Human health no-effect levels of TiO2 nanoparticles as a function of their primary size

As engineered nanomaterials are increasingly introduced on the market into a broad range of commodities or nanoproducts, there is a need for operational, reliable tool, enabling to consistently assess the risks and impacts associated with the releases of nanoparticles. The lack of a developed metric that accurately represents their toxic effects while capturing the influence of the most relevant physicochemical properties is one of the major impediments. Here, we investigate the relationships between the toxic responses of nano-sized and micro-sized particles in in vivo toxicological studies and their physicochemical properties. Our results for TiO2 particles indicate statistically significant associations between the primary particle size and their toxicity responses for combined inhalation and ingestion exposure routes, although the numerical values should be considered with care due to the inability to encompass influences from other relevant physicochemical properties like surface coatings. These findings allow for expressing mass-based adverse effect levels as a continuous function of the primary size of particles. This meaningful, exploratory metric can thus be used for screening purposes and pave the way for reaching adaptive, robust risk assessments of nanomaterials, e.g. for setting up consistent threshold levels, as well as consistent life cycle assessments of nanoproducts. We provide examples of such applications.

General information
State: Published
Organisations: Department of Management Engineering, Quantitative Sustainability Assessment, Department of Informatics and Mathematical Modeling, Department of Environmental Engineering, Michigan State University, Technical University of Denmark, University of Michigan-Dearborn
Authors: Laurent, A. (Intern), Harkema, J. (Ekstern), Andersen, E. W. (Intern), Owsianiak, M. (Intern), Blikra Vea, E. (Ekstern), Jolliet, O. (Ekstern)
Number of pages: 15
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Nanoparticle Research
Volume: 19
Issue number: 130
ISSN (Print): 1388-0764
Ratings:
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BFI (2017): BFI-level 1
The aim of this study was to analyse concordance between Danish adults' recorded diet quality and their own assessment of the healthiness and to examine socio-demographic, health and behavioural characteristics associated with an optimistic or pessimistic self-assessment. Data were derived from The Danish National Survey of Diet and Physical Activity 2011-2013 and included a random sample of 3014 adults (18-75 y). Diet quality was evaluated on the basis of seven-day pre-coded food diaries and categorised 'unhealthy', 'somewhat healthy' and 'healthy'. Self-assessment of the healthiness of own diets was registered via personal interviews and categorised healthy enough 'to a high degree', 'to some degree' or 'not at all/only partly'. Highly and somewhat optimistic self-assessment, respectively, were defined as assessing own diets as healthy enough to a high degree or to some degree while having unhealthy diets. Highly and somewhat pessimistic
self-assessment, respectively, were defined as assessing own diets as not healthy enough or healthy enough to some degree while having healthy diets. Multiple logistic regression models were used to examine characteristics associated with optimistic and pessimistic self-assessments, respectively. Among individuals with unhealthy diets, 13% were highly optimistic and 42% somewhat optimistic about the healthiness of their diets. Among individuals with healthy diets, 14% were highly pessimistic and 51% somewhat pessimistic about the healthiness of their diets. Highly optimistic self-assessment was associated with increasing age, excellent self-rated health, normal weight and a moderate activity level. Highly pessimistic self-assessment was associated with decreasing age, good self-rated health and being overweight or obese. The findings indicate that people seem to use personal health characteristics as important references when assessing the healthiness of their diets.

**General information**
State: Published
Organisations: National Food Institute, Division of Risk Assessment and Nutrition, Research Group for Risk-Benefit, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, University of Copenhagen
Authors: Sørensen, M. R. (Intern), Matthiessen, J. (Intern), Holm, L. (Ekstern), Knudsen, V. K. (Intern), Andersen, E. W. (Intern), Tetens, I. (Intern)
Pages: 15-22
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- Scopus rating (2016): CiteScore 3.71 SJR 1.619 SNIP 1.384
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 1.651 SNIP 1.387 CiteScore 3.43
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 1.403 SNIP 1.358 CiteScore 3.2
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 1.243 SNIP 1.242 CiteScore 3.01
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 1.269 SNIP 1.362 CiteScore 3.1
- ISI indexed (2012): ISI indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 1.128 SNIP 1.261 CiteScore 2.85
- ISI indexed (2011): ISI indexed yes
- BFI (2010): BFI-level 1
- Scopus rating (2010): SJR 1.155 SNIP 1.284
- Web of Science (2010): Indexed yes
- BFI (2009): BFI-level 1
- Scopus rating (2009): SJR 1.103 SNIP 1.264
- BFI (2008): BFI-level 1
- Scopus rating (2008): SJR 1.02 SNIP 1.356
- Web of Science (2008): Indexed yes
- Scopus rating (2007): SJR 0.912 SNIP 1.302
- Scopus rating (2006): SJR 0.83 SNIP 1.023
- Scopus rating (2005): SJR 0.724 SNIP 0.964
Assessment of healthy diets and physical activity: A study of differences between health professionals and lay people

General information
State: Published
Organisations: National Food Institute, Division of Risk Assessment and Nutrition, Department of Applied Mathematics and Computer Science
Authors: Sørensen, M. R. (Intern), Tetens, I. (Intern), Matthiessen, J. (Intern), Andersen, E. W. (Intern)
Number of pages: 88
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Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
PhD_Thesis_Mette_Rosenlund_S_rensen.pdf

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Assessment of healthy diets and physical activity
Publication: Research › Ph.D. thesis – Annual report year: 2017

Gender differences in purchase intentions and reasons for meal selection among fast food customers – Opportunities for healthier and more sustainable fast food

Understanding the factors that influence food selection and dietary behavior is fundamental to support the successful translation of dietary goals into consumer behavior. The present study aims to identify gender differences in fast food consumers' reasons for actual fast food meal selection and their purchase intentions. Based on this background, possible opportunities toward implementing healthier and more sustainable fast food options are discussed. Data were collected at three fast food restaurants from different parts of Denmark among randomly selected customers (aged 15 or above). The customers were approached after having ordered their meal. They filled out a questionnaire on reasons for their actual fast food meal selection and purchase intentions in relation to four hypothesized burger menus, including a regular beef burger menu, a wholegrain beef burger menu, a nutrition labeled beef burger menu and a nutrition labeled chicken burger menu. Results showed that the majority of the fast food customers expressed a wish for healthier menus (55% males vs. 64% females agree or strongly agree, p < 0.001) and more sustainable menus in terms of environmental impact (43% males vs. 52% females agree or strongly agree, p < 0.001), however only 7% of the participants' meals included healthier food choices (n = 740). Habits, taste and price were the main drivers among both genders for the actual meal selection. Compared with women, more men expressed that actual food choice was based on offers and promotions (p < 0.001), and on food perceived as the most satiating (p = 0.001). With regard to purchase intentions, the majority of men preferred a beef burger menu (healthier or regular) over a healthier chicken burger menu or a wholegrain burger menu, whereas the majority of women responded positively to either of the healthier-labeled burger menus (p < 0.001). In conclusion, the study shows that having a focus on gender differences is of particular importance in order to improve the food nutrition environment and support healthier food selections among fast food customers.

General information
State: Published
Organisations: National Food Institute, Division of Risk Assessment and Nutrition, Research Group for Risk-Benefit, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Aalborg University
We followed the progression of healing of deep excisional biopsy punch wounds over the course of 365 days in rainbow trout (Oncorhynchus mykiss) by monitoring visual wound healing and gene expression in the healing muscle at regular intervals (1, 3, 7, 14, 38 and 100 days post-wounding). In addition, we performed muscle texture analysis one year after wound infliction. The selected genes have all previously been investigated in relation to vertebrate wound healing, but only few specifically in fish. The selected genes were interleukin (IL)-1β, IL-6, transforming growth factor (TGF)-β1 and -β3, matrix metalloproteinase (MMP) -9 and -13, inducible nitric oxide synthase (iNOS), fibronectin (FN), tenascin-C (TN-C), prolyl 4-hydroxylase α1-chain (P4Hα1), lysyl oxidase (LOX), collagen type I α1-chain (ColIα1), CD41 and CD163.

Wound healing progressed slowly in the presented study, which is at least partially due to the low temperature of about 8.5 °C during the first 100 days. The inflammation phase lasted more than 14 days, and the genes relating to production and remodeling of new extracellular matrix (ECM) exhibited a delayed but prolonged upregulation starting 1-2 weeks post-wounding and lasting until at least 100 days post-wounding. The gene expression patterns and histology reveal limited capacity for muscle regeneration in rainbow trout, and muscle texture analyses one year after wound infliction confirm that wounds heal with fibrosis. At 100 dpw epidermis had fully regenerated, and dermis partially regenerated. Scales had not regenerated even after one year.

CD163 is a marker of "wound healing"-type M2c macrophages in mammals. M2 macrophage markers are as yet poorly described in fish. The pattern of CD163 expression in the present study is consistent with the expected timing of presence of M2c macrophages in the wound. CD163 may thus potentially prove a valuable marker of M2 macrophages - or a subset hereof - in fish.

We subjected a group of fish to bathing in an immunomodulatory β-glucan product during wound healing, but found this to have very limited effect on wound healing in contrast to a previously published study on common carp.
Optimistic self-assessments of unhealthy diets are associated with positive indicators of health and health behaviours in Danish adults.

**General information**
- **State:** Published
- **Organisations:** National Food Institute, Division of Risk Assessment and Nutrition, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Research Group for Risk-Benefit, University of Copenhagen
- **Authors:** Sørensen, M. R. (Intern), Matthiessen, J. (Intern), Holm, L. (Ekstern), Knudsen, V. K. (Intern), Andersen, E. W. (Intern), Tetens, I. (Intern)
- **Number of pages:** 1
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- **Main Research Area:** Technical/natural sciences

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- **BFI (2012):** BFI-level 1
- **Scopus rating (2012):** SJR 1.151 SNIP 1.174 CiteScore 3.02
- **ISI indexed (2012):** ISI indexed yes
- **Web of Science (2012):** Indexed yes
- **BFI (2011):** BFI-level 1
- **Scopus rating (2011):** SJR 1.196 SNIP 1.265 CiteScore 3.52
- **ISI indexed (2011):** ISI indexed yes
- **Web of Science (2011):** Indexed yes
- **BFI (2010):** BFI-level 1
- **Scopus rating (2010):** SJR 1.131 SNIP 1.056
- **Web of Science (2010):** Indexed yes
- **BFI (2009):** BFI-level 1
- **Scopus rating (2009):** SJR 0.96 SNIP 1.101
- **Web of Science (2009):** Indexed yes
- **BFI (2008):** BFI-level 2
- **Scopus rating (2008):** SJR 0.952 SNIP 1.062
- **Scopus rating (2007):** SJR 0.842 SNIP 1.378
- **Web of Science (2007):** Indexed yes
- **Scopus rating (2006):** SJR 0.954 SNIP 1.298
- **Web of Science (2006):** Indexed yes
- **Scopus rating (2005):** SJR 0.789 SNIP 0.861
- **Web of Science (2005):** Indexed yes
- **Scopus rating (2004):** SJR 0.835 SNIP 1.148
- **Scopus rating (2003):** SJR 0.699 SNIP 1.12
- **Web of Science (2003):** Indexed yes
- **Scopus rating (2002):** SJR 0.733 SNIP 1.244
- **Web of Science (2002):** Indexed yes
- **Scopus rating (2001):** SJR 0.664 SNIP 0.961
- **Web of Science (2001):** Indexed yes
- **Scopus rating (2000):** SJR 0.764 SNIP 1.079
- **Web of Science (2000):** Indexed yes
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**Publication:** Research - peer-review › Journal article – Annual report year: 2016
Symptoms and quality of life in patients with chronic obstructive pulmonary disease treated with aclidinium in a real-life setting

Introduction: Chronic obstructive pulmonary disease (COPD) is a progressive disease with symptoms that can have a major impact on patients' physical health. The aim of this study was to evaluate quality of life (QoL), symptom severity and dyspnoea in COPD patients treated with aclidinium up to 24 weeks.

Methods: In this prospective non-interventional multicentre study (198 centres in Sweden, Denmark, and Norway), COPD patients (age ≥40 years) who started treatment with aclidinium (initial therapy, change of treatment, or add-on therapy) could be included. Health-related QoL was obtained by COPD assessment test (CAT). Symptoms were evaluated on a 6-point Likert scale. The modified Medical Research Council (mMRC) Dyspnoea Scale was used as a simple grading system to assess the level of dyspnoea/shortness of breath from 0 to 4. Patients on treatment with aclidinium who completed baseline and at least one follow-up visit (week 12 or 24) were included in the study population.

Results: Overall, 1,093 patients were enrolled (mean 69 years, 54% females), one-third had ≥1 exacerbation the year prior to baseline. At enrolment, 48% were LAMA naïve. Mean (standard deviation, SD) CAT score decreased from 16.9 (7.7) at baseline to 14.3 (7.3) at week 24 (p <.01) with a decrease in all individual CAT items (p<.05). Mean difference in morning and night-time symptoms from baseline to week 24 was -0.60 (SD 2.51) and -0.44 (SD 2.48), respectively (both p<.001). Mean (SD) mMRC Dyspnoea Scale changed from 1.6 (1.0) at baseline to 1.5 (1.0) at week 24 (p<.001).

Conclusion: In this observational study of a Nordic real-life COPD population, treatment with aclidinium was associated with a clinically important improvement in QoL and morning and night-time symptoms, most pronounced in the LAMA naïve group. However, there is still room for improvement in the management of symptomatic COPD patients.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Technical University of Denmark, University of Copenhagen, Lund University, Vårdcentralen Näsby, Sahlgrenska University Hospital, Clinic of Allergology and Respiratory Medicine, AstraZeneca Nordic-Baltic
Authors: Lange, P. (Ekstern), Godtfredsen, N. S. (Ekstern), Olejnicka, B. (Ekstern), Paradis, B. (Ekstern), Curiac, D. (Ekstern), Humerfelt, S. (Ekstern), Telg, G. (Ekstern), Christensen, H. N. (Ekstern), Bitsch, M. A. (Ekstern), Andersen, E. W. (Intern), Bjermer, L. (Ekstern)
Number of pages: 11
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Main Research Area: Technical/natural sciences

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Journal: European Clinical Respiratory Journal
Volume: 3
Article number: 31232
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Original language: English
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Bibliographical note
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Source: Findit
Source-ID: 2306357168
Publication: Research - peer-review › Journal article – Annual report year: 2016
Validation of Reported Whole-Grain Intake from a Web-Based Dietary Record against Plasma Alkylresorcinol Concentrations in 8- to 11-Year-Olds Participating in a Randomized Controlled Trial

BACKGROUND: Whole-grain (WG) intake is important for human health, but accurate intake estimation is challenging. Use of a biomarker for WG intake provides a possible way to validate dietary assessment methods. OBJECTIVE: Our aim was to validate WG intake from 2 diets reported by children, using plasma alkylresorcinol (AR) concentrations, and to investigate the 3-mo reproducibility of AR concentrations and reported WG intake. METHODS: AR concentrations were analyzed in fasting blood plasma samples, and WG intake was estimated in a 7-d web-based diary by 750 participants aged 8-11 y in a 2 school meal × 3 mo crossover trial. Reported WG intake and plasma AR concentrations were compared when children ate their usual bread-based lunch (UBL) and when served a hot lunch meal (HLM). Correlations and cross-classification were used to rank subjects according to intake. The intraclass correlation coefficients (ICCs) between subjects' measurements at baseline and after the UBL were used to assess reproducibility. RESULTS: Correlations between reported WG wheat + rye intake and plasma AR were 0.40 and 0.37 (P <0.001) for the UBL and the HLM diets, and 78% and 77% were classified in the same or adjacent quartiles for the UBL and HLM diets, respectively. The ICC over 3 mo was 0.47 (95% CI: 0.38, 0.55) for plasma total ARs and 0.64 (95% CI: 0.58, 0.70) for reported WG intake. Correlations were higher when using the AR C17:0 homolog as a biomarker, reflecting rye intake instead of plasma total ARs [UBL: \( r = 0.47 \); HLM: \( r = 0.43 \), P <0.001; ICC = 0.51 (95% CI: 0.43, 0.59)]. CONCLUSIONS: Self-reported WG wheat + rye intake among children showed moderate correlations with plasma AR concentrations. Substantial intraindividual variation was found in WG intake and plasma AR concentrations. The AR homolog C17:0 may be used as a biomarker for WG intake when the WG intake primarily comes from rye as in the present study. This trial was registered at clinicaltrials.gov as NCT01457794.

General information
State: Published
Organisations: National Food Institute, Division of Risk Assessment and Nutrition, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Research Group for Risk-Benefit, University of Copenhagen, Karolinska Institutet, Swedish University of Agricultural Sciences
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Journal: Journal of Nutrition
Volume: 146
Issue number: 2
ISSN (Print): 0022-3166
Ratings:
BFI (2018): BFI-level 2
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.93 SJR 1.956 SNIP 1.335
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.271 SNIP 1.505 CiteScore 4.08
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.089 SNIP 1.596 CiteScore 4.13
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.172 SNIP 1.614 CiteScore 4.6
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.919 SNIP 1.671 CiteScore 4.45
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Accuracy of self-reported intake of signature foods in a school meal intervention study: comparison between control and intervention period

Bias in self-reported dietary intake is important when evaluating the effect of dietary interventions, particularly for intervention foods. However, few have investigated this in children, and none have investigated the reporting accuracy of fish intake in children using biomarkers. In a Danish school meal study, 8- to 11-year-old children (n 834) were served the New Nordic Diet (NND) for lunch. The present study examined the accuracy of self-reported intake of signature foods (berries, cabbage, root vegetables, legumes, herbs, potatoes, wild plants, mushrooms, nuts and fish) characterising the NND. Children, assisted by parents, self-reported their diet in a Web-based Dietary Assessment Software for Children during the intervention and control (packed lunch) periods. The reported fish intake by children was compared with their ranking according to fasting whole-blood EPA and DHA concentration and weight percentage using the Spearman correlations and cross-classification. Direct observation of school lunch intake (n 193) was used to score the accuracy of food-reporting as matches, intrusions, omissions and faults. The reporting of all lunch foods had higher percentage of matches compared with the reporting of signature foods in both periods, and the accuracy was higher during the control period compared with the intervention period. Both Spearman's rank correlations and linear mixed models demonstrated positive associations between EPA+DHA and reported fish intake. The direct observations showed that both reported and real intake of signature foods did increase during the intervention period. In conclusion, the self-reported data represented a true increase in the intake of signature foods and can be used to examine dietary intervention effects.

General information
State: Published
Organisations: National Food Institute, Division of Risk Assessment and Nutrition, Research Group for Risk-Benefit, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, University of Copenhagen, University of Waterloo
Effects of school meals based on the New Nordic Diet on intake of signature foods: a randomised controlled trial. The OPUS School Meal Study

A New Nordic Diet (NND) was developed in the context of the Danish OPUS Study (Optimal well-being, development and health for Danish children through a healthy New Nordic Diet). Health, gastronomic potential, sustainability and Nordic identity were crucial principles of the NND. The aim of the present study was to investigate the effects of serving NND school meals compared with the usual packed lunches on the dietary intake of NND signature foods. For two 3-month periods, 834 Danish children aged 8-11 years received NND school meals or their usual packed lunches brought from home (control) in random order. The entire diet was recorded over 7 consecutive days using a validated Web-based Dietary Assessment Software for Children. The NND resulted in higher intakes during the entire week (% increase) of root vegetables (116 (95 % CI 1.93, 2.42)), cabbage (26 (95 % CI 1.08, 1.47)), legumes (22 (95 % CI 1.06, 1.40)), herbs (175 (95 % CI 2.36, 3.20)), fresh berries (48 (95 % CI 1.13, 1.94)), nuts and seeds (18 (95 % CI 1.02, 1.38)), lean fish and fish products (47 (95 % CI 1.31, 1.66)), fat fish and fish products (18 (95 % CI 1.02, 1.37)) and potatoes (129 (95 % CI 2.05, 2.56)). Furthermore, there was a decrease in the number of children with zero intakes when their habitual packed lunches were replaced by NND school meals. In conclusion, this study showed that the children increased their intake of NND signature foods, and, furthermore, there was a decrease in the number of children with zero intakes of NND signature foods when their habitual packed lunches were replaced by school meals following the NND principles.

General information
State: Published
Organisations: Division of Nutrition, National Food Institute, Department of Informatics and Mathematical Modeling, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Department of Management Engineering, University of Copenhagen
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Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: British Journal of Nutrition
Volume: 114
Issue number: 5
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BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.46 SJR 1.983 SNIP 1.533
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Introduction to Statistics - eNotes
Online textbook used in the introductory statistics courses at DTU. It provides a basic introduction to applied statistics for engineers. The necessary elements from probability theory are introduced (stochastic variable, density and distribution...
function, mean and variance, etc.) and thereafter the most basic statistical analysis methods are presented: Confidence band, hypothesis testing, simulation, simple and multiple regression, ANOVA and analysis of contingency tables. Examples with the software R are included for all presented theory and methods.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Dynamical Systems
Authors: Brockhoff, P. B. (Intern), Møller, J. K. (Intern), Andersen, E. W. (Intern), Bacher, P. (Intern), Christiansen, L. E. (Intern)
Publication date: 2015

Publication information
Main Research Area: Technical/natural sciences
Links:
http://introstat.compute.dtu.dk/enote/
Publication: Education › Internet publication – Annual report year: 2015

Plate waste and intake of school lunch based on the New Nordic Diet and on packed lunches: A randomised controlled trial in 8- to 11-year-old Danish children
The aim of the present study was to compare total food intake, total and relative edible plate waste and self-reported food likings between school lunch based on the new Nordic diet (NND) and packed lunch from home. In two 3-month periods in a cluster-randomised controlled unblinded cross-over study 3rd- and 4th-grade children (n 187) from two municipal schools received lunch meals based on NND principles and their usual packed lunch (control). Food intake and plate waste (n 1558) were calculated after weighing lunch plates before and after the meal for five consecutive days and self-reported likings (n 905) assessed by a web-based questionnaire. Average food intake was 6 % higher for the NND period compared with the packed lunch period. The quantity of NND intake varied with the menu (P < 0·0001) and was positively associated with self-reported likings. The edible plate waste was 88 (sd 80) g for the NND period and 43 (sd 60) g for the packed lunch period whereas the relative edible plate waste was no different between periods for meals having waste (n 1050). Edible plate waste differed between menus (P < 0·0001), with more waste on soup days (36 %) and vegetarian days (23 %) compared with the packed lunch period. Self-reported likings were negatively associated with percentage plate waste (P < 0·0001). The study suggests that portion sizes need to be considered in new school meal programmes. New strategies with focus on reduction of plate waste, children's likings and nutritious school meals are crucial from both a nutritional, economic and environmental point of view.

General information
State: Published
Organisations: National Food Institute, Division of Risk Assessment and Nutrition, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Research Group for Risk-Benefit, University of Copenhagen
Authors: Thorsen, A. V. (Intern), Lassen, A. D. (Intern), Andersen, E. W. (Intern), Christensen, L. M. (Intern), Biltoft-Jensen, A. P. (Intern), Andersen, R. (Intern), Damsgaard, C. T. (Ekstern), Michaelsen, K. F. (Ekstern), Tetens, I. (Intern)
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Web of Science (2016): Indexed yes
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ISI indexed (2013): ISI indexed no
Original language: English
Edible plate waste, School meals, Packed lunches, Food liking
Electronic versions:
15_Thorsen_et_al_Plate_waste_and_intake_of_school_lunch.pdf
DOIs:
Reduction in pedometer-determined physical activity in the adult Danish population from 2007 to 2012

Aims: To examine the development in pedometer-determined physical activity from 2007–2008 to 2011–2012 in the adult Danish population. Methods: The study population comprised two random samples of 18–75-year-old individuals who took part in cross-sectional studies in 2007–2008 (n=224) and 2011–2012 (n=1515). Pedometer data (sealed Yamax SW 200) were obtained for seven consecutive days. Data for 1624 participants (48.2% men) were included in the analysis. An overall step-defined activity level was examined based on a graduated step index (sedentary, low active, somewhat active, active, highly active). The pedometer-determined outcomes were analysed using regression models. Results: A borderline significant decline (p=0.077) from 8788 to 8341 steps/day (−446 (95% confidence intervals −50, 943)) was found between 2007–2008 and 2011–2012. Furthermore, a 23.7% (95% confidence intervals −41.7%, −0.1%) lower overall step-defined activity level was observed in 2011–2012 compared to 2007–2008. These changes were primarily due to a reduced level of activity among women. The proportion of individuals taking 10,000 steps/day decreased non-significantly from 34.8% to 29.3%, whereas the proportion taking...
Short communication: Artificial ultraviolet B light exposure increases vitamin D levels in cow plasma and milk

The number of dairy cows without access to pasture or sunlight is increasing; therefore, the content of vitamin D in dairy products is decreasing. Ultimately, declining vitamin D levels in dairy products will mean that dairy products are a negligible source of natural vitamin D for humans. We tested the ability of a specially designed UVB lamp to enhance the vitamin D-3 content in milk from dairy cows housed indoors. This study included 16 cows divided into 4 groups. Each group was exposed daily to artificial UVB light simulating 1, 2, 3, or 4 h of summer sun at 56 degrees N for 24 d, and the group with simulated exposure to 2 h of summer sun daily continued to be monitored for 73 d. We found a significant increase in 25-hydroxyvitamin D-3 (25OHD(3)) levels in plasma as well as vitamin D-3 and 25OHD(3) levels in milk after daily exposure for 24 d in all treatment groups. Extending daily exposure to artificial UVB light to 73 d did not lead to an increase of vitamin D-3 or 25OHD(3) level in the milk. In conclusion, the change in production facilities for dairy cows providing cows with no access to pasture and sunlight causes a decrease of vitamin D levels in dairy products. This decrease may be prevented by exposing cows to artificial UVB light in the stable.

General information
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Vitamin D intake-status relationship among Danes aged 4-60 years during winter
What do Danish children eat, and does the diet meet the recommendations?: Baseline data from the OPUS School Meal Study

A child’s diet is an important determinant for later health, growth and development. In Denmark, most children in primary school bring their own packed lunch from home and attend an after-school care institution. The aim of the present study was to evaluate the food, energy and nutrient intake of Danish school children in relation to dietary guidelines and nutrient recommendations, and to assess the food intake during and outside school hours. In total, 834 children from nine public schools located in the eastern part of Denmark were included in this cross-sectional study and 798 children (95·7 %) completed the dietary assessment sufficiently (August-November 2011). The whole diet was recorded during seven consecutive days using the Web-based Dietary Assessment Software for Children (WebDASC). Compared with the food-based dietary guidelines and nutrient recommendations, 85 % of the children consumed excess amounts of red meat, 89 % consumed too much saturated fat, and 56 % consumed too much added sugar. Additionally 35 or 91 % of the children (depending on age group) consumed insufficient amounts of fruits and vegetables, 85 % consumed insufficient amounts of fish, 86 % consumed insufficient amounts of dietary fibre, 60 or 84 % had an insufficient Fe intake (depending on age group), and 96 % had an insufficient vitamin D intake. The study also showed that there is a higher intake of fruits and bread during school hours than outside school hours; this is not the case with, for example, fish and vegetables, and future studies should investigate strategies to increase fish and vegetable intake during school hours.

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Common variants in CYP2R1 and GC genes are both determinants of serum 25-hydroxyvitamin D concentrations after UVB irradiation and after consumption of vitamin D3-fortified bread and milk during winter in Denmark

Background: Little is known about how the genetic variation in vitamin D modulating genes influences ultraviolet (UV)B–induced 25-hydroxyvitamin D [25(OH)D] concentrations. In the Food with vitamin D (VitmaD) study, we showed that common genetic variants rs10741657 and rs10766197 in 25-hydroxylase (CYP2R1) and rs842999 and rs4588 in
vitamin D binding protein (GC) predict 25(OH)D concentrations at late summer and after 6-mo consumption of cholecalciferol (vitamin D3)–fortified bread and milk.

Objectives: In the current study, called the Vitamin D in genes (VitDgen) study, we analyzed associations between the increase in 25(OH)D concentrations after a given dose of artificial UVB irradiation and 25 single nucleotide polymorphisms located in or near genes involved in vitamin D synthesis, transport, activation, or degradation as previously described for the VitmaD study. Second, we aimed to determine whether the genetic variations in CYP2R1 and GC have similar effects on 25(OH)D concentrations after artificial UVB irradiation and supplementation by vitamin D3–fortified bread and milk.

Design: The VitDgen study includes 92 healthy Danes who received 4 whole-body UVB treatments with a total dose of 6 or 7.5 standard erythema doses during a 10-d period in winter. The VitmaD study included 201 healthy Danish families who were given vitamin D3–fortified bread and milk or placebo for 6 mo during the winter.

Results: After UVB treatments, rs10741657 in CYP2R1 and rs4588 in GC predicted UVB-induced 25(OH)D concentrations as previously shown in the VitmaD study. Compared with noncarriers, carriers of 4 risk alleles of rs10741657 and rs4588 had lowest concentrations and smallest increases in 25(OH)D concentrations after 4 UVB treatments and largest decreases in 25(OH)D concentrations after 6-mo consumption of vitamin D3–fortified bread and milk.

Conclusion: Common genetic variants in the CYP2R1 and GC genes modify 25(OH)D concentrations in the same manner after artificial UVB-induced vitamin D and consumption of vitamin D3–fortified bread and milk. The VitDgen study was registered at clinicaltrials.gov as NCT01741233. The VitmaD study was registered at clinicaltrials.gov as NCT01184716.
Common Variants in CYP2R1 and GC Genes Predict Vitamin D Concentrations in Healthy Danish Children and Adults

Environmental factors such as diet, intake of vitamin D supplements and exposure to sunlight are known to influence serum vitamin D concentrations. Genetic epidemiology of vitamin D is in its infancy and a better understanding on how genetic variation influences vitamin D concentration is needed. We aimed to analyse previously reported vitamin D-related polymorphisms in relation to serum 25(OH)D concentrations in 201 healthy Danish families with dependent children in late summer in Denmark. Serum 25(OH)D concentrations and a total of 25 SNPs in GC, VDR, CYP2R1, CYP24A1, CYP27B1, C10or88 and DHCR7/NADSYN1 genes were analysed in 758 participants. Genotype distributions were in Hardy-Weinberg equilibrium for the adult population for all the studied polymorphisms. Four SNPs in CYP2R1 (rs1562902, rs7116978, rs10741657 and rs10766197) and six SNPs in GC (rs4588, rs842999, rs2282679, rs12512631, rs16846876 and rs17467825) were statistically significantly associated with serum 25(OH)D concentrations in children, adults and all combined. Several of the SNPs were in strong linkage disequilibrium, and the associations were driven by CYP2R1-rs10741657 and rs10766197, and by GC-rs4588 and rs842999. Genetic risk score analysis showed that carriers with no risk alleles of CYP2R1-rs10741657 and rs10766197, and/or GC rs4588 and rs842999 had significantly higher serum 25(OH)D concentrations compared to carriers of all risk alleles. To conclude, our results provide supporting evidence that common polymorphisms in GC and CYP2R1 are associated with serum 25(OH)D concentrations in the Caucasian population and that certain haplotypes may predispose to lower 25(OH)D concentrations in late summer in Denmark.

General information

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Organisations: National Food Institute, Division of Nutrition, Division of Toxicology and Risk Assessment, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Aarhus University, National Research Center for Working Environment
Dietary effects of introducing school meals based on the New Nordic Diet: a randomised controlled trial in Danish children.

The OPUS School Meal Study

The OPUS (Optimal well-being, development and health for Danish children through a healthy New Nordic Diet (NND)) School Meal Study investigated the effects on the intake of foods and nutrients of introducing school meals based on the principles of the NND covering lunch and all snacks during the school day in a cluster-randomised cross-over design. For two 3-month periods, 834 Danish children aged 8-11 years from forty-six school classes at nine schools received NND school meals or their usual packed lunches brought from home (control) in random order. The whole diet of the children was recorded over seven consecutive days using a validated Web-based Dietary Assessment Software for Children. The NND resulted in higher intakes of potatoes (130 %, 95 % CI 2·07, 2·58), fish (48 %, 95 % CI 1·33, 1·65), cheese (25 %, 95 % CI 1·15, 1·36), vegetables (16 %, 95 % CI 1·10, 1·21), eggs (10 %, 95 % CI 1·01, 1·19) and beverages (6 %, 95 % CI 1·02, 1·09), and lower intakes of bread (13 %, 95 % CI 0·84, 0·89) and fats (6 %, 95 % CI 0·90, 0·98) were found among the children during the NND period than in the control period (all, P< 0·05). No difference was found in mean energy intake (P= 0·4), but on average children reported 0·9 % less energy intake from fat and 0·9 % higher energy intake from protein during the NND period than in the control period. For micronutrient intakes, the largest differences were found for vitamin D (42 %, 95 % CI 1·32, 1·53) and iodine (11 %, 95 % CI 1·08, 1·15) due to the higher fish intake. In conclusion, the present study showed that the overall dietary intake at the food and nutrient levels was improved among children aged 8-11 years when their habitual packed lunches were replaced by school meals following the principles of the NND.

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Scopus rating (2011): SJR 2.079 SNIP 1.661 CiteScore 3.13
Effectiveness of offering healthy labelled meals in improving the nutritional quality of lunch meals eaten in a worksite canteen

Healthier meal selections at restaurants and canteens are often limited and not actively promoted. In this Danish study the effectiveness of a healthy labelling certification program in improving dietary intake and influencing edible plate waste was evaluated in a quasi-experimental study design. Employees from an intervention worksite canteen and a matched control canteen were included in the study at baseline (February 2012), after completing the certification process (end-point) and six month from end-point (follow-up) (total n=270). In order to estimate nutrient composition of the consumed lunch meals and plate waste a validated digital photographic method was used combining estimation of food intake with food nutrient composition data. Food satisfaction was rated by participants using a questionnaire. Several significant positive nutritional effects were observed at the intervention canteen including a mean decrease in energy density in the consumed meals from 561kJ/100g at baseline to 368 and 407kJ/100g at end-point and follow-up, respectively (P<0.001). No significant changes were seen with regard to food satisfaction and plate waste. In the control canteen no positive nutritional effects were observed. The results of the study highlight the potential of using healthy labelling certification programs as a possible driver for increasing both the availability and awareness of healthy meal choices, thereby improving dietary intake when eating out.

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Organisations: Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, National Food Institute, Division of Nutrition
Real-life use of vitamin D₃-fortified bread and milk during a winter season: the effects of CYP2R1 and GC genes on 25-hydroxyvitamin D concentrations in Danish families, the VitmaD study.

Common genetic variants rs10741657 and rs10766197 in CYP2R1 and rs4588 and rs842999 in GC and a combined genetic risk score (GRS) of these four variants influence late summer 25-hydroxyvitamin D (25(OH)D) concentrations. The objectives were to identify those who are most at risk of developing low vitamin D status during winter and to assess whether vitamin D₃-fortified bread and milk will increase 25(OH)D concentrations in those with genetically determined low 25(OH)D concentrations at late summer. We used data from the VitmaD study. Participants were allocated to either vitamin D₃-fortified bread and milk or non-fortified bread and milk during winter. In the fortification group, CYP2R1 (rs10741657) and GC (rs4588 and rs842999) were statistically significantly associated with winter 25(OH)D concentrations and CYP2R1 (rs10766197) was borderline significant. There was a negative linear trend between 25(OH)D concentrations and carriage of 0-8 risk alleles (p <0.0001). No association was found for the control group (p = 0.1428). There was a significant positive linear relationship between different quintiles of total vitamin D intake and the increase in 25(OH)D concentrations among carriers of 0-2 (p = 0.0012), 3 (p = 0.0001), 4 (p = 0.0118) or 5 (p = 0.0029) risk alleles, but not among carriers of 6-8 risk alleles (p = 0.1051). Carriers of a high GRS were more prone to be vitamin D deficient compared to carriers of a low GRS. Furthermore, rs4588-AA carriers have a low but very stable 25(OH)D concentration, and interestingly, also low PTH level.

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Trends in pedometer-measured steps per day in Danish adults: 2007 to 2012

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Vitamin D status and effects of food fortification in families

Background and aims: The importance of vitamin D in bone health is recognised and low concentrations have been associated with increased risk of disease. Cutaneous synthesis is considered the major source of vitamin D, but during winter where sufficient sun exposure is restricted at Northern latitudes, intake from food and dietary supplements become essential. Vitamin D intakes are lower than dietary recommendations in most populations and low vitamin D status is common. The PhD thesis is based on the VitmaD study in which a realistic and model derived fortification strategy was investigated in a real-life setting. The aim was to investigate the effect of increasing vitamin D intake by fortification of milk and bread to the amount recommended in the Nordic Nutrition recommendations (NNR) on serum 25(OH)D concentration in families during winter in Denmark (paper 1). Secondly, the aim was to assess vitamin D status and its determinants at baseline of the study (paper 2). Further, to model the relationship between total vitamin D intake and serum 25(OH)D taking into account potential effect modifiers and estimate required vitamin D intake during winter (paper 3).

Methods: The VitmaD study was a randomized controlled trial in 782 children and adults (4-60 years) recruited as 201 families. Families were randomly assigned to vitamin D fortified or nonfortified milk and bread for 6 months starting from September. The milk and bread replaced the subjects’ usual consumptions of products. Information on dietary intake, supplement use, health and lifestyle was obtained by self-administered web-based questionnaires. Serum 25(OH)D was analysed by liquid chromatography-tandem mass spectrometry (LC/MS-MS). Mixed models with family as a random factor were applied in all the statistical analyses. Results: At baseline of the study (late summer) the geometric mean (IQR) serum 25(OH)D concentration was 72.1 (61.5-86.7) nmol/L with no overall differences between age (P=0.190), gender (P=0.332) or age and gender groups (P=0.223) (paper 2). The prevalence of serum 25(OH)D <50 nmol/L was 9 %. In the multiple analysis of all subjects, vitamin D status was negatively associated with BMI (P<0.001) and positively associated with dietary vitamin D (P<0.008), multivitamin use (P=0.019), solarium use (P=0.006), outdoor stay in light clothes (P=0.001), sun preference (P=0.002) and sun vacation (P<0.001). The intra-family correlation was stronger in children (0.42) compared with adults (0.24). Thus children within a family seemed to be more alike than adults within a family with respect to vitamin D status. The planned fortification strategy was to increase the vitamin D intake to 7.5 µg/day. This succeeded in 66 % of the subjects in the fortification group with a median vitamin D intake (habitual diet plus fortified milk and bread) of 9.4 µg/day compared with 2.2 µg/day in the control group (paper 1). During winter the serum 25(OH)D concentration decreased from 73.1 to 67.6 nmol/L (-5.5 nmol/L) in the fortification group (P<0.001) and from 71.1 to 41.7 nmol/L (-29.4 nmol/L) in the control group (P<0.001). The final serum 25(OH)D concentration was significantly higher in the fortification group compared with in the control group (P<0.001, interpreted estimate 1.59) and the treatment effect was not affected by BMI, multivitamin use and sun vacation. The prevalence of serum 25(OH)D <50 nmol/L remained low in the fortification group (16 %) whereas it increased to 65 % in the control group. The relationship between total vitamin D intake from natural foods, fortified milk and bread and dietary supplements and serum 25(OH)D concentration in winter was best fitted by a non-linear curve (paper 3). The effect of total vitamin D intake on serum 25(OH)D concentration was 4 % higher in men compared with women (P<0.014) and 10 % higher in the group with lowest initial 25(OH)D concentration.
(<61.5 nmol/L) compared with the group with highest initial 25(OH)D concentration (>86.9 nmol/L) (P<0.001). It was not modified by age (P=0.132) or BMI (P=0.884). Estimated required vitamin D intake was 5, 11, 23 and 39 µg/day for 50, 75, 90 and 95 % of the population to maintain vitamin D status >50 nmol/L during winter. These figures were higher for the group with lowest initial 25(OH)D concentration (11, 18, 34 and >34 µg/day) and lower for the group with highest initial 25(OH)D concentration (<1, 3, 8 and 17 µg/day). Conclusions: In the population of Danish families, serum 25(OH)D concentration was above 50 nmol/L in late summer and it was associated with both dietary and sun related factors. Children within a family seemed to be more alike than adults within a family with respect to vitamin D status. Vitamin D fortification of milk and bread reduced the decrease in serum 25(OH)D concentration during winter and ensured concentrations above 50 nmol/L. The relationship between total vitamin D intake and vitamin D status was non-linear. Estimated total vitamin D intake to maintain serum 25(OH)D above 50 nmol/L was largely dependent on the initial vitamin D status.

Vitamin D status and its determinants in children and adults among families in late summer in Denmark. The impact of the familial relationship on vitamin D status has not been investigated previously. The objective of the present cross-sectional study was to assess serum 25-hydroxyvitamin D (25(OH)D) concentration and its determinants in children and adults among families in late summer in Denmark (56°N). Data obtained from 755 apparently healthy children (4-17 years) and adults (18-60 years) recruited as families (n 200) in the VitmaD study were analysed. Blood samples were collected in September-October, and serum 25(OH)D concentration was measured by liquid chromatography-tandem MS. Information on potential determinants was obtained using questionnaires. The geometric mean serum 25(OH)D concentration was 72·1 (interquartile range 61·5-86·7) nmol/l (range 9-162 nmol/l), with 9 % of the subjects having 25(OH)D concentrations <50 nmol/l. The intra-family correlation was 0·27 in all subjects, 0·24 in the adults and 0·42 in the children. Serum 25(OH)D concentration was negatively associated with BMI (P<0·001) and positively associated with dietary vitamin D intake (P= 0·008), multivitamin use (P= 0·019), solarium use (P= 0·006), outdoor stay (P= 0·001), sun preference (P= 0·002) and sun vacation (P<0·001), but was not associated with lifestyle-related factors in the adults when these were assessed together with the other determinants. In conclusion, the majority of children and adults among the families had serum 25(OH)D concentrations >50 nmol/l in late summer in Denmark. Both dietary and sun-related factors were determinants of vitamin D status and the familial component was stronger for the children than for the adults.
Breast cancer in women using digoxin: tumor characteristics and relapse risk

Introduction: Digoxin use is associated with increased incidence of breast and uterus cancers. We postulated that digoxin use might affect tumor characteristics and increase relapse risk in women with breast cancer.

Methods: Incident breast cancer cases in Danish women (n = 49,312; 1995 to 2008) were identified. Analyses were conducted in women 20 to 74 years old. Relapse hazard ratios (HR) were compared in women using and not using digoxin, adjusting for age, calendar period, protocol, tumor size, nodal involvement, histology grade, estrogen-receptor (ER) status, and anti-estrogen therapy in Cox regression models.

Results: At diagnosis, tumors in digoxin users were more likely ER+ (85.4% vs. 78.6%; P = 0.002) and have grade 1 ductal histology (37.2% vs. 25.7; P = 0.004), compared to non-users. 45 relapses occurred in women already using digoxin at breast cancer diagnosis (1,487 person-years; 24 relapses occurred in women later starting digoxin (384 person-years). Overall relapse HR in digoxin users was 1.13 (95% confidence interval: 0.88, 1.46) compared to non-users. Relapse risk in digoxin users was significantly increased in the first year (2.19; 1.26, 3.78) but not thereafter (0.99; 0.74, 1.32) (P = 0.02 for difference in HRs). First-year relapse hazard was high in digoxin-using women with ER+ tumors (2.51; 1.39, 4.55) but not ER- tumors (0.72; 0.10, 5.27). Recurrence hazard was not significantly changed among digoxin-using women also using tamoxifen.

Conclusions: Breast cancers arising in digoxin-using women had better prognostic features. After adjustment for markers, overall breast cancer relapse risk in digoxin users was not increased significantly, although recurrence hazards for ER+ tumors were higher in the first year following diagnosis.

General information
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Effectiveness of offering keyhole labelled meals in improving the nutritional quality of lunch meals eaten in worksite canteens

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Impact of changes in metabolic control on progression to photocoagulation for clinically significant macular oedema: a 20 year study of type 1 diabetes

Aims/hypothesis

Although increasing hyperglycaemia, arterial hypertension and longer duration of diabetes raise the risk of progression of diabetic retinopathy, short-term benefits in terms of improved metabolic control and lowered blood pressure have not been demonstrated. We therefore examined the effect of changes in glycaemia and arterial blood pressure on the incidence of clinically significant macular oedema in a population of diabetic patients.

Methods

We performed a retrospective review of all patients with type 1 diabetes who attended the retinopathy screening clinic at the Steno Diabetes Center from 1988 to 2008, using the endpoint referral to first photocoagulation treatment for clinically significant diabetic macular oedema. The analysis included 1,878 patients (median observation, 8 years). Changes were defined as the inter-visit change; in the case of an event the last event-free interval before referral, where the median screening interval was 6 months.

Results
Risk of progression to photocoagulation for macular oedema increased with duration of diabetes (p < 0.001), current HbA1c (p < 0.0001) and with the magnitude of changes in HbA1c (p = 0.0002) and systolic blood pressure (p < 0.0001) in a multiple regression model. A recent decrease of ≥0.5 percentage points or an increase in HbA1c of >0.5 percentage points per 6 months was associated with HRs of 3.04 and 1.28, respectively, compared with lesser changes in HbA1c.

Conclusions/interpretation
In this study, large recent changes in metabolic control and systolic blood pressure, irrespective of direction, were independent risk factors for progression to photocoagulation for diabetic macular oedema. The effects of metabolic and haemodynamic stability on diabetic retinopathy should be examined in prospective studies.
Randomized controlled trial of the effects of vitamin D–fortified milk and bread on serum 25-hydroxyvitamin D concentrations in families in Denmark during winter: the VitmaD study

Background: Vitamin D intakes are lower than dietary recommendations in most populations, and thus, a low vitamin D status is widespread, especially during winter.

Objective: We investigated the effects of increasing vitamin D intake to the recommended amount by fortification of milk and bread on serum 25-hydroxyvitamin D [25(OH)D] concentrations in families during winter in Denmark.

Design: The study was a randomized controlled trial in 782 children and adults (4–60 y old) recruited as 201 families. Families were randomly assigned to vitamin D–fortified or nonfortified milk and bread for 6 mo starting in September. The milk and bread replaced the participants’ usual consumptions of products.

Results: Median (IQR) vitamin D intakes (habitual diet plus fortified products) were 9.4 μg/d (6.5, 12.3 μg/d) and 2.2 μg/d (1.5, 3.0 μg/d) in fortification and control groups, respectively. Geometric mean (IQR) serum 25(OH)D concentrations decreased from 73.1 nmol/L (61.9, 88.5 nmol/L) to 67.6 nmol/L (56.2, 79.4 nmol/L) in the fortification group and from 71.1 nmol/L (61.2, 85.9 nmol/L) to 41.7 nmol/L (29.5, 58.9 nmol/L) in the control group (both P < 0.001). The final 25(OH)D concentration was significantly higher in the fortification group than in the control group (P < 0.001). By the end of the study, <1% of subjects in the fortification group and 25% of subjects in the control group had 25(OH)D concentrations <30 nmol/L and 16% and 65% of subjects, respectively, had 25(OH)D concentrations <50 nmol/L.

Conclusion: Vitamin D fortification of milk and bread reduces the decrease in serum 25(OH)D concentrations during winter and ensures 25(OH)D concentrations >50 nmol/L in children and adults in Denmark. This trial was registered at clinicaltrials.gov as NCT01184716.
Risk of cardiovascular disease in family members of young sudden cardiac death victims

Aims Descriptive and genetic studies suggest that relatives of sudden cardiac death (SCD) victims have an increased risk of several cardiovascular diseases (CVDs). Given the severe consequences of undiagnosed CVD and the availability of effective treatment, the potential for prevention in this group is enormous if they do have an increased CVD risk. This nationwide prospective population-based cohort study described the risk of CVDs in relatives of young SCD victims, compared with the general population.

Methods and Results All SCD victims aged 1-35 years in Denmark, 2000-2006, were identified (n = 470), along with their first- and second-degree relatives (n = 3073). We compared the incidence of CVD in those relatives with that in the background population using standardized incidence ratios (SIRs). The observed number of CVDs over 11 years of follow-up was 292, compared with 219 expected based on national rates [SIR 1.33, 95% confidence interval (CI) 1.19-1.50]. Risks varied significantly with age; the SIR for those <35 years was 3.53 (95% CI 2.65-4.69), compared with SIRs of 1.59 (95% CI 1.35-1.89) and 0.91 (95% CI 0.75-1.10) for those aged 35-60 years or >60 years, respectively (P-homogeneity < 0.0001). For first-degree relatives <35 years, SIRs for ischaemic heart disease, cardiomyopathy, and ventricular arrhythmia were 5.99 (95% CI 1.95-13.98), 17.91 (95% CI 4.88-45.87), and 19.15 (95% CI 7.70-39.45), respectively.

Conclusion CVDs co-aggregated significantly with SCD in families, with young first-degree relatives at greatest risk. Results clearly indicate that family members of young SCD victims should be offered comprehensive and systematic screening, with focus on the youngest relatives.
The dietary effect of serving school meals based on the new Nordic diet – A randomised controlled trial in Danish children

Background and objectives:
The OPUS study is a school-based intervention study testing selected health effects of New Nordic Diet (NND). Children are served lunch and snacks based on NND. The hypothesis is that Danish school children eat a healthier diet when receiving NND school meals as compared with packed lunch brought from home. To investigate the effects on intake of selected macronutrients in Danish school children when served school meals based on NND compared with packed lunch.

Methods:
In a cluster-randomized controlled unblinded cross-over study children received school meals based on NND for 3 months and their usual packed lunch for 3 months. The daily intake of food and beverages was recorded 3 times during 7 consecutive days using a validated self-administered web-based dietary assessment software tool for children. Statistical analysis was performed by hierarchical mixed models.

Results:
834 children from 9 schools were included and 96%, 89% and 80% filled out the first, second and third dietary assessment sufficiently (4-7 days), respectively. The preliminary results showed that the effect of serving NND resulted in a reduction in fat E% (P<0.0001), total fat (P=0.0007) and saturated fat (P<0.0001) intake for the NND compared to packed lunch; and an increase in protein E% (P<0.0001), and a borderline significant increase in dietary fiber intake (P=0.0471). There was no effect for energy intake, carbohydrate E% and added sugar E% (P>0.05). Effects are adjusted for BMI, season and household education.

Conclusions:
Danish school children’s dietary intake of total and saturated fat decreased, fat E% decreased and protein E% increased when eating NND lunch and snacks compared to packed lunch brought from home. The OPUS project (Optimal well-being, development and health for Danish children through a healthy New Nordic Diet) is supported by the Nordea Foundation.

**General information**

State: Published
Organisations: National Food Institute, Division of Nutrition, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, University of Copenhagen
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.093 SNIP 1.03 CiteScore 2.55
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.284 SNIP 1.12 CiteScore 2.64
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.949 SNIP 1.014 CiteScore 2.46
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.841 SNIP 0.89 CiteScore 2.35
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.872 SNIP 0.951 CiteScore 2.38
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.756 SNIP 0.84
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.668 SNIP 0.899
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 0.783 SNIP 0.78
Scopus rating (2007): SJR 0.687 SNIP 0.74
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.666 SNIP 0.736
Scopus rating (2005): SJR 0.576 SNIP 0.758
Scopus rating (2004): SJR 0.434 SNIP 0.754
Web of Science (2004): Indexed yes
Vitamin D status among families in Denmark: Baseline data from the vitmad study

Background and objectives:
The beneficial effect of vitamin D in bone health is acknowledged and the vitamin has also been associated with several chronic diseases. It is therefore relevant to determine the prevalence of vitamin D insufficiency in different groups, and vitamin D statuses within families have not been studied previously. The objective of the present study was to evaluate serum 25-hydroxyvitamin D (25(OH)D) concentrations among families in Denmark (56 °N) after seasonal UVB peak and to ascertain determining factors.

Methods:
Cross-sectional study with 755 children and adults (4-60 y) recruited as families in the VitmaD study. Blood samples were collected in September-October 2010, and vitamin D status was measured as serum 25(OH)D concentration by LC-MS/MS. Vitamin D intake and life style factors were assessed in self-administered questionnaires. Determinants of vitamin D status were identified in a linear mixed model with family as a random variable.

Results:
Mean (±SD) serum 25(OH)D concentration was 75 ± 20 nmol/l (range 9-162 nmol/l) and only 10 % had 25(OH) D <50 nmol/l. Determinants of serum 25(OH)D were age (p=0.036), BMI class (p=0.001), multi vitamin use (p=0.033), sun behaviour (p=0.005), outdoor stay (p=0.033), sun vacation (p<0.001), and physical activity (p=0.040). Gender (p=0.692) and vitamin D intake (p=0.238) were not associated to serum 25(OH)D.

Conclusions:
The prevalence of vitamin D insufficiency among families in Denmark was low after seasonal UVB peak. Sun vacation was the strongest determinant for vitamin D status at this time of the year.
Purpose: Descriptive studies have indicated clustering of cardiovascular diseases (CVDs) in families with victims of sudden cardiac death (SCD). These studies included highly selected cases often from tertiary referral centers and had no control groups. This population-based cohort study, aimed to prospectively describe the occurrence of CVDs in young relatives of young SCD victims, compared to the background population.

Methods: In Denmark, 2000-2006, all cases of SCD aged 1-35 years were identified. We compared the incidence of CVD in young persons related to those victims of SCD, with the background population in a follow-up study using Standardized Incidence Ratios (SIRs) to estimate relative risks.

Results: For 463 victims of SCD we identified a nationwide cohort of 1,591 first- and second-degree relatives aged <35 years, and followed for more than 7,000 person-years in 2000-2008. The observed number of CVDs were 32 and the expected number based on national rates was 8.4, SIR w. 95% confidence interval (CI) 3.79 (2.68-5.36). For cardiomyopathy and ventricular arrhythmia corresponding SIRs were 15.78 (5.12-36.83) and 11.19 (4.37-25.93), respectively. Sex of SCD victim and/or cohort member had no significant effect on SIRs. The table shows SIR for CVD and subgroups, for those with an SCD in a young first-degree relative.

**Clustering of cardiovascular diseases in family members of young sudden cardiac death victims: A Danish nationwide cohort study**

**Purpose:** Descriptive studies have indicated clustering of cardiovascular diseases (CVDs) in families with victims of sudden cardiac death (SCD). These studies included highly selected cases often from tertiary referral centers and had no control groups. This population-based cohort study, aimed to prospectively describe the occurrence of CVDs in young relatives of young SCD victims, compared to the background population.

**Methods:** In Denmark, 2000-2006, all cases of SCD aged 1-35 years were identified. We compared the incidence of CVD in young persons related to those victims of SCD, with the background population in a follow-up study using Standardized Incidence Ratios (SIRs) to estimate relative risks.

**Results:** For 463 victims of SCD we identified a nationwide cohort of 1,591 first- and second-degree relatives aged <35 years, and followed for more than 7,000 person-years in 2000-2008. The observed number of CVDs were 32 and the expected number based on national rates was 8.4, SIR w. 95% confidence interval (CI) 3.79 (2.68-5.36). For cardiomyopathy and ventricular arrhythmia corresponding SIRs were 15.78 (5.12-36.83) and 11.19 (4.37-25.93), respectively. Sex of SCD victim and/or cohort member had no significant effect on SIRs. The table shows SIR for CVD and subgroups, for those with an SCD in a young first-degree relative.

**General information**

**State:** Published

**Organisations:** Statens Serum Institut, Copenhagen University Hospital

**Authors:** Ranthe, M. F. (Ekstern), Winkel, B. G. (Ekstern), Andersen, E. W. (Intern), Risgaard, B. (Ekstern), Wohlfahrt, J. (Ekstern), Bundgaard, H. (Ekstern), Melbye, M. (Ekstern), Tfelt-Hansen, J. (Ekstern), Boyd, H. A. (Ekstern)

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  BFI (2015): BFI-level 2
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  Scopus rating (2014): SJR 6.801 SNIP 5.099 CiteScore 8.48
  BFI (2013): BFI-level 2
  Scopus rating (2013): SJR 7.003 SNIP 5.292 CiteScore 9.33
  ISI indexed (2013): ISI indexed yes
  Web of Science (2013): Indexed yes
  BFI (2012): BFI-level 2
  Scopus rating (2012): SJR 5.909 SNIP 4.487 CiteScore 7.87
  ISI indexed (2012): ISI indexed yes
  Web of Science (2012): Indexed yes
  BFI (2011): BFI-level 2
  Scopus rating (2011): SJR 4.935 SNIP 4.345 CiteScore 6.66
  ISI indexed (2011): ISI indexed yes
  BFI (2010): BFI-level 2
  Scopus rating (2010): SJR 4.657 SNIP 4.088
  Web of Science (2010): Indexed yes
  BFI (2009): BFI-level 2
  Scopus rating (2009): SJR 5.054 SNIP 3.77
  Web of Science (2009): Indexed yes
  BFI (2008): BFI-level 2
  Scopus rating (2008): SJR 4.575 SNIP 3.334
  Scopus rating (2005): SJR 3.742 SNIP 2.722
  Scopus rating (2004): SJR 3.165 SNIP 2.789
  Scopus rating (2003): SJR 3.196 SNIP 2.649
  Web of Science (2003): Indexed yes
  Scopus rating (2002): SJR 2.613 SNIP 2.165
  Scopus rating (2001): SJR 2.224 SNIP 1.95
  Scopus rating (2000): SJR 1.926 SNIP 1.583
  Scopus rating (1999): SJR 1.377 SNIP 1.626
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Denmark Europe Palearctic region, Danish nationwide cohort study, cardiomyopathy Cardiomyopathy, Congestive (MeSH) heart disease, cardiovascular disease Cardiovascular Diseases (MeSH) heart disease, vascular disease epidemiology, sudden cardiac death Death, Sudden, Cardiac (MeSH) heart disease mortality, ventricular arrhythmia Arrhythmia (MeSH) heart disease, Primates Mammalia Vertebrata Chordata Animalia (Animals, Chordates, Humans, Mammals, Primates, Vertebrates) - Hominidae [86215] human common child, preadolescent child, infant, adult, adolescent, 00520, General biology - Symposia, transactions and proceedings, 14506, Cardiovascular system - Heart pathology, 14508, Cardiovascular system - Blood vessel pathology, 25000, Pediatrics, 37054, Public health: epidemiology - Organic diseases and neoplasms, 37056, Public health: epidemiology - Miscellaneous, Human Medicine, Medical Sciences, Population Studies, Cardiovascular Medicine, Epidemiology
[Commentary on] Serum vaccine antibody concentrations in children exposed to perfluorinated compounds

The article presents insights into a study which examined the role of perfluorinated compounds (PFC) in antibody response to childhood vaccinations. The prevalence of perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) which were mentioned in the study was reported by the U.S. Centers for Disease Control and Prevention (CDC). The adverse effect of PFOS and PFOA on cellular immunity that can cause allergy and autoimmune diseases is also mentioned.

General information
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Organisations: Department of Applied Mathematics and Computer Science
Authors: Grandjean, P. (Ekstern), Andersen, E. W. (Intern), Budtz-Jorgenser (Ekstern)
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- Scopus rating (2013): SJR 1.133 SNIP 2.603
- Scopus rating (2012): SJR 0.936 SNIP 1.385
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- Scopus rating (2011): SJR 0.756 SNIP 1.616
- ISI indexed (2011): ISI indexed yes
- Scopus rating (2010): SJR 0.659 SNIP 1.188
- Scopus rating (2009): SJR 0.613 SNIP 1.1
- Scopus rating (2008): SJR 0.541 SNIP 1.247
- Scopus rating (2007): SJR 0.614 SNIP 0.896
- Scopus rating (2006): SJR 0.584 SNIP 0.718
- Scopus rating (2005): SJR 0.451 SNIP 0.823
- Scopus rating (2004): SJR 0.407 SNIP 0.621
- Scopus rating (2003): SJR 0.366 SNIP 0.62
- Scopus rating (2002): SJR 0.373 SNIP 0.567
- Scopus rating (2001): SJR 0.294 SNIP 0.679
- Scopus rating (2000): SJR 0.245 SNIP 0.571
- Scopus rating (1999): SJR 0.168 SNIP 0.212

Original language: English

High concordance of subtypes of childhood acute lymphoblastic leukemia within families: Lessons from sibships with multiple cases of leukemia

Polymorphic genes have been linked to the risk of acute lymphoblastic leukemia (ALL). Surrogate markers for a low burden of early childhood infections are also related to increased risk for developing childhood ALL. It remains uncertain, whether siblings of children with ALL have an increased risk of developing ALL. This international collaboration identified 54 sibships with two (N = 51) or more (N = 3) cases of childhood ALL (ages <18 years). The 5-year event-free survival for 61 patients diagnosed after 1 January 1990 was 0.83 +/- 0.05. Ages at diagnosis (Spearman correlation coefficient, r(S) = 0.41, P = 0.002) were significantly correlated, but not WBCs (r(S) = 0.23, P = 0.11). In 18 sibships with successful karyotyping in both cases, six were concordant for high-hyperdiploidy (N = 3), t(12;21) [ETV6/RUNX1] (N = 1), MLL rearrangement (N = 1) or t(1;19)(q23/p13) (N = 1). Eleven sibships were ALL-subtype concordant, being T-cell ALL (T-
ALL) (N = 5, of a total of six sibships, where the first-born had T-ALL) or B-lineage ALL belonging to the same cytogenetic subset (N = 6), a finding that differs significantly from the expected chance distribution (kappa: 0.58; P < 0.0001). These data indicate strong genetic and/or environmental risk factors for childhood ALL that are restricted to specific ALL subtypes, which must be taken into account, when performing epidemiological studies to reveal etiological factors. Leukemia (2012) 26, 675-681; doi:10.1038/leu.2011.274; published online 18 October 2011

**General information**

State: Published
Organisations: Copenhagen University Hospital, Hopital Robert Debré, Hospital Infantil Manuel de Jesus Rivera, Erasmus Medical College, Instituto Nacional del Cancer, Statens Serum Institut, St Jude Children's Research Hospital, University of Copenhagen
Authors: Schmiegelow, K. (Ekstern), Lausten Thomsen, U. (Ekstern), Baruchel, A. (Ekstern), Pacheco, C. E. (Ekstern), Pieters, R. (Ekstern), Pombo-de-Oliveira, M. S. (Ekstern), Andersen, E. W. (Intern), Rostgaard, K. (Ekstern), Hjalgrim, H. (Ekstern), Pui, C. (Ekstern)
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- Web of Science (2017): Indexed Yes
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- Scopus rating (2016): SJR 4.929 SNIP 2.213 CiteScore 6.47
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 5.148 SNIP 2.276 CiteScore 6.43
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 4.66 SNIP 1.968 CiteScore 5.83
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 4.643 SNIP 1.744 CiteScore 5.78
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 4.273 SNIP 1.796 CiteScore 6.3
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 2
- Scopus rating (2011): SJR 4.595 SNIP 1.756 CiteScore 5.48
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 2
- Scopus rating (2010): SJR 3.878 SNIP 1.668
- BFI (2009): BFI-level 2
- Scopus rating (2009): SJR 3.416 SNIP 1.622
- BFI (2008): BFI-level 2
- Scopus rating (2008): SJR 3.117 SNIP 1.566
- Web of Science (2008): Indexed yes
- Scopus rating (2007): SJR 2.606 SNIP 1.309
- Scopus rating (2006): SJR 2.434 SNIP 1.396
- Scopus rating (2005): SJR 2.117 SNIP 1.296
Serum Vaccine Antibody Concentrations in Children Exposed to Perfluorinated Compounds

Context Perfluorinated compounds (PFCs) have emerged as important food contaminants. They cause immune suppression in a rodent model at serum concentrations similar to those occurring in the US population, but adverse health effects of PFC exposure are poorly understood. Objective To determine whether PFC exposure is associated with antibody response to childhood vaccinations. Design, Setting, and Participants Prospective study of a birth cohort from the National Hospital in the Faroe Islands. A total of 656 consecutive singleton births were recruited during 1999-2001, and 587 participated in follow-up through 2008. Main Outcome Measures Serum antibody concentrations against tetanus and diphtheria toxoids at ages 5 and 7 years. Results Similar to results of prior studies in the United States, the PFCs with the highest serum concentrations were perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA). Among PFCs in maternal pregnancy serum, PFOS showed the strongest negative correlations with antibody concentrations at age 5 years, for which a 2-fold greater concentration of exposure was associated with a difference of -39% (95% CI, -55% to -17%) in the diphtheria antibody concentration. PFCs in the child's serum at age 5 years showed uniformly negative associations with antibody levels, especially at age 7 years, except that the tetanus antibody level following PFOS exposure was not statistically significant. In a structural equation model, a 2-fold greater concentration of major PFCs in child serum was associated with a difference of -49% (95% CI, -67% to -23%) in the overall antibody concentration. A 2-fold increase in PFOS and PFOA concentrations at age 5 years was associated with odds ratios between 2.38 (95% CI, 0.89 to 6.35) and 4.20 (95% CI, 1.54 to 11.44) for falling below a clinically protective level of 0.1 IU/mL for tetanus and diphtheria antibodies at age 7 years. Conclusion Elevated exposures to PFCs were associated with reduced humoral immune response to routine childhood immunizations in children aged 5 and 7 years.

General information
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Organisations: Harvard School of Public Health, University of Southern Denmark, Statens Serum Institut, Faroese Hospital System, Copenhagen University Hospital, University of Copenhagen
Authors: Grandjean, P. (Ekstern), Andersen, E. W. (Intern), Budtz-Jørgensen, E. (Ekstern), Nielsen, F. (Ekstern), Mølbak, K. (Ekstern), Weihe, P. (Ekstern), Heilmann, C. (Ekstern)
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Web of Science (2016): Indexed yes
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BFI (2014): BFI-level 2
Scopus rating (2014): SJR 6.194 SNIP 9.726 CiteScore 6.16
Trimethoprim use in early pregnancy and the risk of miscarriage: A register-based nationwide cohort study

The antibiotic trimethoprim acts as a folate antagonist. Since trophoblasts are very sensitive to drugs that interfere with the folic acid cycle and thereby inhibit DNA synthesis, use of trimethoprim during the first trimester could be associated with miscarriage. A nationwide cohort study including all women in Denmark with a registered pregnancy between 1997 and 2005 was conducted. We used nationwide registers to identify all women giving birth, having a record of miscarriage or induced abortion. Data on exposure to trimethoprim were obtained from the National Prescription Register. Cox proportional hazard regression analysis with exposure to trimethoprim as a time-dependent variable was used to estimate the risk of miscarriage. The adjusted hazard ratio of having a miscarriage after exposure to trimethoprim in the first trimester compared to non-exposure was 2.04 (95% confidence interval 1.43–2.91). Our results indicate that trimethoprim exposure in the first trimester is associated with a doubling of the hazard of miscarriage.

General information

State: Published
Organisations: Mental Health Centre Amager, Copenhagen University Hospital, University of Copenhagen
Authors: Andersen, J. (Ekstern), Petersen, M. (Ekstern), Jimenez-Solem, E. (Ekstern), Broedbaek, K. (Ekstern), Andersen, E. W. (Intern), Andersen, N. (Ekstern), Afzal, S. (Ekstern), Torp-Pedersen, C. (Ekstern), Keiding, N. (Ekstern), Poulsen, H. (Ekstern)
Association Between Urban Life-Years and Cardiometabolic Risk: The Indian Migration Study

General information
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Organisations: Technical University of Denmark
Authors: Kinra, S. (Ekstern), Andersen, E. W. (Intern), Ben-Shlomo, Y. (Ekstern), Bowen, L. (Ekstern), Lyngdoh, T. (Ekstern), Prabhakaran, D. (Ekstern), Srinath Reddy, K. (Ekstern), Ramakrishnan, L. (Ekstern), Bharathi, A. (Ekstern), Vaz, M. (Ekstern), Kurpad, A. (Ekstern), Smith, G. D. (Ekstern), Ebrahim, S. (Ekstern)
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Scopus rating (2014): SJR 2.975 SNIP 1.948 CiteScore 4.12
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Scopus rating (2011): SJR 3.105 SNIP 2.237 CiteScore 4.79
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
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Scopus rating (2010): SJR 2.977 SNIP 2.077
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.014 SNIP 2.171
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 2.93 SNIP 2.036
Children with acute lymphoblastic leukemia (ALL) receive high doses of glucocorticosteroid as part of their treatment. This may lead to suppression of the hypothalamic-pituitary-adrenal axis, acute adrenal insufficiency, and ultimately to life-threatening conditions. This study explores the adrenal function in 96 children with ALL treated according to common protocols. After cessation of induction glucocorticosteroid therapy, they received hydrocortisone substitution therapy (10 mg/m\(^2\)/24 h) until an adrenocorticotropic hormone test (250 μg tetracosatide) showed a sufficient adrenal response [plasma (\(p\))-cortisol >= 500 nM]. At the first adrenocorticotropic hormone test, 67% of the patients had adrenal insufficiency. When including these patients in a multivariate model, not adjusting for risk factors, the mean elapsed time between end of induction therapy and adrenal sufficiency was 8.5 months (95% confidence interval: 6.3;10.7). Low 0-minute \(p\)-cortisol (P = 0.02) and low rise in \(p\)-cortisol (P < 0.0001) at first test caused a longer time of adrenal insufficiency. In addition, patients with B-cell precursor leukemia reached adrenal sufficiency later than those with T-cell leukemia (P = 0.067). As adrenal insufficiency is frequent in children treated for ALL and as they often experience infections and other stressors, the adrenal response should be determined and hydrocortisone substitution therapy should be considered during such episodes in patients with adrenal insufficiency.
Familial risk of venous thromboembolism: A nationwide cohort study

Background: Venous thromboembolism has genetic determinants, but population-based data on familial risks are limited.

Objectives: To examine the familial risk of venous thromboembolism. Methods: We undertook a nationwide study of a cohort of patients with deep venous thrombosis or pulmonary embolism born after 1952. We used the Danish National Registry of Patients covering all Danish hospitals, for the years 1977 through 2009, to identify index cases of venous thromboembolism, and assessed the incidence among their siblings. We compared standardized incidence ratios (SIRs) of the observed and expected number of venous thromboembolism cases among siblings, using population-specific, gender-specific and age-specific incidence rates. Results: We identified 30 179 siblings of 19 599 cases of venous thromboembolism. The incidence among siblings was 2.2 cases per 1000 person-years, representing a relative risk of 3.08 (95% confidence interval [CI] 2.80-3.39) as compared with the general population. The risk was higher for both men (SIR 3.36, 95% CI 2.96-3.82) and women (SIR 2.81, 95% CI 2.45-3.23). The risk was similar among siblings of index cases with venous thrombosis and those of index cases with pulmonary embolism. Conclusion: Venous thromboembolism has a strong familial component.

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Authors: Sørensen, H. T. (Ekstern), Riis, A. H. (Ekstern), Diaz, L. J. (Ekstern), Andersen, E. W. (Intern), Baron, J. A. (Ekstern), Andersen, P. K. (Ekstern)
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Germ cell numbers in human embryonic and fetal gonads during the first two trimesters of pregnancy: Analysis of six published studies

BACKGROUND: The number of germ cells in human embryonic and fetal ovaries in relation to age is currently based on volumetric estimations from one study including a total of 12 ovaries. Six recent publications present stereological estimations of the number of germ cells in ovaries and testes for the first two trimesters. METHODS: Germ cell numbers from 103 human first and second trimester gonads aged 37–133 days post-conception (p.c.), obtained after legal termination of pregnancy, were collected from six independent studies that all used similar validated stereological methods for estimating germ cell numbers as well as somatic cell numbers. RESULTS: Statistically, the six studies estimated similar number of germ cells (P > 0.05) and no interaction between the studies and age was found (P > 0.05), indicating that the increase in cell numbers in relation to age was of comparable magnitude in each study. The number of germ cells increased from a mean of 7200 to 4 933 000 in fetal ovaries and from 3700 to 1 417 000 in fetal testes, from week 5 to week 19 p.c. A higher rate of increase was found for female germ cells as compared with males (P = 0.004). During the same period, the number of somatic cells increased from a mean of 158 000 to 1 017 000 in ovaries and from 154 000 to 2 035 000 in testes, respectively. CONCLUSIONS: By the use of validated stereological methods, this study provides more accurate and improved information on human germ and somatic cell numbers in ovaries and testes during the first two trimesters of pregnancy.
Individualized toxicity-titiated 6-mercaptopurine increments during high-dose methotrexate consolidation treatment of lower risk childhood acute lymphoblastic leukaemia: A Nordic Society of Paediatric Haematology and Oncology (NOPHO) pilot study

This study explored the feasibility and toxicity of individualized toxicity-titiated 6-mercaptopurine (6MP) dose increments during post-remission treatment with High-dose methotrexate (HDM) (5000 mg/m², ×3) in 38 patients with Childhood (ALL). Patients were increased in steps of 25 mg 6MP/m² per day if they did not develop myelotoxicity within 2 weeks after HDM. 6MP could be increased in 31 patients (81%). Toxicity was acceptable and did not differ significantly between groups. Patients receiving 75 mg/m² per day had significantly shorter duration of treatment interruptions of 6MP than the remaining patients (P = 0.03). This study shows individualized toxicity-titiated 6MP dosing during consolidation is feasible without increased risk of toxicity.

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In human granulosa cells from small antral follicles, androgen receptor mRNA and androgen levels in follicular fluid correlate with FSH receptor mRNA

Human small antral follicles (diameter 3–9 mm) were obtained from ovaries surgically removed for fertility preservation. From the individual aspirated follicles, granulosa cells and the corresponding follicular fluid were isolated in 64 follicles, of which 55 were available for mRNA analysis (24 women). Expressions of androgen receptor (AR) mRNA levels in granulosa cells, and of androstenedione and testosterone in follicular fluid, were correlated to the expression of the FSH receptor (FSHR), LH receptor (LHR), CYP19 and anti-Müllerian Hormone-receptor II (AMHRII) mRNA in the granulosa cells and to the follicular fluid concentrations of AMH, inhibin-B, progesterone and estradiol. AR mRNA expression in granulosa cells and the follicular fluid content of androgens both showed a highly significant positive association with the expression of FSHR mRNA in granulosa cells. AR mRNA expression also correlated significantly with the expression of AMHRII, but did not correlate with any of the hormones in the follicular fluid. These data demonstrate an intimate association between AR expression in immature granulosa cells, and the expression of FSHR in normal small human antral follicles and between the follicular fluid levels of androgen and FSHR expression. This suggests that follicular sensitivity towards FSH stimulation may be augmented by stimulation of androgens via the AR.
Late maternal menopause is associated with stable anti-Müllerian hormone levels and antral follicle count in daughters during reproductive age

Introduction: Maternal age at menopause is hypothesized to influence daughters’ ovarian reserve. We explored this hypothesis by assessing the ovarian reserve through anti-Müllerian hormone levels (AMH) and antral follicle count (AFC) in healthy women of reproductive age.

Material and Methods: A prospective cohort study of 863 healthy female healthcare workers aged 20–40 years employed at Copenhagen University Hospital. We analysed a subpopulation of women (n = 528) whose mother’s age at natural menopause was known. Data were obtained on menstrual cycle, smoking habits including prenatal smoking exposure, reproductive history, and mother’s age at menopause. On menstrual cycle Day 2–6 plasma hormone levels were assessed and a transvaginal sonography was performed measuring AFC. Women taken a combined oral contraceptive were studied on menstrual cycle Day 2–6 (during withdrawal bleeding). Pregnant women (n = 67) were excluded. Multiple linear regression analyses were performed to investigate the effect of participants’ age and their mother’s age at menopause on AMH levels and AFC with adjustment for use of oral contraceptives, follicle-stimulating hormone levels, participants’ smoking habits and mothers’ smoking habits during pregnancy. All mean values are reported as adjusted with 95%CI.

Results: Participants were stratified into three age groups: 20.0–29.9 years, 30.0–34.9 years and 35.0–39.9 years. Age at maternal menopause was normally distributed (mean age 50.2 years). Based on the age at maternal menopause three groups were defined according to the 10th and the 90th percentile: early maternal menopause (≤ 45 years) (n = 68), normal maternal menopause (46–54 years) (n = 383) and late maternal menopause ( ≥ 55 years) (n = 77). In the group with normal maternal menopause the AMH levels and AFC differed significantly according to participants’ age. Participants aged 20.0–29.9 years, 30.0–34.9 years, and 35.0–39.9 years had adjusted mean AMH levels of 16.6 pmol/L [95%CI 13.5–20.6], 12.4 [10.2–15.1], and 8.5 [7.0–10.5], respectively (p < 0.001) and adjusted mean AFC values of 17.1 [95%CI 14.5–20.2], 14.7 [12.6–17.1], and 10.3 [8.7–12.1], respectively (p < 0.001). In the group with early maternal menopause a significant decrease in AMH level (p < 0.001) and AFC (p = 0.002) was shown when comparing participants aged
20.0–29.9 years with participants aged 30.0–34.9 years. The corresponding adjusted mean AMH levels were 18.6 pmol/L [95%CI 12.4–27.9], 9.2 [6.6–12.7], and 6.9 [5.0–9.4], respectively and the adjusted mean AFC values were 17.7 [95%CI 12.9–24.3], 11.4 [8.8–14.7], and 9.9 [7.7–12.7], respectively. In the group with late maternal menopause no significant differences were seen in AMH levels (p = 0.22) and AFC (p = 0.76) across the three age groups. The corresponding adjusted mean AMH levels were 14.4 pmol/L [95%CI 9.2–22.5], 12.2 [9.1–16.3], and 15.4 [11.1–21.4], respectively, and the adjusted mean AFC values were 14.3 [95%CI 10.0–20.2], 14.4 [11.5–18.2], and 15.1 [11.7–19.5], respectively. Crude and adjusted analyses showed consistent effects of age at maternal menopause on AMH and AFC levels in the daughters. Participants' smoking habits and mothers' smoking habits during pregnancy did not influence AMH levels or AFC.

Conclusions: These cross-sectional data showed that women whose mothers entered menopause at a normal age had the expected decline in ovarian reserve with increasing age. However, women whose mothers entered menopause before the age of 45 years had an early, marked decrease in ovarian reserve. In women whose mothers entered menopause after the age of 55 years, the plasma levels of AMH and the antral follicle count remained stable at least up to 40 years of age, indicating that the ovarian follicular depletion may be postponed in these women. Our data support the hypothesis that hereditary factors have a major impact on the ovarian follicular depletion rate.
Paternal smoking habits affect the reproductive life span of daughters

The present study assessed whether the smoking habits of fathers around the time of conception affected the period in which daughters experienced menstrual cycles (i.e., the reproductive life span). The study revealed that the smoking habits of the father shortened the daughters’ reproductive life span compared with daughters whose fathers did not smoke.

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Pneumocystis jiroveci pneumonia prophylaxis during maintenance therapy influences methotrexate/6-mercaptopurine dosing but not event-free survival for childhood acute lymphoblastic leukemia

Trimethoprim-sulfamethoxazole (TMP/SMX) is used in children with acute lymphoblastic leukemia (ALL) to prevent Pneumocystis pneumonia (PCP). We explored to which extent TMP/SMX influenced methotrexate (MTX)/6-mercaptopurine (6MP) dosage, myelosuppression, and event-free survival (EFS) during maintenance therapy. Of 447 study patients treated by the NOPHO ALL92 protocol, 120 patients received TMP/SMX continuously for 2–7 d/wk (TMP/SMX2–7) and 287 patients never received TMP/SMX (TMP/SMXnever). Ten patients (all TMP/SMXnever) developed PCP, eight of which occurred within 7 months from the start of maintenance therapy. The TMP/SMX2–7 group received lower oral 6MP doses than TMP/SMXnever patients (50.6 vs. 63.9 mg/m2/d; P < 0.001) but had lower absolute neutrophil counts (ANC) (median 1.7 vs. 2.0 · 109/L; P < 0.001). In Cox multivariate analysis, higher ANC levels (P = 0.04) and male gender (P = 0.06) were related to reduced EFS. ANC had no effect on EFS among TMP/SMX2–7 patients (P = 0.40) but did for TMP/SMXnever patients (P = 0.02). The difference in the effect on EFS between TMP/SMX2–7 and TMP/SMXnever patients was not significant (P = 0.48). EFS did not differ between TMP/SMX2–7 and TMP/SMXnever patients (0.83 vs. 0.83; P = 0.82). These results suggest that TMP/SMX is effective in preventing PCP and may have an antileukemic effect. TMP/SMX should be given the entire duration of maintenance therapy.
Background: Visceral leishmaniasis is the world's second largest vector-borne parasitic killer and a neglected tropical disease, prevalent in poor communities. Long-lasting insecticidal nets (LNs) are a low cost proven vector intervention method for malaria control; however, their effectiveness against visceral leishmaniasis (VL) is unknown. This study quantified the effect of LNs on exposure to the sand fly vector of VL in India and Nepal during a two year community intervention trial.

Methods: As part of a paired-cluster randomized controlled clinical trial in VL-endemic regions of India and Nepal we tested the effect of LNs on sand fly biting by measuring the antibody response of subjects to the saliva of Leishmania donovani vector Phlebotomus argentipes and the sympatric (non-vector) Phlebotomus papatasi. Fifteen to 20
individuals above 15 years of age from 26 VL endemic clusters were asked to provide a blood sample at baseline, 12 and 24 months post-intervention. Results: A total of 305 individuals were included in the study, 68 participants provided two blood samples and 237 gave three samples. A random effect linear regression model showed that cluster-wide distribution of LNs reduced exposure to P. argentipes by 12% at 12 months (effect 0.88; 95% CI 0.83-0.94) and 9% at 24 months (effect 0.91; 95% CI 0.80-1.02) in the intervention group compared to control adjusting for baseline values and pair. Similar results were obtained for P. papatasi. Conclusions: This trial provides evidence that LNs have a limited effect on sand fly exposure in VL endemic communities in India and Nepal and supports the use of sand fly saliva antibodies as a marker to evaluate vector control interventions.
Cigarette smoking during early pregnancy reduces the number of embryonic germ and somatic cells

BACKGROUND: Cigarette smoking during pregnancy is associated with negative reproductive consequences for male fetuses in adult life such as reduced testicular volume and sperm concentration. The present study evaluates the number of germ and somatic cells present in human embryonic first-trimester gonads in relation to maternal smoking.

METHODS: The study includes 24 human first-trimester testes, aged 37–68 days post-conception, obtained from women undergoing legal termination of pregnancy. A questionnaire was used to obtain information about smoking and drinking habits during pregnancy. Validated stereological methods were used to estimate gonadal cell numbers in histological sections. Results were also evaluated in the context of previously published data on ovaries from our laboratory.

RESULTS: A significant reduction in the number of germ cells by 55% [95% confidence interval (CI) 74–21% reduction, P = 0.004] and somatic cells by 37% (95% CI 59–3%, P = 0.023) was observed in testes prenatally exposed to maternal cigarette smoking, compared with unexposed. The effect of maternal smoking was dose-dependent being higher in the heavy smokers and remained consistent after adjusting for possible confounders such as alcohol and coffee consumption (P = 0.002). The number of germ cells in embryonic gonads, irrespective of gender, was also significantly reduced by 41% (95% CI 58–19%, P = 0.001) in exposed versus non-exposed embryonic gonads.

CONCLUSIONS: Prenatal exposure to maternal cigarette smoke reduces the number of germ and somatic cells in embryonic male and female gonads. This effect may have long-term consequences on the future fertility of exposed offspring. These findings may provide one potential cause of the reduced fertility observed during recent years.
Epidemiology of Leishmania donovani infection in high-transmission foci in Nepal

Objective

Nepal reports a visceral leishmaniasis (VL) incidence of 5 per 10 000 per year on the basis of notification by health facilities, but little community-based epidemiological information exists. We report data on prevalence rates of Leishmania donovani infection in ten communities in East Nepal.

Methods

Ten clusters with highest VL incidence rates were purposefully selected in Nepal. All households were mapped and socio-demographic data and data on past VL incidence were collected. An exhaustive serological survey was performed of individuals aged > 2 years, by collecting finger prick blood on filter paper in November-December 2006. The samples were tested by direct agglutination, and a titre >= 1:1600 was taken as marker of infection. A generalized estimating equation (GEE) model was used to assess risk factors for Direct Agglutination Test (DAT) positivity taking into account the clustering at household and village level.

Results

The sero-survey (n = 5397) showed an infection prevalence rate of 9%, (range 5-15% per cluster) with higher prevalence in men (9.9%) than in women (8.3%) (P = 0.049). Male gender, increasing age and poverty were significant risk factors in the final GEE model.

Conclusion

Leishmania infection rate in high-transmission areas in Nepal is associated with gender, age and socio-economic status.
OBJECTIVE: To test the effectiveness of large scale distribution of longlasting nets treated with insecticide in reducing the incidence of visceral leishmaniasis in India and Nepal. Design Paired cluster randomised controlled trial designed to detect a 50% reduction in incidence of Leishmania donovani infection. Setting Villages in Muzaffarpur district in India and Saptari, Sunsari, and Morang districts in Nepal. Participants 13 intervention and 13 control clusters. 12 691 people were included in the analysis of the main outcome (infection), and 19 810 were enrolled for the secondary (disease) end point.

Intervention Longlasting insecticidal nets (treated with deltamethrin) were distributed in the intervention clusters in December 2006. MAIN OUTCOME MEASURES: Infection was determined by direct agglutination test at 12 and 24 months after the intervention in those who had negative results (titre
The Effect of Rural-to-Urban Migration on Obesity and Diabetes in India: A Cross-Sectional Study

Background: Migration from rural areas of India contributes to urbanisation and may increase the risk of obesity and diabetes. We tested the hypotheses that rural-to-urban migrants have a higher prevalence of obesity and diabetes than rural nonmigrants, that migrants would have an intermediate prevalence of obesity and diabetes compared with life-long urban and rural dwellers, and that longer time since migration would be associated with a higher prevalence of obesity and diabetes.

Methods and Findings: The place of origin of people working in factories in north, central, and south India was identified. Migrants of rural origin, their rural dwelling sibs, and those of urban origin together with their urban dwelling sibs were assessed by interview, examination, and fasting blood samples. Obesity, diabetes, and other cardiovascular risk factors were compared. A total of 6,510 participants (42% women) were recruited. Among urban, migrant, and rural men the age- and factory-adjusted percentages classified as obese (body mass index [BMI] >25 kg/m²) were 41.9% (95% confidence interval [CI] 39.1–44.7), 37.8% (95% CI 35.0–40.6), and 19.0% (95% CI 17.0–21.0), respectively, and as diabetic were 13.5% (95% CI 11.6–15.4), 14.3% (95% CI 12.2–16.4), and 6.2% (95% CI 5.0–7.4), respectively. Findings for women showed similar patterns. Rural men had lower blood pressure, lipids, and fasting blood glucose than urban and migrant men, whereas no differences were seen in women. Among migrant men, but not women, there was weak evidence for a lower prevalence of both diabetes and obesity among more recent (≤10 y) migrants.

Conclusions: Migration into urban areas is associated with increases in obesity, which drive other risk factor changes. Migrants have adopted modes of life that put them at similar risk to the urban population.
The epidemiology of Leishmania donovani infection in high transmission foci in India

Objective

Visceral Leishmaniasis (VL) is highly prevalent in Bihar, India. India and its neighbours aim at eliminating VL, but several knowledge gaps in the epidemiology of VL may hamper that effort. The prevalence of asymptomatic infections with Leishmania donovani and their role in transmission dynamics are not well understood. We report data from a sero-survey in Bihar.

Methods

Demographic and immunological surveys were carried out in July and November 2006, respectively in 16 highly VL
endemic foci in Muzaffarpur district in Bihar. Household and individual information was gathered and capillary blood samples were collected on filter papers. Direct agglutination test (DAT) was used to determine infected individuals (cut-off titre 1:1600). DAT results were tabulated against individual and household variables. A multivariate generalized estimating equation (GEE) model was used to study the prevalence of serologically positive individuals taking into account the clustering at household and cluster levels.

Results

Of study subjects 18% were DAT positive, and this proportion increased with age. Women had a significantly lower prevalence than men > 14 years old. Owning domestic animals (cows, buffaloes or goats) was associated with a higher risk of being DAT positive [OR 1.16 (95% CI 1.01-1.32)], but socio-economic status was not.

Conclusions

Prevalence of leishmanial antibodies was high in these communities, but variable. Demographic factors (i.e. marriage) may explain the lower DAT positivity in women > 14 years of age. Within these homogeneously poor communities, socio-economic status was not linked to L. donovani infection risk at the individual level, but ownership of domestic animals was.
Escitalopram in obsessive-compulsive disorder: Response of symptom dimensions to pharmacotherapy

Introduction: There is a substantial body of evidence that obsessive-compulsive disorder (OCD) symptoms can be grouped into a series of discrete dimensions, and some evidence that not all OCD symptom dimensions respond equally well to pharmacologic or psychotherapeutic intervention. The response of OCD symptom dimensions to 12 weeks of treatment with escitalopram or placebo was investigated. Methods: Data from a randomized, double-blind, placebo-controlled study of escitalopram in 466 adults with OCD were analyzed. Exploratory factor analysis of individual items of the Yale-Brown Obsessive-Compulsive Scale checklist was performed and subscale scores based on the extracted factors were determined. Analyses of covariance were undertaken to determine whether inclusion of each subscale score in these models impacted on the efficacy of escitalopram versus placebo. Results: Exploratory factor analysis of individual Yale-Brown Obsessive-Compulsive Scale items yielded 5 factors (contamination/cleaning, harm/checking, hoarding/symmetry, religious/sexual, and somatic/hypochondriacal). Analyses of covariance including all the subscales demonstrated that escitalopram was more effective than placebo. There was a significant interaction for the hoarding/symmetry factor, which was associated with a poor treatment response. Conclusion: Escitalopram shows good efficacy across the range of OCD symptom dimensions. Nevertheless, hoarding/symmetry was associated with a poorer treatment response. Hoarding/symmetry may be particularly characteristic of an early-onset group of OCD patients, with the involvement of neurotransmitters other than serotonin. Further work is needed to delineate fully the subtypes of OCD, and their correlates with underlying psychobiology and treatment responsibility.

General information
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Escitalopram in obsessive–compulsive disorder: a randomized, placebo-controlled, paroxetine-referenced, fixed-dose, 24-week study

Objective: A randomized, placebo-controlled fixed-dose trial was undertaken to determine the efficacy and tolerability of escitalopram in obsessive–compulsive disorder (OCD), using paroxetine as the active reference. Research design and methods: A total of 466 adults with OCD from specialized clinical centres, psychiatric hospital departments, psychiatric practices, or general practice were randomized to one of four treatment groups: escitalopram 10 mg/day (n = 116), escitalopram 20 mg/day (n = 116), paroxetine 40 mg/day (n = 119), or placebo (n = 115) for 24 weeks. The primary efficacy endpoint was the mean change in the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) total score from baseline to week 12. Secondary efficacy endpoints included remission (defined as Y-BOCS total score ≤10), NIMH-OCS, and CGI-S and CGI-I scores at weeks 12 and 24. Tolerability was based on the incidence of adverse events, and on changes in vital signs (blood pressure and pulse). Main outcome measures; Results: Escitalopram 20 mg/day was superior to placebo on the primary and all secondary outcome endpoints, including remission. Escitalopram 10 mg/day and paroxetine 40 mg/day were also effective on the primary scale as well as some other outcome measures. In the escitalopram 20 mg/day group, the improvement in Y-BOCS total score was significantly better than in the placebo group as early as week 6. The most common AEs in the active treatment groups were nausea (19–27%), headache (17–22%), and fatigue (12–19%). More paroxetine-treated patients withdrew due to adverse events than escitalopram- or placebo-treated patients. Conclusion: Given that escitalopram 20 mg/day was associated with an earlier onset, higher response and remission rates, improved functioning, and better tolerability than the reference drug, escitalopram deserves to be considered as one of the first-line agents in the pharmacotherapy of OCD for longer-term treatment periods.

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Escitalopram versus paroxetine for social anxiety disorder: An analysis of efficacy for different symptom dimensions

Background: A previous factor analysis of pooled data demonstrated that the Liebowitz Social Anxiety Scale (LSAS) can be divided into six subscales. This paper examines data from a fixed-dose trial of escitalopram versus paroxetine, in order to determine the differential effects of these agents on symptom dimensions in social anxiety disorder (SAD).

Methods: Data from a 24-week randomised, placebo-controlled, comparative study of fixed doses of escitalopram (5 mg, 10 mg, 20 mg) versus paroxetine (20 mg) in SAD were examined. The six factors identified in a previous factor analysis of baseline
data from escitalopram studies on the primary efficacy scale, the LSAS, were used to compute subscale scores. These were analysed using analysis of covariance (ANCOVA), and standardised effect sizes were calculated. Results: The combined escitalopram data and the paroxetine data both demonstrated significant superiority to placebo on each of the 6 LSAS factors at week 24 (OC analysis). Escitalopram doses of 5 mg, 10 mg, and 20 mg were generally more effective than placebo for each of the factors. Escitalopram 20 mg was significantly more effective than paroxetine 20 mg on 5 of the 6 symptom dimensions. Conclusion: Factor analysis of the LSAS allows for useful secondary analyses that support and extend the primary efficacy analysis of this instrument. The analysis here indicates that different escitalopram doses are effective across the various symptom dimensions of SAD. D 2005 Elsevier B.V. and ECNP. All rights reserved.

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Scopus rating (2010): SJR 1.691 SNIP 1.086
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.295 SNIP 0.975
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.481 SNIP 1.212
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.602 SNIP 1.385
Scopus rating (2006): SJR 1.367 SNIP 1.179
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.994 SNIP 1.02
Scopus rating (2004): SJR 1.001 SNIP 0.97
Scopus rating (2003): SJR 0.908 SNIP 0.779
Scopus rating (2002): SJR 0.84 SNIP 0.76
Two-Stage Estimation in Copula Models Used in Family Studies

In this paper, register-based family studies provide the motivation for studying a two-stage estimation procedure in copula models for multivariate failure time data. The asymptotic properties of the estimators in both parametric and semi-parametric models are derived, generalising the approach by Shih and Louis (Biometrics vol. 51, pp. 1384–1399, 1995b) and Glidden (Lifetime Data Analysis vol. 6, pp. 141–156, 2000). Because register-based family studies often involve very large cohorts, a method for analysing a sampled cohort is also derived together with the asymptotic properties of the estimators. The proposed methods are studied in simulations and the estimators are found to be highly efficient. Finally, the methods are applied to a study of mortality in twins.

General information
State: Published
Organisations: Technical University of Denmark
Authors: Andersen, E. W. (Intern)
Number of pages: 18
Pages: 333-350
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Lifetime Data Analysis
Volume: 11
Issue number: 3
ISSN (Print): 1380-7870
Ratings:
- BFI (2018): BFI-level 2
- BFI (2017): BFI-level 2
- Web of Science (2017): Indexed Yes
- BFI (2016): BFI-level 2
- Scopus rating (2016): SJR 0.541 SNIP 0.58 CiteScore 0.58
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 0.729 SNIP 0.823 CiteScore 0.59
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 0.943 SNIP 0.962 CiteScore 0.6
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 0.852 SNIP 0.74 CiteScore 0.64
- ISI indexed (2013): ISI indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 1.094 SNIP 0.986 CiteScore 0.91
- ISI indexed (2012): ISI indexed yes
- BFI (2011): BFI-level 2
- Scopus rating (2011): SJR 0.974 SNIP 1.027 CiteScore 1.13
- ISI indexed (2011): ISI indexed yes
- BFI (2010): BFI-level 2
- Scopus rating (2010): SJR 0.738 SNIP 0.524
- BFI (2009): BFI-level 1
- Scopus rating (2009): SJR 0.726 SNIP 0.754
- BFI (2008): BFI-level 1
Composite likelihood and two-stage estimation in family studies

In this paper register based family studies provide the motivation for linking a two-stage estimation procedure in copula models for multivariate failure time data with a composite likelihood approach. The asymptotic properties of the estimators in both parametric and semi-parametric models are derived, combining the approaches of Parner (2001) and Andersen (2003). The method is mainly studied when the families consist of groups of exchangeable members (e.g. siblings) or members at different levels (e.g. parents and children). The advantages of the proposed method are especially clear in this last case where very flexible modeling is possible. The suggested method is also studied in simulations and found to be efficient compared to maximum likelihood. Finally, the suggested method is applied to a family study of deep venous thromboembolism where it is seen that the association between ages at onset is larger for siblings than for parents or for parents and siblings.

General information
State: Published
Organisations: Technical University of Denmark
Authors: Andersen, E. W. (Intern)
Number of pages: 16
Pages: 15-30
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Biostatistics
Volume: 5
Issue number: 1
ISSN (Print): 1465-4644
Ratings:
BFI (2018): BFI-level 2
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): SJR 1.789 SNIP 1.342 CiteScore 1.89
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.969 SNIP 1.335 CiteScore 2.17
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.577 SNIP 1.486 CiteScore 2.44
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.418 SNIP 1.2 CiteScore 2.42
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 2
Escitalopram in the Treatment of Social Anxiety Disorder: Analysis of Efficacy for Different Clinical Subgroups and Symptom Dimensions

Escitalopram has demonstrated efficacy for the acute treatment of social anxiety disorder (SAD) in two placebo-controlled trials and for long-term treatment in a relapse-prevention study. Social anxiety disorder is a heterogeneous disorder. This study questions whether this new selective serotonin reuptake inhibitor is effective across different subgroups of patients. Data from two randomised, placebo-controlled, 12-week escitalopram SAD trials were pooled. General linear models were used to determine the efficacy of escitalopram in different patient subgroups. Furthermore, a factor analysis of the primary efficacy scale, the Liebowitz Social Anxiety Scale (LSAS), was undertaken, and a determination made of whether treatment effects were similar for the different symptom dimensions. Escitalopram was effective in both younger and older patients, in male and female patients, and in patients with more and less severe social anxiety symptoms. The LSAS factor analysis showed six factors, which were differentially associated with different areas of disability. Escitalopram was significantly superior to placebo for all six symptom dimensions. The treatment effects of escitalopram were independent of gender, symptom severity and chronicity, and comorbid depressive symptoms. A six-factor model of social anxiety symptoms is supported by the distinctive association between these symptom dimensions and different areas of disability, but did not predict differential response to escitalopram. Depression and Anxiety 20:175–181, 2004. & 2005 Wiley-Liss, Inc.

General information
State: Published
Organisations: University of Stellenbosch, University of Vienna, Technical University of Denmark, H. Lundbeck A/S, University of London
Authors: Stein, D. J. (Ekstern), Kasper, S. (Ekstern), Andersen, E. W. (Intern), Nil, R. (Ekstern), Lader, M. (Ekstern)
Number of pages: 7
Pages: 175-181
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Depression and Anxiety (Hoboken)
Volume: 20
Issue number: 4
ISSN (Print): 1091-4269
Ratings:
BFI (2018): BFI-level 2
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
It is unclear if depression or depressive symptoms have an effect on mortality in breast cancer patients. In this population-based, nationwide, retrospective cohort study in Denmark, depression was defined as affective or anxiety disorders that necessitated psychiatric hospital admission. All the affective and anxiety disorders were divided and categorized into five ordinal diagnostic groups. Early-stage (N10,382) and late-stage (N10,211) breast cancer patients were analyzed separately with Cox's regression adjusted for well-documented somatic prognostic variables. The authors used survival analysis of data from three central registers and found that breast cancer patients with depression had a modestly but significantly higher risk of mortality depending on stage of breast cancer and time of depression. The same result was found after censoring unnatural causes of death such as accident, suicide, or homicide.

**Depression as a Prognostic Factor for Breast Cancer Mortality**

It is unclear if depression or depressive symptoms have an effect on mortality in breast cancer patients. In this population-based, nationwide, retrospective cohort study in Denmark, depression was defined as affective or anxiety disorders that necessitated psychiatric hospital admission. All the affective and anxiety disorders were divided and categorized into five ordinal diagnostic groups. Early-stage (N10,382) and late-stage (N10,211) breast cancer patients were analyzed separately with Cox's regression adjusted for well-documented somatic prognostic variables. The authors used survival analysis of data from three central registers and found that breast cancer patients with depression had a modestly but significantly higher risk of mortality depending on stage of breast cancer and time of depression. The same result was found after censoring unnatural causes of death such as accident, suicide, or homicide.

**General information**

State: Published
Organisations: Technical University of Denmark
Number of pages: 7
Pages: 24-30
Publication date: 2003
Adjustment for misclassification in studies of familial aggregation of disease using routine register data

This paper discusses the misclassification that occurs when relying solely on routine register data in family studies of disease clustering. A register study of familial aggregation of schizophrenia is used as an example. The familial aggregation is studied using a regression model for the disease in the child including the disease status of the parents as a risk factor. If all the information is found in the routine registers then the disease status of the parents is only known from the time when the register started and if this information is used unquestioningly the parents who have had the disease before this time are misclassified as disease-free. Two methods are presented to adjust for this misclassification: regression calibration and an EM-type algorithm. These methods are used in the schizophrenia example where the large effect of having a schizophrenic mother hardly shows any signs of bias due to misclassification. The methods are also studied in
simulations showing that the misclassification problem increases with the disease frequency. Copyright © 2002 John Wiley & Sons, Ltd.

**General information**
- State: Published
- Organisations: Technical University of Denmark, Statens Serum Institut
- Authors: Andersen, E. W. (Intern), Andersen, P. K. (Ekstern)
- Number of pages: 12
- Pages: 3596-3607
- Publication date: 2002
- Main Research Area: Technical/natural sciences

**Publication information**
- Journal: Statistics in Medicine
- Volume: 21
- Issue number: 23
- ISSN (Print): 0277-6715
- Ratings:
  - BFI (2018): BFI-level 2
  - BFI (2017): BFI-level 2
  - Web of Science (2017): Indexed Yes
  - BFI (2016): BFI-level 2
  - Scopus rating (2016): CiteScore 1.94 SJR 2.022 SNIP 1.419
  - BFI (2015): BFI-level 2
  - Scopus rating (2015): SJR 2.006 SNIP 1.184 CiteScore 1.64
  - BFI (2014): BFI-level 2
  - Scopus rating (2014): SJR 2.443 SNIP 1.584 CiteScore 2.07
  - BFI (2013): BFI-level 2
  - Scopus rating (2013): SJR 2.166 SNIP 1.44 CiteScore 1.93
  - ISI indexed (2013): ISI indexed yes
  - BFI (2012): BFI-level 2
  - Scopus rating (2012): SJR 1.951 SNIP 1.615 CiteScore 2
  - ISI indexed (2012): ISI indexed yes
  - BFI (2011): BFI-level 1
  - Scopus rating (2011): SJR 2.23 SNIP 1.543 CiteScore 2.13
  - ISI indexed (2011): ISI indexed yes
  - BFI (2010): BFI-level 1
  - Scopus rating (2010): SJR 2.115 SNIP 1.439
  - BFI (2009): BFI-level 1
  - Scopus rating (2009): SJR 2.013 SNIP 1.312
  - BFI (2008): BFI-level 2
  - Scopus rating (2008): SJR 1.633 SNIP 1.395
  - Scopus rating (2007): SJR 1.426 SNIP 1.362
  - Web of Science (2007): Indexed yes
  - Scopus rating (2005): SJR 1.635 SNIP 1.476
  - Scopus rating (2004): SJR 1.364 SNIP 1.105
  - Scopus rating (2003): SJR 1.317 SNIP 1.208
  - Scopus rating (2002): SJR 1.102 SNIP 1.106
  - Web of Science (2002): Indexed yes
  - Scopus rating (2001): SJR 1.467 SNIP 1.445
  - Scopus rating (2000): SJR 1.616 SNIP 1.46
  - Scopus rating (1999): SJR 1.533 SNIP 1.406
- Original language: English
- disease register, EM-algorithm, familial aggregation, misclassification, nested case-control study, regression calibration
- DOIs: 10.1002/sim.1319
Predictors of recurrence in affective disorder — analyses accounting for individual heterogeneity

Background: Previous studies suggest that gender, age at onset, and marital status act as risk factors for further recurrence initially during the course of affective disorder but not at a later stage. These studies did, however, not take the individual liability to recurrence into account. Method: The effect of predictors of recurrence was estimated with the use of generalised linear mixed models in a case register study including a random sample of all patients admitted with primary affective disorder in Denmark during 1971–1993. Results: In total, 7047 first admission patients with a diagnosis of affective disorder, depressive or manic/circular type were included in the analyses. The study confirmed that the effect of the type of disorder, age at first admission, and never being married decreased during the course of illness even when the individual liability to recurrence was taken into account. No differences in the effect of gender and in the effect of a recent divorce were found between early and later episodes and the effect of a recent death of a spouse seemed to increase during the course of illness. The risk of recurrence increased with every new episode for all sub-groups of patients. Conclusion: The effect of some, but not all, predictors of recurrence decline during the course of affective illness. The number of previous episodes predicts recurrence in most subgroups of patients. Limitation: The data relate to readmissions rather than recurrence. Clinical relevance: The study underscores the importance of the illness process itself.

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General information
State: Published
Organisations: Copenhagen University Hospital, University of Copenhagen
Authors: Kessing, L. V. (Ekstern), Andersen, E. W. (Intern), Andersen, P. K. (Ekstern)
Number of pages: 7
Pages: 139-145
Publication date: 2000
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Affective Disorders
Volume: 57
Issue number: 1-3
ISSN (Print): 0165-0327
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.967 SNIP 1.362 CiteScore 3.84
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.911 SNIP 1.47 CiteScore 4.05
Affective disorder, Depression, Unipolar, Bipolar, Recurrence, Predictors, Life event, Individual heterogeneity

DOIs: 10.1016/S0165-0327(99)00080-4
Source: dtu
Source-ID: u::8462
Publication: Research - peer-review › Journal article – Annual report year: 2000

Breast cancer risk among women with psychiatric admission with affective or neurotic disorders: a nationwide cohort study in Denmark

General information
State: Published
Organisations: Danish Cancer Society, Aarhus University, Copenhagen University Hospital, University of Copenhagen
Number of pages: 5
Pages: 907-911
Publication date: 1999
Main Research Area: Technical/natural sciences

Publication information
Journal: B J C
Volume: 81
Issue number: 5
ISSN (Print): 0007-0920
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
Recurrence in affective disorder: analyses with frailty models

The risk of recurrence in affective disorder is influenced by the number of prior episodes and by a person's tendency toward recurrence. Newly developed frailty models were used to estimate the effect of the number of episodes on the rate of recurrence, taking into account individual frailty toward recurrence. The study base was the Danish psychiatric case register of all hospital admissions for primary affective disorder in Denmark during 1971-1993. A total of 20,350 first-admission patients were discharged with a diagnosis of major affective disorder. For women with unipolar disorder and for all kinds of patients with bipolar disorder, the rate of recurrence was affected by the number of prior episodes even when the effect was adjusted for individual frailty toward recurrence. No effect of episodes but a large effect of the frailty parameter was found for unipolar men. The authors concluded that the risk of recurrence seems to increase with the number of episodes of bipolar affective disorder in general and for women with unipolar disorder. Am J Epidemiol 1999; 149:404-11.

General information
State: Published
Organisations: Copenhagen University Hospital, University of Copenhagen
Authors: Andersen, E. W. (Intern), Kessing, L. V. (Ekstern), Andersen, P. K. (Ekstern)
Number of pages: 8
Pages: 404-411
Publication date: 1999
Projects:

Food-based solutions for optimal vitamin D nutrition and health

National Food Institute
Period: 01/09/2014 → 25/06/2018
Number of participants: 4
Phd Student:
Grønborg, Ida Marie (Intern)
Supervisor:
Andersen, Elisabeth Wreford (Intern)
Tetens, Inge (Intern)
Main Supervisor:
Andersen, Rikke (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansieret - Andet
Project: PhD

Intervention med målrettede kostråd på risikomarkører for hjertekarsygdom
National Food Institute
Period: 01/11/2012 → 28/03/2018
Number of participants: 5
Phd Student:
Arentoft, Johanne Louise (Intern)
Supervisor:
Andersen, Elisabeth Wreford (Intern)
Overvad, Kim (Ekstern)
Tetens, Inge (Intern)
Main Supervisor:
Andersen, Rikke (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Befolkningens forståelse af kostråd, sund kost- og aktivitetsvaner
National Food Institute
Period: 01/10/2012 → 08/02/2017
Number of participants: 8
Phd Student:
Sørensen, Mette Rosenlund (Intern)
Supervisor:
Andersen, Elisabeth Wreford (Intern)
Holm, Lotte (Ekstern)
Matthiessen, Jeppe (Intern)
Main Supervisor:
Tetens, Inge (Intern)
Examiner:
Mejborn, Heddie (Intern)
Lien, Nanna (Ekstern)
Rasmussen, Mette (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.

Relations
Publications:
Assessment of healthy diets and physical activity
Project: PhD
Betydningen af genotyper for D-vitaminstatus

National Food Institute
Period: 01/09/2010 → 15/12/2015
Number of participants: 9
Phd Student:
Nissen, Ioanna (Intern)
Supervisor:
Andersen, Elisabeth Wreford (Intern)
Ravn-Haren, Gitte (Intern)
Vogel, Ulla Birgitte (Intern)
Wulf, Hans Christian (Ekstern)
Main Supervisor:
Andersen, Rikke (Intern)
Examiner:
Poulsen, Morten (Intern)
Linneberg, Allan (Ekstern)
Meyer, Haakon E. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

ConsumerCheck: Methodology for combining sensory properties with additional information in consumer acceptance studies of food products

Department of Applied Mathematics and Computer Science
Period: 01/05/2010 → 21/09/2015
Number of participants: 6
Phd Student:
Kuznetsova, Alexandra (Intern)
Supervisor:
Christensen, Rune Haubo Bojesen (Intern)
Main Supervisor:
Brockhoff, Per B. (Intern)
Examiner:
Andersen, Elisabeth Wreford (Intern)
Højsgaard, Søren (Ekstern)
Schlich, Pascal (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut, samfinansiering
Project: PhD

Effekten af D-vitamin berigelse i danske familier

National Food Institute
Period: 15/11/2009 → 26/02/2014
Number of participants: 8
Phd Student:
Madsen, Katja Howarth (Intern)
Supervisor:
Andersen, Elisabeth Wreford (Intern)
Andersen, Rikke (Intern)
Mølgaard, Christian (Ekstern)
Main Supervisor:
Rasmussen, Lone Banke (Intern)
Examiner:
Pedersen, Agnes N. (Intern)
Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Activities:

Introduction to Applied Statistics with R for PhD Students
Period: 9 Jun 2017 → 30 Jun 2017
Anders Stockmarr (Lecturer)
Bjarne Kjær Erbsøll (Lecturer)
Elisabeth Wreford Andersen (Guest lecturer)
Murat Kulahci (Lecturer)
Andreas Baum (Lecturer)
Camilla Thyregod (Other)
Jesper Fink Andersen (Other)
Department of Applied Mathematics and Computer Science
Statistics and Data Analysis

Related organisation

Introduction to Applied Statistics with R for PhD Students
Stockmarr, A. (Lecturer), Erbsøll, B. K. (Lecturer), Andersen, E. W. (Guest lecturer), Kulahci, M. (Lecturer), Baum, A. (Lecturer), Thyregod, C. (Other), Andersen, J. F. (Other)
9 Jun 2017 → 30 Jun 2017
Activity: Talks and presentations › Guest lectures, external teaching and course activities at other universities

Comparison of different methods for calculating usual intakes
Period: 26 Jan 2015 → 28 Jan 2015
Anja Pia Biltoft-Jensen (Other)
Elisabeth Wreford Andersen (Speaker)
National Food Institute
Division of Risk Assessment and Nutrition
Department of Informatics and Mathematical Modeling

Description
Det 37. symposium i anvendt statistik 26.-28. januar 2015- Danmarks Tekniske Universitet

Related external organisation

Danmarks Statistik
Denmark
Activity: Talks and presentations › Conference presentations