

# DGEpi Nachwuchspreisträger 2012

## 1. Preis

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### **Adjustment Criteria in Causal Diagrams: An Algorithmic Perspective**

*in: Proceedings of the Twenty-Seventh Conference Annual Conference on Uncertainty in Artificial Intelligence (UAI-11), AUAI Press, Corvallis, Oregon, 2011, 681--688*

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Identifying and controlling bias is a key problem in empirical sciences. Causal diagram theory provides graphical criteria for deciding whether and how causal effects can be identified from observed (nonexperimental) data by covariate adjustment. Here we prove equivalences between existing as well as new criteria for adjustment and we provide a new simplified but still equivalent notion of d-separation. These lead to efficient algorithms for two important tasks in causal diagram analysis: (1) listing minimal covariate adjustments (with polynomial delay); and (2) identifying the subdiagram involved in biasing paths (in linear time). Our results improve upon existing exponential-time solutions for these problems, enabling users to assess the effects of covariate adjustment on diagrams with tens to hundreds of variables interactively in real time.

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### **DAGitty: A Graphical Tool for Analyzing Causal Diagrams**

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Causal diagrams, also known as directed acyclic graphs,<sup>1,2</sup> provide an entirely graphical, yet mathematically rigorous methodology for minimizing bias in epidemiologic studies.<sup>3,4</sup> The analysis of causal diagrams can be cumbersome in practice, and lends itself well to automatization by a computer program. Important first steps in this regard include the development of the DAG program by Knüppel and Stang<sup>5</sup> and dagR by Breitling.<sup>6</sup> We announce the release of DAGitty, which provides a graphical user interface tailored to draw and analyze causal diagrams. DAGitty overcomes some performance obstacles (pointed out by Breitling<sup>6</sup>) that affect earlier software when analyzing large diagrams.

The performance issues are 2-fold. First, previous software employed back-tracking algorithms<sup>5</sup> to enumerate and categorize all paths from exposure to outcome. This is a reasonable approach for small diagrams, but diagrams with tens of variables can already contain millions of paths. A full listing is of little interest to the human user, but can take hours or days to generate. Instead of a path list, DAGitty identifies the subdiagrams involved in causal and biasing paths and highlights them in different colors. This highlighting algorithm<sup>7</sup> scales to very large diagrams. It provides a vivid impression about how causal and biasing effects “flow” in the diagram, that is, by which variables and causal arrows these effects are mediated.

The second problem with previous software has arisen when identifying minimally sufficient adjustment sets (MSA sets). According to causal diagram theory, adjustment for the covariates in an MSA set minimizes bias when estimating the total effect from exposure to outcome. A straightforward approach to find MSA sets is to check each covariate set to see whether it is an MSA set. In a diagram with 50 covariates, this means that 250 sets may have to be tested—a 16-digit number that is too large even for computers. To identify MSA sets more efficiently, we adapted an algorithm proposed recently for a related graph-theoretical problem.<sup>8</sup> This algorithm is guaranteed to output the list of MSA sets reasonably quickly (ie, in polynomial time per MSA set output). Note, however, that very large or very regularly structured diagrams could in theory have millions of different MSA sets. If such diagrams become practically relevant, further research will be

necessary to develop appropriate computational methods for helping the user to choose appropriate MSA sets.

The described algorithms enable DAGitty's graphical interface to instantly reflect changes made to the diagram, such as adding a new arrow or inverting an arrow with unclear causal direction. This way, users can interactively assess the effects of their modifications on minimally sufficient adjustment sets and the flow of causal and biasing effects. We anticipate that these interactive possibilities will help users to develop an intuition about causal diagram theory, and to compare and decide among various causal diagrams.

DAGitty is available under an open-source license, allowing free access, redistribution, and modification. It runs out of the box in most modern web browsers and is available for online use and download at: [www.dagitty.net](http://www.dagitty.net).

## 2. Preis

Anja Rudolph, Deutsches Krebsforschungszentrum Heidelberg  
**Expression of estrogen receptor  $\beta$ ; and prognosis of colorectal cancer**

*in: British Journal of Cancer 2012; 107: 831-839.*

Rudolph A, Toth C, Hoffmeister M, Roth W, Herpel E, Jansen L, Marx A, Brenner H, Chang-Claude J

Previous studies suggest that sex steroids influence colorectal cancer (CRC) carcinogenesis. The oestrogen receptor  $\beta$  (ER $\beta$ ) is the predominantly expressed ER in the colon and loss of ER $\beta$  in CRC has been associated with advanced cancer stages.

Methods: Information on vital status by the end of 2009 was obtained for 1262 CRC patients recruited between 2003 and 2007. The ER $\beta$  expression was immunohistochemically measured and associations of ER $\beta$  scores with overall survival (OS), disease-specific survival (DSS) and disease-free survival (DFS) were evaluated using Cox proportional hazard models adjusted for prognostic factors, such as tumour stage and second primary tumours.

Results: Of the 1101 tumour samples with successful measurement, 535 were ER $\beta$  negative (48.6%), 381 (34.6%) showed moderate and 185 (16.8%) showed high ER $\beta$  expression. Compared with high ER $\beta$  expression, lack of ER $\beta$  was associated with higher cancer stages as well as greater tumour extent. In multivariate analyses, ER $\beta$  negativity was associated with an increased hazard ratio for death (HR=1.61, 95% CI 1.09–2.40,  $P=0.02$ ), death attributed to CRC (HR=1.54, 95% CI 0.99–2.39,  $P=0.06$ ) as well as a poorer DFS (DFS HR=1.64, 95% CI 1.23–3.36,  $P=0.04$ ). The associations were stronger in stage I-III patients (OS HR=2.20, 95% CI 1.28–4.06,  $P=0.007$ , DSS HR=2.38, 95% CI 1.20–5.39,  $P=0.02$ , respectively).

Conclusions: Lack of ER $\beta$  expression is associated with advanced cancer stages and independently associated with poor survival.

## 3. Preis

Ute Mons, Deutsches Krebsforschungszentrum Heidelberg  
**Impact of national smoke-free legislation on home smoking bans; findings from the International Tobacco Control Policy Evaluation Project Europe Surveys**

*in: Tob Control doi:10.1136/tobaccocontrol-2011-050131*

Ute Mons, Gera E Nagelhout, Shane Allwright<sup>5</sup>, Romain Guignard<sup>6</sup>, Bas van den Putte, Marc C Willemsen, Geoffrey T Fong, Hermann Brenner, Martina Pötschke-Langer, Lutz P Breitling  
Objectives: To measure changes in prevalence and predictors of home smoking bans (HSBs) among smokers in four European countries after the implementation of national smoke-free legislation.

Design: Two waves of the International Tobacco Control Policy Evaluation Project Europe Surveys, which is a prospective panel study. Pre- and post-legislation data were used from Ireland, France, Germany and the Netherlands. Two pre-legislation waves from the UK were used as control. Participants 4634 respondents from the intervention countries and 1080 from the control country completed both baseline and follow-up and were included in the present analyses.

Methods Multiple logistic regression models to identify predictors of having or of adopting a total HSB, and Generalised Estimating Equation models to compare patterns of change after implementation of smoke-free legislation to a control country without such legislation.

Results: Most smokers had at least partial smoking restrictions in their home, but the proportions varied significantly between countries. After implementation of national smoke-free legislation, the proportion of smokers with a total HSB increased significantly in all four countries. Among continuing smokers, the number of cigarettes smoked per day either remained stable or decreased significantly. Multiple logistic regression models indicated that having a young child in the household and supporting smoking bans in bars were important correlates of having a pre-legislation HSB. Prospective predictors of imposing a HSB between survey waves were planning to quit smoking, supporting a total smoking ban in bars and the birth of a child. Generalised Estimating Equation models indicated that the change in total HSB in the intervention countries was greater than that in the control country.

Conclusions: The findings suggest that smoke-free legislation does not lead to more smoking in smokers' homes. On the contrary, our findings demonstrate that smoke-free legislation may stimulate smokers to establish total smoking bans in their homes.

## **Preis für eine Arbeit mit besonders hohem Eigenanteil am Forschungsprozess**

Margit Löbner (geb. Zieger), Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP) der Universität Leipzig

### **Affective, anxiety and substance related disorders in patients undergoing herniated disc surgery**

in: *Soc Psychiatry Psychiatr Epidemiol* (2011), 46: 1181-1190

Zieger M, Lupp M, Matschinger H, Meisel HJ, Günther L, Meixensberger J, Toussaint R, Angermeyer MC, König HH, Riedel-Heller SG

**PURPOSE:** At present only a small number of studies have investigated psychiatric comorbidity in disc surgery patients. Objectives of this study are (1) to examine the prevalence rate of comorbid affective, anxiety, and substance-related disorders in nucleotomy patients in comparison to the German general population and (2) to investigate associations between psychiatric comorbidity and socio-demographic and illness-related characteristics.

**METHODS:** The study refers to 349 consecutive disc surgery patients (response rate 87%) between the age of 18 and 55 years. The final study sample consists of 239 lumbar and 66 cervical nucleotomy patients. Face-to-face interviews were conducted approximately 3.45 days (SD 3.170) after disc surgery, during hospital stay. Psychiatric comorbidity was assessed by means of the Composite International Diagnostic Interview (CIDI-DIA-X). The corresponding data of the German general population were derived from the German National Health Interview and Examination Survey (GHS).

**RESULTS:** 12-Month prevalence rates of any affective, anxiety or substance-related disorders range between 33.7% in cervical and 23.5% in lumbar disc surgery patients. Four-week prevalence rates of any affective, anxiety or substance disorder vary between 13.2% in cervical and 14.0% in lumbar nucleotomy patients. Disc surgery patients suffer more often from affective disorders and illicit substance abuse than the general population. Significant associations were found between psychiatric comorbidity and gender, as well as pain intensity.

**CONCLUSIONS:** Disc surgery patients show a higher risk to suffer from mental disorders than the general population. The assessment of psychiatric distress and the assistance by mental health professionals should be considered during hospital and rehabilitation treatment.