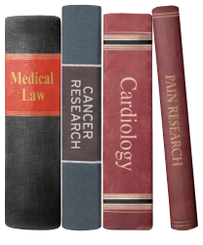
MEDICRES

4th WORLD CONGRESS ON

GOOD MEDICAL RESEARCH



CLINICAL TRIALS
EPIDEMIOLOGICAL STUDIES
PRE-CLINICAL EXPERIMENTS

GOOD PLANNING GOOD ANALYZING GOOD REPORTING
GOOD REVIEWING GOOD PUBLISHING
FOR AUTHORS, REVIEWERS, EDITORS

NEW YORK, USA | OCTOBER 17 - 20, 2014

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MedicReS
Medical Research Support

in memory of the deaths from Ebola pandemic in 2014

MedicReS World Congress 2014
on
Good Medical Research

Research Policy, Research Ethics , Research Education

for Global Health with

Methodological | Biostatistical and Ethical Perspective in

Clinical Trials, Translational Research, Epidemiological Studies,

Pre-Clinical Experiments

International Conferences

on

GOOD BIOSTATISTICAL PRACTICE

GOOD BIOETHICAL PRACTICE

GOOD PUBLICATION PRACTICE

Congress Proceedings Book

Editor

Prof. E. A. KANIK, PhD

October 16-18 | 2014

The Great Hall,The Cooper Union

New York| NY

CONTENT

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PREFACE

A 1

October 7th, 2014, New York

Dear Colleagues,

Humanity's struggle with powerful epidemics started far back in the14th century with the Black Death. Today, this struggle is still going on strong. It seems, one of the most crucial problems of the 21st century, of our age, is going to be the Ebola Outbreak.

As of this moment, more than 3.400 people lost their lives to Ebola Fight and the first Ebola US case diagnosis has taken place in Texas.

Of all the problems that we, the people of Modern Age, face; epidemics, genetic diseases, environmental diseases and their interactions take the front row. Technology has of course been of increasing help to healthcare research, however, human brain is still the most valuable source of healthcare research. In a world where artificial intelligence research in medical field has been rapidly increasing . MedicReS would like to call your attention to the Good Medical Research concept with regards to the points mentioned below.

Burak AKICIER
General Director
MedicReS

B

INVITED SESSIONS

Nicholas P. JEWELL

Nicholas P. Jewell is Professor of Biostatistics and Statistics at the University of California, Berkeley. He has held various academic and administrative positions at Berkeley since his arrival in 1981, most notably serving as Vice Provost from 1994 to 2000. He was educated at the University of Edinburgh where he received a first class Honours degree in Applied Mathematics in 1973 and a PhD in Mathematics in 1976. Immediately following his graduate program he was appointed to a Harkness Fellowship from 1976-1978 which he held at the University of California, Berkeley and at Stanford University. From 1979-1981 he was an Assistant Professor of Statistics at Princeton University. He has also held academic appointments at the University of Edinburgh, Oxford University, and at the University of Kyoto. In 2007, he was a Fellow at the Rockefeller Foundation Bellagio Study Center in Italy, He is a Fellow of the American Statistical Association, the Institute of Mathematical Statistics, and the American Association for the Advancement of Science (AAAS). He is the 2005 winner of the Snedecor Award from COPSS, and won the Distinguished Teaching Award from UC Berkeley's School of Public Health in 2004. In 2000, he was awarded the Director's Award from the Federal Emergency Management Agency for "extraordinary leadership and vision in implementing strategies that enhance the disaster resistance of the University of California, Berkeley, and universities throughout America"; in addition the 2005 Alfred E. Alquist Award was given to UC. Berkeley's SAFER program that he launched and led for many years.

MedicReS' 4th WORLD CONGRESS, INCLUDING THE INTERNATIONAL CONFERENCE ON GOOD BIOSTATISTICAL PRACTICE

Nicholas P. Jewell
MedicReS Word Congress Co-Chair
Professor of Biostatistics & Statistics
University of California, Berkeley

Dear Colleagues,

I write to invite you to attend MedicReS' 4th World Congress, including the International Conference on Good Biostatistical Practice, in New York, USA from October 16-18, 2014. The organizers have arranged a wonderful program of talks and sessions, with many distinguished speakers including Judith Goldberg (NYU), Shelley Hurwitz (Harvard), Arzu Kanik (University of Mersin), David Madigan (Columbia University), Collin O'Neil (Lehman College, CUNY), David Resnik, and Andrea and Douglas Zahn.

I have had the good pleasure to attend two of the previous MedicReS World Congresses—in Istanbul and Vienna—and found them to provide marvelous opportunities to learn about cutting edge issues in Biostatistics and to interact with investigators from across the world. What is particularly special is the scientific and social exchanges with medical researchers and biostatisticians across the world, many representing countries that I do not have the chance to meet at other conferences. The sessions and social events are really terrific venues to make connections, network and form new collegial relations for the future!

I particularly urge young biostatisticians to participate in the conference and I look forward to meeting many of you there in a few months!

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Shelley HURWITZ

Dr. Shelley Hurwitz is the Director of Biostatistics in the Center for Clinical Investigation at Brigham and Women›s Hospital, a teaching hospital of Harvard Medical School. Previously she held leadership positions at the Harvard School of Public Health and the University of Pennsylvania Cancer Center. Dr. Hurwitz has over 100 publications in peer-reviewed journals, and received Partners in Excellence Awards for Leadership and Innovation and for Outstanding Community Contribution for creating and directing the Biostatistics Consulting and Education Programs. She was honored as Fellow of the American Statistical Association for significant contributions to medical research in the field of statistics and mentoring of researchers and clinical faculty. She was appointed to the Committee on Professional Ethics of the American Statistical Association and served as Chair, selected for her dedication to promoting ethical statistical practice and responsibility for statisticians working in biomedical sciences. She was elected to the International Statistical Institute for her expertise and leadership in statistical consulting and mentoring, original research and publications, national and international educational initiatives, and promotion of ethical practice among statisticians in applied settings. She currently serves on the International Statistical Institute's Advisory Board on Ethics.

BIOSTATISTICS AND ETHICS

Shelley Hurwitz, PhD
MedicReS 2014 Word Congress Co Chair
Director of Biostatistics
Center for Clinical Investigation
Brigham and Women's Hospital
Harvard Medical School
Fellow, American Statistical Association
Advisory Board on Ethics, International Statistical Institute

As a consumer, I see exciting reports of scientific breakthroughs almost daily in newspapers and on morning television. Hot topics. Why do most of them turn out to be false? We need to improve our methods, and not settle for status quo. By exchanging ideas and learning opportunities, MedicReS World Congress on Good Medical Research 2014 will bring us closer to Medical Research Excellence.

The world of Big Data is here. In this century, medical research cannot advance without biostatistics and bioinformatics. Biostatisticians must adapt to the changes, and ethical considerations for biostatistical practice must evolve as well.

In my talk on Biostatistics and Ethics, I will discuss the reputation of statistics, the response by the statistical community, some associations' guidelines for the ethical practice of statistics, and the movement toward reproducibility. What is changing? What is new? In the last decade, we've seen a rapid increase in the ability to collect massive amounts of data, with complex structure and often a sensitive nature. Biostatisticians routinely work closely with physicians and scientists and have unique insight into data, often being privy to confidential data. We work in increasingly multidisciplinary teams with potentially divergent ethics codes and sensibilities. These unparalleled advances and opportunities present new ethical concerns for statisticians.

Medical researchers, authors, editors, reviewers, health care professionals, and other research personnel are invited to attend The 4th World Congress on Good Medical Research in New York City, where there will be presentations on methodological, ethical, biostatistical, economic, and legal concerns in medical research. All the up-to-date details about the congress can be found on our web-site. We hope to see you there.

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Emine Arzu KANIK

Dr Kanik is Full Professor of Biostatistics and Chairman of the Department of Biostatistics at the University of Mersin, Faculty of Medicine, Turkey. Founder member of MedicReS (Medical Research Support) Vienna Austria, and MedicReS Scientific Coordinator since 2006, Born in Ankara, Turkey, graduated from Ankara High School, She was optained her PhD degree at the Biometry and Genetics Department of Ankara University. Dr Kanik gained research experience at the Natural and Applied Science Research institute of Ankara University as a research assistant between 1990-1999, She was appointed as founder in Biostatistics department to Mersin University, Medical Faculty in 2000 , Since 2000 she is the chairman of this department. Dr Kanik has authored over 200 research reports and reviews. She concentrates on the postgraduated medical researcher education. She is editor in chief in MedicReS Journals."

COMMENT ON WASTE MEDICAL LITERATURE

Prof. E. Arzu KANIK, PhD.
MedicReS 2014 Word Congress Co Chair
Head of Department of Biostatistics, Faculty of Medicine
Director of Vocational High School of Health Services
Mersin University, Mersin | Turkey
Scientific Director | MedicReS
Editor in Chief | MedicReS Journals
MedicReS - Medical Research Support, New York | USA
Scientific Director | MeStACon Turkey
Director | AEK Research & Education Company, Technoscope, Mersin

"Research: Increasing Value and Reducing Waste" are very important subjects in medical research. Lancet has mentioned this topic many times before and they have published an editorial paper about Good Medical Research after MedicReS World Congress 2012 in Vienna with the title of The truth about good medical research: The Lancet

In the first paper of this series of Lancet, authors have 4 suggestions Research: increasing value, reducing waste - The Lancet. Transparency is one of these suggestions and it is a very remarkable one at that. Regarding with this, we think that the raw data of every published articles should be digitally available in the publishers database. We can only reach transparency if we can achieve this. Another important subject is the 'researcher education' that researchers from medical backgrounds usually lack of it. Researchers with backgrounds other than medicine are more throughly educated especially on topics such as methodology and ethics. Our suggesion is good medical researcher certification and a comment has been sent to FDA about this certification http://federal.eregulations.us/rulemaking/document/fda-2012-d-0847-0003 and has been published in World Medical Journal at Report on MedicReS World Congress 2012 on Good Medical Research MedicReS International Conference on Good Biostatistical Practice

Those who conduct research in the medical field try to conduct those researches only with their knowledge regarding with their professional fields especially in developing countries. This is absolutely not enough at all. Another

topic of importance that was mentioned by the authors is good research ideas. To achieve good medical research, researchers who need financial support and expertise about their research, first of all, should register their hypothesis into hypothesis pool before clinical trial registration Through this hypothesis pool, of course the rights of the original researchers who submit the hypothesis should be protected and a researcher can find both the necessary financial funds and the team who will prepare the research protocol and carry out the research. This topic will be further discussed with researchers around the world who will meet at the 4th World Congress on Good Medical Research which will take place in New York, on October 16th-18th, 2014.

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David MADIGAN

David Madigan is Executive Vice President for Arts and Science and Professor of Statistics at Columbia University in New York City. He received a bachelor's degree in Mathematical Sciences and a Ph.D. in Statistics, both from Trinity College Dublin. He has previously worked for AT&T Inc., Soliloquy Inc., the University of Washington, Rutgers University, and SkillSoft, Inc. He has over 140 publications in such areas as Bayesian statistics, text mining, Monte Carlo methods, pharmacovigilance and probabilistic graphical models. He is an elected Fellow of the American Statistical Association, the Institute of Mathematical Statistics, and the American Association for the Advancement of Science. He recently completed a term as Editor-in-Chief of Statistical Science and is the current editor of Statistical Analysis and Data Mining. Professor Madigan will talk about

WHY MOST PUBLISHED STUDIES ARE WRONG BUT CAN BE FIXED?

David MADIGAN

Executive Vice President for Arts and Science
Professor of Statistics at Columbia University in New York City

" Why most published studies are wrong but can be fixed ? " at MedicReS 4th World Congress on Good Medical Research.

He says that " Observational studies of the effects of healthcare interventions now dominate the medical literature. The ready availability of large-scale patient databases with tens of millions of records provides a chimera of certainty. In reality, while sampling variability diminishes as sample size increases, bias remains ever present.

The analyses of observational studies typically highlight statistical artifacts such as confidence intervals and p-values. However, these artifacts depend on assumptions that might be true in randomized trials but represent untestable leaps of faith in the context observational studies.

The direct consequence of all of this is that the so-called evidence provided by observational studies is often unreliable and indeed the literature is replete with examples of conflicting studies of the same issue, often even in the same database.

Recent work suggests one way forward. By empirically "calibrating" observational studies using test cases, that is, interventions known to cause or known to not cause particular outcomes, statistical artifacts can be adjusted to account not just for sampling variation, but also for sources of bias. The resulting inferences have established operating characteristics and thus can provide useful inputs for decision making. This work is at a nascent stage, however, and many research challenges remain."

Be a part of Good Medical Research and Join Us in New York.

B 5

Collin O'NEIL

Collin O'Neil, PhD, is an assistant professor in the philosophy department at Lehman College, CUNY, specializing in bioethics. Previously he was an assistantprofessor/faculty fellow at the Center for Bioethics, NYU and a post-doctoral fellow in the Department of Bioethics, National Institutes of Health.

IS CONSENT TO RESEARCH NECESSARY IN COMPARATIVE EFFECTIVENESS TRIALS?

Collin O'NEIL
Assistant Professor / Faculty Fellow
Center for Bioethics
New York University

Good Medical Research is research that has the potential to deliver results that can improve the capabilities and decision-making of clinicians, and that obtains its results via methods that respect the rights of human subjects. Settling questions about what counts as good medical research is an interdisciplinary enterprise, requiring contributions from statisticians, scientists, clinicians, and ethicists, and the MedicReS World Congress will be bringing these experts together.

Comparative effectiveness research on already approved therapies can help to improve the decision-making of clinicians and policymakers. But to be considered good medical research, it must be conducted in a way that respects the rights of the subjects. My subject is the question of whether the consent obtained in ordinary clinical practice suffices to respect the rights of the subjects in such trials, or whether explicit consent to research must also be obtained. It is my hope that attendees will come away with a better understanding of the ethics of conducting one critically important kind of human subjects research, randomized comparative effectiveness trials.

Clinicians often must choose between two or more approved therapies for a given condition without good evidence to guide them. Randomized comparative effectiveness trials will help with this problem and must be encouraged. But there is currently a controversy regarding what kind of consent must be obtained to respect the rights of patients enrolled in these trials. I will discuss the function of consent and the conditions under which it successfully waives rights, evaluate the arguments both in favor of and against the necessity of obtaining consent to research in these trials, and address the further question of whether it might sometimes be permissible to make participation in a comparative effectiveness trial a condition on receiving treatment.

I hope you will consider attending the 2014 MedicReS World Congress to hear a variety of presentations on the theme of good medical research, andto participate in the conversations they generate.

Zubin MASTER

Dr. Zubin Master is currently an Assistant Professor at the Alden March Bioethics Institute, Albany Medical College and Research Associate at the University of Alberta's Health Law Institute. He holds an undergraduate degree in genetics from York University and a PhD in molecular and cellular biology from the University of Toronto. He transitioned into bioethics and health policy as a post-doctoral fellow at Dalhousie University and the University of British Columbia. Previously, Dr. Master worked as Senior Policy Advisor at Health Canada where he led the development of Health Canada's Scientific Integrity Framework and beforehand, developed regulations under the Assisted Human Reproduction Act on several laboratory assisted reproductive technologies and embryo research. During his tenure in government, Dr. Master maintained academic ties continuing research as Affiliate Investigator at the Sprott Centre of Stem Cell Research and the Ottawa Hospital Research Institute, University of Ottawa, and held a short post as Guest Researcher at the National Institute of Environmental Health Sciences, National Institutes of Health. His research interests focus on the ethics, policy and commercialization of stem cell research, ethical and policy issues of biobanking and research involving humans, and the responsible conduct of research including authorship and publication ethics. Dr. Master serves on several governmental and non-governmental committees and journal editorial boards and has published over 50 articles in top-tier science, bioethics and law journals.

ETHICAL ISSUES IN AUTHORSHIP OF SCIENTIFIC AND GLOBAL HEALTH RESEARCH

Zubin Master, PhD

Assistant Professor

Alden March Bioethics Institute, Albany Medical College

Current Issues in Publication Ethics
(Friday October 17, 2014, Session 6)

Authorship Ethics in Global Health Research Partnerships Between Researchers from Low or Middle Income Countries and High Income Countries
(Friday October 17, 2014, Session 7)

Dear Colleagues,

The goals of medical research are to increase knowledge, and develop products and services for society. Society trusts that medical research is conducted in a manner upholding the highest standards of research integrity. As such, Good Medical Research is of paramount importance in order to uphold this social contract, and to improve human health by developing safe and effective medical treatments. Good Medical Research captures a range of ethical conduct and responsibilities for medical researchers including the collection and analysis of data, ethical authorship and publication practices, good mentoring, and ethical peer review to name a few.

Authorship and publication ethics is important for medical researchers to understand for several reasons. First, it is the main forum to inform other scientists about medical research in order to reproduce results and build upon. Ethical issues pertaining to open publication practices can impede reproducibility and if research is incorrectly or fraudulently reported, it can cause harm to human subjects, waste resources, diminish trust, and impede scientific discovery. Second, ethical authorship practices are important to all researchers because scientists

are interested in receiving fair recognition for their work despite their position, gender, race, country of origin, or other attributes. Providing fair and deserving authorship shows mutual respect and fosters trust among colleagues. Third, authorship is how researchers are also held accountable for their part of the research project. This is important not only for recognizing one's work, but also to know who might be responsible for errors in results or if results are fabricated or falsified. For these three reasons, medical researchers should be aware of authorship practices and international guidance on authorship and publication ethics.

In my first presentation, I will cover contemporary issues in publication ethics, and in a second presentation, I will discuss specifically authorship ethics in the global health research context. Publication ethics involves various aspects in the conduct of science including selective reporting of data and transparency, plagiarism, deserving authorship, and publication retractions. Authorship and publication practices have shifted throughout the years and differ among the different areas of science and medical research e.g., increased secrecy and selective reporting versus open sharing. I will explain some of the contemporary practices in authorship and publication of medical research and also speak to the factors that might influence such changes. In a subsequent talk, I will outline issues of authorship ethics as it relates to global health research where research groups between high income countries collaborate with groups in low and middle income countries. I will also offer recommendations on how to deal with these authorship ethics issues in a meaningful way.

I hope scientists in a range of medical practices will attend this year's MedicReS World Congress and join us for an excellent selection of speakers covering the many aspects of Good Medical Research.

Best Regards,

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Andrea ZAHN

Andrea spent 10 years in the world of sales and management in the Insurance industry. In 1984, she began supporting Doug in his teaching career and later joined him in working with participants in the UK course providing daily mind-mapsthat summarized content and coaching highlights.

Douglas ZAHN

Doug is a Professor Emeritus of the Department of Statistics at the Florida State University where he taught applied statistics and statistical consulting courses for 35 years. He taught courses for 10 years on how to improve your consulting skills to over 450 professionals at the United Kingdom Office for National Statistics. He received the first W.J. Dixon Award for Excellence in Statistical Consulting awarded by the American Statistical Association. Doug's passion is to transform relationships and interactions from stumbling blocks to stepping stones. He helps professionals tosystematically improve the quality of their services. He continues to grow in these areas by carefully examining what works and what does not work in all aspects of his life.

HOW TO BECOME A MORE EFFECTIVE COLLABORATOR?

Doug Zahn, Professor Emeritus

Department of Statistics

Florida State University

Andrea Zahn, Collaborator

Zahn & Associates

Here are the Titles of My Sessions:

How to Become a More Effective Collaborator ? :

Part 1. (Session 3, Thurs, Oct. 16, 1:30-2:30 p.m.) A Review of the Human Side of Collaboration

Part 2. (Session 7, Friday, Oct. 17, , 1:30-2:15 PM) Identify tough challenges and apply video-based coaching to one of them.

Part 3. (Sat., Oct. 18, 9:00 a.m.-12:00 noon) Workshop: Address more tough challenges

I owe a deep personal debt to Good Medical Research because it has made the difference to me between dying at age 26, as my father did, and living to age 70. My father died of an asthma attack in 1942 and, thanks to Good Medical Research, I survived a similarly severe attack in 1969. Probably every attendee of the MedicReS World Congress 2014 has a similar story. While we are all grateful for the progress that has been made, clearly much Good Medical Research remains to be done.

Doing this work effectively requires successful collaboration among many parties: clinicians, scientists, statisticians, ethicists, administrators, regulatory authorities, and members of staff. Good relationships are at the heart of successful collaboration. The Congress gives its participants an invaluable opportunity to begin creating good face-to-face relationships with individuals from all groups that collaborate to produce Good Medical Research, a rare opportunity in our virtual world.

Doing good medical research inevitably involves interactions with others. Some of these are successful; some are not. My series of three sessions at the Congress will address barriers that must be overcome to be a more effective collaborator. While technical skills are necessary for doing good medical research, they are not sufficient. The researcher must also have interpersonal and intrapersonal skills so that he or she can be an effective collaborator with all coworkers. Each participant will have the opportunity to develop skills to address at least one of the barriers that is now compromising his or her career satisfaction.

The question of how to become a more effective collaborator has been of interest to me during my entire career as an educator and a consultant. Studying it has produced new ideas virtually every day. These studies have produced enough material so that I could easily spend five days talking with you about topics that I think might be of use to you. My goal is to address the topics that you choose as most relevant to improving your practice. To do this, I envision our time together at MedicReS as being a five-hour collaboration using the POWER process.

The POWER process is a structured approach for producing effective collaborations. It consists of five steps:

Prepare: Handle essential matters before you start the interaction.

Open: Agree on a time frame, what each of you want from the interaction, what each is willing and able to do to produce that result.

Work: Address what is wanted from the interaction.

End: Develop a workable plan and close the interaction on time.

Reflect: Consider what worked and what did not work in the interaction.

I will use the POWER process to pursue this goal:

In these five hours each of you will learn

- at least one new skill or concept that will help you address one of your most challenging interpersonal or intrapersonal issues in your own professional practice and
- how to implement this skill or concept effectively in the first two weeks after you return to work.

I will not be examining the technical issues that arise in your professional practice. However, I will address the relational aspects of these technical issues, should you desire.

Here is a summary of how the POWER steps will be applied during my three sessions with you.

Thursday, October 16, Session 3, 1:30-2:30 PM: A Review of the Human Side of Collaboration

Prepare: In a conference collaboration session such as this one, a key part of Prepare is for me to let you know what questions I think I can be helpful on. What have I learned about collaboration in the last 35 years?

My first hour with you (in Session 3) will be devoted to a Prepare conversation. In it I will review consultations that contributed to the development of this work and relate them to your experiences. I will give you an overview of skills and concepts that clients have found most useful over the years. My goal is to equip you to be informed consumers of what I have to offer you. (End of Session 3 assignment: Identify your toughest relational challenge that you are willing to talk about with Congress colleagues in Session 7 and the Workshop. This challenge may be compromising your professional satisfaction and contributing to burnout.)

Friday, October 17, Session 7, 1:30-2:15 PM: Identify tough challenges and apply video-based coaching to one of them.

Open/Work: In Session 7 I will invite you to form groups of four and identify the toughest challenges you encounter. I will then work with a volunteer who is willing to do a role-play relating to his or her toughest problem in front

of the entire group. Another volunteer will be briefed to create the first volunteer's toughest problem in the role-play. The role-play will be videoed, with the video being used to coach the first volunteer. Saturday, October 18, Workshop, 9:00 a.m.-12:00 noon: Address more tough challenges

Work: In the Workshop, we will use role-plays in working groups of four and interactive exercises to address some of the tough challenges participants encounter in interactions.

End: Toward the end of the workshop we will explore remaining open questions.

End: In 15 of the last 20 minutes of the workshop, you will have five minutes to consider how you will implement one new skill or concept you have learned. In the remaining 10 minutes I will invite you to explore your implementation plans with your team members. My hope is that you will receive additional input that will be of assistance to you in implementing your learning when you return to work.

Reflect: In the last 5 minutes workshop I will of the request that you give Andrea and me feedback on what you have learned in this workshop and where you think it may be useful. Any comments or suggestions you have on how the workshop can be improved will be most appreciated.

We invite you to join us at the MedicReS 4th World Congress on "Good Medical Research" to learn a process that you can use to systematically become a more effective collaborator.

Kind Regards,

C

CONTRIBUTED SESSIONS: ORAL PRESENTATIONS

MedicReS

C 1

IMPROVEHEALTH-RELATED MEASUREMENTS: EFFICIENT SCORING IN HEALTH STATUSAND PSYCHOMETRICQUESTION-NAIRES

Caritey, Benoît-Damien,
Department of Biostatistics,
Clinsearch, Bagneux, France, 92220

Presenter contact information:
Name: Caritey Benoît-Damien
Telephone: +33 1 47 35 93 90
Fax: +33 1 47 35 17 18
E-mail: benoit.caritey@clinsearch.fr
Address: 1 rue de l'égalité, Bagneux, 92220, France

ABSTRACT

Subject: Good Biostatistical Practice

Background and Aims: Generic or specificdiscriminative and evaluative questionnaire instruments are currently and since the last twenty five years widely used in orderto create evidence and knowledge for clinical decision making and in clinical research.Questionnaires like the SF-36 Health Survey or the BDI-II are only two famous examples of numerous established and validated questionnaires.Considering that validation guidelines for the construction of questionnaires assessing health status recommenda content validation step studying how the different items composing a particular questionnaire are grouping each other's into consistent and interpretable scales. And, considering that,widely,questionnaires scale scoring are formed by simple summation of item ratings composing the scale. We aim at studying and recommendingthe use of factor loadings provided by Principal Component Analysis during the content validation phase as recommended weightswhen scoring questionnaires factors.

Methods: Factor analysis (FA)is the most popular multivariate statistical techniquesand isa recommended in the development process of health-status assessment questionnaires.PCA is in turnthe preferred factoring method in FA and provide very useful and underused results. Indeed,PCA is a way of representing observations described by several variables, which are generally inter-correlated and to extract information from the individual variabilityexpressing this information in a lower dimensional space by projection, providing new orthogonal variables called factors whichare linear combinations of the original items that should provide a natural way of scoring questionnaires by factors loadings. Scoring a questionnaire by using a simple summation do not respect the underlying PCA structure that led to the construction of the questionnaire scales.Factors are, in case of scoring by summation, only approximated. In this particular study we compare the efficiency of factor loadings in scoring questionnaires scale compare to simple summation by simulating individual data based on published results studying renowned questionnaires and particularly the SF-36 and BDI-II.

Conclusions: PCA factor loadings provide useful and explainableset of weightsin order to efficiently score questionnaires scales.Practical implications could bea greater score precision and a reduced concentrations of extreme scores, a better evaluation of the minimum clinically significant difference and discriminative sensitivity.

C 2

IN THE ABSENCE OF GOLD STANDARD USING LATENT CLASS ANALYSIS IN MICROBIOLOGICAL STUDY AREA

G. Bayram Abiha*, E.A. Kanik**.

** Vocational School of Health Services, Mersin University, Mersin, TURKEY*
*** Departmentof Biostatistics, Faculty of Medicine, Mersin University, Mersin, TURKEY*

Correspondenceauthor:
E-mail: gulbayram78@gmail.com
Tel: +90 324 234 77 23
Fax: +90 324 234 64 10

ABSTRACT

Subject: Good Medical Research

Background and Aims: The research on the effectiveness of diagnostic tests in the absence of a gold standard,analysis for evaluating the performance of these tests is an important problem. Latent class analysis is a statistical analysis method known for many years, especially in the absence of a gold Standard for evaluation of diagnostic tests has found its wide applicationarea.Inparticular researchers has established the performance of this method for identification of dentalcaries, in the evaluation of breast cancer screening tests, colecteral cancer screening tests, diagnosis of *H. pylori*infection in micribiological tests. Latent class analysis in the event of a real disease, a common hidden variables influenced by the different tests for the same disease tha tobserved in the case of incorrect results is a test that is used. We aimed to review availability of latent class analysis method used microbiological diagnosis in various diseases in several studies.

Methods: In this study, in the absence of gold standard, latent class anaysis method was used to assess several diagnostic tests performance.

Results: LCA method is a reliable stastistical method in the assesing microbiological diagnostic test performance in the absence of goldstandard.

Conclusions: During the last decade,latent class analysis method has widely used in for determining sensivity and specifity of different microbiological tests in the diagnosis of *Mycobacteriumtuberculosis Mycobacteriumbovis*, humanpapillomavirus, *Bordetellapertussis, Helicobacterpylori, norovirus*infections. Researchers has compared these different tests for diagnosis of these pathogens. Finally, we supposed that LCA is an useful analysis method to assess different test performances in the absence of gold standard.

Keywords: LCA, diagnostic, microbiological test.

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C 3

OVERCOMING THE BARRIERS TO THE RETIREMENT OF OLD AND NEW WORLD MONKEYS FROM RESEARCH FACILITIES

A. Kerwin
President, Primates Incorporated, U.S.A.

Amy Kerwin
PO Box 7384
Madison, WI 53707, U.S.A.
608-220-2166
amy@primatesinc.com

ABSTRACT

Subject: Good Bioethical Practice

Background and Aims: After working five years in the research business and networking for ten years with those who run sanctuaries, the author discovered first-hand that there are "barriers" to the retirement of laboratory monkey species from research facilities into sanctuaries. Kerwin defines a *barrier* as an opinion or stereotype that prevents primate retirement from occurring on a regular basis.

Her aim is to maximize the retirement of primates by raising awareness among researchers and sanctuary directors to various potential barriers to retiring Old and New World monkeys from research facilities and providing recommendations on how to overcome those barriers.

Methods: Kerwin researched scientific and sanctuary literature about retiring primates, surveyed primate sanctuary directors and primate researchers, and documented her own personal experiences in order to develop a final list of ten barriers to retirement. She then asked survey respondents to provide suggestions on how to overcome the list of barriers.

Results: Barriers compiled included the researcher's concern for the long-term wellbeing of the retired monkey, lack of funding for retirement, unexpected negative publicity after retirement, convenience and affordability of reuse and/or euthanasia, and fear of losing one's job by challenging the status quo and suggesting retirement.

Conclusions: Researchers will increase the frequency of primate retirement by performing the following five actions: (a) increase communication by networking with sanctuaries, (b) prevent negative publicity by developing a confidentiality clause with the sanctuary, (c) increase understanding by reviewing the articles written on retiring monkeys into sanctuaries, (d) increase funding for primate retirement by including funding requests in grant proposals, or (e) raising private funds.

C 4

EFFECTS OF FIBROBLAST GROWTH FACTOR AND OZON APPLICATIONS ON RENAL FAILURE IN HYPOXI-ISCHEMIC RATS

L. Bahar*, M. Gul**, Y. Celik, B. Resitoglu*, S. Erden Erturk*, S. Gul *****

** Vocational School of Health Services, Mersin University, Mersin, TURKEY*

*** Department of Histology and Embryology, Faculty of Medicine, Inönü University, Malatya, TURKEY*

**** Department of Pediatri, Faculty of Medicine, Mersin University, Mersin, TURKEY*

Correspondence author:

E-mail: laylabahar@gmail.com

Tel: +90 324 234 77 23 Fax: +90 324 234 64 10

ABSTRACT

Subject: Good Medical Research

Background and Aims: Fibroblast Growth Factor-2 (FGF2) promotes angiogenesis, proliferation, apoptosis, differentiation, chemotaxis and motility of different cell types. Ozone cleans free radicals that has accumulated in the tissues and neutralizes and thereby has been reported to control the development of tissues damaged. The purpose of this study is to examine the effects of the FGF2 and ozone applications on kidney glomeruli and tubules of created hypoxic-ischemia in newborn rats.

Methods: Enrolling six groups and 7 from each group consisting of a one-week male Wistar rat pups, were included in this study. The first group, hypoxic-ischemia (HI) was not applied which was the sham group. To create hypoxic ischemia, the carotid arteries of the second group were ligated, and to 8% oxygen was performed by taking a chamber of hypoxia. The other two groups, 10µl/ml and 20µl/ml FGF2 were implemented groups . The last two groups, 25 mg/kg and 50 mg/kg ozone were implemented group. For the light microscopic examination, routine tissue processing was performed and stained with hematoxylin-eosin (H-E), Masson's trichromic and periodic acid Schiff (PAS) and was examined by a Nikon Optiphot-2 light microscope. The mean dimension of the glomeruli was semi quantitatively determined by measuring the dimension of a minimum of 100 glomeruli per section. A minimum of 20 fields at 20X magnification were assessed for calculating the mean number of glomeruli. Kidney damage was scored by grading glomerular, tubular and interstitial changes. For statistical analysis of the study "multiple group comparison" was made and the Kruskal-Wallis test was performed.

Results: Especially in kidney sections of the hypoxic ischemia (HI) group,collapse in the glomeruli and sclerotic changes, Collapse in the Bowman's space and in some of the excessive accumulation ultrafiltrate and dilatation was noted. Renal tubule epithelial injury and tubular degeneration was determined. When the average diameter of glomeruli and damage scores were examined, between HI group 20µl FGF and 50mg/kg ozone significant difference was observed.

Conclusions: In summary, having based on this assessment, in the renal glomeruli and tubules for the damage caused by hypoxic ischemia the applied FGF and ozone that provides healing in renal tissue was found. And this result is closely related to the dosage of ozone and the FGF.

Key words: Hypoxia-ischemia, FGF2, ozone applications, renal injury

C 5

HISPOLON INDUCES HUMAN NASOPHARYNGEAL CARCINOMAS CELLS APOPTOSIS THROUGH ERK1/2, JNK1/2 AND P38 MAPK PATHWAY

Ming-Ju Hsieh[1,2], Mu-Kuan Chen[3]

[1]Cancer Research Center, Changhua Christian Hospital, Changhua 50006, Taiwan

[2]Institute of Medicine, Chung Shan Medical University, Taichung 40201, Taiwan

[3]Department of Otorhinolaryngology-Head and Neck Surgery, Changhua Christian Hospital, Changhua 50006, Taiwan

**Present the paper and corresponding author:*
Ming-Ju Hsieh Cancer Research Center, Changhua Christian Hospital, 135 Nanhsiao St, Changhua, Taiwan
Tel: +886-4-7238595#4881; Fax: +886-4-7232942;
Email: 170780@cch.org.tw

ABSTRACT

Subject: Good Medical Research

Background and Aims: Nasopharyngeal carcinoma (NPC) is the most common cancer originating in the nasopharynx, where the nasal passages and auditory tubes join the remainder of the upper respiratory tract. Despite occurring commonly in Southeast Asia and southern provinces of China, rarely occurs in Northern China, Europe, and America. Importantly, It is a metastasis of cancer cells to the neck lymph nodes, which can occur in up to 75% of NPC patients, represents an adverse prognostic factor of the disease.Hispolon, a phenol compound isolated from Phellinuslinteus (PL), possesses anti-inflammatory, antiproliferative, and antioxidant effects. However, the effects of hispolon on human nasopharyngeal carcinomas have yet to be evaluated.

Methods: Here, the molecular mechanism by which hispolon anticancer effects in human nasopharyngeal carcinomas cells was investigated.

Results: The results showed that hispolon significantly inhibited cell proliferation of HONE-1 and NP-039 cell lines. Furthermore, hispolon induced apoptosis through caspases-3, -8, and -9 activations and PARP cleavage in dose- and time-dependent manner in HONE-1 and NP-039 cells. Moreover, hispolon also showed that increase phosphorylation of ERK1/2, p38 MAPK and JNK1/2 in dose - and time - dependent manner by western blot analysis. However, hispolon-induced activation of the caspase-3, -8 and -9 significantly abolished by inhibition of p38 MAPK and JNK1/2 specific inhibitors.

Conclusion: Chemoprevention is an active cancer preventive strategy to suppress, delay, or reverse human carcinogenesis. In this study, we demonstrated that hispolon could induce the phosphorylation of ERK1/2, JNK1/2, and p38 MAPK, stimulate the activation of caspase-3, -8, and -9, which eventually result in the cleaved of PARP and inhibition of proliferation and apoptosis induction of HONE-1 and NPC-039 cells. Our findings revealed that hispolon might be a useful candidate as a chemotherapeutic agent for NPC therapy.

C 6

PON1 L55M POLYMORPHİSM - PARAOXONASE ACTIVITY AND REDUCTION IN THE RISK OF DEVELOPING LEUKEMİA

N. Eras[1], E. Akbas[1], N. Tiftik[2], A. Tombak[2], M. Berkoz[3], S. Kul[4]

[1]Mersin University Faculty of Medicine, Department of Medical Biology and Genetics, Mersin, Turkey
[2]Mersin University Faculty of Medicine, Department of Hematology, Mersin, Turkey
[3]Van University Faculty of Pharmacy, Department of Pharmaceutical Technology, Van, Turkey
[4]Gaziantep University Faculty of Medicine, Department of Biostatistics, Gaziantep, Turkey

Correspondence author:
E-mail:nazaneras@gmail.com

ABSTRACT

Subject: Good Medical Research

Background and Aims: Paraoxonase 1 (PON1) is an antioxidative enzyme, which has been suggested to play a role in tumour biology. The aim of this study was to determine whether PON1 L55M polymorphism was associated with the risk of leukemia and to investigate the relationship between PON1 genotypes and PON1 enzyme activities.

Methods: Genotypes of 102 cases and 112 controls were determined by use of PCR-RFLP. PON1 enzyme activity were kinetically measured using paraoxone as a substrate.

Results: The ratio of MM genotype belonging to PON1 L55M polymorphism in control group was 6.3% and was 7.8% in patients with breast cancer (p=0.39). PON1 enzyme activity was 118.8 ± 115.1 U/mL in control group, while decreased to 75.6 ± 64.4 U/mL in patients with leukemia (p=0.004). PON1 enzyme activities of the cases with MM genotypes belonging to PON1 L55M polimorphism was 57.43 ± 21.61 U/mL in control group and decreased to 39.18±45.61 U/mL in leukemic patients (p=0.028).

Conclusions: PON1 L55M polimorphism genotype ratios do not affect the risk of developing leukemia. PON1 enzyme activity reduces the risk of developing leukemia. Likewise, the combination of PON1 L55M polimorphism - PON1 enzyme activity reduces the risk of developing leukemia.

Key Words: Antioxidant, Paraoxonase, Oxidative stres, Leukemia

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TS1494DEL6 POLYMORPHISM AND INCREASED RISK OF DEVELOPİNG BREAST CANCER

N. Eras [1], E. Akbas[1], E. Nayir[2], A. Arican[2], L. Bahar[3]

[1]Mersin University Faculty of Medicine, Department of Medical Biology and Genetics, Mersin, Turkey
[2]Mersin University Faculty of Medicine, Department of Medical Oncology, Mersin, Turkey
[3]Mersin University Vocational School of Health Service, Mersin, Turkey

Correspondence author:
E-mail:nazaneras@gmail.com

ABSTRACT

Subject: Good Medical Research

Background and Aims: Thymidylate synthase (TS) is an important enzyme involved in folate metabolism that catalyzes reductive methylation of deoxyuridylate to thymidylate, which is the essential precursor of DNA biosynthesis and repair process. Polymorphisms in genes involved in folate metabolism may influence DNA methylation, nucleotide synthesis, and thus individual susceptibility to the development of cancer. We investigated the probable effects of TS1494del6 polymorphism on the risk of developing breast cancer.

Our study population consisted of 298 women with breast cancer (mean age = 50,64±10,28) who were diagnosed at the Oncology Clinic of the Mersin University Hospital and 300 healthy women controls (mean age = 49,14±8,38) matched for ethnicity, sex and age. DNA isolation was performed from blood samples of the subjects and TS1494del6 genotypes was analyzed by using PCR– restriction fragment length polymorphism (RFLP). The resulting RFLP products were separated by electrophoresis. All statistical analyses were performed with SPSS statistical software.

Results: Variant -6bp allele frequency was significantly higher in women with breast cancer than in controls (0.554 vs. 0.467, P=0,003; OR:1,42(1,13-1,78)). The frequency of the -6bp/-6bp genotype was 12% in control group, while increased to 26.8% in women with breast cancer. Putative breast cancer risk factors such as higher BMI (P=0,0001), late age at menopause (P=0,036) and cancer history in first-degree relatives (P=0,001) were related to increased breast cancer.

Conclusions: TS1494del6 gene polymorphism increases the risk of developing breast cancer. Higher BMI, late age at menopause and cancer history in first-degree relatives also increases the risk of developing breast cancer.

Key Words: Breast cancer, TS1494del6, Polymorphism

C 8

THE RELATIONSHIP BETWEEN VEGF-1154 (A/G) GENE POLYMORPHISM AND GLIAL TUMOR PATIENTS IN TURKEY (A Preliminary Study)

***O. Tubay Bagdatoglu* [*], *C. Bagdatoglu* [**], *H. Tuna* [***], *S. Erden Erturk*[*], *G. Polat* [****]**

**Vocational School of Health Services, Mersin University, Mersin, TURKEY*
***Department of Neurosurgery, Faculty of Medicine, Mersin University, Mersin, TURKEY*
****Department of Neurosurgery, Faculty of Medicine, Ankara University, Ankara, TURKEY*
*****Department of Clinical Biochemistry, Faculty of Medicine, Mersin University, Mersin, TURKEY*

Correspondence author:
E-mail: otbagdatoglu@mersin.edu.tr
Tel: +90 324 234 77 23, Fax: +90 324 234 64 10

ABSTRACT

Subject: Good Medical Research

Background and Aims: Glial tumors are the most common tumors in central nervous system. Glioma angiogenesis is related with the angiogenic cytokines releasing from the tumor cells. Single nucleotide polymorphisms (SNP) occur in the promoter regions of proinflammatory cytokine genes influence cytokine production. Vascular endothelial growth factor (VEGF) has a very important role in tumor angiogenesis. In this study, we aimed to investigate whether the VEGF-1154 (A/G) polymorphism is associated with the gliomas.

Methods: The whole bloods of 76 glial tumor patients and 110 healthy controls were collected in EDTA-containing tubes. DNA was extracted by high pure template preparation kit. SNPs were genotyped using polymerase chain reaction (PCR) technique. And finally the genotypes were designed as follows: AA (low VEGF expression), AG (heterozygote) and GG (high VEGF expression).

Results: GG genotype was detected as n=30/76 (39.47%) in glioma patients while n=59/110 (53,64%) in controls (p=0.0583) with an Odds ratio (OR) of 0.5637 (95%CI 0.3115-1.0203). These results suggest that there may not be an association between glial tumors and GG genotype of VEGF-1154 (A/G), which is related with high expression of this cytokine. GG genotype was also detected in both low and high grade glioma patients. GG genotype was detected as n= 7/30 (23.33%) in low grade glioma patients, while n=23/30 (76.67%) in high grade gliomas (p=0.3853) with an OR of 1.5899 (95%CI 0.558-4.5289). According to the p value there isn't a difference between the grades with regard to GG genotype. As well as in terms of angiogenesis high grade glial tumors have 1.6 times more risk than the low grade tumors.

Conclusions: In conclusion, high grade gliomas are known to be high invasion behavior and angiogenesis potential than other tumors and have poor prognosis. However, further work is required in larger patient and control series in these population to explain the possible role of VEGF polymorphism in gliomas.

Key words: Glial tumor, VEGF, tumor invasion

C 9

A SEEKING FOR A WAY TO ILLUSTRATED MEDICAL ETHICS

O. Ogenler *, S.Kadioglu **

**Assistant Professor, Mersin University Faculty of Medicine, Department of History of Medicine and Medical Ethics, Turkey*

*** Associate Professor, Cukurova University Faculty of Medicine, Department of History of Medicine and Medical Ethics, Turkey*

Correspondence author:
E-mail: oyaogenler@gmail.com
Tel: +90 324 3610684, Fax: +90 324 234 64 10

ABSTRACT

Subject: Good Bioethical Practice

Background and Aims: Mersin and Çukurova Universities are located in Mersin and Adana, two sizeable cities in southern Turkey. This presentation contains general information regarding illustration based education approach of Mersin and Çukurova medical ethics departments and also samples of visual materials utilized in lectures.

Methods: Medical ethics courses for medical faculty students of these two universities are in the first and third years of education. Medical ethics courses that mainly have a conceptual and theoretical character are realized in conference format partially open to interaction. It is possible to say that they are lonely and different in human biology based curriculum and students may have focusing and concentration problems with them. Using illustrations seem to be an effective way in the context of making methodological regulations to solve these problems.

Results: In Mersin and Çukurova model, originally prepared or adapted illustrations are placed in slideshows accompanying instructors' speech. In order to understand a lecture prepared in this manner, students must provide integration of its visual and verbal components. This integration activity may be thought as an interesting jigsaw puzzle to challenge for them.

Conclusions: This approach may also be considered as a seeking for a way to an illustrated medical ethics textbook in long term.

Key words: medical ethics, bioethics, illustration, medical education

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RANDOMISED TRIALS IN SPORTS MEDICINE

R. Rylance MSSc, J. Ranstam PhD

Rebecca Rylance (presenter)
Klinikgatan 22, Wigerthuset, plan 1
221 85 LUND
Sweden
Office hours: 8-17 Monday-Friday
mrylance@gmail.com
Tel: +4646708607781, Fax: +46468888328

Jonas Ranstam
Skane University Hospital and Dept of Clinical Sciences, Lund University, Sweden
+4646761412514

ABSTRACT

Subject: Good Biostatistical Practice

Background and Aims: Several discussions have recently focused on the inability of the scientific system to ensure reproducible results in medical research [1, 2]. The problem seems to be greater in laboratory research than in clinical research [3]. Human trials are, in principal, rigorously regulated regarding design and statistical analysis (Good Clinical Practice), have special requirements for pre-registering of endpoints (e.g. clinicaltrials.gov) and reporting guidelines (the CONSORT statement). In practice, however, published reports do not always show compliance to the recommendations [4, 5, 6].

Methods: Much of the evolution of the recommendations have taken place within the framework of drug development. We wished to see to what degree randomized trials published in journals representing a mainly non-pharmacological research area, sports medicine, comply with generally accepted trial recommendations. We have reviewed all reports on randomized trials published during 2013 in the American Journal of Sports Medicine and in the British Journal of Sports Medicine, with special emphasis on trial registration, definition of endpoint and multiplicity issues.

Results: During 2013, the American Journal of Sports Medicine published 25 original articles describing randomized controlled trials. Registration identifiers, from one by ICMJE or WHO approved trial registry, were given in 7, of the reviewed articles. Clearly defined primary endpoints were presented in about half of the articles. All of the 25 articles presented statistical analyses with multiplicity issues, but in none was a clear strategy for addressing them, even if two articles did include a Bonferroni adjustment of the p-values. The British Journal of Sports Medicine also published 16 original articles on randomized controlled trials. A third of those presented an approved registration identifier. Twelve had clearly defined primary endpoints. Again, all the articles presented statistical analyses with multiplicity issues, but none presented a clear strategy for addressing them, even if the problem was mentioned in 5 articles, some of which included Bonferroni adjusted p-values.

Conclusions: Even though these publications give the appearance of high quality; the reality is sub-standard analyses with un-reliable results. Stricter study compliance needs to be to encouraged by journals to improve the quality of randomized controlled trials.

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ACCURATE USAGE OF AGREEMENT METHODS IN THE COMPARISON OF BIOCHMEICAL DIAGNOSTIC TESTS : SAMPLE DATA STUDY

Sema ERDEN ERTURK[a], Sedefgul YUZBASIOGLU ARIYUREK [b]

[a] Vocational School of Health Services , Mersin University, Mersin, TURKEY

[b] Biochemistry Department of Medical Faculty, Cukurova University, Adana, TURKEY

Correspondence author:
E-mail: semaerden@yahoo.com

ABSTRACT

Subject: Good Medical Research

Background and Aims: In the clinical field, many statistical techniques have been used for comparing the diagnostic procedure. Nevertheless, a great deal of researchers do not use the statistical method properly.The aim of this study is to reveal the statistical method which determines the concordance of two measuring techniques.

Methods: In our study, to determine the levels of Serum free beta 2-microglobulin (b2M) of 43 patients; immunonephelometric and immunoturbidimetric biochemical dignostic methods have been used. In the comparison of the diagnostic test's cohesiveness, Bland-Altman Plot, Concordance Correlation Coefficient, İntraclass Correlation ve Deming Regressionstatistical methods will be used and the results found will be evaluted.In addition to these,the mostly used inaccurate methods as Pearson Correlation ve Paired Samples T Test have been applied.

Results: Normal regression tests the parameters of A and B VERSUS 0.Accordance is not adequate to be researched. Deming regression tests alfa versus 0, beta versus 1.It has been observed that the technique that is closest to β"0" AND β"1" ıs the best method.

Conclusions: Including the most appropriate hypothesis test,Deming regression have been used while comparing the cohesiveness.

Key Words: Concordanse Correlation, beta 2-microglobulin, Bland-Altman Plot

C 12

PROTECTIVE EFFECTS OF FIBROBLAST GROWTH FACTOR AND OZON APPLICATIONS ON CORNEA IN HYPOXIC-ISCHEMIA RATS

L. Bahar*, B. Resitoglu*, M. Gul**, Y. Celik, B. Yigitcan **, S. Erden Erturk****

** Vocational School of Health Services, Mersin University, Mersin, TURKEY*
*** Department of Histology and Embryology, Faculty of Medicine, Inönü University, Malatya, TURKEY*
**** Department of Pediatri, Faculty of Medicine, Mersin University, Mersin, TURKEY*

Correspondence author:
E-mail: laylabahar@gmail.com
Tel: +90 324 234 77 23, Fax: +90 324 234 64 10

ABSTRACT

Subject: Good Medical Research

Background and Aims: Recent studies, hypoxic-ischemia-induced damage to repair, new agents and methods are being tested. Fibroblast Growth Factor2 (FGF2)'s protective effects on the retina and the lens epithelial cells have been found. Also ozone application, is used for the treatment of various ocular diseases. The purpose of this study is to examine the effects of the FGF2 and ozone applications on cornea damage of created hypoxic-ischemia in newborn rats.

Methods: Including six groups and 7 from each group consisting of a one-week male Wistar rat pups, were included in this study. The first group, hypoxic-ischemia (HI) was not applied which was the sham group. To create hypoxic ischemia, the carotid arteries of the second group were ligated, and to 8% oxygen was performed by taking a chamber of hypoxia. The other two groups, 10µl/ml and 20µl/ml FGF2 were implemented groups. The last two groups, 25 mg/kg and 50 mg/kg ozone were implemented group.

After enucleation, eyes were fixed in 10% phosphate-buffered formalin and prepared for routine paraffin embedding. Paraffin blocks were cut and stained with the hematoxylin–eosin and periodic acid–Schiff methods. For morphometric examination, a Nikon Optiphot-2 light microscope was used. The full thicknesses of the total cornea, corneal epithelium, and stroma were measured for each section in the one-third central cornea. The grading for corneal epithelium injury and cornea stromal edema were scored. Tukey-Kramer test for all pairwise comparisons was performed for statistical analysis.

Results: The corneal epithelium cells and stroma were normal in histologic appearance in the sections obtained from the sham group. In HI group, the stroma was highly edematous and wide gaps between collagen fiber bundles in some cornea sections. Corneal epithelium, stroma, and total corneal thickness were significantly different between the groups. Histopathological findings in the treatments groups showed a noticeable improvement. The histologic appearances were nearly normal in the treatment groups.

Conclusions: As a result, in the treatment of corneal injury that was induced by hypoxic-ischemia, was found to be helpful to FGF2 and ozone applications. Especially, damage in healing, 20µl FGF and 50mg/kg ozone applications have emerged to be more effective.

C 13

USING PROPENSITY SCORE METHOD IN SURVIVAL ANALYSIS AND MULTI LEVEL TREATMENT STUDIES

E. Ç. Kaspar[1], N. Bekiroglu[2], A. Batirel[3]

1. Yeditepe University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Istanbul, Turkey. Phone number: +90 5353682801 office hours: 09:00- 18:00, e-mail: ecaltunok@yeditepe.edu.tr

2. Marmara University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Istanbul,Turkey. E-mail: nural@marmara.edu.tr

3. Kartal Dr. Lütfi Kırdar Training and Research Hospital, Clinic of Infectious Diseases And Clinical Microbiology, Istanbul,Turkey. E-mail: aysebatirel@yahoo.com

ABSTRACT

Subject: Good Biostatistical Practice

Background and Aims: In observational studies, investigators have no control over the treatment assignment. Therefore, some differences may exist on observed covariates in case-control groups, and these differences could lead to have bias estimates of treatment effects. Propensity score (PS), which can be determined as a balancing score, is the conditional probability of receiving the treatment given pre-treatment variables.PS is aimed to reduce bias, to increase the precision of the estimates, to determine the effects of some covariates. Using estimated PS, new sample which is obtained by resampling can be used to estimate treatment effect. In its original version, it exclusively deals with subjects where dependent variable takes on only two values, butin many subjects the dependent variable takes on more than two values.Despite many papers on PS, few have focused on the analysis of survival data.In this study, it is aimed to observe the difference between the significance in risk factors, when cox-regression models were used for the sample of multi-level treatment groups, before and after adjusting the PS for time-to-end data.

Methods: In this study, the data were taken from N=214 extremely-drug resistant Acinetobacter bloodstream infections (XDR-ABSI) patients who were treated in 27 tertiary-care centers in 7 provinces of Turkey from January 2009, to August 2012. Significant factors were tested by Cox-regression analysis in order to determine the independent risk factors for the mortality. Cox-regression was performed with 16 risk factors, regarding patients with different colistin (COL) based treatment combinations. PS was calculated by multinomial logistic regression and Cox-regression was performed for the new sample.

Results: After resampling, groups had similar characteristics in risk factors and bias was reduced.

Risk Factors	Before PS Matching		After PS Matching	
	HR (%95 CI)	P value	HR (%95 CI)	P value
Age	1.04 (1.02-1.05)	<0.0001	1,02 (1.02-1.06)	<0.0001
Gender	0.88 (0.59-1.32)	0.111	0.93 (0.62-1.58)	0.993
Hospital stay prior to XDR-ABSI	1.2 (1.1-1.3)	0.02	1.2 (0.98-0.99)	0.024
ICU stay prior to XDR-ABSI	1.3 (1.2-1.4)	0.01	1.3 (1.2-1.4)	0.042
Pitt bacteremia score	1.19 (1.1-1.29)	0.02	1.2 (1.1-1.4)	<0.0001
APACHE 2 score Charlson Co-morbidity Index	1.05 (1.05-1.08) 1.2 (1.1-1.3)	<0.0001 <0.0001	1.06 (1.02-1.1) 1.2 (1.03-1.3)	0.007 0.017
Early vs late therapy	0.76 (0.47-1.22)	0.7	1.19 (0.67-1.93)	0.629
Concomitant other infection	1.26 (0.84-1.91)	0.8	1.41 (0.87-2.29)	0.161

Conclusions: The significance in risk factors, when Cox- regression was used for the sample of treatment groups' patients before and after adjusting the PS, was observed some differences. PS can be used for reducing bias between multi-level treatment groups and to increase the precision of estimates in survival analysis.

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COMPARISON OF NRI AND LOGISTIC REGRESSION ANALYSIS RESULTS THROUGH A SIMULATION IN THE DETERMINATION OF THE EFFICACY OF A NEW BIOMARKER

Emine Arzu Kanik, PhD [1,]
Vedia Bennu Ozcomert [2],
Gülhan Orekici Temel,PhD [3]

[1]*Department of Biostatistics, Mersin University, Mersin,Turkey*
[2] *Department of Biostatistics, Mersin University, Mersin,Turkey*
[3] *Department of Biostatistics, Mersin University, Mersin,Turkey*

Correspondence author:
Emine Arzu KANIK
E-mail: arzukanik@gmail.com
Tel: +90 531 367 06 53

ABSTRACT

Subject: Good Biostatistical Practice

Background and Aims: There are several multivariate statistical analysis methods that set forth whether a new risk factor can be included in a model. In the recent years, it is emphasized in the literature that also the NRI (Net Reclassification Improvement) statistic can be used for this purpose. The primary functioning of this statistic is to decide by focusing on the increasing improvement in patients when the new biomarker is included in the model and the decreasing improvement in the control group. Although NRI is expressed as if it is a ratio, it is in fact a statistic between the values of $-2 \ll NRI \ll 2$. Its statistical significance istested through z test. The purpose of the present study is to introduce NRI (Net Reclassification Improvement) as a method used in the determination of a new risk factor to be included in the model for estimating risk factors for diseases, to discuss whether a new risk factor can be included in the model through this method and to test NRI method in comparison with the widely used logistic regression method through simulation.

Methods: In this study a simulation was carried out in order to exhibit the activity of a new biomarker and the data were generated in Minitab 15.0 package software. The simulation process was repeated 100 times. In order to exhibit the activity of a new biomarker as a classification method, bivariate logistic regression analysis was employed. For this purpose, two test plans were made. In the first test plan, in order to show that the second determinant is efficacious, 30 data were generated in each group for the two continuous determining variables. The data in the patient and control groups of the two determining variables were generated from normal distribution with the mean to be zero and the standard deviation to be 1, and with the mean to be 1 and the standard deviation to be 1. On the other hand, in the second test plan for the purpose of showing the inefficacy of the second determinant, while the data in the patient and control groups for the first determinant were generated from normal distribution with the mean being zero and the standard deviation being 1 and the mean being 1 and the standard deviation being 1,

the second determinant was generated from the patient and control groups with the mean being 1 and the standard deviation being 1. Within the scope of the analyses, at first logistic regression analysis was carried out with a single explanatory variable. Later on, logistic regression analysis was conducted by including the second variable to the model. NRI value was calculated by utilizing the classification tables belonging to the logistic regression estimations. Significance of the NRI analysis was measured through z test.

Results: In both of the test plans the regression result of the new determinant, NRI value and the related statistical significance levels were reported. Among the 100 tests carried out for the first test plan, while logistic regression determined the new determinant to be significant 90 tests, if found the new determinant insignificant in 10 tests. According to the results obtained from NRI on the other hand, the new determinant was found out to be significant in 13 tests, while it was determined to be insignificant in the remaining 87 tests. As for the 100 tests carried out for the second test plan, while logistic regression set forth the new determinant to be insignificant in 93 tests, it was determined to be significant in 7 tests. On the other hand, according to the results obtained from NRI, the new determinant was found out to be insignificant in 93 tests, while it was determined to be significant in the remaining 7 tests.

Conclusions: In comparison with other statistical analyses, NRI is a more selective test and the conducted simulation supports this conclusion. It was observed that logistic regression analysis is used for the estimation of the risks of particularly cardiovascular diseases and that this analysis is not as successful as NRI in terms of determining the efficacy of a new biomarker. Therefore, it is suggested to use NRI in such studies.

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DEVELOPING A RODENT MODEL FOR INVESTIGATION OF ILEAL-POUCHITIS

N Curran, M Thompson-Fawcett***

** General Surgery Department, Middlemore Hospital*

*** General Surgery Department, Dunedin Hospital*

ABSTRACT

Background and Aims: Pouchitis is an important long-term complication of ileal pouch-anal anastamosis (IPAA). Such inflammation of the surgical pouch is the most frequently observed long-term complication in pouch recipients. The aetiology is uncertain but pouch bacteria is believed to play a central role. A study in humans has revealed interesting differences in the microflora of healthy pouches versus those with pouchitis [1]. From this data, we hypothesised that a particularly abundant bacterium, *Bifidobacteriaceae catenulatum,* may protect from pouchitis.

Following a previously described rodent model [2], we intended to surgically create pouches in rats, and conduct a controlled trial if the model proved successful. We aimed to assess both the viability of the probiotic and any histological differences between the pouches of the two groups.

Methods: Appropriate ethical approval and animal welfare guidance were established. General anaesthesia was by inhalational halothane. Surgery involved defunctioning of the colon and formation of ileal pouch-rectal anastamosis (IPRA). Twelve Sprague-Dawley rats underwent surgery and eventual necrosectomy. The originally IPRA model [2] was unsatisfactory and the pouch was eventually abandoned in favour of an ileorectal anastamosis (IRA) with successful outcome.

Results: Six of the twelve rats died from anaesthetic complications, four died from functional obstruction at the IPRA and one from haemorrhage. We progressively modified the anastamosis, and eventually performed IRA in the final animal, which thrived. Histological assessment at day 106 showed minimal inflammation at the IRA.

Conclusions: The previously described pouch is an unsatisfactory model. The IRA model is a possible alternative. The anaesthesia used in this study requires re-evaluation given the number of anaesthetic deaths. The probiotic is viable through the rodent gut but no conclusions on its prophylactic benefit can be drawn from this study. Another animal study may be contemplated but there is current interest in commencing human trials.