Basel Institute **ceb**
for Clinical Epidemiology and Biostatistics

EVIDENCE FOR DECISION MAKING IN HEALTH CARE

ANNUAL REPORT 2019

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FOREWORD OF THE PRESIDENT OF THE BOARD OF TRUSTEES

Dear reader

It is a delight to present, in the name of the board of trustees of the foundation, the 2019 report of the Basel Institute for Clinical Epidemiology and Biostatistics (CEB). The output of this small, agile and internationally well-connected team is again outstanding and deserves our full respect.

The board of trustees is pleased to see a growing number of researchers who were able to initiate their career with support of our foundation at CEB and who are now increasingly gaining impressive and well-funded research grants. The consolidation of the research portfolios and independent project funding from competitive funds fulfills the foundation with great satisfaction and was always at the forefront of the foundation's goal. Nevertheless, the provision of funding and academic prospects for senior investigators, research associates and fellows of CEB by the University of Basel will be fundamental to build on the achievements of CEB.

CEBs' teaching engagement at the Department of Health Science and Technology at ETH Zurich is another development that was well received by the board. A collaboration within the Bachelor Medicine Program will hopefully soon open doors for research collaborations with the most prominent and prestigious university in continental Europe.

CEB is a thriving research institute with a strong focus on improving clinical research methodology and patient outcomes by real world evidence generation. This team under the lead of Prof. Bucher deserves our full respect and support.

Reto Guetg MD
President of the Board of Trustees
Foundation Institute for Clinical Epidemiology

The Board of Trustees
Stefan Kaufmann lic. rer. pol, Prof. Jörg D. Leuppi MD, PhD, Reto Guetg MD

BASEL INSTITUTE FOR CLINICAL EPIDEMIOLOGY AND BIOSTATISTICS (CEB)

OUR MISSION IS TO IMPROVE DECISION MAKING IN HEALTH CARE

We generate and appraise evidence of medical interventions by own research and evidence synthesis.
We use innovative analytical techniques to investigate how new interventions perform in a real world setting.
We invest in clinical research methodology development to improve the quality of clinical research.

OUR STRATEGY

We evaluate whether new or established interventions and technologies improve patient relevant outcomes without safety concerns in the real world setting and represent added benefit to the health care system.

Improve patient outcomes by evidence-based decision making and implementation of effective interventions into clinical care

RESEARCH & CONSULTING

CEB combines excellence in research and clinical expertise with an extensive consulting activity – a unique distinction from other academic institutions. Services offered range from consulting in clinical trial design to large-scale observational and clinical trial data analysis, individual patient data, network and standard meta-analyses, Health Technology Assessments and methodological support for clinical researchers, governmental agencies, health insurers, and industry.

TEACHING

We teach principles of evidence-based medicine, research methodology, and medical statistics to medical students at University of Basel and the Eidgenössische Technische Hochschule (ETH) Zurich and in postgraduate courses.

The team of CEB

RESEARCH HIGHLIGHTS OF CEB IN 2019

Oseltamivir plus usual care versus usual care for influenza-like illness in primary care: an open-label, pragmatic, randomised controlled trial. Butler CC, van der Velden AW, Bongard E, Saville BR, Holmes J, Coenen S, Cook J, Francis NA, Lewis RJ, Godycki-Cwirko M, Llor C, Chlabicz S, Lionis C, Seifert B, Sundvall PD, Colliers A, Aabenhus R, Bjerrum L, Jonassen Harbin N, Lindbaek M, **Glinz D**, **Bucher HC**, Kovacs B, Radzeviciene Jurgute R, Touboul Lundgren P, Little P, Murphy AW, De Sutter A, Openshaw P, de Jong MD, Connor JT, Matheeussen V, Ieven M, Goossens H, Verheij TJ. ***Lancet*** 2019 Dec 12.

Background: Antivirals are infrequently prescribed in primary care for influenza-like illness (ILI).

Method and results: In an open pragmatic, adaptive, randomised controlled trial run during three influenza seasons in 15 European countries, 1629 patients were treated with oseltamivir and 1637 by usual care with 52% having PCR-confirmed influenza. Return to usual daily activity with oseltamivir was in all patients 1·02 day (95% [BCrI] 0·74-1·31) and in older patients or with comorbidities 3·20 days (95% BCrI 1·00-5·50) shorter.

Conclusion and Relevance: Patients with ILI and treated with oseltamivir recovered one day earlier than with symptomatic treated but older and sicker patients profited more.

The comparative effectiveness of NRTI-sparing dual regimens in emulated trials using observational data from the Swiss HIV Cohort Study (SHCS). **Young J**, Scherrer AU, Calmy A, Tarr PE, Bernasconi E, Cavassini M, Hachfeld A, Vernazza P, Gunthard HF, **Bucher HC**. ***Antivir Ther*** 2019 Apr 15.

Background: Nucleoside (or nucleotide) reverse transcriptase inhibitors (NRTIs) cause side effects in some HIV infected patients, prompting the use of either partly or fully NRTI-sparing regimens.

Method and results: Based on data from the SHCS we estimated the 48 weeks effectiveness (therapy switch or measurable viral load equals failure) of two new dolutegravir dual regimens relative to the alternative NRTI-sparing dual regimens. We used a Bayesian Cox model and emulated two trials by propensity score matching of 58 case patients on dolutegravir with 17 control patients on partly NRTI sparing regimens with darunavir (both with lamivudine or emtricitabine) (trial 1) and by matching with 32 control patients with fully NRTI sparing regimens with raltegravir (both with boosted darunavir) (trial 2). The estimated difference in effectiveness was in trial 1 15% (95% credible interval [CrI] 2 - 33) and 12% (95% CrI 0 - 26) in two sequential analyses 1 year apart and in trial 2 9% (95% CrI -1 - 21) and 5% (95% CrI -4 - 15).

Conclusion and Relevance: Estimates of relative effectiveness suggest that both dolutegravir regimens are not inferior to these alternative regimens.

Current use and costs of electronic health records for clinical trial research: a descriptive study. **Mc Cord KA**, **Ewald H**, **Ladanie A**, **Briel M**, **Speich B**, **Bucher HC**, **Hemkens LG**. ***CMAJ Open*** 2019 Jan-Mar; 7(1): E23-E32.

Background: Electronic health records (EHRs) may support randomized controlled trials (RCTs). We describe the current use and costs of EHRs in RCTs, with a focus on recruitment and outcome assessment.

Method and results: Based on a PubMed search of RCTs and cost information from RCT investigators we identified 189 RCTs using EHRs. 17 RCTs (9.0%) involving a median of 732 (interquartile range 73-2513) patients explored interventions not related to EHRs, including quality improvement, screening programs, and disease management interventions. In these trials, EHRs were used for recruitment (14 [82%]) and outcome measurement (15 [88%]). In most of the trials (158 [83.6%]), the outcome was measured with the use of EHRs. The per-patient cost in the 17 EHR-supported trials varied from US$44 to US$2000, and total RCT costs from US$ 67,750 to US$ 5,026,000. In the remaining 172 RCTs (91.0%), EHRs were used as a modality of intervention.

Conclusion and Relevance: RCTs are frequently and increasingly conducted with the use of EHRs, but mainly as part of the intervention. Costs may be reduced once the data infrastructure is established.

MOST CITED PUBLICATION 2019

Tate JP, Sterne JAC, Justice AC, Akgun KM, Brown ST, Bryant K, Chang CC, Gibert CL, Goetz MB, So-Armah K, Marconi VC, McGinnis KA, Oursler KAK, Rentsch CT, Rimland D, Rodriguez-Barradas MC, May MT, Trickey A, Zangerle R, Gill MJ, Bonnet F, Reiss P, Monforte AD, **Bucher HC**, Teira R, Sterling TR, Crane HM. Albumin, white blood cell count, and body mass index improve discrimination of mortality in HIV-positive individuals. ***AIDS*** 2019 Apr 1; 33(5): 903-12.

IMPACT OF RESEARCH FROM CEB AND CITATION FREQUENCY

Our research is frequently cited as reflected by the h-index of senior researchers. The citation frequency of publications of senior staff from CEB is a further measure of the relevance of our research activity.

Senior Researcher	h-Index	Citation frequency in 2019
Prof Dr. M. Briel	51	1369
Prof. H.C. Bucher	71	1697
PD Dr. S Dell-Kuster	14	100
PD Dr. L.G. Hemkens	18	280
PD Dr. B. Kasenda	21	282
PD Dr. M. Koller	49	946
Prof. Dr. Alain Nordmann	25	365

Per 20.1.2020; Scopus.com Author search, citation overview

CEB RESEARCH

In 2019, researchers of CEB have published 58 publications in peer-reviewed journals.

Methodological research

In 2019, CEB Researchers have published 16 meta-research studies (5, 12, 13, 25, 27-29, 32, 33, 36, 46, 48, 50-52, 57)[1]. New publications deal with adherence to guidelines for clinical trial reporting (51). One study found sub-optimal reporting of confounding in observational studies in psychiatry (36). Two studies focus on approval evidence provided by the FDA to guide healthcare decisions (22, 24). Two studies deal with treatment effects in observational studies and randomized controlled trials investigating the same research question (12, 13). Two studies examined the use of electronic health records and routinely collected data for the conduct of randomized clinical trials (32, 33). One study at the protocol stage will systematically investigate monitoring strategies in trials and their impact on quality of trial conduct (27). Three publications deal with costs for the preparatory phase of investigator initiated trials, and budget planning tools for trials (32, 50, 52). The third work investigated planning costs for trials before and after the implemention of the new Swiss human research legislation, but limited data precluded any conclusions on cost differences (52). Two studies deal with disparity for the reimbursement of off-label drugs in oncology (22), and on single pivotal trials in FDA approvals of anticancer drugs (28). One publication evaluated missing outcome data reporting in RCTs (25), another evaluated the impact of early stopping trials on estimated treatment effect sizes (57).

[1] Number refers to the list of publication (see section "Publications of CEB in 2019").

Evidence synthesis

Evidence synthesis is important for decision making. We published and cooperated in nine meta-analyses investigating therapies for Wilson disease (1), complications after non-surgical management of proximal humerus fractures (6), antibiotic prophylaxis in the management of open fractures (9), acetylcholinesterase inhibitors combined with memantine for moderate to severe Alzheimer's disease (19), mannitol bronchials challenge test to identify asthma (26), risk of hospital admission in atrial fibrillation (34), and rituximab in primary central nervous system lymphoma (47).

Randomized controlled trials

CEB contributed as a network partner to the oseltamivir trial (see research highlights, (7)) and participated in trials in surgery of abdominal midline laparotomy and mesh use (17, 18), in a trial from neurology on different drug treatment in Duchenne muscular dystrophy (21), and in a trial of different prophylactic antibiotic treatment durations in transurethral prostate resection (49). A large nationwide trial of routine prescription feedback and monitoring to reduce antibiotic use in primary care (NFP 72 Antimicrobial Resistance) is still ongoing. In another pilot trial we are investigating a new diagnostic device for acute bacterial rhinosinusitis which continues to recruit patients. We submitted a trial protocol to the investigator initiated clinical trial call by the Swiss National Science Foundation where we intend to investigate the comparative effectiveness of a test and treat approach in patients with influenza like illness in primary who will be randomized to point of care PCR testing by Roche Cobas plus treatment of influenza positive patients with the new antiviral drug baloxavir marboxil versus symptomatic treatment.

Non-randomized real world evidence

Three publications from the international HIV Causal Collaboration deal with different monitoring and treatment strategies in HIV, with mortality risks from transmitted antiretroviral drug resistance, and with a comparison of the effects of immediates versus defer antiretroviral therapy initiation as investigate in clinical trial and observational study data (8, 30, 31). One international collaborative project investigated new prediction models for mortality in HIV that additionally included non HIV related prognostic parameters (55). Two projects from the Swiss HIV Cohort Study investigated the impact of immune reconstitution on cancer risk, on the effect of new dual antiretroviral drug combinations in patients with drug-toxicity related limited treatment options (45, 58). **Eric Remera** and **Sabin Nsanzimana** current and former PhD students contributed four publications, two of them dealing with retention in care and outcomes of HIV infected children and adolescents in Rwanda (38, 49).

In a very large international collaboration with experts in the field of real world evidence, CEB researchers were involved in the development of the reporting guideline for pharmocoepidemiological research (RECORD-PE)(29).

Team of Biostatisticians
Frédérique Chammartin, PD Dr. Salome Dell-Kuster,
Florian Halbeisen, Dr. Soheila Aghlmandi
(James Young absent)

Clinical Epidemiology & Methodology Team
Research Groups Prof. Dr. Matthias Briel and PD Dr. Lars Hemkens
Ala Taji Heravi, Dr. Viktoria L. Gloy, Prof. Dr. Matthias Briel,
Stefan Schandelmaier, PD Dr. Lars G. Hemkens
(Kimberly McCord, Dmitry Gryaznov, absent)

Clinical Epidemiology & Methodology Team
Research Group Prof. Dr. Heiner Bucher
Florian Halbeisen, Frédérique Chammartin, Diana Grauwiler,
Dr. Soheila Aghlmandi, Dr. Dominik Glinz, Prof. Dr. Heiner Bucher
(James Young, Eric Remera, absent)

Teamleaders of Swiss Transplant Cohort Study
PD Dr. Michael Koller, Madeleine Wick

CEB TEACHING

CEB teaches principles of evidence-based medicine, critical appraisal skills, basics in clinical epidemiology and clinical research methodology to medical students in the bachelor and masters program at the University of Basel and at ETH Zurich. Total undergraduate teaching obligations in 2019 were 206 hours. In 2019, CEB was training six PhD students and three master students.
PhD and master students have been involved in eleven publications (10, 12, 19, 22, 32, 33, 35, 38, 39, 51, and 52) and were first authors in three publications (27, 32, 33).

CEB CONSULTING

CEB is providing clinical epidemiology consultancy services within the Department of Clinical Research at the University Hospital Basel. Five publications originated from collaborative projects with the Department of Surgery (17, 18, 23, 44, 53), one with the Division of Infectious Diseases (49) and two publications were done with the Swiss Cohort of Acute Coronary Syndrome. **H.C. Bucher** and **L.G. Hemkens** were instrumental in the protocol development of two randomized controlled trials on the use of prednisone in post-infection chronic cough in primary care (Lead Prof. Andreas Zeller) and on pre- versus sub-pectoral implant-based breast reconstruction after nipple-sparing mastectomy for prevention and treatment of breast cancer (Lead Prof. Walter Weber) that were funded by the Swiss National Science Foundation in the context of the Investigator initiated trial call (IICT) with the total amount of CHF 2.4 millions.

HEALTH TECHNOLOGY ASSESSMENT (HTA)

CEB has a consultancy mandate from the Swiss Federal Office of Public Health (BAG) for a Health Technology Assessment report on the effectiveness of iron therapy in non-anemic patients with iron deficiency to be finished in early 2020 and another consultancy mandate from the German "Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen" (IQWIG). The HTA report on knee arthroscopy for the treatment of degenerative changes mandated by the Swiss Medical Board and the BAG was published in 2019.

SWISS TRANSPLANT COHORT STUDY

The Swiss Transplant Cohort Study (STCS), founded in 2007 with major support of CEB included by the end of 2019, a total of 5817 patients enrolled in the STCS and the active cohort involved 4813 patients (for details on these publications see www.stcs.ch).

PROMOTIONS, NEW POSTIONS

G Moffa was appointed as assistant professor of biostatistics at the Department of Mathematics and Informations, University of Basel.
S Aghlmandi was promoted to a senior biostatistician at CEB.
S Nsanzimana who finished his PhD in 2018 at CEB was appointed as the new General Director of Rwanda Biomedical Center in Kigali Rwanda.

Senior Investigators
PD Dr. Salome Dell-Kuster, Prof. Dr. Matthias Briel, PD Dr. Michael Koller,
PD Dr. Lars G. Hemkens, Prof. Dr. Laurent Audigé, Prof. Dr. Heiner C. Bucher
(James Young absent)

COMPETITIVELY ACQUIRED FUNDING

Associated researchers of CEB acquired substantial funding for innovative projects:

Project Funding agency	Principle investigator	Duration (months)	Funds in CHF 1000
Surgical safety and effectiveness in orthopedics: Swiss-wide multicenter evaluation and prediction of core outcomes in arthroscopic rotator cuffreconstruction SNF	**Prof. L. Audigé**	36	504
Making clinical trials more affordable – systematic investigation of trial costs and tool development SNF	**Prof. M. Briel**	36	667
Generalizability, applicability and pragmatism of clinical trials and their impact on treatment effect estimates: a meta-epidemiological study SNF	**PD L.G. Hemkens**	36	464
Emerging trends and developments in cancer treatment innovation: expansion of the CEIT-cancer project (exCEIT) Krebsforschung Schweiz	**PD L.G. Hemkens**	24	234
Increasing value of biomedical research: development of a methodological decision support system to assist health scientists in research design, conduct, and analysis SNF/SPARK	**Dr. S. Schandelmaier**	12	100

OUTLOOK

CEB has further expanded its collaborative network at the local, national and international level. Associated researchers have acquired substantial funding, which allows to keep and hire new staff and to create new PhD positions. This relatively small team is extremely productive and achieves to publish every year several important scientific publications in high impact factor journals. Expanding the teaching activities to ETH Zurich will help us to further attract highly motivated medical students to clinical research.

I would like to thank the entire team and Diana Grauwiler, my clinical research manager for their excellent work. I also would like to express my deep gratitude to the foundation for the long-lasting and generous financial support of the institute.

Prof. Heiner C. Bucher MD MPH
Director of the Institute

PUBLICATIONS OF CEB IN 2019

Original Publications in Peer Reviewed Journals

1. Appenzeller-Herzog C, Mathes T, Heeres MLS, Weiss KH, Houwen RHJ, **Ewald H**. Comparative effectiveness of common therapies for Wilson disease: A systematic review and meta-analysis of controlled studies. ***Liver International*** 2019 39(11): 2136-52.

2. Bachmann N, von Siebenthal C, Vongrad V, Turk T, Neumann K, Beerenwinkel N, Bogojeska J, Fellay J, Roth V, Kok YL, Thorball CW, Borghesi A, Parbhoo S, Wieser M, Böni J, Perreau M, Klimkait T, Yerly S, Battegay M, Rauch A, Hoffmann M, Bernasconi E, Cavassini M, Kouyos RD, Günthard HF, Metzner KJ, Anagnostopoulos A, Battegay M, Bernasconi E, Böni J, Braun DL, **Bucher HC**, Calmy A, Cavassini M, Ciuffi A, Dollenmaier G, Egger M, Elzi L, Fehr J, Fellay J, Furrer H, Fux CA, Günthard HF, Haerry D, Hasse B, Hirsch HH, Hoffmann M, Hösli I, Huber M, Kahlert C, Kaiser L, Keiser O, Klimkait T, Kouyos RD, Kovari H, Ledergerber B, Martinetti G, Tejada BM, Marzolini C, Metzner KJ, Müller N, Nicca D, Paioni P, Pantaleo G, Perreau M, Rauch A, Rudin C, Scherrer AU, Schmid P, Speck R, Stöckle M, Tarr P, Trkola A, Vernazza P, Wandeler G, Weber R, Yerly S, the Swiss HIVCS. Determinants of HIV-1 reservoir size and long-term dynamics during suppressive ART. ***Nature Communications*** 2019 10(1).

3. Becker C, Lecheler L, Hochstrasser S, Metzger KA, Widmer M, Thommen EB, Nienhaus K, **Ewald H**, Meier CA, Rueter F, Schaefert R, Bassetti S, Hunziker S. Association of Communication Interventions to Discuss Code Status With Patient Decisions for Do-Not-Resuscitate Orders: A Systematic Review and Meta-analysis. ***JAMA Netw Open*** 2019 Jun 5; 2(6): e195033.

4. Bogoch, II, **Speich B**, Lo NC, Moser W, Croll D, Ali SM, Ame SM, Utzinger J, Andrews JR, Keiser J. Clinical evaluation for morbidity associated with soil-transmitted helminth infection in school-age children on Pemba Island, Tanzania. ***PLoS Negl Trop Dis*** 2019 Jul; 13(7): e0007581.

5. **Briel M**, **Speich B**, von Elm E, **Gloy V**. Comparison of randomized trials discontinued or revised for poor recruitment and completed trials with the same research question: a matched qualitative study. ***Trials*** 2019;20(1):800.

6. Brorson S, Alispahic N, Bahrs C, Joeris A, Steinitz A, **Audige L**. Complications after non-surgical management of proximal humeral fractures: a systematic review of terms and definitions. ***BMC Musculoskelet Disord*** 2019 Feb 23; 20(1): 91.

7. Butler CC, van der Velden AW, Bongard E, Saville BR, Holmes J, Coenen S, Cook J, Francis NA, Lewis RJ, Godycki-Cwirko M, Llor C, Chlabicz S, Lionis C, Seifert B, Sundvall PD, Colliers A, Aabenhus R, Bjerrum L, Jonassen Harbin N, Lindbaek M, **Glinz D**, **Bucher HC**, Kovacs B, Radzeviciene Jurgute R, Touboul Lundgren P, Little P, Murphy AW, De Sutter A, Openshaw P, de Jong MD, Connor JT, Matheeussen V, Ieven M, Goossens H, Verheij TJ. Oseltamivir plus usual care versus usual care for influenza-like illness in primary care: an open-label, pragmatic, randomised controlled trial. ***Lancet*** 2019 Dec 12.

8. Caniglia EC, Robins JM, Cain LE, Sabin C, Logan R, Abgrall S, Mugavero MJ, Hernandez-Diaz S, Meyer L, Seng R, Drozd DR, Seage Iii GR, Bonnet F, Le Marec F, Moore RD, Reiss P, van Sighem A, Mathews WC, Jarrin I, Alejos B, Deeks SG, Muga R, Boswell SL, Ferrer E, Eron JJ, Gill J, Pacheco A, Grinsztejn B, Napravnik S, Jose S, Phillips A, Justice A, Tate J, **Bucher HC**, Egger M, Furrer H, Miro JM, Casabona J, Porter K, Touloumi G, Crane H, Costagliola D, Saag M, Hernan MA. Emulating a trial of joint dynamic strategies: An application to monitoring and treatment of HIV-positive individuals. ***Stat Med*** 2019 Jun 15; 38(13): 2428-46.

9. Chang Y, Bhandari M, Zhu KL, Mirza RD, Ren M, Kennedy SA, Negm A, Bhatnagar N, Naji FN, Milovanovic L, Fei Y, Agarwal A, Kamran R, Cho SM, **Schandelmaier S**, Wang L, Jin L, Hu S, Zhao Y, Lopes LC, Wang M, Petrisor B, Ristevski B, Siemieniuk RAC, Guyatt GH. Antibiotic Prophylaxis in the Management of Open Fractures: A Systematic Survey of Current Practice and Recommendations. ***JBJS Rev*** 2019 Feb; 7(2): e1.

10. Donenberg GR, Cohen MH, Ingabire C, Fabri M, Emerson E, Kendall AD, **Remera E**, Manzi O, **Nsanzimana S**. Applying the Exploration Preparation Implementation Sustainment (EPIS) Framework to the Kigali Imbereheza Project for Rwandan Adolescents Living With HIV. ***J Acquir Immune Defic Syndr*** 2019 Dec; 82 Suppl 3: S289-S98.

11. Duggan BT, **Roth JA**, Dangel M, Battegay M, Widmer AF. Impact of health insurance status on surgical site infection incidence: A prospective cohort study. ***Infect Control Hosp Epidemiol*** 2019 Jul 16: 1-3.

12. **Ewald H**, Ioannidis JP, **Ladanie A**, **Cord KM**, **Bucher HC**, **Hemkens LG**. Non-randomized studies using causal-modelling may give different answers than RCTs: a meta-epidemiological study. ***J Clin Epidemiol*** 2019 Nov 5.

13. **Ewald H**, **Speich B**, **Ladanie A**, **Bucher HC**, Ioannidis JPA, **Hemkens LG**. Marginal structural models and other analyses allow multiple estimates of treatment effects in randomized clinical trials: Meta-epidemiological analysis. ***J Clin Epidemiol*** 2019 Mar; 107: 12-26.

14. Gabriel L, **Young J**, Hoesli I, Girard T, **Dell-Kuster S**. Generalisability of randomised trials of the programmed intermittent epidural bolus technique for maintenance of labour analgesia: a prospective single centre cohort study. ***Br J Anaesth*** 2019 Aug; 123(2): e434-e41.

15. Gencer B, Rigamonti F, Nanchen D, Vuilleumier N, Kern I, **Aghlmandi S**, Klingenberg R, Raber L, Auer R, Carballo D, Carballo S, Heg D, Windecker S, Luscher TF, Matter CM, Rodondi N, Mach F. Prognostic Value of Elevated Lipoprotein(a) In Patients With Acute Coronary Syndromes. ***Eur J Clin Invest*** 2019 Apr 2: e13117.

16. Gencer B, Vuilleumier N, Nanchen D, Collet TH, Klingenberg R, Raber L, Auer R, Carballo D, Carballo S, **Aghlmandi S**, Heg D, Windecker S, Luscher TF, Matter CM, Rodondi N, Mach F. Prognostic value of total testosterone levels in patients with acute coronary syndromes. ***Eur J Prev Cardiol*** 2019 Jun 1: 2047487319853343.

17. Glauser PM, Brosi P, **Speich B**, Kaser SA, Heigl A, Rosenberg R, Maurer CA. Prophylactic Intraperitoneal Onlay Mesh Following Midline Laparotomy-Long-Term Results of a Randomized Controlled Trial. ***World J Surg*** 2019 Mar 1.

18. Glauser PM, Brosi P, **Speich B**, Kaser SA, Heigl A, Rosenberg R, Maurer CA. Correction to: Prophylactic Intraperitoneal Onlay Mesh Following Midline Laparotomy-Long-Term Results of a Randomized Controlled Trial. ***World J Surg*** 2019 Jul; 43(7): 1676.

19. **Glinz D**, **Gloy VL**, Monsch AU, Kressig RW, **Patel C**, **McCord KA**, Ademi Z, Tomonaga Y, Schwenkglenks M, **Bucher HC**, **Raatz H**. Acetylcholinesterase inhibitors combined with memantine for moderate to severe Alzheimer's disease: a meta-analysis. ***Swiss Med Wkly*** 2019 Jun 17; 149: w20093.

20. Gran JM, Hoff R, Røysland K, Ledergerber B, **Young J**, Aalen OO. Estimating the treatment effect on the treated under time-dependent confounding in an application to the Swiss HIV Cohort Study. ***Journal of the Royal Statistical Society: Series C (Applied Statistics)*** 2018 67(1): 103-25.

21. Hafner P, Bonati U, Klein A, Rubino D, Gocheva V, Schmidt S, Schroeder J, Bernert G, Laugel V, Steinlin M, Capone A, Gloor M, Bieri O, **Hemkens LG**, **Speich B**, Zumbrunn T, Gueven N, Fischer D. Effect of Combination l-Citrulline and Metformin Treatment on Motor Function in Patients With Duchenne Muscular Dystrophy: A Randomized Clinical Trial. ***JAMA Netw Open*** 2019 Oct 2; 2(10): e1914171.

22. Herbrand AK, Schmitt AM, **Briel M**, Diem S, **Ewald H**, Hoogkamer A, Joerger M, **Mc Cord KA**, Novak U, **Sricharoenchai S**, **Hemkens LG**, **Kasenda B**. Contrasting evidence to reimbursement reality for off-label use (OLU) of drug treatments in cancer care: rationale and design of the CEIT-OLU project. ***ESMO Open*** 2019 4(6): e000596.

23. Hatz CR, Msallem B, **Aghlmandi S**, Brantner P, Thieringer FM. Can an entry-level 3D printer create high-quality anatomical models? Accuracy assessment of mandibular models printed by a desktop 3D printer and a professional device. ***Int J Oral Maxillofac Surg*** 2019 Jul 9.

24. Kaderli RM, Spanjol M, Kollar A, Butikofer L, Gloy V, Dumont RA, Seiler CA, Christ ER, Radojewski P, **Briel M**, Walter MA. Therapeutic Options for Neuroendocrine Tumors: A Systematic Review and Network Meta-analysis. ***JAMA Oncol*** 2019 Feb 14.

25. Kahale LA, Guyatt GH, Agoritsas T, **Briel M**, Busse JW, Carrasco-Labra A, Khamis AM, Zhang Y, Hooft L, Scholten R, Akl EA. A guidance was developed to identify participants with missing outcome data in randomized controlled trials. ***J Clin Epidemiol*** 2019 Jul 9; 115: 55-63.

26. Kernen P, Steveling-Klein EH, **Saccilotto RT**, **Raatz H**, **Briel M**, **Koller MT**, Westwood M, **Bucher HC**, Miedinger D, Leuppi JD. The sensitivity and specificity of the mannitol bronchial challenge test to identify asthma in different populations: a systematic review. ***Swiss Med Wkly*** 2019 Aug 26; 149: w20100.

27. **Klatte K**, Pauli-Magnus C, Love S, Sydes M, Benkert P, Bruni N, **Ewald H**, Jimenez PA, Mi Bonde M, **Briel M**. Monitoring strategies for clinical intervention studies. (Protocol). ***CochrDatabaseSysRevs*** 2019 Dec 13.

28. **Ladanie A**, **Speich B**, **Briel M**, Sclafani F, **Bucher HC**, Agarwal A, Ioannidis JPA, Pereira TV, **Kasenda B**, **Hemkens LG**. Single pivotal trials with few corroborating characteristics were used for FDA approval of cancer therapies. ***J Clin Epidemiol*** 2019 May 31.

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48. **Speich B**. Adequate reporting of the sample size calculation in surgical randomized controlled trials. ***Surgery*** 2019 Nov 28.

49. **Speich B**, Bausch K, **Roth JA**, **Hemkens LG**, **Ewald H**, Vogt DR, Bruni N, Deuster S, Seifert H-H, Widmer AF. Single-dose versus 3-day cotrimoxazole prophylaxis in transurethral resection or greenlight laser vaporisation of the prostate: study protocol for a multicentre randomised placebo controlled non-inferiority trial (CITrUS trial). ***Trials*** 2019 February 19; 20(1): 142.

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53. Steffen L, **Moffa G**, Muller PC, Oertli D. Secondary hyperparathyroidism: recurrence after total parathyroidectomy with autotransplantation. ***Swiss Med Wkly*** 2019 Dec 2; 149: w20160.

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57. Walter SD, Guyatt GH, Bassler D, **Briel M**, Ramsay T, Han HD. Randomised trials with provision for early stopping for benefit (or harm): The impact on the estimated treatment effect. ***Stat Med*** 2019 Mar 19.

58. **Young J**, Scherrer AU, Calmy A, Tarr PE, Bernasconi E, Cavassini M, Hachfeld A, Vernazza P, Gunthard HF, **Bucher HC**. The comparative effectiveness of NRTI-sparing dual regimens in emulated trials using observational data from the Swiss HIV Cohort Study. ***Antivir Ther*** 2019 Apr 15.

HTA Reports

1. **Bucher HC**, **Glinz D**, **Gloy V**, **Patel C**, **Raatz H**, Schwenkglenks M, Tomonaga Y. Health Technology Assessment of knee arthroscopy for the treatment of degenerative changes. Zurich, Switzerland: Swiss Medical Board, 2019 November 23.

Editorials, Research Letters, Letters and Non-Peer Reviewed Publications

1. **Glinz D**. C-Reactive Protein for Antibiotic Use in COPD Exacerbations. ***N Engl J Med*** 2019 Dec 12; 381(24): 2371.

2. **Mc Cord KA**, **Hemkens LG**. Using electronic health records for clinical trials: Where do we stand and where can we go? ***CMAJ*** 2019 Feb 4; 191(5): E128-E33.

3. **Roth JA**, Widmer AF. Reply to Yoshioka et al. ***Clin Infect Dis*** 2019 Aug 12.

Presentations

1. **Dell-Kuster S**. Classification des complications intra-opératoires. ***Enseignement – Cours Post-Gradues***, Hôpitaux Universitaires de Genève, Switzerland. 2019 October 14.

2. **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – CLASSification of Intraoperative Complications. ***Jahreskongress der Schweizerischen Gesellschaft für Chirurgie***, Bern, Switzerland. 2019 May 16.

3. **Deutschmann E**, **Bucher HC**, Jaeckel S, Gibbons S, McAllister K, Scherrer A, Braun D, Cavassini M, Hachfeld A, Calmy A, Battegay M, Cipriani A, Elzi L, Young J, Lopez-Centeno B, Berenguer J, Khoo S, Moffa G, Marzolini C, The Swiss HIVCS. Prevalence of potential drug-drug interactions in patients of the Swiss HIV Cohort Study in the era of HIV integrase inhibitors. ***European AIDS Conference***, Basel, Switzerland. 2019 November 6-9 (Oral Presentation).

4. **Speich B**, Open access budget tools for the planning of randomised controlled trials: a scoping review. ***Evidence Based Medicine Live (EBMLive)***, Oxford, United Kingdom. 2019 Jul 15-17 (oral presentation).

5. **Speich B**, Are reporting guidelines fit for purpose or are they neither use nor ornament? ***NIHR Statistics Group Driving Interprofessional Collaboration***, Sheffield, United Kingdom. 2019 Jun 20 (oral presentation).

6. Benkert P, **Briel M**. Beschreibende Statistik der Forschung im Geltungsbereich des Schweizer Humanforschungsgesetzes. ***Swiss Federal Office of Public Health 2019***, Bern-Liebefeld, Switzerland. 2019 Jan 15 (invited talk).

7. **Briel M**. More STEAM to improve trial efficiency: current research-on-research. ***CTU rounds Zurich***, Zurich, Switzerland. 2019 February 28 (invited talk).

8. **Briel M**. Research-on-research to improve clinical trial efficiency. ***Colloquium Evidence-based Health Services Research***, Cologne, Germany. 2019 May 8 (invited talk).

9. **Briel M**. Latest Insights on Research-on-Research. ***Nursing Sciences Research Roundtable Meeting***, Basel, Switzerland. 2019 May 21 (invited talk).

10. **Briel M**. Research-on-research. ***Basics of Ethics in Health Sciences Research SSPH+***, Bern, Switzerland. 2019 May 28-29 (invited talk).

11. **Briel M**. Learning from failure: Research on clinical research. ***International Psychiatry Summer School***, Basel, Switzerland. 2019 July 15-19 (invited talk).

12. **Briel M**. Trial Forge Centre Basel & use of trial resources. ***2nd Trial Forge Meeting***, Brighton, United Kingdom. 2019 Oct 5 (invited talk).

13. **Briel M**. Clinical Trial Design – partnering pragmatism with complexity to achieve excellence. ***5th Annual Trial Methodology Symposium Health Research Board Trial Methodology Research Network (HRB-TMRN)***, Dublin, Ireland. 2019 Dec 6 (invited talk).

14. **Hemkens LG**. Registries and Routine Data for Better Research and Patient Care [Register und Routinedaten für bessere Forschung und Patientenversorgung]. ***1st Symposium der Cochrane Deutschland Stiftung***, Freiburg, Germany. 2019 Feb 1 (invited lecture).

15. **Hemkens LG**. Evaluation approaches for reporting statement impact. CONSORT Extension for Trials Conducted Using Cohorts and Routinely Collected Health Data. ***Reporting Guideline Development Meeting***. London, United Kingdom. 2019 May 14.

16. **Hemkens LG**. Disruptive clinical trial technologies for systematic innovation in oncology. ***Personalized Oncology 2019***. Basel, Switzerland. 2019 June 26 (invited lecture).

17. **Hemkens LG**. More useful evidence – new ways to better healthcare research. ***DayOne Experts – Next Generation Clinical Trials***. Basel, Switzerland. 2019 June 26 (invited lecture).

18. **Hemkens LG**. Routine data and healthcare decisions: concepts, chaos and chances. Increasing value of research in health care. ***25th Anniversary of Cochrane Netherlands symposium***. Utrecht, the Netherlands. 2019 Oct 4 (invited lecture).

19. **Hemkens LG**. RCTs with routinely collected data: How does this work? [RCTs mit Routinedaten: Wie geht das?]. ***Gemeinsamer Bundesausschuss (G-BA)***. Berlin, Germany. 2019 Oct 17 (invited lecture).

20. **Hemkens LG**. Using routinely collected data to assess effects of medical innovations: promises, evidence and future. ***Swissmedic***. Berne, Switzerland. 2019 Nov 4 (invited lecture).

21. **Hemkens LG**. Ioannidis JPA. Randomized real world evidence: promises, opportunities and real world challenges. ***9th International Conference for EBHC Teachers and Developers***. Taormina, Italy. 2019 Nov 8 (workshop).

Posters and Abstracts

1. **Aghlmandi S**. Record linkage of claims and cohort data for health economic analyses: Swiss HIV Cohort Study ***40th Annual Conference of the International Society for Clinical Biostatistics***, Leuven, Belgium. 2019 July 14-18.

2. Engel A, Murugesan J, Gomes NV, **Gawria L**, Kirchhoff P, Villarino L, Solis A, Trulls C, Martin R, Gie O, Blanc C, Hahnloser D, Van Goor H, ten Broek R, Rosman C, Schumacher P, Brandt C, Schmid R, Joller S, Goebel B, Mayr J, Meier S, Kang SJ, Aduse-Poku M, Delrio P, Rega D, Pace U, Loveday B, Bissett I, O'Grady G, Herbst F, Ghaffari S, Ozcelik M, Gecim IE, Ioannidis O, Galanos K, Vrochides D, Passeri M, Ridgway PF, Clancy C, Nally DM, Bruppacher HR, Ranter B, Rabanser S, Steiner LA, Clavien PA, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – Classification of Intraoperative Complications. ***General Surgery Section of the Royal Australasian College of Surgeons (RACS) Annual Scientific Congress 2019*** Bangkok, Thailand. 2019 May 6-10.

3. **Gawria L**, Gomes NV, Kirchhoff P, Van Goor H, Rosenthal R, **Dell-Kuster S**. Classification Of Intraoperative Complications (CLASSIC): Reliability And Practicability. ***Annual Academic Surgical Congress 2019***, Houston, United States of America. 2019 Feb 5-7. (oral presentation)

4. **Gawria L**, Gomes NV, Kirchhoff P, Villarino L, Solis A, Trulls C, Martin R, Gie O, Blanc C, Hahnloser D, Van Goor H, Ten Broek R, Rosman C, Schumacher P, Brandt C, Schmid R, Joller S, Goebel B, Mayr J, Meier S, Kang SJ, Aduse-Poku M, Delrio P, Rega D, Pace U, Loveday B, Bissett I, O'Grady G, Herbst F, Ghaffari S, Engel A, Murugesan J, Ozcelik M, Gecim IE, Ioannidis O, Galanos K, Vrochides D, Passeri M, Ridgway PF, Clancy C, Nally DM, Bruppacher HR, Ranter B, Rabanser S, Steiner LA, Clavien PA, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – Classification of Intraoperative Complications. ***Clinical Research Day 2019 University Hospital Basel***, Basel, Switzerland. 2019 Jan 24.

5. **Gawria L**, Ten Broek R, Rosman C, van Goor H, Clavien PA, Kirchhoff P, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC - Classification of intraoperative complications. ***World Congress of Surgery***, Krakow, Poland. 2019 August 11-15.

6. Gomes NV, **Gawria L**, **Aghlmandi S**, Aduse-Poku M, Bissett I, Blanc C, Brandt C, Ten Broek R, Bruppacher HR, Clancy C, Delrio P, Espin E, Galanos K, Gecim IE, Ghaffari S, Gie O, Goebel B, Hahnloser D, Herbst F, Ioannidis JP, Joller S, Kang SJ, Martin R, Mayr J, Meier S, Murugesan J, Vrochides D, Engel A, O'Grady G, Loveday B, Van Goor H, **Bucher HC**, Clavien PA, Steiner LA, Kirchhoff P, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of ClassIntra® – Classification of intraoperative adverse events. ***SwissAnaesthesia 2019***, Interlaken, Switzerland. 2019 November 7-9.

7. Gomes NV, **Gawria L**, Kirchhoff P, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – Classification of Intraoperative Complications. ***EuroAnaesthesia 2019*** Vienna, Austria. 2019 June 1-3.

8. Kirchhoff P, Gomes NV, **Gawria L**, Villarino L, Rochera MI, Solis A, Martin R, Blanc C, Gie O, Hahnloser D, Van Goor H, Ten Broek R, Rosman C, Schuhmacher P, Brandt C, Schmid R, Joller S, Goebel B, Mayr J, Meier S, Kang SJ, Aduse-Poku M, Delrio P, Rega D, Pace U, Loveday B, Bissett I, O'Grady G, Herbst F, Ghaffari S, Engel A, Murugesan J, Ozcelik M, Gecim IE, Ioannidis O, Galanos K, Vrochides D, Passeri M, Ridgway PF, Clancy C, Nally DM, Bruppacher HR, Ranter B, Rabanser S, Steiner LA, Clavien PA, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – Classification of Intraoperative Complications. ***106th Annual Congress of the Swiss Society of Surgery***, Bern, Switzerland: European Journal of Surgery. 2019 May 15-17.

9. Kirchhoff P, Gomes NV, **Gawria L**, Villarino L, Solis A, Trulls C, Martin R, Gie O, Blanc C, Hahnloser D, Van Goor H, Ten Broek R, Rosman C, Schumacher P, Brandt C, Schmid R, Joller S, Goebel B, Mayr J, Meier S, Kang SJ, Aduse-Poku M, Delrio P, Rega D, Pace U, Loveday B, Bissett I, O'Grady G, Herbst F, Ghaffari S, Engel A, Murugesan J, Ozcelik M, Gecim IE, Ioannidis O, Galanos K, Vrochides D, Passeri M, Ridgway PF, Clancy C, Nally DM, Bruppacher HR, Ranter B, Rabanser S, Steiner LA, Clavien PA, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – Classification of Intraoperative Complications. ***106th Annual Meeting of the Swiss Society of Surgery (SGC)*** Bern, Switzerland. 2019 May 15-17.

10. Klingenberg R, **Aghlmandi S**, Räber L, Gencer B, Carballo D, Nanchen D, **Bucher HC**, Von Eckardstein A, Matter CM, Lüscher TF. Cysteine-rich Angiogenic inducer 61 (CYR61) provides independent incremental prognostic information after acute coronary syndromes beyond cadiovascular biomarkers and GRACE risk score. ***European society of cardiology (ESC 2019)*** Davos, Switzerland. 2019 Feb 18.

11. Krielen P, **Gawria L**, Stommel MWJ, **Dell-Kuster S**, Rosenthal R, Ten Broek R, Van Goor H. Interrater agreement of the CLASSification of Intra-operative Complications (CLASSIC). ***Annual Academic Surgical Congress 2019***, Houston, United States of America. 2019 Feb 5-7.

12. Murugesan J, Engel A, Kirchhoff P, Rosenthal R, **Dell-Kuster S**. International multicentre cohort study for the external validation of CLASSIC – Classification of Intraoperative Complications. ***International Surgical Congress of the Associations of Surgeons of Great Britain and Ireland*** Telford, England. 2019 May 7-9.

13. Nussbaumer J, **Dell-Kuster S**, Gomes NV, Heinzelmann-Schwarz V, Kind AB. Validation study of ClassIntra - Classification of Intraoperative Adverse Events - application in operative gynecology. ***Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe***, St.Gallen, Switzerland. 2019 June 26-28.

14. **Remera E**, Musengimana G, Semakula M, Sebuhoro D, Mulindabigwi A, Mugwaneza P, **Nsanzimana S**, **Bucher HC**. Index testing and intensified case finding for efficiency in HIV testing in Rwanda. ***European AIDS Conference***, Basel, Switzerland. 2019 November 6-9.

15. **Young J**, Scherrer A, Calmy A, Tarr P, Bernasconi E, Cavassini M, Hachfeld A, Vernazza P, Guenthard HF, **Bucher HC**. Comparing NRTI-sparing dual regimens using data from the Swiss HIV cohort study ***European AIDS Conference***, Basel, Switzerland. 2019 November 6-9.

16. Walter SD, Guyatt GH, Bassler D, **Briel M**, Ramsay T, Han HD. Mis-estimation of the treatment effect in trials that stop early for benefit. ***40th Annual Conference of the International Society of Clinical Biostatistics***, Leuven, Belgium. 2019 July 14-18 (poster presentation).

17. Deschodt M, Blozik E, **Briel M**, Probst-Hensch N, Schwenkglenks M, Zeller A, De Geest S on behalf of the INSPIRE consortium. Implementation of an integrated nurse-led care program for community-dwelling older adults in Canton Baselland: the INSPIRE project. ***International Jerusalem Conference on Health Policy***, Jerusalem, Israel. 2019 Sept 15-17 (oral presentation).

18. **Klatte K**, Love S, Sydes M, **Ewald H**, Benkert P, Bruni N, Arnaiz P, Pauli-Magnus C, **Briel M**. Systematic review of prospective studies comparing different monitoring strategies in clinical intervention studies. ***5th International Clinical Trials Methodology Conference***, Brighton, United Kingdom. 2019 Oct 6-9 (short oral & poster presentation).

19. **Gryaznov D**, **Kasenda B**, von Elm E, von Niederhäusern B, **Speich B**, **Hemkens LG**, **Schandelmaier S**, Ojeda Ruiz E, **Saccilotto R**, Tomonaga Y, Amstutz A, **Briel M**. Longitudinal evaluation of the reporting quality of clinical trial protocols – evidence for improvement? ***5th International Clinical Trials Methodology Conference***, Brighton, United Kingdom. 2019 Oct 6-9 (poster presentation).

20. **Speich B**, **Gryaznov D**, **Gloy V**, **McCord KA**, **Kasenda B**, **Briel M**. What proportion of ethically approved randomized clinical trials can be found in a trial registry? ***5th International Clinical Trials Methodology Conference***, Brighton, United Kingdom. 2019 Oct 6-9 (short oral & poster presentation).

21. **Gryaznov D**, Odutayo A, Copsey B, Monk P, **Speich B**, Roberts C, Vadher K, Dutton P, Hopewell S, **Briel M**, Altman DG. Design, Analysis and Reporting of Multi-Arm Trials and Strategies to Address Multiple Testing. ***5th International Clinical Trials Methodology Conference*** Brighton, United Kingdom. 2019 Oct 6-9 (short oral & poster presentation).

22. **Schandelmaier S**, **Briel M**, Varadhan R, Schmid CH, Devasenapathy N, Hayward RA, Gagnier J, Borenstein M, van der Heijden GJMG, Dahabreh IJ, Sun X, Sauerbrei W, Walsh MW, Ioannidis JPA, Thabane L, Guyatt GH. A new instrument to assess the credibility of effect modification analyses (ICEMAN) in randomized controlled trials and meta-analyses. ***5th International Clinical Trials Methodology Conference*** Brighton, United Kingdom. 2019 Oct 6-9 (short oral & poster presentation).

ACCOMPLISHED PROJECTS IN 2019[2]

HIV INFECTION, SWISS HIV COHORT STUDY AND MULTICOHORT PROJECTS

SHCS 832 Estimating the effectiveness of NRTI sparing regimens in patients with limited treatment options and then re-estimating as data accrue*

Novel NRTI sparing regimens with dolutegravir are already in use within the SHCS. There is no good evidence that these regimens are better than earlier regimens used to treat NRTI intolerant patients. We will develop a framework based on Bayesian methods for routinely updating estimates of effectiveness as data accrue. This would provide the best information currently available about novel regimens for clinicians treating patients with limited treatment options. We will: (1) Develop an appropriate measure of regimen durability given the information available from the SHCS ; (2) Describe a Bayesian statistical method for estimating the relative effectiveness of novel regimens given limited time to event data and for then updating those estimates; (3) Provide up-to-date estimates of the relative durability of novel regimens used to treat NRTI intolerant patients.
Start of project: 01.10.2017 – End of project: 31.01.2019

METHODOLOGICAL RESEARCH PROJECTS

Development of a reporting guideline for RCTs using routinely collected data (RCD)*

This project assesses the reporting gaps in RCD trials, followed by a stakeholder qualitative process for the development of a reporting guideline and checklist. The qualitative process will encompass a survey of stakeholders such as clinical researchers, clinicians, publishers and pharmaceutical industry representatives and we will closely collaborate with the RECORD and CONSORT groups.
Start of project: 01.03.2018 – End of project: 31.12.2019

Coronary syndromes and inflammation: Cysteine-rich angiogenic inducer 61 (Cyr61)±

Clinical scores and biomarkers improve risk stratification of patients with acute coronary syndromes. However, little is known about their value in patients referred for coronary angiography. Consecutive patients admitted at four Swiss university hospitals with a diagnosis of the acute coronary syndrome were enrolled in the SPUM-ACS Biomarker Cohort between 2009 and 2012. Patients were followed at 30 days and 1 year with assessment of adjudicated events including all-cause mortality and the composite of all-cause mortality or non-fatal recurrent myocardial infarction. We know that the Global Registry of Acute Coronary Events (GRACE) risk score has good predictive accuracy for death or myocardial infarction and allows identification of high-risk patients. Cyr61 (also called CCN1) is a novel biomarker currently evaluated for diagnostic and prognostic performance in addition to the GRACE score. It is shown that Cyr61 is a novel early biomarker reflecting myocardial injury that improves risk stratification in ACS patients, however, how much benefit we might gain from the incremental value of other biomarkers hsTnT, NT-proBNP, and, hsCRP combined with Cyr61 and GRACE risk score remains unknown. The objective of this project is to compare the result of previous Cyr61 publication by adding these known cardiac biomarkers to assess if the incremental value of existing model improves or not.
Start of project: 20.10.2017 – End of project: 31.12.2019

[2] *Project Leadership ± Project Partner

Prediction of recruitment in randomized clinical trial*

The objectives of this study are 1) to establish a comprehensive sample of randomized clinical trials with individual patient recruitment data; and 2) to develop tools to monitor and predict recruitment. The overall goal of this project is to provide clinical research, trial lists, ethics committees and funding bodies with guidance how to effectively improve patient recruitment in clinical studies.

Start of project: 01.01.2017 – End of project: 31.12.2019

Epidemiology and publication of discontinued randomised trials; DISCO

DISCO - design features DISCO 2*

This study is a matched comparison between discontinued RCTs and completed RCTs. Based on key characteristics of the trials discontinued due to poor recruitment (i.e. patient population, intervention, comparator, and outcome) we will conduct systematic searches of electronic databases to identify similar RCTs that were completed as planned. We will then analyse the pairs of completed and discontinued RCTs for differences in design features, logistics, and trial conduct.

Start of project: 03.02.2014 – End of project: 31.12.2019

ONCOLOGY

Comparison of results of pivotal randomized trials for novel oncology drugs reported in journal articles, trial registries and FDA approval documents*

Availability and consistency of trial information are crucial for assessment of newly approved drugs. We aimed to determine the availability of trial reports and treatment effect data for pivotal randomized controlled trials used for FDA approval of oncology were available in the Clinicaltrial.gov registry. We also compared the treatment effect estimates in clincialtrial.gov and published articles using the FDA approval documents as references.

Start of project: 01.06.2018 – End of project: 01.07.2019

Rituximab in Primary Central Nervous System Lymphoma – A Systematic Review and Meta-analysis?*

Primary central nervous system (CNS) lymphoma (PCNSL) is a diffuse large B-cell lymphoma solely confined to the CNS. We summarized and appraised the available randomized trial evidence on the role of rituximab in the treatment of patients with PCNSL in a systematic review and meta-analysis.

Start of project: 01.01.2015 – End of project: 01.01.2019

Confounding in Psychiatry?*

Confounding bias is probably the most pervasive threat to the validity of non-randomized, observational studies. Authors should explicitly discuss the potential for confounding and other biases. This systematic literature analysis of 120 high impact articles published in the field of psychiatry found that - with one exception - authors never expressed any caution, limitation, or uncertainty in relation to confounding or other bias in the conclusions or in the abstract of their articles.

Start of project: June 2018 – End of project: 31.12.2019

Online Randomized Controlled Experiments at Scale: Lessons and Extensions to Medicine?±

Many technology companies conduct hundreds of concurrent randomized controlled experiments on millions of users. In collaboration with experts from Airbnb/Microsoft, LinkedIn, Google and Stanford University, we provide an overview of key lessons learned in the technology field. There are many differences between the technology and medical world, but it is worth considering whether and how similar designs can be applied.

Start of project: Fall 2018 – End of project: 31.12.2019

ANESTHESIOLOGY

Programmed intermittent epidural bolus technique: external validity of trial results*

This retrospective cohort study aims at investigating the effects of programmed intermittent epidural bolus (PIEB) combined with patient- controlled epidural bolus (PCEA) on maternal motor function and labour outcome in a typical trial patient (healthy nulliparous) as compared to non-trial patients (multiparous, non healthy women). The results of the RCTs on PIEB in regards of motor function seem to be generalizable to women not eligible in these trials, but these women (non-trial patients) required a higher time-weighted number and volume of additional rescue top-ups. This higher number and volume of rescue top-ups in non-trial patients suggests that their labor is more intense, which should be considered in the dosing scheme for PIEB labor analgesia in non-trial patients.

Start of project: 11.02.2015 – End of project: 31.03.2019

ONGOING PROJECTS IN 2019

HIV INFECTION, SWISS HIV COHORT STUDY AND MULTICOHORT PROJECTS

SHCS 805 Prevalence and predictors of potential and contraindicated drug-drug interactions in patients receiving antiretroviral therapy*

Potential drug-drug interactions (DDI) are the most common drug-related problem in ambulatory care and a growing problem in HIV infection due to increasing comorbidities and age of HIV infected patients. In this study of the Swiss HIV Cohort Study (SHCS) we assess the prevalence of contraindicated and potential clinically relevant DDIs and determine major patients and provider related predictors of DDIs in patients receiving antiretroviral therapy. Finally, we validate drug data entered into the new Webmed database of the SHCS with a probability matched patient sample of claims data of Helsana, the largest Swiss health insurer.

Start of project: 01.03.2019 – End of project: 31.05.2020

SHCS 820 HIV and co-morbidity related costs in Switzerland: A large scale data linkage study*

Studies based on representative data on costs and resource use of chronic conditions in Switzerland are scare. Likewise, in HIV there is a lack of high quality cost data. With the success of antiretroviral therapy (ART) HIV infection has become a chronic condition but comorbidities due to cardiovascular diseases, cancer and liver cirrhosis are becoming increasingly important. Therefore, HIV infection is an important and prominent disease to study the cost and consequences of comorbidity in a condition requiring lifelong care and drug treatment. We propose to investigate health resource use and consequences for management of HIV and non-HIV related comorbidities by matching claims data from health insurers with data from the Swiss HIV Cohort Study by anonymous privacy preserving linkage.

Start of project: 01.05. 2018 – End of project: 31.12.2020

Smartphone app and CO self-monitoring for smoking cessation: A randomised controlled trial nested into the Swiss HIV Cohort Study*

This a randomized controlled trial nested in the Swiss HIV cohort comparing the effectiveness of a smartphone app and carbon monoxide self-monitoring support for smoking cessation. The primary outcome is the combination of self-reported continuous abstinence biochemically verified by a carbon monoxide test in-person, with a cut-off of 7 ppm, at 6 months.

Start of project: 09.08.2017 – End of project: 31.03.2020

Risk of non-AIDS defining and AIDS defining malignancies with early versus delayed initiation of antiretroviral therapy: an international multicohort study*

The objective of this study is to investigate the relationship between delayed versus early initiation of antiretroviral therapy (ART) and the risks of non-AIDS defining (NADM) and AIDS defining malignancies (ADM). The analysis will be based on data from European cohorts including HIV infected individuals, and more specifically from the Data Collection on Adverse events of Anti-HIV Drugs (D:A:D) database, a prospective multi-cohort study of HIV-1 positive persons (https://chip.dk/Studies/DAD). The aim of our study is to compare and model different ART initiation strategies in relation to the risk of NADM, ADM and death using state of the art statistical methods to adjust for baseline and time-varying confounders.

Start of project: 01.07.2018 – End of project: 31.03.2020

INFECTIOUS DISEASES, OPTIMIZING ANTIBIOTIC PRESCRIBING FOR UPPER RESPIRATORY INFECTIONS AND DIAGNOSIS OF ACUTE RHINOSINUSITIS IN PRIMARY CARE

NFP72: Routine Antibiotic Prescription*

Antibiotic resistance is a worldwide problem and associated with the direct use of antibiotics in the population. Most antibiotics are used in primary care for acute respiratory tract infections, although primarily of viral origin, and urinary tract infections (UTI). In a nationwide pragmatic randomized intervention trial we use routinely collected fully anonymized claim data from 3 large health insurers covering 40% of insurers in Switzerland and investigate whether routine antibiotic prescription feedback in primary care physicians reduce antibiotic use. We will link claim data with national antibiotic resistance data by anonymized probabilistic record linkage to investigate whether the intervention affects resistance of bacteria against broad-spectrum antibiotics for URTI. A health economic evaluation will be integrated part of the trial.
Start of project: 01.01.2017 – End of project: 31.12.2020

Sinus-endoscopy for the diagnosis of acute bakterial rhinosinusitis*

Acute rhinosinusitis is one of the most common reasons for consultations and the most common reason for antibiotic prescriptions in primary care, although the condition is primarily of viral origin. Antibiotic overuse in acute rhinosinusitis is mainly due to the lack to objectively diagnose acute bacterial rhinosinusitis. Endoscopy of the rhinopharynx and collection of diagnostic material from the ostium draining the sinus is the most reliable method to diagnose acute bacterial rhinosinusitis but is only used by specialists (otolaryngologists). We have developed a one-way usable device the JGG endoscope® (patent number PA 2016 00657) which can be attached to pocket otoscopes that allows for the diagnosis of acute bacterial rhinosinusitis in primary care.
Start of project: 01.10.2018 – End of project: 31.06.2020

METHODOLOGICAL RESEARCH PROJECTS

Routinely collected health data for randomized trials – The RCD for RCT initiative*

Large and simple pragmatic mega-trials may be conducted with only a fraction of costs when using routinely collected health data (RCD). The RCD for RCT initiative aims on improving how clinical trials are made, driven by a strong believe that most of the problems of randomized clinical trial (RCT) evidence are man-made and routine data can be a key to solve many of these issues.
Start of project: 01.02.2016 – End of project: 31.12.2040

Development and validation of an instrument to assess the credibility of putative subgroup effects in randomized controlled trials and meta-analyses*

The overall goal of this project is to provide clinicians, researchers, and decision-makers with a reliable, valid, and functional instrument for assessing the credibility of subgroup effects found in randomized trials and meta-analyses. In a first step, we will conduct a systematic survey of the methodological literature addressing the conduct and interpretation of subgroup analyses. We will identify and summarize currently suggested credibility criteria and the rationale offered for these criteria, in the process generating a list of potential instrument items and evidence or opinion about the relative merits of the criteria.
Start of project: 13.11.2013 – End of project: 31.07.2020

Learning from failure - Understanding the mechanisms of trial discontinuation DISCO 2*

In a first project we will conduct semi-structured interviews with principal investigators of RCTs discontinued for insufficient recruitment and with key stakeholders of clinical research in Switzerland. A second project will examine health-care RCTs funded by the SNSF to explore whether a rigorous selection of trials for funding and monitoring decreases the risk of trial discontinuation including potential effects of full versus partial funding. In a third project we will perform an analysis of recruitment patterns from about 500 completed and discontinued RCTs conducted in different countries and settings. It will explore whether insufficient recruitment can reliably be identified at an early stage and determine optimal time points and criteria for the assessment of recruitment progress in RCTs.

Start of project: 01.12.2013 – End of project: 31.12.2020

Longitudinal evaluation of the accuracy and completeness of clinical trial protocols - evidence for improvement?*

The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) were published in 2013 and the new Swiss federal Law on Research in Humans (Humanforschungsgesetz, HFG) came into effect in January 2014. The present project aims to investigate the accuracy and completeness of clinical trial protocols approved by Research Ethics Committees before the introduction of SPIRIT & HFG and thereafter. In addition, we will evaluate the extent of appropriately registered protocols before the introduction of SPIRIT & HFG and thereafter (in national or international registries).

Start of project: 07.11.2014 – End of project: 31.07.2020

Making clinical trials more affordable – systematic investigation of trial costs and tool development*

The overall aim is to make clinical trials more affordable. In Project A we will gather empirical resource use and cost data from 180 investigator-initiated RCTs in Switzerland, Germany, Canada, and the UK to investigate cost patterns, empirically identify major cost drivers, examine planned versus actual RCT costs, and explore heterogeneity of costs across medical fields and countries. Project B will consist of semi-structured interviews to explore current practices, attitudes, needs, and preferences of trial investigators, trial funders, and trial support organizations with respect to budget planning, funding acquisition for RCTs, and managing costs during RCT conduct. In Project C we will develop reliable and user-friendly budget calculation and cost monitoring tools for RCTs with stakeholder consensus.

Start of project: 01.11.2019 – End of project: 31.10.2022

Multicentre assessment of the completion, registration, and publication of randomized clinical trials approved in 2012 and in 2016*

The DISCO II study builds on a sample of RCTs approved by Ethics Committees in CH, Germany, UK, and Canada in 2012 and in 2016 that we used in a previous project on RCT protocol quality (EURO-SPIRE). Objectives are 1) To empirically assess the proportions of registered RCTs and published RCTs that received ethical approval in 2012 and 2016; 2) To assess the proportions of discontinued RCTs and to investigate the reasons for trial discontinuation; 3) To investigate the extent to which unpublished RCTs (in particular those that were prematurely discontinued) can be identified through registries of clinical trial protocols; and 4) To investigate whether the proportions under 1) - 3) vary across countries.

Start of project: 01.09.2019 – End of project: 31.12.2023

Scoping review of available feasibility assessment tools and checklists for clinical trials*
The aims of this scoping review are to investigate (1) how many and what kind of feasibility assessment tools or checklists for clinical trials are available through electronic literature databases and the internet; and (2) what components identified feasibility tools and checklists consist of.
Start of project: 15.09.2019 – End of project: 29.02.2020

Descriptive statistics of the research covered by the Swiss Human Research Act (HRA; project 1) and a national survey of researchers about the implementation of the HRA (project 2)*
Starting January 2016 all applications to research ethics committees (RECs) in Switzerland need to be submitted and managed through a central online portal (BASEC). This project comprises 3 parts: 1) A descriptive analysis of the BASEC content (all studies sent to Swiss RECs) for 2016/2017 and then yearly updates until 2021; 2) a survey of researchers/principal investigators of studies submitted via BASEC in 2017; and 3) to describe research projects for which applicants were uncertain whether they are within the scope of the Human Research Act or not. The project is done in collaboration with the Swiss Clinical Trial Organisation and Cochrane Switzerland.
Start of project: 15.12.2017 – End of project: 31.12.2022

Abbreviating literature for rapid reviews*
Searching multiple data sources for systematic reviews and health-technology-assessments requires costs and resources and delays answers to health care decision makers. Searching less data sources may reduce the number of studies, study participants, and observed events contributing to meta-analyses. If such abbreviated literature searches give similar treatment effect estimates as comprehensive literature searches is not clear. It may be argued that given the already well described publication bias in many clinical fields, the potential risk of missing some information in abbreviated searches would be acceptable and paid off by faster answers to more clinical questions. We quantified the impact of abbreviating searches on the actual treatment effect estimates, beyond just assessing how many studies would be missed.
Start of project: 01.09.2016 – End of project: 31.01.2020

PragMeta: Generalizability, applicability and pragmatism of clinical trials and their impact on treatment effect estimates: a meta-epidemiological study*
It is often claimed that results from some randomized clinical trials (RCT) are difficult to transfer into real life situations. Pragmatic RCTs provide decision-oriented, real world evidence that is perceived as highly applicable and generalizable to routine care. The cornerstone of real world evidence is that treatment effects under real world conditions in routine care may differ from that in highly controlled research settings, such as in drug approval trials. The PragMeta includes an analysis of over 2000 randomized trials to provide a better understanding of pragmatic trials and the generation and interpretation of real world evidence. It will give practical guidance for clinicians, researchers, regulators, health insurers and health-care policy makers, developers of reporting guidelines, and other stakeholders who develop, fund, conduct, assess or otherwise use clinical trials. Ultimately, it may help to generate report and use evidence that is more relevant for patients, clinicians and other key health care decision-makers.
Start of project: 01.11.2019 – End of project: 2022

Development of a reporting guideline for RCTs using routinely collected data (RCD)*
This project assesses the reporting gaps in RCD trials, followed by a stakeholder qualitative process for the development of a reporting guideline and checklist. The qualitative process will encompass a survey to stakeholders such as clinical researchers, clinicians, publishers and pharmaceutical industry representatives; and we will closely collaborate with the RECORD and CONSORT groups.
Start of project: 01.03.2018 – End of project: 31.12.2020

ONCOLOGY

exCEIT-Cancer: Emerging trends and developments in cancer treatment innovation*

In the Comparative Effectiveness of Innovative Treatments for cancer (CEIT-Cancer) project, we assessed the early evidence described in FDA approval documents for all 92 cancer drugs approved between 2000 and 2016. In exCEIT we expand the current database and aim to analyze all novel therapies up to 2020, overall more than 150 drugs. We will establish a new online database accessible through a dedicated website and linked to other research resources. The overarching goal is a systematic, comprehensive and transparent analysis of latest developments and innovations in oncology, better support of evidence-based decision-making in policy and practice, and translation of our findings into research and patient care.

Start of project: 01.04.2020 – End of project: 01.04.2022

CEIT – Cancer (Comparative Effectiveness of Innovative Treatments for Cancer)*

In this project, the approval studies for all cancer drug treatments that were approved since the year 2000 are systematically reviewed and their methods, size, and treatment effects evaluated. We will also evaluate the post-approval generation of clinical evidence on effects on overall survival, patient-important outcomes, and the most important cancer specific surrogate outcomes progression-free survival and tumor response. The ultimate goal is to provide decision-makers with guidance to identify early indications, which innovative drugs likely fulfil, the promise of therapeutic success in the long run and which should be used cautiously until more evidence is generated.

Start of project: 01.10.2015 – End of project: 31.12.2021

CEIT-RWE: Comparative Effectiveness for Innovative Cancer Treatments in so-called real-world evidence*

With the emergence of so-called "real world evidence" (RWE), non-randomized studies using routinely collected data (RCD) are increasingly perceived as complementary to randomized trials for assessing treatment effects for drug approval. We use a large number of RCD-studies and explore to what degree these studies address research gaps, detect or confirm for example subgroups of patients with better treatment response, if such studies truly include less selected and more typical patient populations and how such studies deal with common challenges and limitations of non-randomized studies, for example issues of confounding bias.

This project aims to understand the research agenda of real world evidence in the field of cancer and innovative drug treatments. It is closely embedded in the Comparative Effectiveness of Innovative Treatments for cancer (CEIT) project.

Start of project: 01.06.2019 – End of project: 30.06.2020

Real World Off-label Reimbursement in Cancer Care*

Off-label use (OLU) of a drug is common in oncology and frequently regulated by reimbursement restrictions. For evidence-based healthcare, treatment reimbursement would be closely associated with the supporting evidence for treatment benefit. This project aims to investigate the relationship of reimbursement decisions with the underlying clinical evidence using routinely collected data from medical records of more than 5000 patients treated in three Swiss oncology centers. It will provide a systematic overview and assessment of OLU and its reimbursement reality in Switzerland and provide a better understanding of the access to cancer care that is regulated by health insurers.

Start of project: 02.01.2018– End of project: 31.12.2020

Use of heparin for cancer: indivdual patient data meta-analysis*

Study level systematic reviews on this topic indicate a reduction in venous thromboembolism and provide moderate confidence that a small survival benefit exists. We will perform an individual patient data meta-analysis (IPDMA) to explore the magnitude of the suggested survival benefit and address whether or not specific subgroups and characteristics of cancer patients are more likely to benefit from parenteral anticoagulants.

Start of project: 01.04.2013 – End of project: 31.07.2020

ANESTHESIOLOGY

International multicentre validation study of CLASSIC – Classification of Intraoperative Complications*

Quantifiable evidence-based methods for reporting complications are needed to improve perioperative patient safety. While there are several validated systems for reporting postoperative complications, there are only a few (none prospectively validated) for reporting intraoperative complications. Our group developed a definition and classification for intraoperative complications within a Delphi study involving international interdisciplinary experts. As both surgery and anaesthesia may be involved in complications, all patient-related intraoperative complications are considered. This current cohort study aims to assess the validity and feasibility of this newly derived classification in an international multicentre cohort study. Providing a well-applicable internationally validated classification system for intraoperative complications is an important contribution to the quality of health care and perioperative patient safety.

Start of project: 01.01.2015 – End of project: 31.12.2020

HTA REPORTS

HTA report – Iron therapy for iron deficiency without anaemia*

Iron deficiency with no anaemia (IDNA) appears to be associated with different symptoms such as fatigue or restless legs that may be alleviated by iron therapy. The effectiveness of iron therapy in symptomatic patients with IDNA is unclear and there is no consensus regarding the relevant diagnostic markers and thresholds that should be used to to treat IDNA. The aims of this reports are: 1) to assess the effectiveness of iron therapy in populations with symptomatic IDNA with a systematic review, 2) to assess diagnostic markers with an individual patient data meta-analysis in population with relevant treatment effect which were identified within the systematic review and 3) to assess costs of intravenous versus oral treatment in the populations identified in the systematic review.

Start of project: 01.02.2017 – End of project: 31.03.2020

TEACHING

Undergraduate

University of Basel

H.C. Bucher, **M. Briel**, **S. Dell-Kuster**, **L.G. Hemkens**, **B. Kasenda** and **A.J. Nordmann** teach principles of evidence-based medicine, critical appraisal skills, basics in clinical epidemiology and clinical research methodology to medical students in the Bachelor and Master's program at the University Basel. Total teaching obligations in 2019 were 206 hours. **H.C. Bucher** and **M. Briel** coordinate three teaching blocks in undergraduate medical training (Wissenschaftliche Kompetenz, Patienten Orientierte und Evidenz-basierte Medizin (POEM), and Wissenschaftsmonat). **S. Dell-Kuster** is responsible for teaching medical statistics to medical students in the Bachelor program at the University Basel. Total teaching obligations at the University of Basel were 170 hours corresponding to 344 LAS.

ETH Zurich

H.C. Bucher has been appointed to set up the Clinical Research Methodology course for the bachelor programme in Medicine at ETH Zurich, which started in February 2019. Total teaching obligations were 36 hours corresponding to 82 LAS. **S. Dell-Kuster**, **B. Kasenda** and **A.J. Nordmann** were teaching critical appraisal skills in seminars for the bachelor program in Medicine at ETH Zurich.

University of Paris / Sorbonne Paris Cité

L.G. Hemkens has been appointed to teach latest methods and advances in the field of real world evidence and comparative effectiveness research (CER) as one-week module "Routinely collected data in CER" within the Master of Public Health in Comparative Effectiveness Research program offered by the Centre of Research in Epidemiology and Statistics, Sorbonne Paris Cité, France

Postgraduate

1. **Matthias Briel**. Randomized Clinical Trials - part 1. PPHS - Essentials in Health Research Methodology, University Hospital Basel
2. **Matthias Briel**. Randomized Clinical Trials - part 2. PPHS - Essentials in Health Research Methodology, University Hospital Basel
3. **Matthias Briel**. Systematische Reviews und Meta-Analysen. GCP – Aufbaukurs, University Hospital Basel
4. **Matthias Briel**. Von der Forschungsfrage zur Studie. GCP – Aufbaukurs, University Hospital Basel
5. **Matthias Briel**. Roundtable. PhD Day of PPHS, University of Basel
6. **Matthias Briel**. RCT Design. RCT course - HRM Programme McMaster, Online
7. **Matthias Briel**. Research on Research. Basics of Ethics in Health Science, ISPM Bern
8. **Matthias Briel**. Randomization. RCT course - HRM Programme McMaster, Online
9. **Matthias Briel**. Experimental Studies. Fundamentals of producing, interpreting and using evidence in health care, Swiss TPH Basel
10. **Matthias Briel**. Measurement issues. RCT course - HRM Programme McMaster, Online
11. **Matthias Briel**. Study population. RCT course - HRM Programme McMaster, Online
12. **Matthias Briel**. Outcome events. RCT course - HRM Programme McMaster, Online
13. **Matthias Briel**. Methods Workshop Clin Research. Summer School - Pediatric Psychiatry, University of Basel

14. **Matthias Briel**. Learning from failure: Research on Clinical Research. Summer School - Pediatric Psychiatry, University of Basel
15. **Matthias Briel**. Tipps for PhD students. PPHS Welcome Day, University of Basel
16. **Matthias Briel**. How much is an RCT? DKF Research Lunch, University Hospital Basel
17. **Matthias Briel**. Study selection, risk of bias assessment, data extraction. An Introduction to Systematic Reviewing, University Library of Basel
18. **Matthias Briel**. Einführung in die Patientenorientierte Forschung. CAS Study Nurses/ Coordinators, University Hopitals Basel
19. **Salome Dell-Kuster**. Classification of intraoperative adverse events. Education and Training, Department of Surgery, University Hospital Basel
20. **Salome Dell-Kuster**. Classification of intraoperative adverse events. Education and Training, Department of Anaesthesiology, University Hospital Geneva
21. **Salome Dell-Kuster**. Reporting and Statistics. Annual meeting of SGAR, Interlaken
22. **Salome Dell-Kuster**. Inferential Statistics – Populations. ESA Masterclass, Athens
23. **Salome Dell-Kuster**. Normality & Transforms (exercise). ESA Masterclass, Athens
24. **Salome Dell-Kuster**. Proportions – Chi-square & Fisher Exact tests. ESA Masterclass, Athens
25. **Salome Dell-Kuster**. Diagnostic tests. ESA Masterclass, Athens
26. **Salome Dell-Kuster**. Systematic Review & Meta-analysis. ESA Masterclass, Athens
27. **Lars Hemkens**. Concepts and chaos - what is real world evidence and how is it useful? DKF Research Lunch, University Hospital Basel
28. **Lars Hemkens**. Routine data & registries for better RCTs. PPHS - Essentials in Health Research Methodology, University Hospital Basel
29. **Lars Hemkens**. The crucial issue: Why clinical trials can be useful and not useful at the same time. PPHS - Essentials in Health Research Methodology, University Hospital Basel
30. **Lars Hemkens**. Study designs and critical appraisal – Overview. Swiss TPH Fundamentals of producing, interpreting and using evidence in health care, Swiss TPH Basel
31. **Lars Hemkens**. An introduction to systematic reviewing: From literature search to meta-analysis. An introduction to systematic reviewing: From literature search to meta-analysis, University of Basel
32. **Lars Hemkens**. Why does evidence matter? Swiss TPH Fundamentals of producing, interpreting and using evidence in health care, Swiss TPH Basel
33. **Lars Hemkens**. Routinely collected data (RCD) & Real World Evidence (RWE) – Concepts. Master Comparative effectiveness research. University of Paris
34. **Lars Hemkens**. Nonrandomized Real World Evidence – Promises and Challenges. Master Comparative effectiveness research. University of Paris
35. **Lars Hemkens**. Routinely collected data – Reporting: RECORD. Master Comparative effectiveness research. University of Paris
36. **Lars Hemkens**. Pragmatic Trials. Master Comparative effectiveness research. University of Paris
37. **Lars Hemkens**. Randomized Real World Evidence – Concepts. Master Comparative effectiveness research. University of Paris
38. **Lars Hemkens**. Randomized Real World Evidence – Examples. Master Comparative effectiveness research. University of Paris
39. **Soheila Aghlmandi**. Introduction to Meta Analysis. An Introduction to systematic reviewing: From literature search to a meta-analysis, University of Basel
40. **Soheila Aghlmandi**. Meta-analysis in R. An Introduction to systematic reviewing: From literature search to a meta-analysis, University of Basel

Supervision of Master Theses

1. **Ala Taji Heravi**. MSc Epidemiology. Faculty of Science, University of Basel. Comparison of planned and actual costs of investigational medical products in clinical trials supervised by **M. Briel**.
2. **Luzius Angehrn**. Faculty of Medicine, University of Basel. Epidemiology of multimorbidity in the perioperative population and their effect on outcome supervised by **S. Dell-Kuster**.
3. **Wenyan Ma**. MSc Epidemiology. Faculty of Science, University of Basel. Comparative effectiveness for innovative cancer treatments in so-called real-world evidence (CEIT-RWE): a meta-epidemiological study supervised by **L.G. Hemkens**.
4. **Sirintip Sricharoenchai**. MSc Epidemiology. Faculty of Science, University of Basel. Comparison of results of pivotal randomized trials for novel oncology drugs reported in journal articles, trial registries and FDA approval documents supervised by **L.G. Hemkens**.

Supervision of MD Theses

1. **Amar Polutak**. Discrepancy in reporting of perioperative complications supervised by **S. Dell-Kuster**.
2. **Bettina Gruber**. Multicentre double-blind randomised controlled trial "EEG in general anaesthesia – more than a BIS value supervised by **S. Dell-Kuster**.
3. **Olga Bossong**. Prospective cohort study for the validation of ClassIntra® in patients undergoing eye surgery supervised by **S. Dell-Kuster**.

PhD Students

1. **Dmitry Gryaznov**. MD, MSc. Longitudinal evaluation of the accuracy and completeness of clinical trial protocols, 2017 – 2020
2. **Eric Remera**. MSc. Evaluating the effectiveness of HIV treatment and preventions in Rwanda, 2018 – 2021
3. **Katharina Klatte**. Development and assessment of evidence-based strategies towards increased feasibility and transparency of investigator-initiated clinical trials in Switzerland, 2018 – 2021
4. **Kimberly McCord**. MSc. Routinely collected data for randomized trials, 2017 – 2020
5. **Larsa Gawria**. MD. Complications in perioperative care, 2018 – 2021
6. **Maddalena Favaretto**. Big data ethics in research, 2017 – 2020

STAFF AS OF 31.12.2019

Name	Position	Employment
Prof. Dr. med. Heiner C. Bucher, MPH	Head of Institute	100%
Prof Dr. med. Matthias Briel, MSc	Senior Scientist	Associated Collaborator
PD Dr. med. Salome Dell-Kuster, MSc	Senior Scientist	Associated Collaborator
PD Dr. med. Lars G. Hemkens, MPH	Senior Scientist	Associated Collaborator
PD Dr. med. Dr. phil. Benjamin Kasenda	Senior Scientist	Associated Collaborator
PD Dr. med. Michael Koller, MSc	Senior Scientist	Associated Collaborator
Prof. Dr. med. Dr. med. dent. Pedram Sendi, PhD	Senior Scientist	Associated Collaborator
James Young, PhD	Senior Biostatistician	Associated Collaborator
Soheila Aghlmandi, PhD	Senior Biostatistician	100%
Frédérique Chammartin, PhD	Biostatistician	80%
Florian Halbeisen PhD	Biostatistician	80%
Dominik Glinz, PhD	Research Fellow	80%
Viktoria Gloy, PhD	Research Fellow	50%
Dr. med. Stefan Schandelmaier PhD	Research Fellow	100%
Diana Grauwiler	Clinical Research Manager	60%
Prof. Dr. med. vet. Laurent Audigé	Research Associate	Associated Collaborator
Hannah Ewald PhD	Medical information specialist	Associated Collaborator
Dr. med. Jan Adam Roth	Research Associate	Associated Collaborator
Dr. med. Ramon Saccilotto, MAS	Research Associate	Associated Collaborator
Benjamin Speich, PhD	Research Associate	Associated Collaborator
Dr. med. Dmitry Gryaznov, MSc	PhD Student Clinical Research	
Katharina Klatte	PhD Student Clinical Research	
Kimberly McCord, MSc	PhD Student Epidemiology	
Eric Remera, MSc	PhD Student Epidemiology	
Ala Taji Heravi	Master Student Epidemiology	

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