Institute of Medical Informatics, Biometry, and Epidemiology

Chair of Medical Biometry and Epidemiology

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Research focus
- Computational biostatistics
- Statistical learning methods and medical data analysis
- Dermatoepidemiology
- Cooperative epidemiological and clinical studies

Structure of the Chair

Professorships: 2
Personnel: 13
- Scientists: 12 (thereof funded externally: 5)
- Graduate students: 5

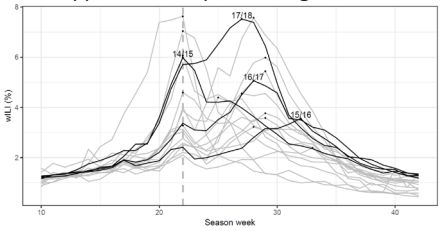
Research

The focus of the Chair's scientific activity is on three distinct areas: Methods development in the realm of machine learning (Computational Biostatistics), statistical modelling of infectious diseases, Statistical learning methods and medical data analysis, and dermato-epidemiological research, respectively. Moreover, the Chair cooperates with numerous research projects addressing different topics with different departments or institutes. Usually, the Chair is responsible for statistical aspects of study design and analysis.

Computational biostatistics
PI: Dr. E. Waldmann
The statistical analysis of high-dimensional data containing large numbers of features has become increasingly important in biomedical practice. Consequently, statistical methods for analyzing data with complex dependency patterns and for separating informative features from non-informative ones are needed. Boosting is a promising statistical method to address these issues. The project focuses on improving and developing boosting methodology for data structures that cannot yet be analyzed with the help of classical boosting techniques. For example, classical boosting methods were further extended to generalized additive models for location, scale, and shape (GAMLSS). GAMLSS is a popular statistical approach for simultaneously modeling multiple parameters of a response distribution in regression models. Current fitting procedures for GAMLSS are infeasible for high-dimensional data setups and require heuristic (or potentially biased) feature selection methods. The new algorithm allows for simultaneous estimation of predictor effects and feature selection in GAMLSS. In the course of the project, boosting methods were further analyzed with regard to their general performance as optimization method for AUC-based performance criteria in classification and survival analysis. Furthermore, boosting methods are developed and evaluated which target the analysis of so-called joint models, addressing modeling of two related outcome variables, one a time-to-event- component, the other a longitudinally observed outcome, related by a parameter of association.

Statistical learning methods and medical data analysis
PI: PD Dr. W. Adler
In the statistical evaluation of clinical studies in collaboration with the University Hospital Erlangen, in addition to the usual questions that can be solved with conventional test procedures and multiparametric models, studies with very small sample sizes and / or complex data structure often arise, for which, in addition to complex statistical models, non-parametric analysis procedures that do not rely on statistical distribution assumptions are also suitable. Among the latter, especially the bootstrap method plays an important role, which, in addition to the estimation of confidence intervals or the determination of statistical significance when examining the group difference of different statistical measures, can also be used, for example, to generate ensembles of classification and regression trees, since a flexible adaptation to the data structure at hand is possible. Mixed linear models, by suitable manipulation of the covariance matrix, allow the determination of correlation for data with appropriate data structure, such as the presence of repeated measures. Moreover, GEE models have an important role, for example, for efficient evaluation of data sets where both eyes are partially available from glaucoma patients. GEE models take the data structure into account not so much by modeling the magnitude of parameters, but rather by determining their uncertainty.

Statistical analysis of infectious disease spread
PI: Dr. S. Meyer
Infectious pathogens such as influenza and noro viruses cause epidemics. Public health surveillance records age-stratified and spatial data on the occurrence of notifiable infectious diseases; in Germany, this is handled by the Robert Koch Institute. Based on such surveillance data, statistical models enable probabilistic forecasts of key measures relevant to public health authorities, eg. the incidence or peak week of the epidemic. A particular scientific focus was to investigate proper scoring rules for such probabilistic forecasts. Furthermore, epidemic models can support the understanding of disease spread, for example to estimate the impact of environmental or socioeconomic factors and vaccination coverage on disease dynamics. For this purpose, we have developed specialized regression models and associated statistical software, which has already been employed also by other epidemiological research groups. We are working on extensions of these methods for multidimensional time series of proportions, for example, regionally stratified consultation rates of influenza-like illness or influenza-attributable hospitalization rates in different age groups. Moreover, we evaluate statistical models for point processes, which allow for a more detailed picture of epidemic spread given individual-level surveillance data. All methodological developments are implemented in open source research software to facilitate scientific progress and broad application in epidemiological research.



Seasonal flu activity in the USA, 1998-2017, as measured by the (population-weighted) proportion of patients with influenza-like illness (ILI) among all monitored outpatient visits. Season week 22 (calendar week 52) is indicated with a vertical dashed line, where a peak or secondary peak occurs in most seasons. A forecasting challenge of different statistical models was performed for the last four seasons (black lines). From: Lu & Meyer, IJERPH, 2020. License: CC BY 4.0.

Dermatoepidemiology
PI: Prof. Dr. A. Pfahlberg, Prof. Dr. W. Uter
In clinical contact allergy research, a close co-operation with the German contact dermatitis group (DKG) e.V. and the multi-centric project Information Network of Departments of Dermatology (IVDK), maintained by an institute at the University of Göttingen, has been established. Pooled data collected in the participating allergy departments are analyzed in terms of contact allergy surveillance, i.e. early detection of trends in contact allergy (increase, possibly in particular subgroups). Moreover, the network European Surveillance System on Contact Allergies – Data Centre (ESSCA-DC) has been collecting and analyzing such data on a European level since 2002, with the data center located at the Chair of Medical Biometry and Epidemiology. Currently, the so-called European Baseline Series for patch testing is being updated based on ESSCA results.
The epidemiology of malignant melanoma and acquired melanocytic nevi is a further research interest: Acquired melanocytic nevi, surrogates or potential precursors of malignant melanoma, are addressed by the current MONA-study which

includes standardized assessment of student cohorts. Currently, results of two surveys ("Erlking Sun", "Francis") addressing knowledge on prevention of UV exposure in kindergarten staff and actual protective measures (shading etc.) in the institutions are being analyzed with the aim of identifying targets of improvement of primary prevention, with a special focus on the concept of the UV-index.

Cooperative epidemiological and clinical studies

This area of activity comprises diverse research topics addressed in cooperation with different departments and institutes. Usually, biometrical aspects of study design and statistical analysis have been performed by the Chair in these co-operative projects. The most important projects in the reporting period include:

- Studies in cooperation with the Center for medical healthcare research of the Chair of Psychiatry and Psychotherapy concerning nonpharmacological interventions for dementia (DeTa-MAKS, Senior-Go, MAKS-kog-ls, MAKS-s)
- A multi-centric European studying on "Accelerated Partial Breast Irradiation" and a controlled clinical trial on radiochemotherapy in patients with locally advanced head/neck tumors stage III and IVA-B (PACCIS) and radiochemotherapy after induction chemotherapy with gemcitabine and FOLFIRINOX, resp. (CONKO-007 study), all chaired by the Department of Radiation Oncology
- The research network PRO PRICARE (see separate report) targeting the identification of unnecessary diagnostic and therapeutic interventions, their causes, and possible strategies for a future reduction of such measures. The Chair is involved in a sub-project addressing so-called cascade effects and their causes in thyroid disease
- A European multicenter study "SCOPE" ("Screening for Chronic Kidney Disease among Older People across Europe") in co-operation with the Institute for Biomedicine of Aging
- The transsectoral TIGER Study assessing daily home support of elderly patients by "pathfinders" to reduce re-admission rates after discharge from inpatient treatment
- The ANFOLKI-36 study, which examines the effects of general anesthesia in children on their cognitive function, in cooperation with the Department of Anesthesiology and the Chair of Medical Informatics
- The clinical study EUPHORIA to enhance ultrasound & photoacoustic for recognition of intestinal abnormalities using a new imaging modality called Multispectral Optoacoustic Tomography (MSOT).
- The population-based epidemiological cohort study TiCoKo examining the seroprevalence of SARS-CoV-2 longitudinally in the county of Tirschenreuth based on a random sample of more than 4200 inhabitants as well as determinants of morbidity
- A qualitative study regarding knowledge and use of the UV-index during consultations on the subject of sun protection in pharmacies in the Rhine-Main region in cooperation with the Institute for Public Health at Mannheim University Medical Center
- The statistical-epidemiological study SUSPend to analyse the impact of social distancing policies on the spatio-temporal spread of COVID-19.

Teaching

The Chair of Medical Biometry and Epidemiology contributes to curricular teaching in terms of mandatory and optional courses in Medicine, Molecular Medicine, Medical Technology, Life Science Engineering, Logopedics, and Medical Process Management. Concerning inter-disciplinary teaching, the cooperation in the context of "Querschnittsbereich I" with the Chair of Medical Informatics and the Institute and Outpatient Clinic of Occupational, Social, and Environmental Medicine is of note.
The Chair supervises Bachelor's and Master's theses as well as MD and PhD doctoral theses.

Selected publications

Gayawan E, Adebayo SB, Waldmann E. Modeling the spatial variability in the spread and correlation of childhood malnutrition in Nigeria. Stat Med. 2019 May 10;38(10):1869-1890.

Kaiser I, Pfahlberg AB, Uter W, Heppt MV, Veierød MB, Gefeller O. Risk Prediction Models for Melanoma: A Systematic Review on the Heterogeneity in Model Development and Validation. Int J Environ Res Public Health. 2020 Oct 28;17(21):7919.

Lehmann M, Sandmann H, Pfahlberg AB, Uter W, Gefeller O.. Erythemal UV Radiation on Days with Low UV Index Values-an Analysis of Data from the German Solar UV Monitoring Network over a Ten-year Period. Photochem Photobiol 2019;95(4):1076-1082

Lu J, Meyer S. Forecasting flu activity in the United States: Benchmarking an endemic-epidemic beta model. International Journal of Environmental Research and Public Health. 2020;17(4):1381

Uter W, Aalto-Korte K, Agner T, Andersen KE, Bircher AJ, Brans R, Bruze M, Diepgen TL, Foti C, Giménez Arnau A, Gonçalo M, Goossens A, McFadden J, Paulsen E, Svedman C, Rustemeyer T, White IR, Wilkinson M, Johansen JD. The epidemic of methylisothiazolinone contact allergy in Europe: follow-up on changing exposures. J Eur Acad Dermatol Venereol. 2020;34(2):333-339

Uter W, Gefeller O, Mahler V, Geier J. Trends and current spectrum of contact allergy in Central Europe: results of the Information Network of Departments of Dermatology (IVDK) 2007-2018. Br J Dermatol. 2020 Nov;183(5):857-865.

International cooperation

Multicentric:
Prof. J.D. Johansen (1), Prof. C.M. Bonefeld (1), Dr. I. R. White (2), Prof. J.-P. Lepoittevin (3), Prof. M.B. Veierød (4)
(1) Copenhagen University, (2) Kings College London, (3) Université de Strasbourg, (4) University of Oslo