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Evaluation eines multimodalen Programmes zur Prävention von Übergewicht in Kindergärten (TigerKids) nach zwei Jahren Laufzeit

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Short and mid term effects of a setting based prevention programme to reduce obesity risk factors in children: a cluster-randomized trial

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Running title:

Prevention of obesity risk in preschool children

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Abstract (264 words)

Objectives: To assess effects of a prevention programme in a preschool setting on obesity risk factors.

Design: Cluster randomized trial. Outcome assessed during school entrance health examinations in two cross sectional samples.

Setting: 64 kindergartens in 4 Bavarian regions, randomly assigned as intervention or controls in a 2 : 1 ratio.

Participants: Samples of 1318 and 1340 children in the school entrance health examination 5.7 ± 2.6 and 17.6 ± 2.3 months (mean ± standard deviation for first and second sample) after programme start.

Interventions: The behavioural intervention aimed at modifying physical activity and food and drink choices at the kindergarten setting.

Main outcome measures: Prevalence of high fruit and vegetable consumption, low consumption of high caloric drinks assessed in food questionnaires filled by parents, of overweight and obesity, and secondary, further dietary habits and results of motoric testing.

Results: An increased proportion of children with a high fruit and vegetable consumption was found already after 6 months, which was sustainable with adjusted odds ratios of 1.59 (1.26 to 2.01) and 1.48 (1.08 to 2.03) after 18 months. Subgroup analyses by gender, overweight and parental education, performed in order to assess consistency of effects, showed similar results. Prevalence of overweight, obesity and motoric testing results were not statistically different between intervention and control groups.

Conclusions: This low cost setting based behavioural intervention achieved sustainable effects on fruit and vegetable consumption in young children 18 months after start of the intervention. A large scale study to assess whether these and potentially unmeasured effects will also result in a reduction of childhood overweight is therefore warranted.

ClinicalTrials.gov ID: NCT00336128

Key Words: children, overweight, prevention, dietary habits, physical activity

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What this paper adds

What is already known on this subject

- Obesity is an increasing problem and is grounded in early childhood.
- There are few studies on prevention programmes in children younger than seven years.

What this study adds

- With a low cost intervention programme in the kindergarten setting sustainable improvement in eating behaviour can be attained.
- A large scale study to assess potential effects on the prevalence of overweight and obesity appears to be warranted.

Introduction

Prevalence and severity of childhood obesity have markedly increased worldwide in recent decades, but the effects and availability of therapeutic interventions remain far less than satisfactory (1, 2). The observed increase of obesity prevalence already at primary school entry with 5-6 years over the last two decades (3) suggests that the basis of obesity development is already established in early childhood. Therefore, the development and implementation of effective prevention strategies at an early age is of utmost importance, but at present only very limited data on the effectiveness of childhood obesity prevention programmes from randomized controlled trials are available, and no generalisable conclusions can be drawn (4-6). We developed and evaluated (phase II trial according to the Medical Research Council (7)) a low-cost behavioural intervention programme for use in Kindergarten day care settings in a cluster-randomized study.

Participants and methods

Intervention and setting

The "TigerKids" behavioural intervention programme was developed with the primary aims to modify habits of food and drink intakes and physical activity in preschool children (www.tigerkids.de). A setting approach was chosen because almost all children in our population attend the Kindergarten setting (97 % of all children) and can thus be reached, and because the cost per participating subject can be kept low. The intervention focussed on improving health behaviour, such as regular physical activity, regular consumption of water and other low energy drinks as well as fruit and vegetables. The intervention was offered on a daily basis in the day care setting, aiming at establishing a health promoting behaviour pattern that might also be maintained outside of the daycare setting, e.g. at home. For a period of one year, modules for use in Kindergarten settings were developed in collaboration with experts in pre-school education, sport and nutrition science, and paediatrics, and tested for suitability and acceptance in two day care centres one in the city of Munich and one in Kaufbeuren, Germany. In Germany Kindergarten day-care centres are usually (> 90 %) attended by children in the age range of 3 – 6 years for half a day during weekdays. The key targets set were that children should reach:

- at least 30 minutes/day of vigorous physical activity at the Kindergarten setting,
- consumption of at least two portions/day of vegetables and fruits,

- intake of not more than one glass/day of sugared drinks and juices

A folder for Kindergarten teachers with information materials and modules ready for use in the day to day activities of the Kindergarten (374 printed pages) and a CD with songs for use in the day care was produced, along with information materials for parents in the form of four newsletters/Kindergarten year and twelve "Tippcards" providing simple messages on health related behaviour for parents, such as to engage in regular physical activity together with their children, or to encourage consumption of vegetables and fruits and of water and low-energy drinks. A box of materials for use in the Kindergarten setting was produced in close collaboration with the publisher of Germany's largest health insurance AOK (AOK Verlag, Remagen, Germany) at a low cost of 150 € for the materials for one day care setting with up to 75 children, including the information folders for teachers, materials for use in the Kindergarten setting, as well as newsletters and TippCards for families and a large wooden train used for structured exploration of foods and drinks by children. An Internet platform with supporting information for Kindergarten teachers and families was established (www.tigerkids.de). All materials were provided in German language.

At the start of the intervention, all teachers of participating day care centres were asked to participate in a two day training workshop in which they were introduced into the concept and practical application of the TigerKids programme. A telephone hotline with the coordinating centre at the Dr. von Hauner Children's Hospital, University of Munich was established for counselling of teachers and problem solving. At the start of the TigerKids programme after the summer holidays, two information evenings were offered for parents at each Kindergarten setting to introduce the parents into the concepts, goals and practical aspects of the project, in collaboration with the health insurance AOK Bavaria. At the start of the second Kindergarten year after the onset of the intervention, the Kindergarten teachers were encouraged to continue using the programme. During the second year the telephone hotline at the coordinating centre was maintained, and one workshop was held to motivate the educators.

Design and study population

In July 2004 64 kindergartens in four regions were randomly assigned (2 :1) to receive the intervention or not. Kindergartens assigned to the control group were asked to maintain their usual programme. The outcome measures were assessed in children eligible for school entry (age 5-6 years) during the 2005 (first sample) and 2006 (second sample) school entry health

examinations. Eating habits were assessed by questions embedded in a parental questionnaire of the Bavarian Health Survey (8). Anthropometrics and motoric testing were carried out during the obligatory school entrance health examination offered to all children in the state of Bavaria. Thus two samples were analysed at a time interval of 5.7 ± 2.6 and 17.6 ± 2.3 months (mean ± standard deviation) after the start of the intervention. Figure 1 illustrates the sequence of intervention and evaluation. 81.0/83.6 % and 83.8/82.8 % of the parental questionnaires were returned and informative in the intervention/control group of the first and second sample, respectively.

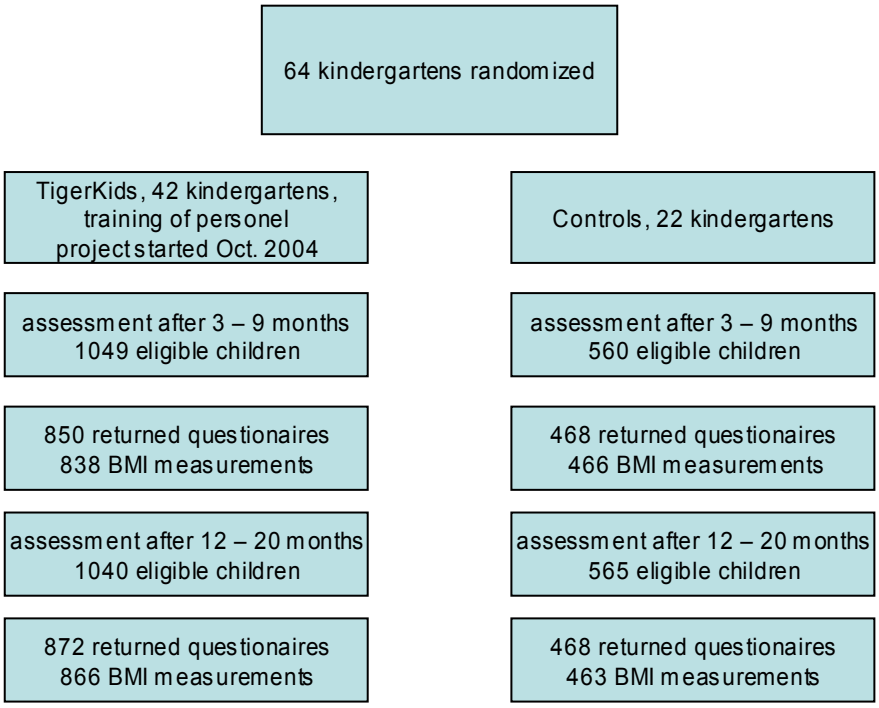

Figure 1: Flowchart of evaluation

According to the key targets of the programme, we defined the main outcomes as follows.

Main outcomes

Food frequency data as obtained from the questionnaire were categorized into foods with low caloric (desirable) and high caloric densities (less desirable).

High fruit and vegetable consumption (9, 10): Two or more portions daily were regarded as high. A portion is defined as a children's hand full of food.

Low consumption of high caloric drinks (11): A maximum of one glass (200 ml) a day of such drinks (e. g. high sugar soft drinks, sugared teas, undilutes juices etc.) was regarded as low. A number of high caloric drinks were listed. Classification of a child as exposed to low consumption of high caloric drinks required answers to be complete for each type of high caloric drinks listed.

Overweight/obesity: Weight and height were measured using standard stadiometers and calibrated digital scales and transformed into body mass index (BMI), using age and gender specific cutoff values established by Cole et al (13) to define overweight and obesity.

Secondary outcomes

High Consumption of low caloric drinks (11): A list of low caloric drinks was provided. At least one glass/day of low caloric drinks was counted as high.

Low Consumption of energy dense sweets (9): A list of energy dense sweets (e. g. chocolate bars, ice cream) was presented: for each of these products not more than three portions per week were considered as low. Again, to be rated as low required answers for each energy dense sweets item.

The following variables were also measured:

Purchase of low fat milk products (9): At least two low-fat diary products which may be purchased for the child or the family. Participants with positive answers for two or more products were considered valid, even if not all items in this category were answered.

Infrequent snacking in front of TV (14): Yes, if less than once per week.

Motoric testing consisted of one task from the "Karlsruher Motorik-Screening für Kindergartenkinder (KMS 3 – 6)" (12): Side to side jumps: Number of jumps over a bar a child can perform within 15 s. The child should jump and land with both feet simultaneously. The numbers of two runs were added up.

Ethical and data protection aspects

The study protocol was reviewed by the Ethical Committee of the Bavarian Board of Physicians (Bayerische Landesärztekammer), Munich, by the local Data Protection Officer, and the Bavarian Ministry for Environment, Health and Consumer Protection, and no objections were raised. Parents had given written consent to the data collection.

Statistical analysis

Chi-square or t-tests as appropriate were used to compare population characteristics. In bivariate analyses of the outcome measures binomial confidence intervals are given for binary outcomes; for side-to-side jumps, a likelihood based interval for Poisson-distributed data was computed (R version 2.3, www.r-project.org). To account for the cluster-randomized design we used a Generalized Estimating Equations model for multivariate analysis (as implemented

in SAS version 9.1, PROC GENMOD). In addition to the cluster levels defined by region and kindergarten adjustment for parental education and non-German-nationality was done.

Results

Table 1 shows descriptors of the two samples. While in the first sample there was some difference in terms of German nationality between children randomized for the intervention and controls, randomization worked very well in the second sample.

Table 1: Population descriptives and potential confounders of the control and intervention samples. The first and second values in each cell represent the first and second sample, respectively.

	missing	**Controls n = 468**	**Intervention n = 872**	**χ^2-value**	**p-value**
2 or more siblings	4	150 (11.4 %)	245 (18.7 %)	1.65	0.20
	8	130 (28.0 %)	235 (27.1 %)	0.11	0.74
without German nationality	5	404 (13.5 %)	775 (8.4 %)	8.53	0.0035
	3	41 (8.8 %)	66 (7.6 %)	0.587	0.44
medium to high educational level	43	327 (71.9 %)	585 (71.3 %)	0.04	0.84
	50	318 (71.0 %)	615 (73.0 %)	0.619	0.43
smoking during pregnancy	59	59 (13.2 %)	87 (10.7 %)	1.74	0.19
	55	48 (10.7 %)	84 (10.1 %)	0.117	0.73
sex (male)	0	245 (52.4 %)	431 (63.8 %)	0.33	0.57
	0	242 (51.7 %)	451 (51.7 %)	0.00	1.00
		mean ± standard deviation		t-value	p-value
Age	16	6.12 ± 0.42	6.12 ± 0.41	0.13	0.89
	3	6.0 ± 0.42	6.0 ± 0.42	-0.04	0.97

There was a reproducible higher (with non-overlapping confidence intervals) consumption of fruits and vegetables reported in the intervention group in both samples (Table 2). A lower consumption of high caloric drinks and snacks while watching TV was only observed in the first sample. In the second sample the proportion of children with a low consumption of high caloric drinks had increased in the intervention group. An even more marked increase in the control group, however, rendered the difference between the control and intervention group in the second sample non significant.

Table 2: Prevalence of overweight, obesity, reported eating habits (95%-CI) and motoric testing (95%-CI of mean) by intervention group with main outcomes listed in the upper part of the table. Again values for the first and second sample are listed in the first and second line of each cell. Significant differences are typeset in boldface.

Outcome	Cases with valid information	Intervention	Controls
Overweight	1295	13.9 % (11.6 to16.5)	18.0 % (14.6 to 21.8)
	1326	15.6 % (13.2 to 18.2)	16.7 % (13.4 to 20.5)
Obesity	1295	3.4 %(2.2 to 4.8)	5.4 % (3.5 to 7.9)
	1326	3.8 % (2.6 to 5.3)	4.3 % (2.7 to 6.6)
High fruit consumption	1299	**66.6% (63.3 to 69.8)**	**55.7 % (51.0 to 60.3)**
	1314	**66.7 % (63.4 to 69.9)**	**56.3 % (51.6 to 60.9)**
High vegetable consumption	1294	**45.1% (42.4 to 47.8)**	**33.9 % (29.6 to 38.5)**
	1307	**42.7 % (39.4 to 46.1)**	**33.6 % (29.2 to 38.1)**
Low consumption of high caloric drinks	1022	**60.4 % (56.6 to 64.2)**	**47.7 % (42.4 to 52.9)**
	1163	63.5 % (60.0 66.9)	60.8 % (55.9 to 65.7)
Purchase of low fat milk products for child or family	1301	74.5 % (71.4 to 77.4)	74.7 % (70.5 to 78.6)
	1251	85.3 % (82.7 to 87.7)	85.7 % (82.1 to 88.9)
Low consumption of energy dense sweets	1178	39.7% (36.2 to 43.2)	37.7 % (33.1 to 42.5)
	1245	44.2 % (40.8 to 47.7)	42.0 % (37.3 to 46.8)
High consumption of low caloric drinks	1062	49.9% (46.0 to 53.7)	51.3% (46.2 to 56.5)
	1186	50.6 % (47.0 to 54.2)	48.2 % (43.2 to 53.1)
Infrequent snacking in front of TV	1266	68.7 % (65.4 to 71.9)	63.4% (58.7 to 67.9)
	1305	69.9 % (66.7 to 72.9)	67.5 % (62.9 to 71.8)
# side to side jumps within 2 x 15 s	1318	24.9 (24.4 to 25.3)	24.0 (23.4 to 24.6)
	1340	24.9 (24.5 to 25.3)	24.5 (23.9 to 25.1)

These interdependencies were expressed as odds ratios (Table 3), which were calculated taking account of the cluster randomization and adjustment for possible confounders and confirm the findings of the bivariate analysis.

Table 3: Intervention effects (OR, controls used as reference) on main and secondary outcomes as obtained from the cluster randomized multivariate analysis, adjusting for parental education and German nationality. Overweight, obesity and side to side jumps were additionally adjusted for age and sex. Significant effects are denoted by *, **, * for alpha < 0.05, 0.01, 0.001, respectively.**

Outcome	OR
Overweight	0.73 (0.51 to 1.04) 0.89 (0.66 to 1.22)
Obesity	0.58 (0.31 to 1.10) 0.79 (0.35 to 1.77)
High fruit consumption	1.64 (1.26 to 2.12) *** 1.59 (1.26 to 2.01) ***
High vegetable consumption	1.26 (0.98 to 1.61) 1.48 (1.08 to 2.03) *
Low consumption of high caloric drinks	1.66 (1.16 to 2.38) ** 1.15 (0.88 to 1.51)
Purchase of low fat milk products for child or family	0.94 (0.71 to 1.24) 0.97 (0.73 to 1.29)
Low consumption of energy dense sweets	1.01 (0.78 to 1.31) 1.11 (0.85 to 1.45)
High consumption of low caloric drinks	0.95 (0.72 to 1.25) 1.05 (0.83 to 1.33)
Infrequent snacking in front of TV	1.18 (0.90 to 1.55) 1.13 (0.86 to 1.49)
# side to side jumps within 2 x 15 s	1.02 (0.94 to 1.11) 1.02 (0.95 to 1.10)

Subgroup analyses

Subgroup analyses were attempted for German vs. non German nationality, boys vs. girls, high vs. lower parental education, and overweight vs. non overweight children. Subgroup analyses revealed no differential intervention effect in boys and girls (data not shown). The subgroup of children without German nationality (even not as second nationality) was too small (127 and 98 in first and second sample) for sensible subgroup analyses (data not shown). An important issue in public health is the benefit of the intervention for children of different socioeconomic background. We used level of parental education as a proxy measure. Estimates for the effect of the intervention were stratified by the highest school-leaving qualification of their parents: if at least one of them had passed secondary school qualification examination after ten years ("Realschulabschluss") or a higher level of education, they were categorized as "higher parental education" (Table 4). The intervention effects seemed to reach children from both the lesser and the higher educated subgroups, with trends to desired effects observed in both groups. The effect on fruit and vegetable consumption appears to be slightly

higher in the higher parental education subgroup. A higher consumption of low fat diary products was found in families with lower parental education exposed to TigerKids, whereas no such an effect was observed in the children from families with a higher educational background.

Table 4: Intervention effects (OR, controls used as reference) as obtained from the cluster randomized multivariate analysis, adjusting for parental education and German nationality. Overweight, obesity and side to side jumps were additionally adjusted for age and sex. Significant effects are typeset in boldface. Results for subgroups by parental education

Outcome	Lower parental education 1st sample: 361 2nd sample: 355	Higher parental education 1st sample: 910 2nd sample: 932
High fruit consumption	1.03 (0.58 to 1.84) 1.36 (0.93 to 1.98)	1.90 (1.45 to 2.49) 1.70 (1.26 to 2.31)
High vegetable consumption	1.18 (0.73 to 1.90) 1.41 (0.91 to 2.17)	1.27 (0.96 to 1.70) **1.49 (1.01 to 2.21)**
Low consumption of high caloric drinks	1.52 (0.87 to 2.67) 1.41 (0.90 to 2.20)	**1.73 (1.10 to 2.73)** 1.05 (0.77 to 1.44)
Purchase of low fat milk products for child or family	0.78 (0.48 to 1.27) **1.60 (1.10 to 2.33)**	0.95 (0.65 to 1.38) 0.83 (0.60 to 1.15)
Low consumption of energy dense sweets	0.99 (0.61 to 1.61) 1.31 (0.78 to 2.19)	1.03 (0.75 to 1.41) 1.05 (0.79 to 1.38)
High consumption of low caloric drinks	0.85 (0.53 to 1.38) 0.91 (0.63 to 1.33)	0.97 (0.71 to 1.33) 1.11 (0.84 to 1.49)
Infrequent snacking in front of TV	1.24 (0.85 to 1.82) 1.49 (0.94 to 2.37)	1.14 (0.79 to 1.64) 0.98 (0.70 to 1.36)

Although a healthy diet and a high level of physical activity is likely to be beneficial for all children irrespective of whether they are overweight or not, effects of overweight children are of particular interest in such a preventive programme. We therefore analysed the effects on eating habits in the normal and overweight subgroups (Table 5), even though the sample of overweight children is rather small. The adjusted odds ratios comparing fruit and vegetable consumption between the control and intervention groups are similar. A stronger effect on the consumption of sweets and the consumption of snacks/sweets while watching TV in children with overweight was reported in the second sample after a longer observation period.

Table 5: Intervention effects (OR, controls used as reference) as obtained from the cluster randomized multivariate analysis, adjusting for parental education and German nationality. Overweight, obesity and side to side jumps were additionally adjusted for age and sex. Significant effects are typeset in boldface: Results for subgroups by overweight.

Outcome	Overweight 1st sample: 187 2nd sample: 203	Normal weight 1st sample: 1062 2nd sample: 1070
High fruit consumption	1.65 (0.91 to 3.01) 1.42 (0.72 to 2.80)	**1.65 (1.27 to 2.15)** **1.65 (1.27 to 2.14)**
High vegetable consumption	1.17 (0.65 to 2.12) 1.22 (0.68 to 2.20)	1.29 (0.99 to 1.69) **1.56 (1.09 to 2.24)**
Low consumption of high caloric drinks	1.42 (0.61 to 3.30) 0.93 (0.48 to 1.80)	1.75 (1.23 to 2.50) 1.19 (0.90 to 1.57)
Purchase of low fat milk products for child or family	0.67 (0.30 to 1.48) 0.87 (not determinable)	0.99 (0.74 to 1.33) 0.99 (0.73 to 1.34)
Low consumption of energy dense sweets	0.61 (0.30 to 1.25) 1.85 (1.06 to 3.23)	1.12 (0.86 to 1.45) 1.01 (0.77 to 1.32)
High consumption of low caloric drinks	1.13 (0.53 to 2.39) 1.16 (0.69 to 1.97)	0.88 (0.67 to 1.17) 1.04 (0.80 to 1.36)
Infrequent snacking in front of TV	1.22 (0.72 to 2.08) **1.92 (1.01 to 3.68)**	1.18 (0.87 to 1.61) 0.97 (0.72 to 1.30)

Discussion

This multimodal behavioural intervention programme in the kindergarten setting aiming at promoting healthy dietary choices and regular physical activity was associated with a higher fruit and vegetable consumption in the home environment in two different samples assessed six and eighteen months after the initiation of the programme. Subgroup analyses suggested similar effects for boys and girls, children of families with higher or lower school education and for overweight and non overweight children. An additional effect on consumption of energy rich drinks was only seen in the first sample. No significant effects on the prevalence of overweight, obesity and on a test for physical fitness were observed.

Increasing fruit and vegetable consumption is considered a useful intervention for the prevention of overweight and obesity. A large study in 1013 school children with a baseline prevalence of obesity of 35 % (15) found an increase in fruit and vegetable consumption accompanied by a 2 % reduction in overweight. Epstein and colleagues (9) report a significant decrease of parental overweight in a family based setting after one year associated with high fruit and vegetable intake, which had also significantly influenced fat and sugar intake. In contrast, a longitudinal study in a very small sample of only 213 preschool children (16) found no effects on the prevalence of overweight, and a CDC review (17) concluded that the effectiveness of increasing fruit and vegetable consumption to prevent or reduce overweight has not been conclusively demonstrated. Other authors have emphasized that the energy density of the diet, i.e. the amount of calories per 100 g or per portion of food, is closely related to the total energy intake and hence to the risk of developing overweight and obesity (1, 18). Indeed, frequent consumption of fast food with a high energy density by young adults led to an increased occurrence of obesity (19). Regular consumption of fruits and vegetables, which have a low energy density, will replace energy dense foods and thus should result in a lower energy density of the total dietary intake and lower long-term risk of overweight.

Most studies find an independent association between sugared soft drinks and overweight (20, 21). Ludwig and colleagues report an odds ratio of 1.6 for occurrence of overweight per daily glass of soft drink consumed (22). Accordingly, the Christchurch obesity prevention project in schools (11) reports a reduction of overweight prevalence by propagating low consumption of such drinks. A sustainable reduction in the consumption of high caloric drinks would undoubtedly be a desirable effect of the intervention.

Since five main outcomes were considered, multiple testing might be an issue. However, the p-values of the OR presented in Table 3 are smaller than the required values according to the

Holm/Hochberg method and thus remain significant on an overall level of alpha = 0.05, except for one (high vegetable consumption in the second sample).

A potential drawback of our study is the absent ascertainment of diet habits both before and after the intervention. Therefore it might be possible that the presumed intervention effects reflect rather differences in baseline exposures. This, however, appears to be unlikely, at least regarding the effects on fruit and vegetable consumption. As part of the first and second survey in the setting of the health monitoring units (GME 2004/05 and 2005/06) in Bavaria, dietary habits were also ascertained for children in the respective regions attending kindergartens not enrolled in the programme either in the intervention or control groups. The proportion of children with a high consumption of fruits and vegetables in both surveys was almost identical or less for children in these kindergartens and controls. High fruit consumption for controls vs. children not enrolled in the study was 55.7 (51.0 to 60.3) vs. 55.7 (54.2 to 57.3) % in the first and 55.5 (53.9 to 57.2) vs. 56.3 (51.6 to 60.9) % in the second sample. High vegetable consumption for controls vs. children not enrolled in the study was 28.4 (27.0 to 29.9) vs. 33.9 (29.6 to 38.5) % in the first and 31.1 (29.6 to 32.7) vs. 33.6 (29.2 to 38.1) % in the second sample. The presumed intervention effect on a low consumption of high caloric drinks in the first sample, however, might partially be explained by a low baseline prevalence in the controls. In the first sample the proportion of children with a low consumption of high caloric drinks (47.7 (42.4 to 52.9) %) was below that observed among children outside the study (55.9 (54.1 to 57.7) %). A – certainly favourable – spread of the message of the intervention to control kindergartens may have contributed to close the gap between intervention and control children in the second sample, since the proportion of children with low consumption of high caloric drinks increased in children outside the study from 55.9 (54.1 to 57.7) to 60.3 (58.6 to 62.0) % as well.

Effect estimates on reported diet habits were based on parental reports, because measures independent of parental reports are difficult if not impossible to obtain in a large sample of children of this age group. It is possible that reports of parents of children in the intervention group might have been influenced by the messages they received with the intervention. It can also not be excluded that reporting bias might have influenced the observed intervention effect on low consumption of energy rich sweets and infrequent consumption of sweets in front of TV in overweight children observed in the second sample.

There was no advantage in the motoric testing results obtained in the intervention group. Physical activity, which influences BMI, is difficult to measure, even when technical

equipment is used (23). The motoric testing performed in our study might have been a poor surrogate marker for increased physical activity.

A major characteristic advantage of our intervention is its setting approach at a group level. Therefore we chose a group randomized design for evaluation. We accounted for cluster effects on the regional and kindergarten level following the recommendations of the CONSORT-statement and chose a GEE-model considering the prerequisites (number of clusters > 40) in accordance with the biostatistical literature (24).

We found no significant effects on the prevalence of overweight and obesity which may be attributed to two possible causes. The duration of exposure might not have been long enough, but the observation period of almost two years in our second sample is equal or even longer than in other studies that showed an improvement in BMI in children even though they were older than six years (5, 6), and hence different intervention strategies were used. Lack of power appears to be a more likely explanation. On the basis of our data we estimated the number of participants needed to detect a 1 % difference in prevalence with 80 % power on an alpha = 5 % level taking into account the cluster structure, which would require about 20 000 participants in each group. Since the potential size of the intervention effect could not be predicted before study onset, no prior sample size estimation for detection of a reduction in overweight and obesity could be performed.

Conclusion:

A low intensity behavioural intervention at low cost, to promote physical activity and healthy diet at the kindergarten setting, resulted in significant and sustainable improvements in the consumption of fruits and vegetables. Whether these or potentially other not measured intervention effects might also result in a reduction of the prevalence of overweight and obesity needs to be addressed in a large scale study with pre- and post intervention assessment of BMI.

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2 Checkliste nach dem CONSORT-Statement (2001)

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomized", or "randomly assigned").	title
INTRODUCTION Background	2	Scientific background and explanation of rationale.	5
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	6
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	5
Objectives	5	Specific objectives and hypotheses.	5,7
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	7
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	(n. a., see 7, 16)
Randomization, Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (e.g., blocking, stratification)	6

Randomization, Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	6
Randomization, Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	6
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No blinding, evident from setting based approach
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	8
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	Fig. 1
Recruitment	14	Dates defining the periods of recruitment and follow-up.	6, Fig. 1

Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50 %).	Top of the respective tables
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95 % confidence interval).	yes
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	Main and secondary outcomes 7, tables divided, discussion 14
Adverse events	19	All important adverse events or side effects in each intervention group.	
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	14ff
Generalizability	21	Generalizability (external validity) of the trial findings.	15
Overall evidence	22	General interpretation of the results in the context of current evidence.	14

3 Bemerkung zu Subgruppenanalysen

Subgruppenanalysen stellen ein anschauliches Mittel dar, um auf vermutete Wirkunterschiede frei von Modellvoraussetzungen (z. B. Loglinearität bei der logistischen Regression) zu untersuchen. Dies geschieht freilich auf Kosten der statistischen Power, da sich die vorhandene Fallzahl auf die Untergruppen verteilt. Wenngleich diese Analysen gelegentlich im Verdacht des Mißbrauchs stehen, aus Studien mit nicht signifikanten Gesamtergebnissen doch noch Effekte zu berichten, ist die getroffene Auswahl hypothesengeleitet und gerechtfertigt: Im Gegensatz zur Zwischenauswertung von 2005[8] wurde in dieser Arbeit eine Subgruppenanalyse nach Über- und Normalgewichtigen durchgeführt. Es scheint durchaus plausibel, wenn Übergewichtige sich von einem Programm zur Gewichtsreduktion mehr angesprochen fühlen, als Normalgewichtige, die keine Notwendigkeit sehen, ihr Ernährungs- und Bewegungsverhalten i. S. einer Gewichtsreduktion zu ändern. Auch wäre ein Fokus auf übergewichtige Kinder ganz im Sinne des Programms. Dieser, als Effektmodifikation zu bezeichnende Sachverhalt hätte zu einer "Verdünnung" des Interventionseffektes in der Gesamtauswertung führen können.

4 Modellwahl und -diagnostik

In diesem Kapitel werden Überlegungen zur Wahl und Diagnostik des verwendeten Modells angestellt. Wie bereits im Publikationsmanuskript beschrieben, ist bei den vorliegenden Daten von einer Cluster-Struktur auszugehen, was angesichts des Setting-Ansatzes der Intervention unvermeidlich ist. Konkret heißt dies, daß Kinder innerhalb eines Kindergartens bzw. Gesundheitsamt Einzugsbereiches ähnlicher sind, als würde man einzelne Kinder aus verschiedenen Gebieten zufällig ziehen. Damit ist die Annahme der Unabhängigkeit der Beobachtungen in der Stichprobe verletzt. Diese Besonderheit kann in gemischten Modellen mit Zufallseffekten (random effects) und GEE-Modellen (generalized estimating equations)

berücksichtigt werden.[3]
Beim Zufallseffekt-Modell wird jeder Beobachtungseinheit (Kindergarten) ihre eigenen Parameter (β)[1] zugestanden, so daß man schließlich eine Verteilung für das β jeder Kovariable erhält. Ein Restfehler (ε) bleibt deshalb noch übrig, da eine *Vielzahl* der Messungen (Kinder) innerhalb einer Beobachtungseinheit (Kindergarten) durch *eine* $\beta_0 \ldots \beta_k$ Parameterkombination imperfekt modelliert werden.
Das marginale GEE-Modell dagegen, paßt einen Parameter β (pro Kovariable) für alle Beobachtungen über alle Beobachtungseinheiten (Kindergärten) hinweg an; etwaige Unterschiede zwischen den Beobachtungseinheiten werden zunächst ignoriert (Stichwort: population average). Da die Beobachtungen innerhalb einer Einheit aber nicht unabhängig sind, werden die Residuen als korreliert behandelt, um der Clusterstruktur Rechnung zu tragen.
Bei der hier verwendeten Modellierung mittels GEE wird also von einem festen Effekt ausgegangen, der sich in allen Kindergärten entfaltet unter Berücksichtigung der Clusterstruktur der Daten und adjustiert für weitere Kovariablen.

4.1 QIC

Da GEE-Modelle nicht likelihood-basiert sind, steht das bekannte AIC (Aikaike Information Criterion) zum Modellvergleich nicht zur Verfügung. Als Analogon entwickelte Pan[7] das QIC (Quasilikelihood under the Independence model Criterion). Dieses erlaubt auch den Vergleich nicht hierarchischer Modelle und kann mit einem SAS-Makro[5] berechnet werden. Wie in Tabelle 1 zu sehen ist, weist das verwendete Modell mit den Kovariablen Intervention, elterliche Bildung und deutsche Staatsangehörigkeit für beide Stichproben den jeweils kleinsten Wert auf, was für dessen Überlegenheit im Vergleich zu den Übrigen spricht.

[1] Die Parameter $\beta_0 \ldots \beta_k$ repräsentieren die Effektstärken der dazugehörigen Kovariablen und können über die entsprechende Linkfunktion (z. B. logit) in gewohnte Effektmaße (z. B. $OR = e^{\beta}$) umgewandelt werden.

Kovariablen im Modell			QIC für Outcome		
Intervention	elterliche Bildung	dt. Staats-angehörigkeit	Obst	Gemüse	hochkalorische Getränke
+	+	+	1662,25 1663,01	1653,12 1691,27	1306,28 1453,28
+	+		1665,26 1668,00	1659,52 1692,92	1337,25 1472,15
+		+	1702,53 1715,88	1700,77 1748,57	1355,49 1518,74
+			1705,18 1720,75	1706,60 1749,97	1394,48 1543,28

Tabelle 1: QIC für verschiedene Modellierungen der die Ernährung betreffenden Hauptzielvariablen. Die erste bzw. zweite Angabe in jeder Zelle bezieht sich auf die erste und zweite Stichprobe.

Für die Zielvariablen Übergewichts-/Adipositasprävalenz und die Ergebnisse des motorischen Tests "Seitliches Hin- und Herhüpfen" wurden im Manuskript noch die Variablen Alter und Geschlecht ins Modell aufgenommen. Dieses Vorgehen erscheint für den motorischen Test einleuchtend, könnte aber im Falle der Übergewichts-/Adipositasprävalenz hinterfragt werden, da diese Größen ja bereits von alters- und geschlechtsspezifischen Kurven[2] abgeleitet sind. Für die Adjustierung sprechen mögliche Unterschiede zwischen der hier untersuchten und der Referenzpopulation, oder Wirkunterschiede der Intervention bei Jungen und Mädchen.
Der Modellvergleich für die beiden Prävalenzen und das motorische Testergebnis fällt etwas unübersichtlicher aus (Tabelle 2), als im Falle der eingangs beschriebenen Ernährungs-bezogenen Variablen. Für Übergewicht und Adipositas wird das Alter in keinem der aufgeführten Modelle in keiner der beiden Stichproben signifikant (auf eine mögliche Überadjustierung wurde hingewiesen). Mädchen haben in

Kovariablen im Modell					QIC für Outcome		
Inter-vention	elterliche Bildung	dt. Staats-angehörig-keit	Alter	Ge-schlecht	Über-gewicht	Adi-positas	SHH
+	+	+	+	+	1036,88 1101,53	409,64 401,27	-57531,50 -66921,35
+	+		+	+	1056,06 1104,24	418,39 411,21	-57435,87 -67041,05
+		+	+	+	1084,58 1157,02	435,15 445,30	-59160,71 -69323,12
+			+	+	1110,05 1160,38	445,70 456,51	-59058,39 -69430,87
+	+	+	+		1041,49 1110,92	409,91 398,79	-57503,39 -66882,42
+	+	+		+	1036,33 1099,55	407,89 398,50	-54527,37 -61540,66
+	+	+			1040,65 1109,17	408,04 395,95	-54556,50 -61597,56
+	+				1059,73 1111,91	417,02 406,19	-54622,98 -61673,80
+		+			1087,55 1165,30	433,60 440,02	-55898,93 -63898,91
+					1113,40 1168,68	444,27 451,39	-55987,78 -64025,02

Tabelle 2: QIC für verschiedene Modellierungen der Zielvariablen Übergewicht, Adipositas und seitliches Hin- und Herhüpfen (SHH). Die erste bzw. zweite Angabe in jeder Zelle bezieht sich auf die erste und zweite Stichprobe.

allen Modellen ein signifikant höheres Übergewichtsrisiko. Für Adipositas (kleinere Fallzahlen) liegt der p-Wert für Geschlecht um 0,15. Das nach QIC zu favorisierende Modell für Übergewicht und Adipositas beinhaltet neben der Intervention, die nie eliminiert wurde, da sie das Thema der Arbeit darstellt, die elterliche Schulbildung, deutsche Staatsangehörigkeit und das Geschlecht. Letzteres fällt für Adipositas in der zweiten Stichprobe heraus. Das im Manuskript gewählte Modell für Übergewicht und Adipositas belegt jeweils den 2., für Adipositas in der zweiten Stichprobe den 4. Platz.
Beim motorischen Testergebnis ist das Alter in beiden, das Geschlecht, die elterliche Bildung und die deutsche Staatsangehörigkeit nur in der ersten Stichprobe signifikant. Ordnet man die QIC-Werte in Tabelle 2 liegt das volle Modell an dritter bzw. vierter Stelle (erste bzw. zweite Stichprobe).
Zusammenfassend ist festzuhalten, daß die getroffene Variablenauswahl im Sinne eines gemeinsamen Modells für verschiedene Zielgrößen auch nach den hier diskutierten Kriterien gut vertretbar erscheint. Das Alter stünde bei den Modellierungen der Adipositas- und Übergewichtsprävalenz zur Disposition.

4.2 Residuen

Im Rahmen der lokalen Modelldiagnostik kommen Residuen als vergleichsweise anschauliche Größen zum Einsatz. Sie berechnen sich für jede einzelne Beobachtung aus der Differenz der tatsächlichen Ausprägung der Zielgrößen und der Vorhersage des angepaßten Modells. Die Interpretation der Residuen ist beim vorliegenden Modell mit kategoriellen Variablen jedoch weniger einfach, als etwa bei einer linearen Regression mit metrischen Größen, wo Ausreißer schnell auffallen. Abbildung 1 zeigt beispielhaft die Residuen für die Zielvariable hoher Obstkonsum. Links oben sieht man die tatsächlich berichteten "Obstesser" ($p = 1$) der Kontrollgruppe, denen das Modell je nach Ausprägung der anderen berücksichtigten Einflußgrößen eine Wahrscheinlichkeit $\hat{p}$ zwischen 0,5 und 0,6 vorhersagt. Blickt man weiter nach

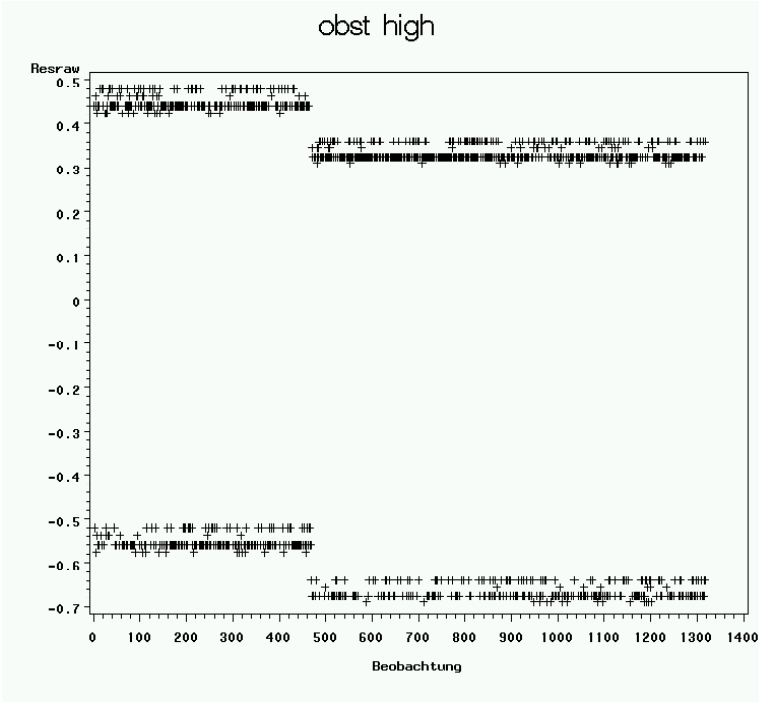

Abbildung 1: Rohe Residuen für die Zielvariable hoher Obstkonsum der 2. Stichprobe.

rechts ergibt sich eine Stufe zu den "Obstessern" der Interventionsgruppe, denen mit einem $\hat{p}$ zwischen 0,6 und 0,7 (daher kleinere Residuen) einer höhere Wahrscheinlichkeit viel Obst zu essen vorhergesagt wird. Analoges gilt für die tatsächlich berichteten "Nichtobstesser" (quasi die Falsch-Positiven) im unteren Teil des Plots. Immerhin ergibt sich aus den verschiedenen Kombinationen (2^3) der drei Kovariablen acht bzw. 16 mögliche Werte, die der lineare Prädiktor bzw. ein Residuum des Modells annehmen kann. Der Half-Normal-Plot (Abbildung 2) ist ein weiterer diagnostischer Plot, der auf der nach Größe geordneten Folge der Residuen beruht, deren tatsächliche Werte (Ordinate) gegen die erwarteten (Abszisse) aufgetragen werden. Da das GEE-Modell nicht die benötigten Devianzresiduen berechnet, wurde der abgebildete Plot für ein generalisiertes lineares Modell mit binominaler Linkfunktion unter Verwendung derselben Kovariablen erstellt (also ein Modell ohne Berücksichtigung der Cluster-Struktur der Daten). In der derzeiti-

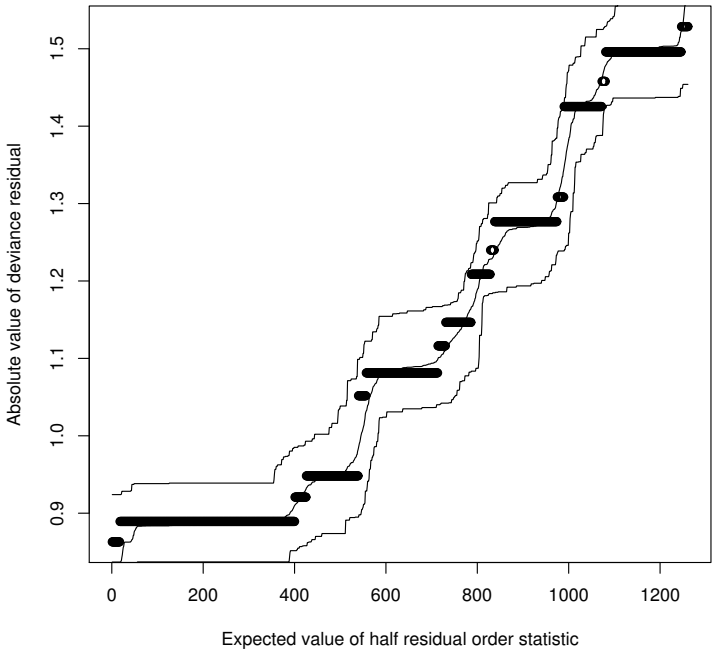

Abbildung 2: Half-Normal-Plot für die Zielvariable hoher Obstkonsum der 1. Stichprobe. Mittelwert und 95%-Quantilen (Linien) der Residualwerte an Position i wurden mittels parametrischem Bootstrap konstruiert[6].

gen Literatur waren keine einheitlichen Empfehlungen zu finden, welche Residuendiagnostischen Verfahren für den hier vorliegenden Fall von GEE-Modellen mit kategoriellen Variablen anzuwenden sind, so daß die hier angedeuteten Methoden in ihrer Aussagekraft fraglich sind. Es sei deshalb auf die globale Diagnostik im Abschnitt 4.1 verwiesen.

5 Weitere Analysen

Während im Zentrum der vorigen Kapitel die Effekte der Intervention im Vergleich zu den Kontrollkindergärten standen, behandelt dieses Kapitel den Zusammenhang zwischen berichtetem Ernährungsverhalten und Übergewicht.

5.1 Zusammenhang zwischen Ernährungsverhalten und Übergewicht

Der eingesetzte Fragebogen erlaubt mit überschaubarem Aufwand - und daher auch epidemiologisch praktikabel - einen Einblick in das Ernährungsverhalten der Kinder. Darüber hinaus enthält der Datensatz Angaben zum BMI. Es liegt daher nahe, evtl. Assoziationen zwischen dem erhöhten Konsum bestimmter Nahrungsmittel und Übergewicht zu untersuchen. Dies ist zum einen von ernährungswissenschaftlichem Interesse, zum anderen wichtig zum Setzen von Schwerpunkten in der Prävention (z. B. "Was bringt Reduktion des Schokoladenkonsums?", "TigerKids erhöht den Obstkonsum. Welche Effekte auf Übergewicht sind davon überhaupt zu erwarten?"). Wie bereits in der Diskussion des Publikationsmanuskripts angedeutet wurde, bringt das Querschnittsdesign der Studie einige Beschränkungen mit sich. Im Zusammenhang mit den eben skizzierten Fragestellungen gewinnt ein weiteres Problem an Bedeutung, welches im folgenden Abschnitt behandelt wird. Andererseits bietet der Datensatz grundsätzlich schon die Möglichkeit valider Prävalenzschätzungen, da die Teilnehmer weder nach Expositions- noch nach Krankheitsstatus (hier Übergewicht, Adipositas) selektiert wurden.

5.2 Problem der reverse causation

Nicht immer lassen sich Ursache und Wirkung in epidemiologischen Studien klar unterscheiden. So führt, um am Beispiel kindlicher Adipositas zu bleiben, hoher Konsum hochkalorischer Lebensmittel mittelfristig zu Übergewicht. Nachdem die-

	O+	O-
E+	a $p(O+ \mid E+)\cdot(\mathbf{1}-\mathbf{s})\cdot\mathbf{p}(\mathbf{E})$	b $p(O- \mid E+)\cdot p(E)$
E-	c $p(O+ \mid E-)\cdot(1-p(E))+\mathbf{s}\cdot\mathbf{p}(\mathbf{E})\cdot\mathbf{p}(\mathbf{O}+ \mid \mathbf{E}+)$	d $p(O- \mid E-)\cdot(1-p(E))$

E Exposition, O Outcome, s "Überläuferquote" (s. Text)

a, b, c, d tatsächlich beobachtete Zellbesetzungen

Tabelle 3: Viefeldertafel: Kinder, die aufgrund von Übergewicht die Exposition aufgeben, wandern von Zelle a nach c. Damit sinkt scheinbar das Risiko unter Exposition (obere Zeile), während das baseline-Risiko (untere Zeile) steigt. Im unteren Teil jeder Zelle ist die Wahrscheinlichkeit angegeben, daß ein zufällig aus einer Population gezogenes Individuum in die entsprechende Zelle gelangt. Der durch reverse causation bedingte Anteil des jeweiligen Terms ist **fettgedruckt**.

ser Kausalzusammenhang den meisten Eltern bekannt sein dürfte, ist es wahrscheinlich, daß gerade übergewichtige Kinder in ihrem Konsum adipogener Lebensmittel eingeschränkt werden, was nicht immer, oder erst nach längerer Zeit zur gewünschten Gewichtsabnahme führt. Verdeutlicht man sich dies an einer Vierfeldertafel (Tabelle 3), kommt es zu "Überläufern" unter den Übergewichtigen. Es resultiert eine Verzerrung, die im Extremfall dazu führt, daß etwa das relative Risiko für eine an sich schädliche Exposition kleiner eins wird, also einen protektiven Effekt vorspiegelt. Dieses Phänomen ist als "reverse causation" bekannt. Da die in der Literatur gefundenen Studien das Problem meist durch Auschluß bestimmter Teilnehmer (was hier nicht möglich ist) behandeln, wird im Folgenden eine Methode entwickelt, die es zumindest erlaubt, das Ausmaß der Verzerrung i. S. einer Sensitivitätsanalyse zu schätzen.

5.3 Formales Vorgehen

Die Wahrscheinlichkeiten für die Zellbesetzungen sind Tabelle 3 zu entnehmen. Um den Schreibaufwand zu reduzieren, werden drei Kurzbezeichnungen eingeführt: die Expositionswahrscheinlichkeit $p := p(E)$, die Wahrscheinlichkeit eines Exponierten zu erkranken $pPlus := p(O+ \mid E+)$, und die Wahrscheinlichkeit eines nicht Exponierten nicht zu erkranken $pMinus := p(O- \mid E-)$. Damit ist die logarithmierte Likelihood

$$\begin{aligned} LL = a \cdot (log(1-s) + log(p) + log(pPlus)) + \\ c \cdot log(pMinus \cdot (1-p) + s \cdot p \cdot pPlus) + \\ b \cdot (log(p) + log(1-pPlus)) + \\ d \cdot (log(1-p) + log(1-pMinus)) \end{aligned} \tag{1}$$

Die zur Berechnung der Standardfehler benötigte Informationsmatrix beinhaltet die Ableitungen dieser LogLikelihood nach allen Kombinationen aus pPlus, pMinus und p (Element[1,1] = LL nach pPlus abgeleitet, dann das Ergebnis nochmal nach pPlus, Element[1,2] = LL nach pPlus abgeleitet, dann das Ergebnis nach pMinus usw.). Um die Schreibarbeit wiederum zu vermindern, wird $h1 := (1-p) \cdot pMinus + p \cdot pPlus \cdot s$ gesetzt.

$$\begin{aligned} InfMat = [[& \frac{-b}{(1-pPlus)^2} - \frac{a}{pPlus^2} - \frac{c \cdot p^2 \cdot s^2}{h1^2}, -\frac{c \cdot (1-p) \cdot p \cdot s}{h1^2}, \\ & -\frac{c \cdot p \cdot s \cdot (-pMinus + pPlus \cdot s)}{h1^2} + \frac{c \cdot s}{h1}] \\ [& \frac{c \cdot (1-p) \cdot p \cdot s}{h1^2}, -\frac{d}{(1-pMinus)^2} - \frac{c \cdot (1-p)^2}{h1^2}, \\ & -\frac{c \cdot (1-p) \cdot (-pMinus + pPlus \cdot s)}{h1^2} - \frac{c}{h1}], \\ [& -\frac{c \cdot p \cdot s \cdot (-pMinus + pPlus \cdot s)}{h1^2} + \frac{c \cdot s}{h1}, \\ & -\frac{c \cdot (1-p) \cdot (-pMinus + pPlus \cdot s)}{h1^2} + \frac{c}{h1}, \\ & -\frac{d}{(1-p)^2} - \frac{a}{p^2} - \frac{b}{p^2} - \frac{c \cdot (-pMinus + pPlus \cdot s)^2}{h1^2}]] \end{aligned} \tag{2}$$

Um die Maximum-Likelihood-Schätzer für pPlus, pMinus und p zu finden, muß die Likelihood-Funktion maximiert werden. Es ist jedoch effizienter, das Minimum der negativen logarithmierten Likelihood-Funktion (-LL, Gleichung 1 mit negativem Vorzeichen) rechnergestützt zu ermitteln. Nun kann das relative Risiko (RR) oder die odds ratio (OR) für die Exposition korrigiert für die "Überläuferquote" s berechnet werden (p, pPlus und pMinus wurden ja oben als die "wahren" Wahrscheinlichkeiten, d. h. ohne Vorliegen von reverse causation definiert).

$$RR = \frac{pPlus}{pMinus} \tag{3}$$

$$OR = \frac{pPlus \cdot (1 - pMinus)}{pMinus \cdot (1 - pPlus)} \tag{4}$$

Zur Berechnung der Standardfehler von RR und OR wird ein Vektor mit deren Ableitungen nach pPlus und pMinus und 0 benötigt:

$$dRR = [\frac{1}{pMinus}, -\frac{pPlus}{pMinus^2}, 0] \tag{5}$$

$$\begin{aligned} dOR = [&\frac{1 - pMinus}{pMinus \cdot (1 - pPlus)} + \frac{(1 - pMinus) \cdot pPlus}{pMinus \cdot (1 - pPlus)^2}, \\ &-\frac{(1 - pMinus) \cdot pPlus}{pMinus^2 \cdot (1 - pPlus)} - \frac{pPlus}{pMinus \cdot (1 - pPlus)}, 0] \end{aligned} \tag{6}$$

Nun werden die Quadrate der Standardfehler berechnet.

$$se(RR)^2 = dRR * (-Inv(InfMat)) * dRR \tag{7}$$

$$se(OR)^2 = dOR * (-Inv(InfMat)) * dOR \tag{8}$$

Schließlich lassen sich damit und mit $z_{\alpha/2} = 1,96$ symmetrische 95%-Konfidenzintervalle von RR und OR berechnen.

$$KI(RR) = RR \pm 1,96 \cdot se(RR) \tag{9}$$

$$KI(OR) = OR \pm 1,96 \cdot se(OR) \tag{10}$$

Dieses Vorgehen wurde mit einem selbstgeschriebenen R[1]-Programm unter Verwendung der zusätzlichen Pakete `DEoptim` (Minimierung von -LL), `MASS` (Bildung der Inversen von InfMat) und `gplots, gdata, gtools` (graphische Darstellung, s. 5.4) implementiert.

	Übergewichtig	Normalgewichtig
hoher Konsum	151	716
niedriger Konsum	177	1112

Tabelle 4: Beobachtete Häufigkeiten von Übergewicht nach Konsum hochkalorischer Getränke, gepoolt aus beiden Stichproben.

5.4 Anwendung

Die vorgestellte Methodik soll nun anhand der realen Daten zum Einsatz kommen und wurde auf verschiedene Variablen des berichteten Ernährungsverhaltens angewendet. Beispielhaft wird die Variable hochkalorische Getränke herausgegriffen, jedoch in umgekehrter Kodierung wie im Publikationsmanuskript. 1 bedeutet also hoher Konsum dieser Getränke (exponiert), 0 dagegen niedriger Konsum. Die Vierfeldertafel mit den beobachteten Häufigkeiten ist in Tabelle 4 gezeigt. Abbildung 3 zeigt die Assoziation von Übergewicht und hohem Konsum hochkalorischer Getränke. Die RR wurden für verschiedene Werte von s berechnet. Würde man reverse causation vernachlässigen (s = 0), d. h. keiner der (noch) Übergewichtigen hat die Exposition wegen seines Übergewichts aufgegeben, ergibt sich ein RR von 1,27 [1,02 1,52]. Der Punktschätzer kann anhand der Vierfeldertafel in Tabelle 4 leicht nachgerechnet werden: 151/(151+716)/ (177/(177+1112))=1,27. Nimmt man für s einen Wert zwischen 5 und 30 % an, ergibt sich ein signifikantes RR zwischen 1,38 und 2,52[1]. Ab einem s von 50 % werden die Risikoschätzer unrealistisch hoch und gehen gegen unendlich; dies gilt auch für die anderen Expositionen. Eine derartig hoher Wert für s scheint indes auch unplausibel, würde er doch bedeuten, daß die Hälfte aller Übergewichtigen mit hohem Konsum hochkalorischer Getränke auf diesen verzichten, aber immer noch übergewichtig sind.

Die Assoziationen weiterer Hauptzielgrößen (main outcomes im Publikationsma-

[1]Auf die Problematik der Unabhängigkeit der Stichproben/Clusterstruktur wurde bereits ausführlich eingegangen. Sie wird hierbei nicht berücksichtigt.

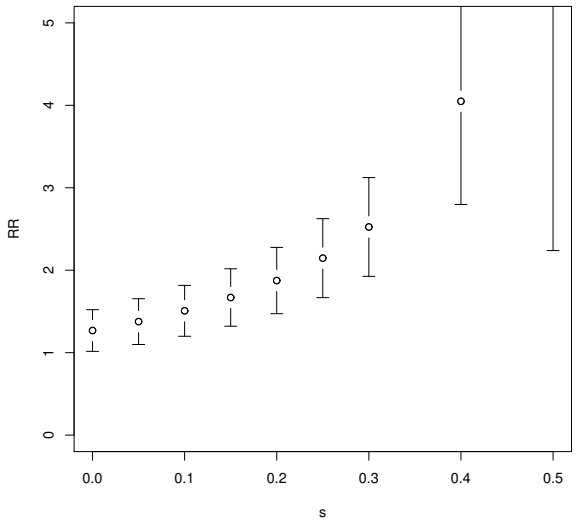

Abbildung 3: RR mit 95%-KI für Übergewicht durch hohen Konsum hochkalorischer Getränke unter Annahme verschiedener "Überläuferquoten" s.

nuskript) der Intervention mit Übergewicht seien noch kurz dargestellt. Das RR durch niedrigen Obstkonsum beträgt 1,16 [0,94 1,37] für s = 0, 1,24 [1,01 1,47] für s = 0,05 und 2,08 [1,66 2,49] für s = 0,3. Das RR durch niedrigen Gemüsekonsum beträgt 0,86 [0,71 1,02] für s = 0, 0,96 [0,78 1,14] für s = 0,05 und 2,58 [1,75 3,41] für s = 0,3. Das RR durch niedrigen Gemüsekonsum wird erst ab einer unterstellten "Überläuferquote" s von 20 % signifikant[1] und spricht damit gegen einen starken Effekt auf Übergewicht. Auf Literaturergebnisse bezüglich des Zusammenhangs von Konsum bestimmter Nahrungsmittel und Übergewicht wurde bereits in der Diskussion innerhalb des Publikationsmanuskripts eingegangen.
Prinzipiell wäre auch eine Modellierung der Zielgröße Übergewicht mit multiplen Einfluß-/Störgrößen (Obst-, Gemüsekonsum, Bildung etc.) denkbar mit Diskussion evtl. Kollinearitäten. So macht erhöhter Obst- und Gemüsekonsum isoliert vermutlich nicht schlank, kann aber den Konsum adipogener Nahrungsmittel günstig beeinflussen[4]. Dies würde jedoch den Rahmen dieser Arbeit sprengen.

5.5 Weitere Überlegungen zur Anwendung und Ausblick

Ergebnisse in der Statistik hängen vielfach kritisch von korrekter Methodenwahl und Spezifikation ab. Während hier Risikofaktoren, d. h. Expositionen, von denen eine Erhöhung des Risikos erwartet werden kann berechnet wurden, kommen in der Realität auch protektive Faktoren vor. Solche Fälle erfordern Änderungen in den Formeln der Vierfeldertafel (Tabelle 3). Der daraus folgende formale Aufwand (5.3) läßt es zweckmäßiger erscheinen, in solchen Fällen die Zeilen der Vierfeldertafel der beobachteten Häufigkeiten vor dem Einsetzen zu vertauschen, so daß die dem protektiven Faktor nicht Exponierten in die obere Zeile gelangen (hohes Risiko), die Exponierten in die untere (niedriges Risiko). Als Endergebnis erhält man den Kehrwert des RR bzw. OR.

Die Spezifikation der Richtung der reverse causation ist von entscheidender Bedeutung. Geht man davon aus, daß die Erkrankten eher Risikofaktoren meiden und protektive Faktoren suchen, arbeitet die reverse causation immer gegen den tatsächlichen Effekt der Exposition, bis hin zur (scheinbaren) Umkehr der Assoziation. Richtung und Ausmaß der reverse causation dürften erheblich von Risikowahrnehmung (schädliche Faktoren als harmlos oder sogar gesund bekannt) und evtl. auch Fatalismus (z. B. Weiterrauchen, da sowieso schon multiple Metastasen) beeinflußt sein. Die in Klammern gegebenen Szenarien könnten sogar die andersherum gerichtete Beeinflussung der Exposition durch die Erkrankung bewirken, also eine Richtungsumkehr der reverse causation. Hier verspricht Zusammenarbeit mit dem Forschungszweig der Gesundheitskommunikation einen interessanten Abgleich zwischen empirisch gefundenen Maßen für die Wanderung zwischen den Expositionsgruppen und rechnerisch plausiblen Werten für s.

Abschließend ist zu bemerken, daß die dargestellte Methode es erlaubt,

1. die Auswirkungen (Verzerrung der Risikoschätzer) der reverse causation zu überprüfen

2. sinnvolle a priori-Annahmen über s und damit das Ausmaß der (ansonsten schwer zugänglichen) reverse causation zu treffen.

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7 Autorenrichtlinien

Im Folgenden sind die für dieses Manuskript relevanten Auszüge der Autorenrichtlinien des British Medical Journal wiedergegeben, abgerufen am 28.9.2007.
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8 Anlage

8.1 Erklärung über die selbständige Anfertigung der Arbeit

Die vorliegende Magisterarbeit wurde nach §12(5) der Prüfungsordnung des Studiengangs Öffentliche Gesundheit und Epidemiologie von mir selbständig angefertigt.

München, September 2007 Dr. med. Otmar Bayer

8.2 Einverständniserklärung des Betreuers

Ich bin mit der Veröffentlichung der Magisterarbeit in der vorliegenden Form einverstanden.

München, September 2007 Prof. Dr. med. Rüdiger von Kries, MSc

8.3 Einverständniserklärung der Mitautoren

Alle Mitautoren erklärten sich mit der Veröffentlichung des vorliegenden Publikationsmanuskriptes einverstanden. Die von den Mitautoren unterzeichneten Formblätter liegen vor.

8.4 Spezifikation des Eigenanteils

S. a. Publikationsmanuskript unter “Contributorship” und “Acknowledgements”

Leistungsbereich	Eigenanteil	Anteil anderer Personen (wer, was, wieviel)
Konzeption	Kleine Verbesserungen der Dichotomisierung einiger Variablen, soweit im bestehenden Konzept vertretbar. Subgruppenanalyse/Effektmodifikation durch Übergewicht	Prof. Dr. R. von Kries, Institut für soziale Pädiatrie und Jugendmedizin der LMU, Prof. Dr. B. Koletzko, Dr. von Haunersches Kinderspital der LMU
Feldarbeit	Einholen fehlender Informationen über Teilnehmerzahlen von den Gesundheitsämtern zur Berechnung der Response	Prof. Dr. B. Koletzko und Mitarbeiter
Auswertung	Publikationsmanuskript: Rekonstruktion/Programmierung in SAS. Der Anhang wurde vor mir konzeptioniert und erstellt. Reverse causation: Aufstellung der Vierfeldertafel mit Wahrscheinlichkeiten, Implementation der formalen Vorgehens in R.	Ich danke Herrn Prof. Dr. U. Mansmann für die statistische Unterstützung (Reverse causation: Aufstellung des ML-Schätzers, Berechnung d. Standardfehler).
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9 Lebenslauf

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Wissenschaftliche Arbeiten

Promotion über Sakkaden zu bewegten und stationären Zielen bei Prof. Dr. U. Büttner, Neurologie, Klinikum Großhadern der LMU München im Rahmen eines Doktorandenstipendiums der DFG

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