Postgradualer Studiengang
Öffentliche Gesundheit und Epidemiologie
Ludwig-Maximilians-Universität München

Magisterarbeit

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

vorgelegt von
Dr. med. Otmar Bayer

im
Sommersemester 2007

In Zusammenarbeit mit dem Institut für soziale Pädiatrie und Jugendmedizin
und dem Dr. von Haunerschen Kinderspital der LMU München

Inhaltsverzeichnis

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

Otmar Bayer, MD* (epidemiologist), Rüdiger von Kries, MD, MSc* (professor for paediatric epidemiology), Angelika Strauss, PhD (study coordinator), Christine Mitschek (nutritionist), A. Michael Toschke, MD, MSc, MPH (senior lecturer in health services research), Alexander Hose (epidemiologist), Berthold V. Koletzko, MD (professor for paediatrics, principal investigator)

**contributed equally*

Running title:

Prevention of obesity risk in preschool children

Institute for Social Paediatrics and Adolescent Medicine
Ludwig-Maximilians University
Heiglhofstr. 63, 81377 Munich, Germany

Div. Metabolic Diseases and Nutritional Medicine
Dr. von Hauner Children's Hospital
Ludwig-Maximilians-University
Lindwurmstr. 4, 80337 Munich, Germany

Bavarian State Institute for Health and Food Safety
Pfarrstr. 3, 80538 Munich, Germany

King's College London
Division of Health and Social Care Research
Department of Public Health Sciences Floor 7
Capital House, 42 Weston St, London SE1 3QD, United Kingdom

Correspondence:
Berthold Koletzko, MD, Professor of Paediatrics
Dr. von Hauner Children's Hospital, Klinikum der Universität München
Lindwurmstraße 4, D-80337 München, Germany
Phone: +49-89-5160-2826, Fax: +49-89-5160-3336
e-mail: Berthold.Koletzko@med.uni-muenchen.de

Competing interests: None declared by any of the authors.

Contributorship: OB performed the statistical analysis and contributed to writing the manuscript; RvK conceived the evaluation concept and contributed to the statistical analysis and to writing the manuscript; AS contributed to the development of the intervention and coordinated the execution of the intervention and the training of kindergarten staff; CM: contributed to the development of the intervention and the training of kindergarten staff; MT consulted on the statistical analysis, AH contributed to data management and analysis, BK conceived the study and intervention concept, contributed to writing the manuscript and acts as the guarantor.

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

84

85

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.

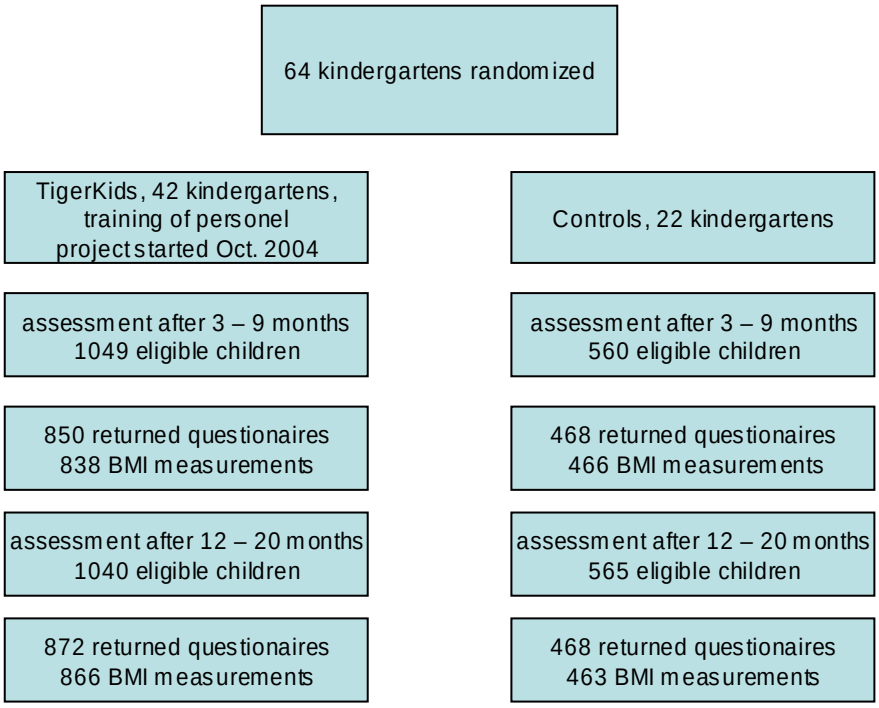

Figure 1: Flowchart of evaluation

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.

Acknowlegements:

The authors thank the participating Kindergarten teachers and families as well as the colleagues involved in the preparation of the intervention programme and materials and in taking the measurements for their enthusiastic support, and the AOK Verlag Remagen for their help in designing and producing the materials for the intervention programme. The development, pilot testing and evaluation of the intervention was financially supported by the

Bavarian Ministry of Environment, Health and Consumer protection (Grant 36-G8203.1-2005/12). OB was funded by the University of Munich - Munich Center of Health Sciences (MCHealth). Additional support was provided by Allgemeine Ortskrankenkasse (AOK) Bavaria, Lions Club Munich, Südzucker AG, Mannheim, and Kraft Foods, Munich. BK is the recipient of a Freedom to Discover Award of the Bristol Myers Squibb Foundation, New York, NY, USA. We're indebted to the monitoring units (GME) for providing a framework for the measurements and questionnaire study, Ladan Baghi and PD Dr. Gabriele Bolte for providing the datasets.

References

1. Koletzko B, Girardet JP, Klish W, Tabacco O. Obesity in children and adolescents worldwide: current views and future directions--Working Group Report of the First World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2002;35 Suppl 2:S205-12.
2. Fisberg M, Baur L, Chen W, Hoppin A, Koletzko B, Lau D, et al. Obesity in children and adolescents: Working Group report of the second World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2004 Jun;39 Suppl 2:S678-87.
3. Kalies H, Lenz J, von Kries R. Prevalence of overweight and obesity and trends in body mass index in German pre-school children, 1982-1997. Int J Obes Relat Metab Disord. 2002 Sep;26(9):1211-7.
4. Collins CE, Warren J, Neve M, McCoy P, Stokes BJ. Measuring effectiveness of dietetic interventions in child obesity: a systematic review of randomized trials. Arch Pediatr Adolesc Med. 2006 Sep;160(9):906-22.
5. Stice E, Shaw H, Marti CN. A meta-analytic review of obesity prevention programs for children and adolescents: the skinny on interventions that work. Psychol Bull. 2006 Sep;132(5):667-91.
6. Summerbell CD, Waters E, Edmunds LD, Kelly S, Brown T, Campbell KJ. Interventions for preventing obesity in children. Cochrane Database Syst Rev. 2005(3):CD001871.
7. MRC. A framework for development and evaluation of RCTs for complex interventions to improve health. April 2000.
8. Bolte G HA, von Kries R, Zapfl A, Wildner M, Fromme H. Gesundheits-Monitroing-Einheiten (GME) in BAyern: Konzept, Ziele und thematische Schwerpunkte des 1. Surveys zu Umwelt und Gesundheit von Kindern. . Bundesgesundheitsblatt - Gesundheitsforschung - GEsundheitsschutz 2007;50:476-83.
9. Epstein LH, Gordy CC, Raynor HA, Beddome M, Kilanowski CK, Paluch R. Increasing fruit and vegetable intake and decreasing fat and sugar intake in families at risk for childhood obesity. Obes Res. 2001 Mar;9(3):171-8.
10. Prentice A, Jebb S. Energy intake/physical activity interactions in the homeostasis of body weight regulation. Nutr Rev. 2004 Jul;62(7 Pt 2):S98-104.
11. James J, Thomas P, Cavan D, Kerr D. Preventing childhood obesity by reducing consumption of carbonated drinks: cluster randomised controlled trial. Bmj. 2004 May 22;328(7450):1237.
12. Boes K BS, Tittlbach S, Woll A. Karlsruher-Motorik-Screening für Kindergartenkinder (KMS 3-6). Sportunterricht. 2004;53(3).
13. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. Bmj. 2000 May 6;320(7244):1240-3.
14. O'Brien TP, Walley PB, Anderson-Smith S, Drabman RS. Naturalistic observation of the snack-selecting behavior of obese and nonobese children. Addict Behav. 1982;7(1):75-7.
15. Spiegel SA, Foulk D. Reducing overweight through a multidisciplinary school-based intervention. Obesity (Silver Spring). 2006 Jan;14(1):88-96.
16. Warren JM, Henry CJ, Lightowler HJ, Bradshaw SM, Perwaiz S. Evaluation of a pilot school programme aimed at the prevention of obesity in children. Health Promot Int. 2003 Dec;18(4):287-96.
17. Sherry B. Food behaviors and other strategies to prevent and treat pediatric overweight. Int J Obes (Lond). 2005 Sep;29 Suppl 2:S116-26.

18. Prentice AM, Jebb SA. Fast foods, energy density and obesity: a possible mechanistic link. Obes Rev. 2003 Nov;4(4):187-94.
19. Pereira MA, Kartashov AI, Ebbeling CB, Van Horn L, Slattery ML, Jacobs DR, Jr., et al. Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. Lancet. 2005 Jan 1-7;365(9453):36-42.
20. James J, Kerr D. Prevention of childhood obesity by reducing soft drinks. Int J Obes (Lond). 2005 Sep;29 Suppl 2:S54-7.
21. Raben A, Vasilaras TH, Moller AC, Astrup A. Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. Am J Clin Nutr. 2002 Oct;76(4):721-9.
22. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. Lancet. 2001 Feb 17;357(9255):505-8.
23. Toschke JA, von Kries R, Rosenfeld E, Toschke AM. Reliability of physical activity measures from accelerometry among preschoolers in free-living conditions. Clin Nutr. 2007 Aug;26(4):416-20.
24. Murray DM, Varnell SP, Blitstein JL. Design and analysis of group-randomized trials: a review of recent methodological developments. Am J Public Health. 2004 Mar;94(3):423-32.

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

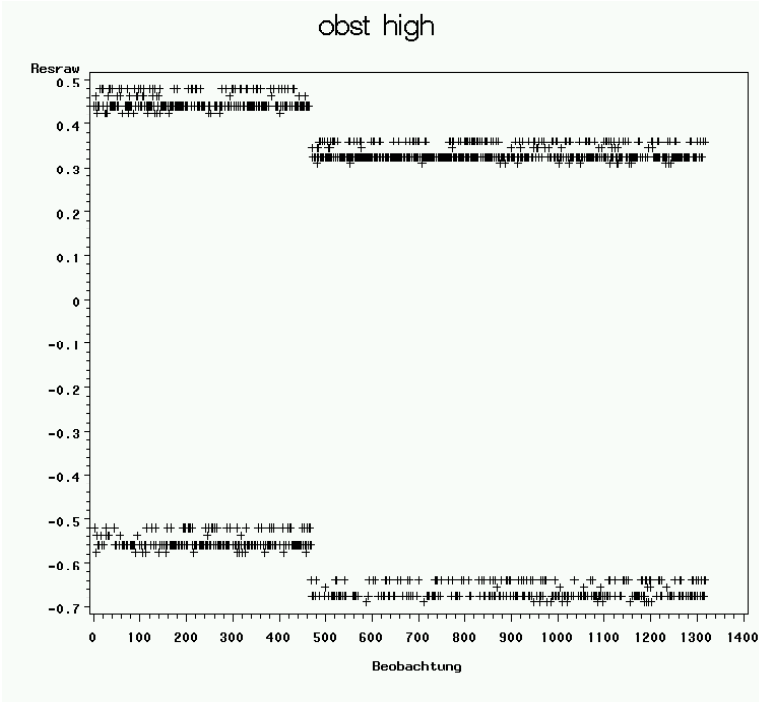

Abbildung 1: Rohe Residuen für die Zielvariable hoher Obstkonsum der 2. Stichprobe.

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-

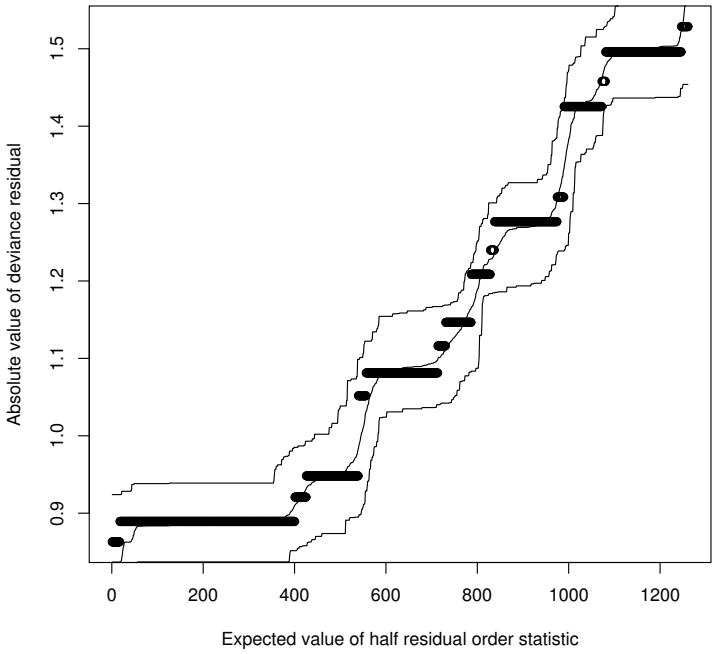

Abbildung 2: Half-Normal-Plot für die Zielvariable hoher Obstkonsum der 1. Stichprobe. Mittelwert und 95%-Quantilen (Linien) der Residualwerte an Position i wurden mittels parametrischem Bootstrap konstruiert[6].

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.

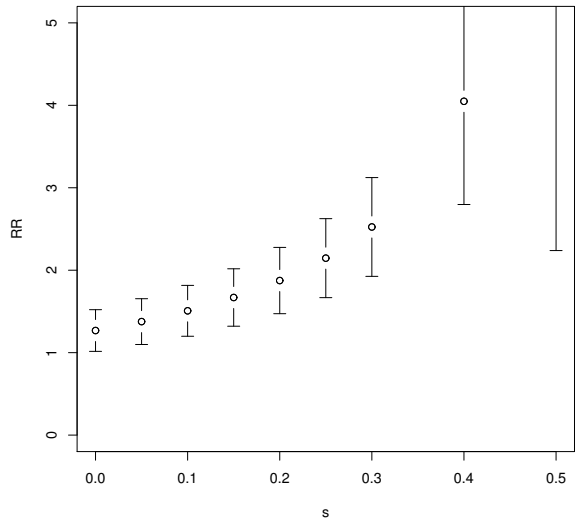

Abbildung 3: RR mit 95%-KI für Übergewicht durch hohen Konsum hochkalorischer Getränke unter Annahme verschiedener "Überläuferquoten" s.

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.

Literatur

[1] R version 2.5.1 for Linux. `http://www.r-project.org`, 2007.

[2] T. J. Cole, M. C. Bellizzi, K. M. Flegal, and W. H. Dietz. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*, 320(7244):1240–1243, May 2000.

[3] Peter J. Diggle, Patrick J. Heagerty, Kung-Yee Liang, and Scott L. Zeger. *Analysis of Longitudinal Data*, chapter 7 - 9, pages 126 – 189. Oxford Statistical Science Series. Oxford University Press, 2nd edition, 2002.

[4] L. H. Epstein, C. C. Gordy, H. A. Raynor, M. Beddome, C. K. Kilanowski, and R. Paluch. Increasing fruit and vegetable intake and decreasing fat and sugar intake in families at risk for childhood obesity. *Obes Res*, 9(3):171–178, Mar 2001.

[5] SAS Institute Inc. *Sample 1686: QIC goodness of fit statistic for GEE models.* `http://support.sas.com/ctx/samples`.

[6] U. Mansmann. Modelldiagnostik und Modellvalidierung. Vorlesung Epidemiologie III am IBE der LMU München, 2007.

[7] W. Pan. Akaike's information criterion in generalized estimating equations. *Biometrics*, 57(1):120–125, Mar 2001.

[8] Rüdiger von Kries and Ladan Baghi. TigerKids: Effekte auf Ernährungsverhalten, BMI und motorische Geschicklichkeit – Basierend auf den Daten der SEU 2004/05. Bericht an das Bayerische Staatsministerium für Umwelt, Gesundheit und Verbraucherschutz, 2006.

7 Autorenrichtlinien

Im Folgenden sind die für dieses Manuskript relevanten Auszüge der Autorenrichtlinien des British Medical Journal wiedergegeben, abgerufen am 28.9.2007.
`http://resources.bmj.com/bmj/authors/article-submission/article-requirements`

Please ensure that anything you submit to the BMJ conforms to the International Committee of Medical Journal Editors uniform requirements for manuscripts submitted to biomedical journals. We have found that it is easiest for everyone if all the information we require (see below) is contained in your manuscript. Therefore the manuscript file that you attach should include:
Title - All manuscripts
Names, addresses, and positions of all authors plus email address for corresponding author - All manuscripts Copyright - All manuscripts - A statement in the manuscript that "The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd, and its Licensees to permit this article (if accepted) to be published in BMJ editions and any other BMJPGL products and to exploit all subsidiary rights, as set out in our licence (`bmj.com/advice/copyright.shtml`)." We no longer need to see a hard copy of the signed form.
A competing interest statement - All manuscripts- A statement in the manuscript describing the interests of all authors or a declaration in the manuscript that "All authors declare that the answer to the questions on your competing interest form are all No and therefore have nothing to declare". We no longer need to see a hard copy of the signed form.
Details of contributors and the name of the guarantor - All original research articles
Details of ethics approval (or a statement that it was not required) - All original research articles
Details of funding - All original research articles
Description of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication (see further advice below) - All original research articles
Statement of the independence of researchers from funders - All original research articles

If you are submitting a randomised controlled trial please send with your manuscript the following:
a checklist and flowchart in accordance with the CONSORT guidelines. Please submit the checklist as a supplementary file and the flowchart as figure 1 in the manuscript.
the trial protocol, submitted as a supplementary file. We do not intend to publish this but we do need it to appraise and peer review your paper.
the registration number of the trial and the name of the trial registry. Please add these to the last line of your papers structured abstract. If your trial is not yet registered please register it now: you can do this retrospectively. The BMJs criteria for a suitable public trial registry are: free to access, searchable, and identifies trials with a unique number; registration is free or has minimal cost; registered information is validated; registered entry includes details to identify the trial and investigator and includes the status of the trial; and the research question, methodology, intervention, funding, and sponsorship must all be disclosed.

`http://resources.bmj.com/bmj/authors/types-of-article/research`

These articles should report original research relevant to clinical medicine in a way that is accessible to readers of a general journal. They should follow the IMRaD style (introduction, methods, results and discussion) and should have a structured abstract and a structured discussion. Please see our requirements for all BMJ manuscripts which give full details of what you should include

with your manuscript. In particular, please note that we need, as appropriate:
...
CONSORT checklist and flowchart for a randomised controlled trial as supplemental files to your article when you submit it to our online editorial office
trial registration number and name of register for a clinical trial in the last line of the structured abstract
...
We do not set fixed limits for the length of BMJ research articles and can be flexible. We produce abridged versions of research articles in the printed BMJ while publishing their full versions on bmj.com. Nonetheless, please try to make your article concise and make every word count. Think hard about what really needs to be in the paper to get your message across accurately and what can be left out. We do want your piece to be easy to read but also want it to be as scientifically accurate as possible. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:
...
For a cohort study:
Absolute event rates over time (eg 10 years) among exposed and non-exposed groups
RRR (relative risk reduction)
...
Please do not use the term "negative" to describe studies that have not found statistically significant differences, perhaps because they were too small. There will always be some uncertainty, and we hope you will be as explicit as possible in reporting what you have found in your study. Using wording such as "our results are compatible with a decrease of this much or an increase of this much" or "this study found no effect" is more accurate and helpful to readers than "there was no effect/no difference". Please use such wording throughout the article, including the structured abstract, and the box stating what the paper adds. Please also provide within your research article's manuscript:
Title page
This should give the title of the article, including the study design. Please give for each author his or her name and initials, full address including postal code and one main work position (job title) at the time of writing the paper. We do not need authors qualifications. For the corresponding author please provide an email address and the best contact address: this may differ from his or her work address.
Structured abstract
Please ensure that the structured abstract is as complete, accurate, and clear as possiblebut not unnecessarily longand has been approved by all authors. We may screen original research articles by reading only the abstract. Please note the general rules for abstracts in the BMJ: should be 250 - 300 words long. (MEDLINE allows a maximum of 4096 characters and will truncate longer abstracts)
use active voice but avoid "we did" or "we found"
numbers over 10 do not need spelling out at the start of sentences
sentences starting with a number do not require a capital letter
p values should always be accompanied by supporting data and denominators should be given for percentages
abstracts do not need references
The first few items (objective, design, setting) may be note-like and need not form full sentences. The results and conclusions sections should be written properly. Do not mix notes and full sentences in one section.
If the standard headings do not suit the type of study, substitute something sensible such as ppopulationäs a heading instead of participantsïn an economics article. Please do not simply delete the heading. For standard original research articles please provide the following headings and

information
objectives - a clear statement of the main aim of the study and the major hypothesis tested or research question posed.
design - including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests etc
setting - include the level of care eg primary, secondary; number of participating centres. Be general rather than give the name of the specific centre, but give the geographical location if this is important participants (instead of patients or subjects) - numbers entering and completing the study, sex, and ethnic group if appropriate. Give clear definitions of how selected, entry and exclusion criteria interventions - what, how, when and for how long. This heading can be deleted if there were no interventions but should normally be included for randomised controlled trials, cross over trials, and before and after studies.
main outcome measures - those planned in protocol, those finally measured (if different, explain why)
results - main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm.
conclusions primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article. Conclusions are important because this is often the only part that readers look at.
trial registration - registry and number (only for clinical trials)
Please note that confidence intervals should be written in the format (15 to 27) within parentheses, using the word "to" rather than a hyphen.
...
Structured discussion
Please ensure that the discussion section of your article follows this structure:
statement of principal findings
strengths and weaknesses of the study
strengths and weaknesses in relation to other studies, discussing important differences in results
meaning of the study: possible explanations and implications for clinicians and policymakers
unanswered questions and future research

"What this paper adds" box
Please produce a box offering a thumbnail sketch of what your article adds to the literature, for readers who would like an overview without reading the whole article It should be divided into two short sections, each with 1-3 short sentences.
section 1: What is already known on this subject
In two or three short sentences please summarise the state of scientific knowledge on this subject before you did your study and why this study needed to be done. Be clear and specific, not vague. For example you might say: ...
section 2: What this study adds
In one or two short sentences give a simple answer to the question "What do we now know as a result of this study that we did not know before?" Be brief, succinct, specific, and accurate. For example: ...

Other items to include with your original research article
a word count for the main text (excluding the abstract, references, tables, boxes, or figures): you will be asked to enter this when you upload your manuscript at submit.bmj.com
original data if you think they will help our reviewers or if we specifically request them
copies of any non-standard questionnaires and assessment schedules used in the research
copies of patient information sheets used to obtain informed consent
copies of related articles you have published. This is particularly important where details of the

study methods are published elsewhere
copies of any previous reviewers' reports on this article. We appreciate that authors may have tried other journals before sending their work to the BMJ. Please let us know how you have responded to previous reviewers' comments before submission
names and contact details (including email addresses) of suitable peer reviewers; we often find authors' suggestions helpful
...

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).
Manuskript	Erstellung der Rohfassung, federführender Autor	s. Publikationsmanuskript unter “Contributorship”

9 Lebenslauf

Name	Dr. med. Otmar Bayer
Anschrift	xxxxxxxx D-81543 München
Geburtsdatum	xxxxxxxx
Geburtsort	München
Eltern	Dr. Eberhard Bayer, Physiker, verstorben 1994 Sigrun Bayer, geb. Meyer, Krankengymnastin
Kinder	Theresa L. M. Bayer, * xxxxxxxx Jakob Konstantin Bayer, * xxxxxxxx
1980 - 1983	Herterichschule, München-Solln
1983 - 1985	Deutsche Schule Tokyo-Yokohama
1986 - 1993	Pestalozzi-Gymnasium, München
1994 - 2000	Studium der Jazz- und Popularmusik, Bruckner-Konservatorium, Linz Seminararbeit: "Musik und Neuronale Netze - Vorstellung einer Programmumgebung zur gemeinsamen Anwendung von NN und algorithmischer Analyse"
1996 - 2002	Studium der Humanmedizin, Ludwig-Maximilians-Universität, München
seit 2006	Postgradualer Studiengang Öffentliche Gesundheit und Epidemiologie (MPH), LMU
5/2002 - 7/2004, 7/2005 - 6/2007	AiP/Assistenzarzt in Neurologie am Klinikum Großhadern der LMU
8/2004 - 3/2005	Assistenzarzt in Neurologie am Klinikum Rosenheim
1/2007 - aktuell	Akademischer Rat in der Abteilung Epidemiologie des Instituts für soziale Pädiatrie der LMU

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

Y. Guan, T. Eggert, O. Bayer, U. Büttner, "Saccades to stationary and moving targets differ in the monkey". Exp Brain Res. 2005 Feb; 161(2): 220 - 32

R. Brzezny, O. Bayer, S. Glasauer, U. Büttner, "Age-Related Changes in Three Dimensional Vestibulo-Ocular Reflex". J Vestib Res. 2004; 14(2,3): 294. Abstract for Bárány Society 13th International Congress

O. Bayer, U. Heininger, C. Heiligensetzer, R. von Kries, "Metaanalysis of vaccine effectiveness in varicella outbreaks". Vaccine 2007;25(37-38): 6655 - 60.