SPEAKERS AND LECTURE SYNOPSES

Peter Tugwell is Professor of Medicine, and Epidemiology & Community Medicine at the University of Ottawa. He holds the Canada Research Chair in Health Equity. He is a staff physician and practicing rheumatologist at the Ottawa Hospital, Ottawa, Canada. In 2001, Dr. Tugwell took the post of Director for the Centre for Global Health at the Institute of Population Health, University of Ottawa. He has built a research program and multidisciplinary team around his Canada Research Chair in Health Equity. Dr. Tugwell was Founding Director of the International Clinical Epidemiology Network Training Centre at McMaster University (1982 – 1991) and currently serves as Secretary General to INCLEN's North American group (CanUSAClen). He is the past Chair of the Epidemiology Committee of the International League of Associations for Rheumatology (1989 – 1997) and of the Canadian Association of Professors of Medicine (2000-2001). He is a Fellow of the Royal College of Physicians of Canada, the American College of Physicians,the American College of Rheumatology and the United Kingdom Royal College of Physicians. Dr. Tugwell is co-director of a WHO Collaborating Center for Knowledge Translation and Health Technology Assessment in Health Equity as well as a member of the Organizing Committee of OMERACT (Outcome Measures in Rheumatology Clinical Trials). Dr. Tugwell is the Coordinating Editor of the Cochrane Musculoskeletal Review Group, is the Co-Convenor of the Campbell and Cochrane Equity Methods Group and Co-Chair of the Campbell International Development Coordinating Group. He is also on the Steering Group of the Campbell Collaboration. Dr. Tugwell is Co-Editor of the Journal of Clinical Epidemiology. He is past chair of the Oversight committee of the Canadian Medical Association Journal.

GRADE and application to Guidelines: Grading the quality of evidence and the strength of recommendations

Judgments about evidence and recommendations in healthcare are complex. For example, those making recommendations must agree on which outcomes to consider, which evidence to include for each outcome, how to assess the quality of that evidence, and how to determine if therapy does more good than harm.

Systematic reviews of the effects of healthcare provide essential, but not sufficient information for making well informed decisions. Reviewers and people who use reviews draw conclusions about the quality of the evidence, either implicitly or explicitly. Such judgments guide subsequent decisions. Similarly, practice guidelines and people who use them draw conclusions about the strength of recommendations, either implicitly or explicitly. A systematic and explicit approach to making judgments such as these can help to prevent errors, facilitate critical appraisal of these judgments, and can help to improve

communication of this information. Since the 1970's a growing number of organizations have employed various systems to grade the quality (level) of evidence and the strength of recommendations. Unfortunately, different organizations use different systems to grade evidence and recommendations. This is confusing and impedes effective communication. The GRADE system has been adopted by the World Health Organisation and over 50 other organisations.

Nichole Taske is a Senior Technical Adviser in the Centre for Clinical Practice at the National Institute for Health and Care Excellence. She graduated with a PhD in clinical genetics from the Australian National University in 1997. She has worked as a postdoctoral research fellow both in Australia and the UK specialising in inherited chanelopathies. In the UK, she undertook further studies in health policy, planning and financing at University College London and the London School of Economics. In 2003 she joined Bazian Ltd, a private company that provides evidence-based health reports for governments, insurers, publishers and research organisations. Nichole joined NICE in 2004 and is responsible for overseeing the technical quality assurance of clinical guidelines in development in addition to leading on the development and evaluation of guideline development processes and methodologies.

Clinical guideline development – the UK perspective

NICE guidelines make evidence-based recommendations on a wide range of topics, from preventing and managing specific conditions, improving health and managing medicines in different settings, to providing social care to adults and children, and planning broader services and interventions to improve the health of communities. They aim to promote integrated care where appropriate, for example, by covering transitions between health and social care. New guidelines developed by NICE are usually chosen from a library of topics for quality standards and then agreed with the relevant commissioning body (NHS England or the Department of Health). An outline of the NICE guideline development process will be presented. All NICE guidelines are developed according to the following key principles: they are based on the best evidence available whilst also taking into account social values and equity considerations; the methods and processes employed are open and transparent; recommendations are developed by independent advisory committees with input from topic experts, patients and carers, and all guidelines are subject to genuine consultation with stakeholders before publication. NICE clinical guidelines are a key source for the development of NICE quality standards and performance metrics developed for those providing and commissioning health, public health and social care services. To

date, NICE has produced almost 200 clinical guidelines and some of the ongoing challenges with maintaining and updating the library of guidelines will also be discussed.

Silvia Minozzi graduated in "Medicine and Surgery" with honours at the University of Milan (Italy) in 1983. She received postgraduate degree on Hygiene and preventive medicine in 1992 with honours. Since then I worked at epidemiology departments of Public Hospitals or Health Organization within the Italian National health Service with the task of conducting systematic reviews, preparing the evidence base for guideline production (WHO guidelines, European and Italian guidelines). I attended several international courses on epidemiology, evidence based medicine, methodology for the conduct of systematic reviews. My main areas of interest are: methods for clinical research, methodology of systematic reviews and meta-analysis Principles and method of Evidence based medicine; quality assessment and risk of bias assessment of systematic reviews, randomized controlled trials, diagnostic accuracy studies, observational studies, clinical practice guidelines; production of clinical practice guidelines; GRADE methods. I taught at many EBM courses for nurses, physiotherapists and medical doctors in various Italian hospitals and also at the University Master on: "Methodology of systematic reviews" organized by the University of Milan and the University of Modena and Reggio Emilia. Since 2002 I am a member of the editorial base of the Cochrane Drugs and Alcohol group with the role of quality advisor and assistant editor. In October 2014 I became an editor of the Group. First author or co-Author of 82 scientific articles published in peer-reviewed journals. Among these I am the first authors of 15 systematic reviews and first author or co-authors of 29 Cochrane Systematic Reviews.

Criteria for assessing risk of bias of studies used to formulate guidelines recommendation: RCTs, non randomized studies, diagnostic accuracy studies and systematic reviews

Evidence based guidelines realized following a rigorous methodology are informed by a systematic search of existing evidence answering the clinical questions posed by the panel responsible for formulating recommendation. A critical step of any systematic review is the risk of bias / quality of evidence assessment of the retrieved studies. Risk of bias concerns with the internal validity of study results, i.e. the systematic (as opposed to random) deviation of the results of a study from the 'true' results, which is caused by the way the study is designed or conducted, whereas the quality of evidence, as defined by the GRADE approach, is a more extensive evaluation considering also other domains (inconsistency of the results across the studies, imprecision, indirectness, risk of publication bias, magnitude of the effect, dose response gradient). Several validated tool have been elaborated by international working groups for each kind of study. The quality of conduct

/risk of bias should not be confused with the quality of reporting, i.e. the completeness and the clarity by which the methods and the results of a study are reported in the published paper, even if quite often a poor quality of reporting could be expression of poor quality of conduct. The following tools assessing risk of bias (quality of conduct) will be described and commented: the Cochrane tool for randomized controlled trial, ACROBAT for non randomized studies, QUADAS 2 for diagnostic accuracy studies, AMSTAR checklist for systematic review and meta-analysis.

Joerg Meerpohl is a Pediatrician and Pediatric Hematologist & Oncologist by training. Since 2011, he is the Deputy Director of Cochrane Germany at the Medical Center, University of Freiburg. In 2006, he joined part time as a senior researcher Cochrane Germany with a main interest in systematic reviews, reporting bias/quality and guideline development (GRADE methodology). In 2011 he became methodological advisor for WHO guideline panels such as Nutritional Guidance Expert Advisory Group (NUGAG Subgroup Diet and Health), HIV Consolidated Guidelines, SAGE vaccine hesitancy working group as well as other organizations such as Robert Koch Institute, Germany (Standing Vaccination Committee). In 2013 he was founding director of the GRADE center in Freiburg. He is a board member of the German Network for Evidence-based Medicine, and an advisory board member for the Cochrane Child Health Field and the WHO ICTRP portal. Since 2014, he is also a member of the GRADE Guidance Committee and the Cochrane Steering Group.

Ad-a-lopment of guidelines: a way forward for Croatia?

In many healthcare areas, well-done clinical practice guidelines do exist. However, these are not always up-to-date and/or directly applicable to other countries. Accordingly, decision-makers need to consider whether adoption, adaptation or de novo development of guidelines is appropriate.
Drawing on experiences from a large project led by Prof. Schünemann from McMaster University, Hamilton, a strategy to approach these decisions will be presented and discussed. The concept of Ad-a-lopment of guidelines will be introduced and advantages and disadvantages discussed.

Ana Marušić is Professor of Anatomy and Chair of the Department of Research in Biomedicine and Health at the University of Split School of Medicine, Split, Croatia. Since 2012, she is Honorary Professor of the Edinburgh University, Edinburgh, Scotland, UK. Prof. Marušić was the Editor in Chief of the *Croatian Medical Journal* for 20 years, and is now the Founder and Co-editor in Chief of the *Journal of Global Health*. Prof. Marušić is Past President of the World Association of Medical Editors and Council of Science Editors. She is currently the Vice President of the European Association of Science Editors. Prof. Marušić is

the founder of the Croatian branch of the Cochrane Collaboration and creator of the Croatian public registry of clinical trials. She is on the Steering Group of the EQUATOR Network, an international initiative for promoting transparent and accurate reporting of health research.

Using AGREE II tool to evaluate methodological rigour and transparency of Croatian clinical practice guidelines in neurology

We evaluated the methodological rigour and transparency of guideline development in neurology formulated by professionals in a local medical community. We analyzed clinical guidelines in neurology publicly available at the web-site of the Physicians' Assembly in Croatia in 2012: 6 guidelines developed by Croatian authors and 1 adapted from the European Federation of Neurological Societies. The quality was assessed by 2 independent evaluators using the AGREE II instrument. We also conducted a search of the Cochrane Library to identify potential changes in recommendation from Cochrane systematic reviews included in guideline preparation. The methodological quality of the guidelines greatly varied across different domains. "Scope and Purpose" and "Clarity of Presentation" domains received high scores (100% [95% confidence interval (CI) 98.5–100] and 97% [77.9–100], respectively), the lowest scores were in "Stakeholder Involvement" (19% [15.5–34.6]) and "Editorial Independence" (0% [0–19.2]). Conclusions of 3 guidelines based on Cochrane systematic reviews were confirmed in updated versions and one update provided new information on the effectiveness of another antidepressant. Two Cochrane reviews used in guidelines were withdrawn and split into new reviews and their findings are now considered to be out of date. We recommend to national societies and professional groups to develop a more systematic and rigorous approach to the development of the guidelines, timely inclusion of best evidences and an effort to involve target users and patients in the guideline development procedures.

Vanja Giljača finished high school in the United States. He graduated from the University of Rijeka, School of Medicine in 2003. He conducted research within the Cochrane Collaboration from 2011 to 2012 at the University College London, and in 2013 obtained a PhD degree on systematic reviews and meta-analysis of diagnostic accuracy of different methods in the diagnosis of choledocholithiasis. Since 2007 he has been working at the Department of Gastroenterology and Hepatology at the Internal Medicine Clinic of the University Hospital Rijeka, with a special interest in invasive Gastroenterology, Gastrointestinal Endoscopy and hepatobiliary diseases. His specialty is internal medicine, and he is currently attending sub-specialization in gastroenterology and hepatology. He is an assistant and lecturer at the School of Medicine in Rijeka. He is an editor in the Cochrane

hepatobiliary group. Dr. Giljača published several Cochrane systematic reviews and meta-analyzes, as well as other scientific papers in international peer-reviewed journals. He is a co-author and examiner on several randomized controlled trials. He is the author of one university textbook. He collaborated on the translation of 'Harrison - Principles of Internal Medicine' manual from English into Croatian.

Evidence based diagnostic guidelines for common bile duct stones

- what are diagnostic algorithms?
- how are diagnostic algorithms developed?
- what is evidence based diagnostic algorithm?
- how are diagnostic algorithms made for and who uses them?
- do consumers need to know about diagnostic test accuracy?
- Cochrane and diagnostic test accuracy reviews
- common bile duct stones (CBDs): introduction
- diagnosis of common bile duct stones
- current diagnostic algorithm for CBDs
- Cochrane diagnostic accuracy review for diagnosis of CBDs
    - brief methods and statistics
    - results
    - evidence based diagnostic algorithm
- what next?

Livia Puljak obtained her medical degree in 2002 from University of Zagreb School of Medicine and her PhD in 2008 from University of Split School of Medicine. She has been trained at the University of Nijmegen, Belgium, University of Colorado Health Sciences Center in Denver, CO, USA, University of Texas Southwestern Medical Center in Dallas, TX, USA and University of Ottawa. Since 2006 she has been employed at the University of Split School of Medicine. She was inaugural director of the Croatian Cochrane Branch and from 2009 she has been volunteering as the Knowledge Translation Coordinator at Cochrane Croatia. She is managing the translation of Cochrane plain language summaries into Croatian as well as the social media sites of Cochrane Croatia and edits the internet portal *Evidence in medicine*. Her research interests include pain and evidence-based medicine. She has published over 70 manuscripts in international peer-reviewed journals, mentored 16 MD, MSc and PhD theses and serves as a peer reviewer for numerous journals.

'Evidence in Medicine': a new Croatian website

Internet portal Evidence in medicine (Croatian: *Dokazi u medicini*) was established in 2014 in order to protect consumers from false advertising and unsubstantiated medical claims about alternative and complementary therapies and other products claiming effects on human body, health and disease. Evolution of the portal and literature search methods for answering citizens' questions on the portal will be described.

Karmela Krleža-Jerić is a strong advocate of transparency of health research, especially of open access to clinical trial data and she promotes the development of ethical and other related standards to support these goals. Karmela is the one of co-founders and a leader of the Ottawa Group on Trial Registration (OG) and its IMProving Access to Clinical Trial data- IMPACT- initiative. As a NewFelPro fellow and the Principal investigator of the IMPACT Observatory of clinical trials and data sharing, she is working at the Department for Research in Biomedicine and Health, University of Split School of Medicine. She spent ten years (2002-2012) at the Canadian Institute of Health Research where she mainly worked on clinical research and its transparency, including participation in creation of the International standards for trial registration as a member of the WHO Scientific Advisory Group, leading an analysis of transparency of clinical trials in the Americas, OG recommendations for the 7th revision of the Declaration of Helsinki and comments on the NIH Expansion of the Clinical Trial Registry and Results Data Bank. At the time she was also a Regional Editor of the Croatian Medical Journal, and an Adjunct Professor at the University of Ottawa. She is a member of the SPIRIT working group, Cochrane consumers' network, Campbell and Cochrane Equity, Bias Methods, and PRISMA IPD groups. Over the years, Karmela has acted as a consultant to the World Health Organisation (WHO) on health planning, health economics, the HFA (Health for all by the year 2000), Healthy Cities, and clinical trials.

Setting up an Observatory of Data Sharing and Clinical Trials: IMPACT (IMProving Access to Clinical Trials data) Observatory

Opening of clinical trial data is expected to increase the reliability of evidence needed for evidence informed medicine and for speeding up knowledge creation and consequent development of health and medical interventions. Observatories or natural experiments monitor the impact that an intervention which is outside the control of the researcher performing it and can point to trends and suggest directions.

The IMPACT Observatory aims at analysing ongoing transition in clinical research regarding data sharing, including opportunities and barriers. Funded by the NewFelPro fellowship (Marie-Curie and the Croatian Ministry for Science, Education and Sport), the

IMPACT Observatory started in October 2014, hosted by the Department for Research in Biomedicine and Health of the Split University School of Medicine, and it is closely connected with the Split Cochrane Branch. The Observatory is part of the IMPACT initiative, which has its roots in the Ottawa Statement on Trial Registration.

Clinical trials are an international enterprise and many constituencies are involved in shaping it which creates a specific challenge for this observatory. While usually observatories study the effect of one intervention, this observatory needs to study the impact of interventions of several key players and of their interactions.

Experiences in setting-up the Observatory will be shared. They consist of finding a host institution, forming a local team, building a network, setting the baseline, and defining the methodology of observation.