BIOGRAPHICAL SKETCH

NAME: Andreae, Michael H.

eRA COMMONS USER NAME: andrem10

POSITION TITLE: Associate Professor of Anesthesiology

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE | Completion Date | FIELD OF STUDY |
| --- | --- | --- | --- |
| Friedrich-Wilhelm-University, Bonn, Germany | M.D. | 06/1994 | Medicine |
| Imperial College, London, United Kingdom | M.Sc. | 06/1996 | Physics and Engineering in Medicine |
| Columbia University, NYC, NY | M.A. | 05/2015 | Quantitative Methods in Social Science |

# A. Personal Statement

We are proposing to develop and disseminate software packages and tools to make advanced hierarchical modeling more accessible to clinical data scientists for data driven outcomes research. Together with Dr. Benjamin Goodrich, I will lead this project as co-principal investigator.

Our goal is to transform electronic records based outcomes research by making software and modeling tools accessible to clinical data scientists so they can take advantage of novel algorithms and cutting edge software that accelerate by several orders of magnitude model complexity and speed of computational implementation of hierarchical models for Big Data. I will be co-principal investigator leading an exceptionally diverse group of outstanding data scientist in a tight knight collaboration, building a bridge from clinical outcomes research to fundamental statistical innovation and back.

As an anesthesiologist, how did I get into building statistical software? Passionate for regional anesthesia, I set out to prove its long term benefits. The varied design and disparate outcome reporting of existing clinical trials hampered classical meta-analysis and make me look for more advanced statistical methods. I am about to complete my mentored research training in Bayesian evidence synthesis under the guidance of my mentor Dr. Hall. This included a master in quantitative methods at Columbia University, where I focused on Bayesian multi-level hierarchical modeling and realized the enormous potential of electronic health records based outcomes research. Through this Columbia program, I started my collaboration with Drs. Goodrich, Gelman and Gong and we build the prototype software we want to further develop in the proposed grant.

My previous training and experience prepared me well for this role as co-principal investigator for this project:

(a) **Domain Expertise:** Board certified in anesthesiology and critical care, I am a nationally recognized expert in the domain of perioperative (long term) outcomes research, leading and mentoring clinical research (training), the departmental grand rounds journal club and the research endeavors in my department.

(b) **Advanced Statistical Modeling:** I completed two quantitative graduate programs, (1) at Imperial College, London and (2) at Columbia University, New York, respectively; they included intensive quantitative and statistical coursework emphasizing Bayesian hierarchical modeling and computational implementation. I fitted and published several hierarchical Bayesian and classical models investigating perioperative and chronic pain outcomes and health care disparity using various statistical software packages including BUGS, STAN, Stata and R, also applying them to large electronic medical records datasets. With my collaborators at Columbia, we build an interactive software suite for graphical exploration of hierarchical and Bayesian models.

(c) **Teaching Statistics:** I teach workshops at the American Society of Anesthesiology Annual Meeting in data science and taught in graduate courses in evidence based medicine s at the Albert Einstein College of Medicine. I lead our departmental grand rounds journal club and organize the clinical research methods mini course for our fellows, where we introduce physicians to statistical software and analysis.

(d) **Managing Diverse Teams:** Under the auspices of my mentor Dr. Sacks, I lead a multidisciplinary research team to conduct focus groups to (1) investigate ethical barriers to research and (2) conduct evidence synthesis of alternative and complementary medicine for HIV comorbidities, (see letter of support by Dr. Sacks).

# B. Positions and Honors

## Positions and Employment

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| --- | --- |
| 1994-1995 | Junior House Officer, Surgery, Buckland Hospital, Dover, UK |
| 1995-1995 | Junior House Officer, Radiology, Euskirchen, Germany |
| 1997-1998 | Japanese Government Monbusho Scholar at Kyoto University, Kyoto, Japan |
| 1998-1999 | Transitional Internship, The Miriam Hospital, Providence, RI |
| 1999-2002 | Anesthesiology Residency, UCSF, San Francisco, CA |
| 2002-2003 | Anesthesiology Residency, Robert Wood Johnson, New Brunswick, NJ |
| 2/2003-4/03 | Doctors of the World-Medical Mission in Seguela, Ivory Coast |
| 2003-2004 | Critical Care Fellowship, Columbia University, New York, NY |
| 2004-2006 | Assistant Professor of Anesthesiology, UMDNJ, Newark, NJ |
| 2006-2007 | Regional Anesthesia Fellowship, Freiburg University, Freiburg, Germany |
| 2007-2008 | Paternity Leave |
| 2008-2010 | Consultant Anaesthesist, Vienna University, Vienna, Austria |
| 2010-2011 | Assistant Professor of Anesthesiology, Mount Sinai School of Medicine, New York, NY |
| 2011-2015 | Assistant Professor of Anesthesiology, Albert Einstein College of Medicine, Bronx, NY |
| 2015-present | Associate Professor of Anesthesiology, Albert Einstein College of Medicine, Bronx, NY |

## Professional Experience

|  |  |
| --- | --- |
| 2004-2006 | Assistant Professor of Anesthesiology, UMDNJ, Newark, NJ |
| 2008-2010 | Consultant Anaesthesist, Vienna University, Vienna, Austria |
| 2010-2011 | Assistant Professor of Anesthesiology, Mount Sinai School of Medicine, New York, NY |
| 2011-2015 | Assistant Professor of Anesthesiology, Albert Einstein College of Medicine, New York, NY |
| 2015-present | Associate Professor of Anesthesiology, Albert Einstein College of Medicine, Bronx, NY |
| 2013-present | Institutional Review Board Member, Albert Einstein College of Medicine, Bronx, NY |

## Honors and Awards

Einstein Mentored Research Training Award 2014

Columbia University Student Scholarship 2013

Einstein Clinical Research Training Scholar 2012

American Society of Regional Anesthesia First Abstract Prize 2012

European Society of Regional Anaesthesia Congress Third Abstract Prize 2011

Monbusho Award (Japanese Ministry of Education and Science Scholarship) 1998

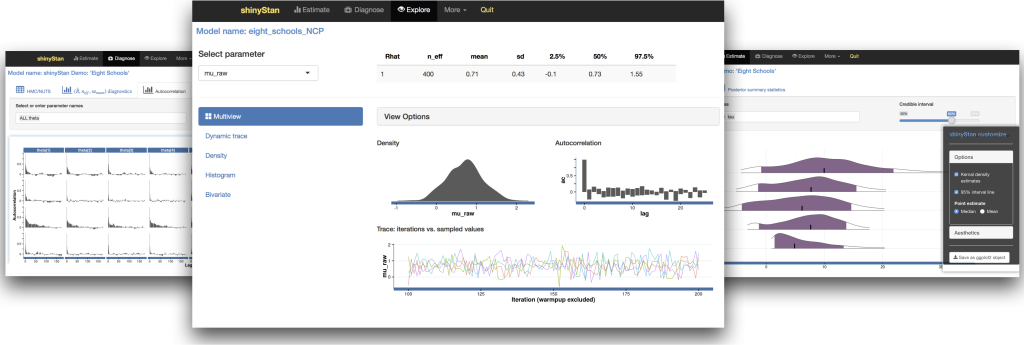
Imperial College, Student Scholarship in 1995/1996

European Community, Erasmus-Scholarship, twice in 1990 & 1992

German Academic Exchange Service, Elective Travel Grant in 1990

# C. Contribution to Science

## 1. Statistical software package for multi-level hierarchical Bayesian models

Exploratory and confirmatory data analyses complement each other in the comparison of data to implicit or explicit statistical models, but can be cumbersome to realize and interpret in the face of complex hierarchical models. The availability of drastically increased computer power and advanced graphical software routines allows novel approaches to integrate exploratory and confirmatory analysis for complex hierarchical models.

As part of dynamic model fitting for Big Data, statisticians need to quickly assess convergence and mixing of Markov Chain Monte Carlo simulations. 3D visualization of asymmetric distribution of prior and posterior statistics on the log scale against the log likelihood offers new insight into model misspecifications, for example explaining slow model convergence and low effective sample size in Hamiltonian MCMC while offering practical indications on how to overcome these by non-centered parametrization. We developed an interactive interface with tools to facilitate exploration and visualization of Bayesian models, and published our toolbox on GitHub. Graphs can be downloaded as ggplot objects, facilitating post-processing for publication. [ShinyStan](http://mc-stan.org/interfaces/shinystan.html) has been discussed in [blogs](http://andrewgelman.com/2015/03/02/introducing-shinystan/), on twitter and [YouTube](https://www.youtube.com/watch?v=X31xqNHcvQs). I

shinyStan Team. (2015). shinyStan: R package for interactive exploration of Markov chain monte carlo output, version 0.1. Retrieved from <https://github.com/stan-dev/shinystan>

Galbry J, **Andreae MH**, Yuanjun Gao, Dongying Song. Interactive graphical analysis, exploration and posterior predictive checking of multi-level hierarchical Bayesian models. Oral Presentation at the Annual Meeting of the International Society of Clinical Biostatistics, Utrecht, NL, 2015.

## 2. Multi-level models for hierarchically structured data

### a) Antiemetic prophylaxis as a surrogate marker for anesthesia health care disparities

Health care disparities in anesthesia have barely been investigated. We investigate the hypothesis that individual providers provide disparate treatment predicted by patient health insurance status. We chose antiemetic prophylaxis as a surrogate marker for anesthesia health care disparities attributable to individual providers. We fit a hierarchical Bayesian logistic regression mixed effects model in the subset of anesthesia cases in the National Anesthesia Clinical Outcomes Registry. Based on 176,334 anesthesia cases, bivariate analysis, multivariate logistic regression and the Bayesian hierarchical model consistently a strong and statistically significant association between insurance status and the odds of receiving antiemetic prophylaxis; insensitive to controlling for patient characteristics. Our results point to potential unappreciated healthcare disparities in anesthesia at the provider level.

**Andreae MH**, White R, Galbry J. Hall C. Utilization of antiemetic medication as a marker of health care disparities in anesthesia. Abstract at the Translational Science Conference, Washington, 2015.

**Andreae MH**, White R, Galbry J. Hall C. Utilization of antiemetic medication as a marker of health care disparities in anesthesia. Oral Presentation at the Anesthesia Quality Institute, Chicago, 2015.

### b) Patient characteristics predict failure to attend inner-city chronic pain clinic

US Health care disparities persist despite repeated countermeasures. We investigated healthcare disparities in anesthesiology and pain medicine; so far little research exists in in either domain. Patients often fail to attend appointments in chronic pain clinics for unknown reasons. Based on a retrospective cohort of 1,394 chronic pain patients, we examined the effect of demographic factors on appointment status, fitting a marginal logistic regression using generalized estimating equations with exchangeable correlation. Spanish spoken as a primary language and distance to the pain clinic predicted failure to attend a scheduled appointment in our cohort and may constitute systematic barriers to access, a hypothesis, we are currently testing in subsequent follow up randomized clinical trial. We have completed enrollment [n=1000] and are analyzing the data.

Shaparin N, White R, **Andreae M**, Hall C, Kaufman A. A longitudinal linear model of patient characteristics to predict failure to attend an inner-city chronic pain clinic. J Pain. 2014 Jul;15(7):704-11. doi: 10.1016/j.jpain.2014.03.004. Epub 2014 Apr 18. PubMed PMID: 24747766.

## 3. Bayesian and classical evidence synthesis of long term patient centered outcomes

Different follow-up intervals, variable outcomes measure and incomplete reporting hamper evidence synthesis of clinical outcomes needed to inform evidence-based medicine. Bayesian inference allows a more flexible implementation of hierarchical models and can incorporate all available data at all follow-up intervals. We developed hierarchical Bayesian models to synthesize aggregate and individual patient data to summarize the evidence on cannabis for chronic neuropathic pain and multivitamins for HIV progression. Individual patient data meta-analysis is considered the gold standard and Bayesian evidence synthesis is still very novel.

### Inhaled cannabis alleviates chronic neuropathic pain: an individual patient meta-analysis.

Chronic neuropathic pain is very frequent, but currently without satisfying conventional treatment options. Classical meta-analysis of the results of five randomized trials was hindered by their disparate and heterogeneous outcome reporting. We obtaining the individual patient data from all primary study authors and build a hierarchical model to integrate the reported dichotomous and continuous outcomes in a novel Bayesian responder analysis, pooling the estimated number of patients whose pain improved meaningfully; this new approach provided compelling evidence that inhaled cannabis alleviates chronic neuropathic pain with a Number Needed to Treat of 4-5, which is better than current standard therapy (gabapentin). Our analysis helps to rationalize the current heated debate on legalization of medicinal marihuana.

Forest plot 1: Odds of responding to therapy. Each square in the forest plot shows the odds ratios for a study (or study arm); the black diamond below shows the pooled odd ratio.

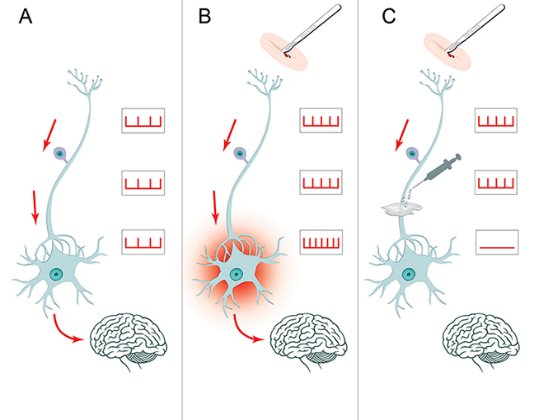
**Andreae MH**, Carter GM, Shaparin N, Suslov K, Ellis RJ, Ware MA, Abrams DI, Prasad H, Wilsey B, Indyk D, Johnson M, Sacks HS. Inhaled Cannabis for Chronic Neuropathic Pain: A Meta-analysis of Individual Patient Data. J Pain. 2015 Dec;16(12):1221-32. PubMed PMID: 26362106.

### Micronutrients in HIV: A Bayesian meta-analysis

Micronutrient supplementation may mitigate disease progression and mortality in HIV disease. We built a hierarchical Bayesian random effects model to synthesize the clinical evidence analogous to the Distrogram below. MNS significantly and substantially slows disease progression in HIV+ adults not on ARV, and possibly reduces mortality. Considering MNS low cost and lack of adverse effects, MNS should be standard of care for HIV+ adults not yet on ARV.

Carter GM, Indyk D, Johnson M, **Andreae M**, Suslov K, Busani S, Esmaeili A, Sacks HS. Micronutrients in HIV: a Bayesian meta-analysis. PLoS One. 2015 Apr 1;10(4):e0120113. PMID: 25830916

### Regional anesthesia for the prevention of chronic postsurgical pain: A Bayesian model

Persistent postsurgical pain (PPP) is a devastating condition and difficult to treat. PPP is most frequent (30-50%) after breast surgery and thoracotomy, but also after cesarean section and even hernia repair (10%). Our classical Cochrane model showed that epidural anesthesia and paravertebral block reduces the risk of PPP, with a number needed to treat of 3-5, a very strong preventive effect. Emphasizing the impact of our work, our Cochrane review was co-published in the British Journal of Anasthesia, where it was selected as “Editor's choice” and for continuing medical education credit.

**Andreae MH**, Andreae DA. Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis. Br J Anaesth. 2013 Nov;111(5):711-20. doi: 10.1093/bja/aet213. Epub 2013 Jun 28. Review. PubMed PMID: 23811426;

### Regional anesthesia for improved long term function after total joint replacement

Regional analgesia is more effective than conventional analgesia for controlling pain and may facilitate rehabilitation after large joint replacement in the short term but it was unclear if regional anesthesia improves functional outcomes beyond three months after surgery. We synthesized five studies with 290 participants followed-up for at least three months, but found insufficient evidence to support the hypothesis that regional analgesia improves function after major joint replacement.

Atchabahian A, Schwartz G, Hall CB, Lajam CM, **Andreae MH**. Regional analgesia for improvement of long-term functional outcome after elective large joint replacement. Cochrane Database Syst Rev. 2015 Aug 13;8:CD010278. doi: 10.1002/14651858.CD010278.pub2. Review. PubMed PMID: 26269416.

## 4. An ethical exploration of barriers to research on controversial controlled drugs

Heroin, marijuana, ketamine and cocaine have shown therapeutic benefit in randomized controlled trials (RCTs) and systematic reviews, they are used routinely in Europe even in children and for labor pain. The dearth of research in the US suggests that overly strict regulations, fear of legal consequences, associated stigma, and lack of funding hinder their scientific evaluation. Our review of ethical concerns germane to the research with illicit and addictive substances (undue inducement, informed consent, risk to participants, researchers and institutions, justice and liberty) was accepted for publication in the American Journal of Bioethics, arguably the leading bioethics journal the below cartoon illustrates this **Catch 22:** We cannot study the benefits of illicit drugs because they are illegal; they are illegal because there is no evidence to support benefit.

**Andreae MH**, Rhodes E, Bourgoise T, Carter G, Indyk D, Sacks HS, Rhodes R. An ethical exploration of barriers to research on controlled drugs. AJOB 2016 [In press].

Supported through a Conduit CTSA grant (UL1 TR000067) from the *National Center for Advancing Translational Sciences (NCATS),* we collected preliminary data using mixed methods, (focus groups of the three main stakeholder groups in research: members of the institutional review boards, clinical researchers investigating controversial substances like cannabis and potential research participants living with HIV). Our work has been presented as panels and abstracts at international several conferences.

**Andreae MH**, Carter GM, Rhodes R. Bucking Tradition: Questioning Barriers to Research on Controlled Drugs ASBH Panel on research ethics, 15th Annual Meeting of American Society for Bioethics and Humanities, October 24–27, 2013. Hilton Atlanta, Atlanta, GA, 2013

Evelyn Rhodes E, Bourgoise T, **Andreae MH**, Indyk D, Rhodes R, Sacks H.Ethical, social and regulatory barriers to research on controlled drugs for HIV. Aids 2014. Melborne, Australia. June 20-25th 2014

**Andreae MH**, Evelyn Rhodes E, Bourgoise T, Indyk D, Rhodes R, Sacks H. Discordant perspectives on barriers to research on the therapeutic potential of controversial controlled drugs. Anesthesiology 2015. San Diego, CA, 2015

## Complete List of Published Work in [MyBibliography](http://www.ncbi.nlm.nih.gov/sites/myncbi/michael.andreae.1/bibliography/45912673/public/?sort=date&direction=descending): <[Link](http://www.ncbi.nlm.nih.gov/sites/myncbi/michael.andreae.1/bibliography/45912673/public/?sort=date&direction=descending)>

# D. Current NIH Research Support

1) Bayesian evidence synthesis of long term pain outcomes

CTSA Grant 1 UL1 TR001073-01, 1 TL1 TR001072-01, 1 KL2 TR001071-01 7/2014 - 6/2016

* + *National Center for Advancing Translational Sciences (NCATS) –* [80% salary support, PI]

3UL1 RR025750-0253, (Albert Einstein College of Medicine) Fall/2012 - one time

* + *National Center for Advancing Translational Sciences (NCATS) –* [Enhancement funds: $1,500]

**Completed NIH Research Support**

2) Bayesian methods for evidence synthesis of complementary and alternative therapies for HIV

R01-AT005824 (Dr. Sacks) 12/01/2010 – 06/30/2015

*NIH, Center for drug evaluation and research (CDER) –* [Co-Investigator – 10% salary support]

3) Research ethics of controlled substances for HIV related disease

CTSA grant (UL1 TR000067) (Mount Sinai School of Medicine) Fall 2013 - Summer 2015

*National Center for Advancing Translational Sciences (NCATS) -* [$40.000 Co-Investigator]

Conduits Community–Engaged Research pilot project program.

**4) Bayesian evidence synthesis to impute missing data for evidence synthesis of pain outcomes**

CTSA Grant UL1 RR025750, (Albert Einstein College of Medicine) 07/2012 - 07/2013

National Center for Advancing Translational Sciences (NCATS) – [Clinical Research Training Scholar]