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General Discussion

Although much work has been done in the field of childhood obesity prevention, the global prevalence of childhood obesity is still high. This is partly due to the lack of our understanding of the causal influences of behavior on weight gain trajectories and indivudial and environmental determinants of behavior change in children. The overall aim of this thesis was contributing to filling the knowledge gap in our understanding of the limited success of previous school-based obesity prevention interventions, by;

1. exploring the mediating and moderating mechanisms of school-based obesity prevention interventions targeting energy balance-related behaviors (EBRBs);
2. exploring measurement issues of physical activity (PA) and sedentary behavior (SB) using accelerometers;
3. exploring social and environmental determinants of EBRBs.

In this final chapter, first the main findings and the methodological issues of the previous chapters will be presented. Secondly, reflections in a broader perspective and recommendations for future research will be provided. Lastly, key recommendations for research and practice will be provided. This chapter will end with concluding remarks.

Main Findings

Working mechanisms of school-based obesity prevention interventions

The first two parts of the thesis provided insight into the working mechanisms of school-based obesity prevention interventions aimed at EBRBs. In Chapter 2 behavioral mediators of longitudinal changes in adiposity measures in the Dutch Obesity Intervention in Teenagers-study (DOiT) were investigated. Results showed that sugar-containing beverages intake mediated the DOiT intervention effect on the changes in body mass index (BMI). We found that the intervention decreased sugar-containing beverages consumption, which, in turn led to a smaller increase in BMI over time. We also found a positive association between computer time and BMI. However, due to the lack of a significant intervention effect on computer time, we could not confirm a significant mediating effect of computer time.

The systematic review on moderators of the school-based interventions aimed at EBRBs (Chapter 3) concluded that there is no strong evidence for any of the studied moderators due to the lack of significant and consistent results. Gender was the most prominent moderator, as girls appeared to benefit more from school-based interventions than boys. The quality of the moderation analyses in the included studies was generally not satisfactory, due to selection of moderators without a specific priori rationale, failing to report statistical power of moderation analyses and assumption of homogeneity of (error) variances across moderator groups. The systematic review on mediators of school-based interventions targeting EBRBs (Chapter 4) concluded that there is consistent evidence for a mediating effect of self-efficacy and intention on PA behavior. Some evidence was found for attitude, knowledge and habit strength as mediators of intervention effects on dietary behaviors. The majority of interventions failed to significantly change the hypothesized mediators, suggesting the need for more effective intervention strategies. Furthermore, only a limited range of potential mediators was investigated in the included studies.

Measurement issues of physical activity and sedentary behavior

Part 3 examined the measurement issues of PA and SB. Chapter 5 describes a standardized protocol for the accelerometer sub-study within the ENERGY cross-European survey. Best evidence for the specific age group of the ENERGY project (10-12yr) was explored for the decisions on data collection and data processing.

There is a lack of evidence regarding the influence of cut-point decisions on calculating SB time from accelerometer data. In Chapter 6, we compared the commonly used accelerometer cut-points (100, 300, 800, 1100 counts per minute (cpm)) for SB with observed sedentary time. A standard protocol was used for observing children involved in different activities, i.e., playing computer games, non-electronic sedentary games, watching television and playing outdoor while wearing an accelerometer. Results of this study showed that estimated time spent sedentary varied considerably using the various cut-points for SB. Our results suggest that the cut-point of <100 cpm is most appropriate.

Social and environmental determinants of EBRBs

Part 4 examined the social and environmental determinants of EBRBs. Influences of migration to a Western country on EBRBs and adiposity measures were explored in Chapter 7. We compared EBRBs, adiposity measures and prevalence of overweight/obesity between Turkish adolescents in Turkey (TR-TR) and Turkish immigrant adolescents living in the Netherlands (TR-NL). Results showed that TR-NL adolescents were more overweight/obese, reported significantly higher consumption of sugar-containing beverages, lower fruit and vegetable intakes, higher PA levels, and less screen time and computer use than their peers living in Turkey (TR-TR).

The association of a natural physical environmental factor (i.e., rainfall and outdoor temperature) on objectively assessed PA and SB in the ENERGY study was explored in Chapter 8. We found that lower maximum daily temperature and higher amount of total rainfall per day was associated with lower children's light, moderate-to-vigorous intensity PA and average overall level of PA (cpm). Higher total rainfall was associated with more sedentary time. The association between maximum temperature and light PA was moderated by gender, with girls' light PA being stronger related to maximum temperature than boy's light PA.

Chapter 9 examined the interpersonal and environmental mediators of the mid-intervention effects on objectively measured PA during school recess and lunchtime in the Transform-Us! study. The Transform-Us! study is an Australian school-based intervention with four groups: SB intervention (SB-I), PA intervention (PA-I), combined PA+SB-I and control group. Results showed that none of the interpersonal or environmental variables mediated the interventions effects. The PA-I and PA+SB-I had a significant positive intervention effect on perceived social support from the teacher for being active. The perceived school play environment was positively associated with moderate-to-vigorous PA during recess among girls. Additionally, we found a significant suppression effect of social support from teachers on LPA during recess in the PA+SB-I group, meaning that social support from teachers was associated with lower LPA during recess.

Methodological Concerns

This thesis consists of systematic reviews and secondary data analyses using data from the ENERGY cross-European survey, baseline data from the ENDORSE, Pro-Children, DOiT - AGAIN and Jump-In intervention studies and longitudinal data from the school-based interventions DOiT and Transform-Us!. Strengths and limitations of these studies are discussed elsewhere (1-5). In this section overall methodological concerns that should be considered when interpreting the findings of this thesis will be elaborated on.

A strong and innovative aspect of this thesis is exploring mediating and moderating mechanisms of the school-based interventions by multiple methods, i.e., systematic reviews and secondary data analyses.

Systematic reviews; We applied an extensive search strategy and selection procedure that yielded the most relevant publications in the literature about mediators and moderators of school-based interventions targeting EBRBs. The methodological quality assessment gave us confidence on grading the level of evidence obtained from the included studies. However, as well as other systematic reviews the quality of our reviews is limited by the quality of the included studies, which was moderate. In the systematic mediators review, we did not specify the potential moderated mediating effects (that is the level of mediation varied by the moderator). Only two studies included in the systematic mediators review explored mediating effects in gender groups separately. The majority of the included studies in both reviews found significant effects on the outcome variable. This may bring the question of publication bias in mind. Meta-analyses were not applied in the systematic reviews, because of the high variety in (the measures of) the outcome variables.

Mediation and moderation analyses; Mediation and moderation analyses are only recently applied in school-based obesity prevention interventions, and they provide valuable information. We applied mediation and moderation analyses in two chapters of this thesis (Chapter 2 and Chapter 9). Chapter 2 describes the first study investigating behavioral mediators of longitudinal changes in adiposity measures; Chapter 9 describes the first study on interpersonal and environmental mediators of PA change during recess and lunchtime in a school-based intervention. In Chapter 2 we used an advanced statistical method (latent growth modeling) for testing the mediating effects in a longitudinal dataset. Parallel process latent growth modeling (PPLGM) is considered as an advanced method for longitudinal mediation analysis (6). However, PPLGM needs careful priori considerations and preliminary analyses to identify the growth trajectories of the examined variables, i.e., coding of time loadings, testing non-linearity. In our study we observed that non-linearity in the growth trajectories of mediators and outcomes caused difficulties and uncertainties in calculation of mediating effect in the PPLGM. There is no priori simulation study on how to calculate mediating effects when having non-linearity in growth trajectories of mediators and/or outcome variables. Therefore, we preferred to linearize the growth function instead of choosing a more complicated model with uncertainties (7). Moreover, PPLGMs are complex statistical models, e.g., combining

individual latent growth models into a single complex model to test mediation. Our PPLGM models could not be adjusted for the multilevel nature of the data and also did not cover multiple mediation models due to non-convergence problems. However, analyzing multiple mediators in one model can clarify to what extent a specific mediator mediates the intervention effect while adjusting for the other mediators (8). Ongoing developments of the statistical programs will allow researchers to apply more integrative PPLGM mediation models. Generally, longitudinal data adds considerable complexity to the mediation model and the use of latent growth modeling is rather new for mediation analysis (9). Considering the large amount of time in developing PPLGMs and the related uncertainties of non-linear growth models, PPLGMs may still not be considered as a gold standard in longitudinal mediation analysis. However, PPLGM may be preferred when the research interest is in development of trajectories of change of mediators and outcomes over time (9). There is a growing interest in this kind of statistical modeling, which will improve the understanding of complex mediation analyses using PPLGM.

Furthermore, the mediation analysis provide exploration of a causal mediation pathway, but do not truly test such causal chains, due to a lack of randomization on potential mediators. The relationship between the mediator and outcome may not indicate a causal effect because it is correlational, not the result of random assignment (10).

Data analyses in Chapter 9 are an example of a combination of mediation and moderation in a single study. Based on previous studies we explored potential differential intervention effects on mediators (a-path in Figure 1) in subgroups according to gender or parental education. Theoretically we did not expect that the examined relationships between the mediator and the outcome in Chapter 9 would be moderated, therefore, we did not assess moderation of that relationship (b-path in Figure 1).
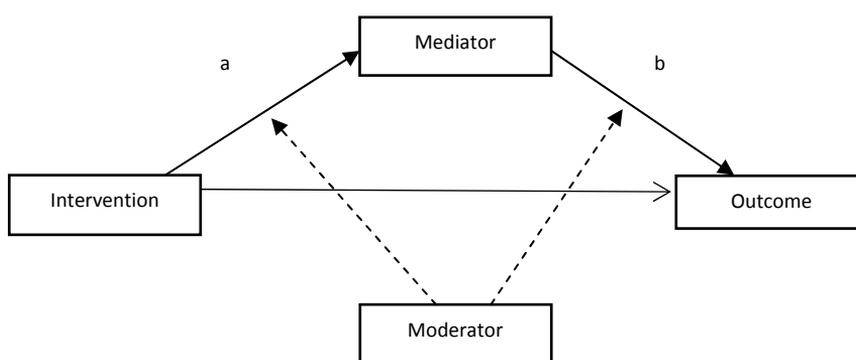
Figure 1. A conceptual framework of mediating and moderating effects.

Measurement issues; In behavioural epidemiology obtaining reliable and valid measurement of behaviors, as well as mediators of these behaviors or behavior change, is an ongoing challenge. Accurate measurement of PA and SB is needed to examine intervention effects or associations with health outcomes. Accelerometry provides

objective assessment of PA and SB time and has been shown a valid and reliable method in children (11,12). However, the data reduction and analysis includes a number of subjective decisions complicating comparison between studies. The accelerometer protocol paper in this thesis (Chapter 5) is the first publication describing a standardized protocol for accelerometer measurements used in a cross-European school-based survey. In our protocol paper we used the best evidence for decisions on accelerometer use in 10-12yr old children. However, accelerometer measurement brings its own limitations to the studies. They are less accurate in detecting activities such as carrying, lifting weight, cycling and also water-based activities (due to limited waterproofing, however the newest versions are mostly water resistant) (13). Accelerometers can assess time spent in SB, however current types cannot distinguish between different types of sedentary activities, i.e., reading, TV viewing, PC use. The newest versions of accelerometers work with pattern recognition and in the near future distinguishing between different types of sedentary activities may be possible. Compliance is another common limitation with accelerometer use (14). In the ENERGY study approximately 30% of children were excluded from further analysis due to insufficient wearing time.

In the studies from Chapter 2 and Chapter 7, EBRBs were assessed using self-reports. Self-reports are limited by potential recall bias and social desirability, and low sensitivity to subtle change. Furthermore, assessing a specific SB and PA behavior using self-reports, such as TV time or active transport to/from school may not accurately reflect overall PA and SB (15,16). Without measuring overall PA and SB, compensatory increase or descrease on PA and SB would bias the results (e.g., an active participation in school physical education class may lead to compensatory decrease in after school PA). Moreover, in Chapter 7 combining the survey data from multiple studies using different self-report instruments limits the comparability of the different studies.

Valid and reliable measures of psychosocial and environmental mediators are largely lacking (17) limiting the accuracy of the associations examined in Chapter 9. Questionnaires need to be compact to limit respondent burden, especially in school-based studies. Therefore, mediating variables were frequently assessed by one item, e.g., liking the school environment or not. Although assessing more mediators by one item was chosen instead of assessing fewer mediators with more items, the broad range of mediators included in the studies still prevented us to fully understand which specific aspects of the environment were associated with behavior change. The included one-item questions were very general, e.g., liking the school environment, and not specific about what aspects of the school environment were appreciated or not.

Reflections and future research

This thesis explored various aspects of school-based obesity prevention by means of promotion of healthy EBRB as well as measurement issues when using accelerometers for the measurements of PA and SB, and social and environmental determinants of EBRBs. The findings and the methods used in this thesis contribute to the understanding of obesity prevention programs. There are three basic questions - Who? What? Why? - that guide us to reflect on our findings: 1. for whom is the intervention effective and for whom

it is not? (who-question) 2. What works and what doesn't (what-question)? and 3. Why is the intervention effective or not (why-question)?

WHO?

The results of this thesis, shows us that the 'one size fits all' approach does not cover the needs and characteristics of the different subgroups within the target population of school children. For instance, boys and girls may have different preferences and need different approaches in order to change their behavior. Knowledge of moderators provides guidance to intervention developers regarding for whom, when, or where specific intervention strategies are effective and this evidence, in turn, will inform further specification of theoretical models (18).

The systematic review suggests that current interventions targeting EBRBs tend to work better among girls. Thus, future research should give special consideration to differences between boys and girls when developing interventions. Different choices for promoting health may be provided for boys and girls. For example, boys and girls may enjoy PA in different ways. Different determinants (e.g., perceived school environment for girls) may be targeted for gender groups.

The moderating effect of ethnicity and socio-economic status on intervention effect on EBRBs are not frequently studied or reported. However, both are known as independent risk factors of obesity (19). Non-Western immigrant children have higher prevalence rates of obesity and unhealthy EBRBs than their native counterparts (20,21). Immigrant groups may be more vulnerable to the obesogenic environments in developed countries (21,22). The findings from Chapter 7 showed that immigrant children living in a Western country oriented their EBRBs to the host culture leading to unfavorable dietary habits i.e., higher sugar-containing beverages consumption and lower fruit and vegetable intake. Future research should focus on intervention strategies that match the immigrant's culture and environment.

Overall, the quality of moderation analyses in school-based obesity prevention interventions should be improved. Studies should be adequately powered and moderators should only be explored with specific a priori reasoning and not data driven. In addition, qualitative research is needed for further understanding why different subgroups respond better than others. This will guide adjustments in intervention development and implementation (different dose or different intervention strategies for specific subgroups) in order to make interventions more effective and efficient.

WHAT?

To make interventions more (cost-)effective only those behaviors that are related to overweight and excessive weight gain, should be identified and included. Therefore, the behavioral influence on adiposity measures should be identified in order to eliminate the risk of selecting ineffective EBRBs to be targeted in the intervention (23). The results from Chapter 2 showed the importance of targeting sugar-containing beverages consumption for preventing excessive weight gain among Dutch children. The ENERGY cross-European survey showed that Dutch children consume the highest amount of sugar-containing

beverages compared to six other European countries (1), suggesting that addressing these behaviors in Dutch children is very timely.

We also found that children who increased their computer time showed a larger increase in BMI (Chapter 2). Previous studies also showed associations between computer time and increased risk of obesity among adolescents (24,25). The results indicate that decreasing computer use may be an effective strategy in order to prevent weight gain among Dutch adolescents. However, the DOiT intervention was not successful in reducing computer time, so more research is needed on effective strategies to change computer time. A recent review that explored effective strategies to reduce screen time among children indicated that future studies may use contingent feedback systems, electronic monitoring devices and parental involvement to successfully decrease children's screen time (26).

After identifying the right EBRBs to target, better understanding of the right determinants is needed (23). Based on the findings of Chapter 4, school-based PA promotion interventions should focus on improving self-efficacy (a person's perceived ability with respect to performing PA) and intention, whereas nutrition interventions may focus on knowledge, attitude and habit. Thus working mechanisms of interventions are different for PA and dietary behaviors, which should be considered in multi-component intervention development. Still, there is a lack of evidence to conclude which determinants should be targeted for EBRB change. Even less knowledge exists on mediators of SB change.

It is generally acknowledged that EBRBs are complex behaviors influenced by multiple factors (27). There is a shift in research from behavioral theories to use ecological models to explain multiple dimensions of influences (intrapersonal, sociocultural and environmental) on EBRBs (28). Influence of social and physical environmental factors on EBRBs in school settings has not been explored extensively (29). In this thesis, we showed the significant impact of daily temperature and rainfall on children's PA and SB. It seems intuitive that weather influences attitudes, confidence and behaviors of children, however weather is not modifiable. Thus, weather conditions should be taken into account, e.g., by developing effective intervention strategies that are less dependent on weather conditions or different strategies depending on season and climate. An example is the forest school concept in which children are encouraged and inspired to play in woodlands in all weathers and eventually aims to develop positive learning towards physical challenges (30). We further examined the perceptions of social support and physical environmental factors on PA during school breaks. The physical environment appears to have an important influence on PA levels of children, especially in girls. Further research is needed to understand whether and via which cognitive mediators (e.g., self-efficacy, attitude) the environmental factors influence EBRBs (31).

WHY?
Intervention strategies and implementation
Both the systematic review and the secondary data analyses showed that interventions were often not successful in achieving significant changes in the targeted mediators. This might be due to selecting the wrong strategies or inadequate implementation. Therefore,

more research is needed to develop effective intervention strategies changing potential mediators. Studies that succeeded in changing important EBRBs are recommended to report their effective intervention strategies as described in the standardized taxonomy developed by Abraham and Michie (32). A process evaluation is essential to better understand the quality of implementation as well as whether the participants complied with the intervention strategies. For example in Chapter 3 the process evaluation indicated that girls complied better with the intervention strategies than boys.

Behavior change theories

Up to now, most theories that guided intervention development are health behavior theories developed and tested in adults. Children do not have the same capacity of abstract thinking, reasoning, information processing and often have less autonomy in making choices as adults have and are exposed to different environments, therefore those theories may be less suitable for explaining children's behavior. Schoolchildren's behavior may be stronger influenced by their physical and social environment, e.g., parents and peers (33). Recently there has been a shift to ecological models proposing that human behavior is an interaction between the person and its environment. Since mediators and moderators are the building blocks of theory, testing them in childhood obesity prevention studies is needed for developing, testing, and refining theory (18).

Adequate measurement of behavior and/or its mediators

One of the reasons of why obesity prevention intervention did not affect the targeted outcomes is likely due to the limited quality of measurement of EBRBs and their determinants (34). Measurement errors distort estimates of relations between variables, thus influence detection of existing relationships (10). Without accurate measurement of EBRBs, identifying their determinants is difficult (33). Once the relevant behaviors and mediators are selected adequate measurement of these behaviors and mediators is needed. Since no gold standard exists for the EBRBs explored in this thesis, we used a combination of accelerometers and self-report. Measures of psychosocial and environmental mediators were based on self-report and parent-report. Both are prone to response bias and social desirability. Future studies should select and/or develop valid, reliable and sensitive measurement tools for schoolchildren.

Recommendations; Where to go from here
For research

Key recommendations for future studies based on the observations described in the thesis are summarized below;
- Develop further understanding of how sugar-containing beverages consumption and computer use influence the weight gain trajectories among youth;
- Gain a deeper understanding of the determinants of EBRB change and especially SB change;
- Seek further understanding of the characteristics of the environment that support healthy behavior;

- Properly report intervention strategies using a standardized taxonomy to facilitate replication;
- Reliable, valid and responsive measures of EBRBs and psychosocial and environmental determinants suitable for children should be developed;
- Reach consensus on an evidence-based standard protocol for data reduction and analysis of accelerometers to assess PA and SB;
- Perform process evaluations to see if the intervention was implemented as planned and if intervention fidelity is indeed associated with better effects;
- Conduct correct mediation analyses - even when a significant main effect was not found - in order to understand why and how an intervention was (not) effective so that it can be improved;
- Evaluate moderating effects in evaluation of interventions so that interventions can be adapted to specific subgroups.

For practice

Key recommendations for future childhood obesity prevention practice based on the observations described in the thesis are summarized below;

- Intervention components: Sugar-containing beverages consumption and computer use appeared to be promising EBRBs to target with school-based obesity prevention interventions.
- Increasing children's self-efficacy and intention is important for PA promotion and increasing children's knowledge, improving attitude and changing habit are important for the promotion of healthy dietary habits. School-based PA promotion studies should also take into account the influence of the school play environment on children's PA.
- Intervention strategies: Results of this thesis suggest that advice on changing EBRBs of children should take into account gender and culture- sensitive issues. Obesity prevention intervention strategies could take into account different weather conditions to promote PA among youth. Feasibility of implementation practices should be assured for optimizing the implementation of the intervention strategies.

Conclusions

Childhood obesity prevention is an important public health challenge. Identifying and evaluating relevant and irrelevant mediators and moderators should be a common approach for obesity prevention researchers. Subsequent intervention development should be based on the results of such studies. Accurate measurement, consideration of the environmental influences, applying effective intervention strategies while taking into account the needs and the characteristics of the various subgroups and also targeting the right mediators will help enhancing the effectiveness of future school-based obesity intervention programs. Understanding the interaction between moderators and mediators will help to support further modification and development of both theory and practice (18). We should remember that even small changes, can when taken together, will contribute to combatting the childhood obesity epidemic in the coming decades.

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