP z-score	-0.005	-0.009; -0.001	0.006
Well-being score→LIF→WAIST z-score→BP z-score	-0.001	-0.002; -0.001	0.003
Well-being score→WAIST z-score→HOMA z-score	-0.018	-0.031; -0.006	0.005
Well-being score→LIF→HOMA z-score	-0.009	-0.016; -0.002	0.015
Well-being score→LIF→WAIST z-score→HOMA z-score	-0.003	-0.006; -0.001	0.002
Well-being score→WAIST z-score→HDL-C z-score	0.013	0.004; 0.022	0.005
Well-being score→LIF→HDL-C z-score	0.006	0.000; 0.011	0.032
Well-being score→LIF→WAIST z-score→HDL-C z-score	0.002	0.001; 0.004	0.002
Well-being score→WAIST z-score→TRG z-score	-0.010	-0.017; -0.003	0.006
Well-being score→LIF→TRG z-score	-0.009	-0.016; -0.003	0.005
Well-being score→LIF→WAIST z-score→TRG z-score	-0.002	-0.003; -0.001	0.003

CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region; *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S11 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of cross-sectional associations between well-being and cardio-metabolic markers at second follow-up – analysis by sex – girls

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Whole group N=3,290		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	-0.043	-0.083;-0.003	0.034
Well-being score→BP z-score	-0.013	-0.037; 0.011	0.296
Well-being score→HOMA z-score	-0.040	-0.079; -0.001	0.042
Well-being score→HDL-C z-score	0.032	0.000; 0.065	0.051
Well-being score→TRG z-score	-0.017	-0.051; 0.017	0.322
Indirect effects*			
Well-being score→LIF→WAIST z-score	-0.015	-0.023; -0.007	<0.001
Well-being score→WAIST z-score→BP z-score	-0.006	-0.011; 0.000	0.038
Well-being score→LIF→BP z-score	-0.001	-0.006; 0.003	0.640
Well-being score→LIF→WAIST z-score→BP z-score	-0.002	-0.003; -0.001	0.001
Well-being score→WAIST z-score→HOMA z-score	-0.013	-0.025; -0.001	0.037
Well-being score→LIF→HOMA z-score	-0.004	-0.012; 0.004	0.334
Well-being score→LIF→WAIST z-score→HOMA z-score	-0.005	-0.007; -0.002	<0.001
Well-being score→WAIST z-score→HDL-C z-score	0.008	0.000; 0.016	0.038
Well-being score→LIF→HDL-C z-score	0.002	-0.004; 0.008	0.491
Well-being score→LIF→WAIST z-score→HDL-C z-score	0.003	0.001; 0.004	<0.001
Well-being score→WAIST z-score→TRG z-score	-0.006	-0.012; 0.000	0.040
Well-being score→LIF→TRG z-score	-0.002	-0.008; 0.004	0.495
Well-being score→LIF→WAIST z-score→TRG z-score	-0.002	-0.003; -0.001	0.001

CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region; *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S12 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between change in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up – analysis by sex – boys

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=704		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.016	-0.062; 0.031	0.509
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	-0.072	-0.138; -0.006	0.033
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	0.045	0.006; 0.083	0.023
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	0.070	0.014; 0.126	0.014
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	-0.051	-0.102; 0.001	0.054
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	-0.068	-0.144; 0.008	0.078
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.018	-0.027; 0.063	0.430
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	0.055	-0.005; 0.116	0.070
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	0.002	-0.045; 0.049	0.949
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.028	-0.106; 0.049	0.471
Indirect effects*			
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	-0.015	-0.026; -0.004	0.007
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.011	-0.022; 0.000	0.060
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.003	-0.010; 0.005	0.516
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.012	-0.024; 0.000	0.052
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.003	-0.011; 0.006	0.525
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.004	-0.011; 0.004	0.366
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.005; 0.000	0.017
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.004; 0.000	0.074
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.004	-0.017; 0.008	0.515
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.019	-0.038; 0.000	0.047
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.014	-0.030; 0.003	0.103

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=704		
	Estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.014	-0.032; 0.004	0.129
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.004	-0.007; -0.001	0.013
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	-0.003	-0.006; 0.000	0.068
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	-0.006; 0.011	0.512
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.013	0.000; 0.025	0.045
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	0.008	-0.002; 0.017	0.109
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	0.005	-0.004; 0.015	0.273
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	0.001; 0.005	0.014
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.002	0.000; 0.004	0.072
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.003	-0.011; 0.005	0.518
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.012	-0.025; 0.000	0.054
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.008	-0.019; 0.002	0.120
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.006	-0.015; 0.002	0.136
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.003	-0.005; 0.000	0.019
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.004; 0.000	0.074

CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, country, parental education (all at baseline), pubertal status (at FU2) and included an indicator for residence in intervention vs. control region; [*]indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S13 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between change in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up – analysis by sex – girls

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=689		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.019	-0.063; 0.024	0.379
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	-0.045	-0.098; 0.009	0.100
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	-0.013	-0.047; 0.022	0.469
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	-0.009	-0.053; 0.034	0.672
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	0.003	-0.057; 0.064	0.915
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	0.047	-0.023; 0.118	0.186
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.054	0.010; 0.097	0.016
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	0.074	0.016; 0.131	0.012
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	-0.023	-0.072; 0.027	0.371
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.034	-0.107; 0.040	0.369
Indirect effects*			
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	-0.012	-0.022; -0.001	0.027
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.014	-0.030; 0.001	0.068
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.006; 0.002	0.388
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.004	-0.010; 0.001	0.143
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.004	-0.010; 0.002	0.173
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.008	-0.019; 0.002	0.131
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.093
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.003; 0.000	0.142
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.004	-0.013; 0.005	0.391
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.009	-0.020; 0.002	0.121
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→HOMA $z\text{-}score_{FU2}$	0.000	-0.010; 0.010	0.986

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=689		
	Estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	0.004	-0.014; 0.021	0.670
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.002	-0.004; 0.000	0.040
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	-0.003	-0.006; 0.000	0.088
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.004	-0.005; 0.012	0.387
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.008	-0.002; 0.019	0.115
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	-0.001	-0.007; 0.005	0.747
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	-0.001	-0.011; 0.010	0.896
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.002	0.000; 0.004	0.037
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	0.000; 0.006	0.080
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.004	-0.013; 0.005	0.390
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.009	-0.020; 0.002	0.124
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	0.000	-0.008; 0.009	0.984
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	0.006	-0.009; 0.021	0.422
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.004; 0.000	0.041
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.003	-0.006; 0.000	0.079

CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, country, parental education (all at baseline), pubertal status (at FU2) and included an indicator for residence in intervention vs. control region; [*]indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S14 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of cross-sectional associations between well-being and cardio-metabolic markers at second follow-up – additional adjustment for self- vs. proxy-report

Cross-sectional analysis (Well-being score: 1 unit ≙ 4 points)	Whole group N=6,519		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being score→WAIST z-score	-0.054	-0.084; -0.024	<0.001
Well-being score→BP z-score	0.006	-0.012; 0.025	0.495
Well-being score→HOMA z-score	-0.039	-0.068; -0.011	0.007
Well-being score→HDL-C z-score	0.017	-0.008; 0.042	0.180
Well-being score→TRG z-score	-0.002	-0.027; 0.023	0.886
Indirect effects*			
Well-being score→LIF→WAIST z-score	-0.014	-0.019; -0.008	<0.001
Well-being score→WAIST z-score→BP z-score	-0.007	-0.011; -0.003	0.001
Well-being score→LIF→BP z-score	-0.004	-0.006; -0.001	0.015
Well-being score→LIF→WAIST z-score→BP z-score	-0.002	-0.002; -0.001	<0.001
Well-being score→WAIST z-score→HOMA z-score	-0.016	-0.025; -0.007	0.001
Well-being score→LIF→HOMA z-score	-0.006	-0.011; -0.001	0.025
Well-being score→LIF→WAIST z-score→HOMA z-score	-0.004	-0.006; -0.002	<0.001
Well-being score→WAIST z-score→HDL-C z-score	0.011	0.005; 0.017	0.001
Well-being score→LIF→HDL-C z-score	0.004	0.000; 0.008	0.033
Well-being score→LIF→WAIST z-score→HDL-C z-score	0.003	0.002; 0.004	<0.001
Well-being score→WAIST z-score→TRG z-score	-0.008	-0.013; -0.003	0.001
Well-being score→LIF→TRG z-score	-0.006	-0.010; -0.002	0.007
Well-being score→LIF→WAIST z-score→TRG z-score	-0.002	-0.003; -0.001	<0.001

CI: confidence interval, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education, pubertal status and included an indicator for residence in intervention vs. control region and an indicator for self- vs. proxy-report; *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S15 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between change in well-being score between baseline and first follow-up as well as between first and second follow-up and cardio-metabolic markers at second follow-up – additional adjustment for self- vs. proxy-report

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=1,393		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.019	-0.052; 0.013	0.246
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$	-0.060	-0.103; -0.017	0.006
ΔWell-being $score_{FU1\text{-}baseline}$→BP $z\text{-}score_{FU2}$	0.017	-0.009; 0.044	0.194
ΔWell-being $score_{FU2\text{-}FU1}$→BP $z\text{-}score_{FU2}$	0.024	-0.011; 0.060	0.176
ΔWell-being $score_{FU1\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	-0.022	-0.061; 0.017	0.271
ΔWell-being $score_{FU2\text{-}FU1}$→HOMA $z\text{-}score_{FU2}$	-0.007	-0.057; 0.043	0.798
ΔWell-being $score_{FU1\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.031	-0.001; 0.063	0.056
ΔWell-being $score_{FU2\text{-}FU1}$→HDL-C $z\text{-}score_{FU2}$	0.058	0.016; 0.100	0.006
ΔWell-being $score_{FU1\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	-0.005	-0.040; 0.029	0.761
ΔWell-being $score_{FU2\text{-}FU1}$→TRG $z\text{-}score_{FU2}$	-0.025	-0.078; 0.027	0.345
Indirect effects*			
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	-0.011	-0.017; -0.004	0.001
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.013	-0.021; -0.004	0.003
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.007; 0.002	0.251
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.008	-0.014; -0.002	0.012
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.004	-0.009; 0.000	0.063
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.004	-0.010; 0.001	0.142
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.005
ΔWell-being $score_{FU2\text{-}FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.002	-0.003; 0.000	0.009
ΔWell-being $score_{FU1\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.004	-0.012; 0.003	0.254
ΔWell-being $score_{FU2\text{-}FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.014	-0.024; -0.003	0.010
ΔWell-being $score_{FU1\text{-}baseline}$→$LIF_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.006	-0.015; 0.003	0.217

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=1,393		
	Estimate	*95% CI*	*p-value*
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HOMA z-score$_{FU2}$	-0.005	-0.016; 0.006	0.381
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.003	-0.004; -0.001	0.002
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score $_{FU2}$	-0.003	-0.005; -0.001	0.005
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.004	-0.002; 0.010	0.251
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.011	0.003; 0.019	0.009
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	-0.002; 0.008	0.274
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	0.003	-0.003; 0.010	0.288
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.002	0.001; 0.003	0.002
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.002	0.001; 0.004	0.005
ΔWell-being score$_{FU1\text{-}baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.004	-0.010; 0.003	0.257
ΔWell-being score$_{FU2\text{-}FU1}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.012	-0.020; -0.003	0.011
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.008; 0.004	0.531
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.001	-0.009; 0.006	0.728
ΔWell-being score$_{FU1\text{-}baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.003; -0.001	0.002
ΔWell-being score$_{FU2\text{-}FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.002	-0.004; -0.001	0.005

CI: confidence interval, FU1: first follow-up; FU2: second follow-up; WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education (all at baseline), pubertal status (at FU2) and included an indicator for residence in intervention vs. control region and an indicator for self- vs. proxy-report; *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S16 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between change in well-being score between baseline and second follow-up and cardio-metabolic markers at second follow-up

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=1,393		
	Estimate	*95% CI*	*p-value*
Direct effects			
ΔWell-being $score_{FU2\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$	-0.084	-0.149; -0.018	0.012
ΔWell-being $score_{FU2\text{-}baseline}$→BP $z\text{-}score_{FU2}$	0.043	-0.011; 0.097	0.120
ΔWell-being $score_{FU2\text{-}baseline}$→HOMA $z\text{-}score_{FU2}$	-0.011	-0.088; 0.065	0.769
ΔWell-being $score_{FU2\text{-}baseline}$→HDL-C $z\text{-}score_{FU2}$	0.082	0.017; 0.146	0.013
ΔWell-being $score_{FU2\text{-}baseline}$→TRG $z\text{-}score_{FU2}$	-0.024	-0.102; 0.053	0.539
Indirect effects*			
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$	-0.022	-0.035; -0.008	0.002
ΔWell-being $score_{FU2\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.011	-0.020; -0.002	0.020
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→BP $z\text{-}score_{FU2}$	-0.008	-0.017; 0.002	0.104
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.003	-0.005; -0.001	0.006
ΔWell-being $score_{FU2\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.019	-0.035; -0.003	0.018
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.010	-0.029; 0.009	0.292
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	-0.005	-0.008; -0.002	0.003
ΔWell-being $score_{FU2\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→HDL-C $z\text{-}score_{FU2}$	0.015	0.003; 0.028	0.017
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→HDL-C $z\text{-}score_{FU2}$	0.006	-0.004; 0.017	0.232
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→HDL-C $z\text{-}score_{FU2}$	0.004	0.001; 0.007	0.003
ΔWell-being $score_{FU2\text{-}baseline}$→WAIST $z\text{-}score_{FU2}$→TRG $z\text{-}score_{FU2}$	-0.016	-0.030; -0.003	0.019
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→TRG $z\text{-}score_{FU2}$	-0.003	-0.015; 0.010	0.680
ΔWell-being $score_{FU2\text{-}baseline}$→$LIF_{FU2}$→WAIST $z\text{-}score_{FU2}$→TRG $z\text{-}score_{FU2}$	-0.004	-0.007; -0.001	0.003

CI: confidence interval, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education (all at baseline), pubertal status (at FU2) and included an indicator for residence in intervention vs. control region; *indirect effects via LIF are the sum of indirect effects via the five single LIF.

Table S17 Sensitivity analysis – Unstandardized effect estimates of direct and indirect effects and corresponding p-values obtained from path analysis of longitudinal associations between baseline well-being score and well-being at first follow-up, respectively, and cardio-metabolic markers at second follow-up

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=1,393		
	Estimate	*95% CI*	*p-value*
Direct effects			
Well-being $score_{baseline}$→WAIST $z\text{-}score_{FU2}$	0.047	-0.013; 0.108	0.123
Well-being $score_{FU1}$→WAIST $z\text{-}score_{FU2}$	0.011	-0.044; 0.066	0.685
Well-being $score_{baseline}$→BP $z\text{-}score_{FU2}$	0.010	-0.042; 0.061	0.710
Well-being $score_{FU1}$→BP $z\text{-}score_{FU2}$	0.023	-0.023; 0.068	0.331
Well-being $score_{baseline}$→HOMA $z\text{-}score_{FU2}$	0.019	-0.060; 0.099	0.632
Well-being $score_{FU1}$→HOMA $z\text{-}score_{FU2}$	-0.031	-0.100; 0.038	0.378
Well-being $score_{baseline}$→HDL-C $z\text{-}score_{FU2}$	-0.021	-0.084; 0.042	0.518
Well-being $score_{FU1}$→HDL-C $z\text{-}score_{FU2}$	0.010	-0.045; 0.066	0.720
Well-being $score_{baseline}$→TRG $z\text{-}score_{FU2}$	-0.024	-0.090; 0.041	0.467
Well-being $score_{FU1}$→TRG $z\text{-}score_{FU2}$	0.014	-0.047; 0.075	0.646
Indirect effects*			
Well-being $score_{baseline}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	0.001	-0.008; 0.010	0.875
Well-being $score_{FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$	-0.014	-0.024; -0.004	0.008
Well-being $score_{baseline}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	0.004	-0.001; 0.010	0.137
Well-being $score_{FU1}$→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	0.001	-0.004; 0.006	0.687
Well-being $score_{baseline}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.001	-0.004; 0.003	0.628
Well-being $score_{FU1}$→LIF_{FU2}→BP $z\text{-}score_{FU2}$	-0.006	-0.012; 0.000	0.056
Well-being $score_{baseline}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	0.000	-0.001; 0.001	0.876
Well-being $score_{FU1}$→LIF_{FU2}→WAIST $z\text{-}score_{FU2}$→BP $z\text{-}score_{FU2}$	-0.001	-0.002; 0.000	0.018
Well-being $score_{baseline}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	0.011	-0.003; 0.025	0.129
Well-being $score_{FU1}$→WAIST $z\text{-}score_{FU2}$→HOMA $z\text{-}score_{FU2}$	0.003	-0.010; 0.015	0.685
Well-being $score_{baseline}$→LIF_{FU2}→HOMA $z\text{-}score_{FU2}$	0.000	-0.008; 0.008	0.926
Well-being $score_{FU1}$→LIF_{FU2}→HOMA $z\text{-}score_{FU2}$	-0.008	-0.020; 0.004	0.196

Longitudinal analysis (ΔWell-being score: 1 unit ≙ 1 point per year)	Whole group N=1,393		
	Estimate	*95% CI*	*p-value*
Well-being score$_{baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	0.000	-0.002; 0.002	0.875
Well-being score$_{FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HOMA z-score$_{FU2}$	-0.003	-0.006; -0.001	0.012
Well-being score$_{baseline}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	-0.009	-0.020; 0.003	0.130
Well-being score$_{FU1}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	-0.002	-0.012; 0.008	0.685
Well-being score$_{baseline}$→LIF$_{FU2}$→HDL-C z-score$_{FU2}$	0.001	-0.003; 0.005	0.590
Well-being score$_{FU1}$→LIF$_{FU2}$→HDL-C z-score $_{FU2}$	0.004	-0.003; 0.011	0.242
Well-being score$_{baseline}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.000	-0.002; 0.002	0.876
Well-being score$_{FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→HDL-C z-score$_{FU2}$	0.003	0.001; 0.005	0.010
Well-being score$_{baseline}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	0.009	-0.003; 0.020	0.132
Well-being score$_{FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	0.002	-0.008; 0.012	0.684
Well-being score$_{baseline}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	0.000	-0.005; 0.004	0.861
Well-being score$_{FU1}$→LIF$_{FU2}$→TRG z-score$_{FU2}$	-0.003	-0.011; 0.005	0.405
Well-being score$_{FU1}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	0.000	-0.002; 0.002	0.876
Well-being score$_{FU2}$→LIF$_{FU2}$→WAIST z-score$_{FU2}$→TRG z-score$_{FU2}$	-0.003	-0.005; -0.001	0.012

CI: confidence interval, FU1: first follow-up, FU2: second follow-up, WAIST: waist circumference, BP: blood pressure, HOMA: homeostasis model assessment, HDL-C: high-density lipoprotein cholesterol, TRG: triglycerides, LIF: lifestyle factors; LIF comprised snack/salty foods intake (times/week), fruit and vegetables intake (times/week), sports club physical activity (hours/week), nocturnal sleep duration (age-standardized z-score) and electronic media time (hours/week). Path model was adjusted for age, sex, country, parental education (all at baseline), pubertal status (at FU2) and included an indicator for residence in intervention vs. control region; [*]indirect effects via LIF are the sum of indirect effects via the five single LIF.

Text S6: Detailed discussion on the directionality of associations

Especially in the cross-sectional analysis the direction of the associations cannot be determined. Nevertheless, we considered this analysis worthwhile because well-being may influence cardio-metabolic markers within short time intervals. Furthermore, in our longitudinal analysis a clear temporal sequence of exposure and outcomes can only be established for associations between change in well-being $score_{FU1\text{-}baseline}$ and cardio-metabolic markers at FU2. This is not the case for associations between change in $well\text{-}being_{FU2\text{-}FU1}$ and cardio-metabolic markers at FU2, i.e. there is no time lag between the exposure and outcome measurement and therefore reverse causality cannot be precluded. The approach of calculating well-being change scores was chosen because of the long time lag of six and four years between baseline and FU2 and between FU1 and FU2, respectively, over which effects of single measurements of well-being may have most likely dissipated (1). Lastly, lifestyle factors and cardio-metabolic markers were both measured at FU2 precluding the establishment of cause and effect.

Nevertheless, we acknowledge the interest in temporal relationships and therefore conducted a sensitivity analysis using well-being scores measured at baseline and FU1 as predictors. As expected, no direct effects of baseline well-being $score_{baseline}$ and well-being $score_{FU1}$, respectively, on cardio-metabolic markers at FU2 were found (Text S5, Table S17).

Reference

1. Kline RB. Principles and practice of structural equation modeling. New York, NY, USA: The Guilford Press; 2011.