Introduction and Overview

R. Ziegler

Verein für Krebsforschung, Arlesheim, Switzerland

Main Focus and Participants

The symposium had its focus on methodological questions concerning different types of comparative observational studies, with the main emphasis on prospective studies. The aim of this conference was to answer the following question: How should comparative observational studies be conducted and reported in order to get the highest, or at least high scores via the in-depth quality assessment of a systematic review?

The meeting brought together 25 specialists from the areas of clinical trial design, trial practice, statistical methodology for observational trials, and systematic reviews. The primary field of study is health care interventions, in particular interventions within complementary and alternative medicine. The subjects of the talks and discussions encompassed theoretical, methodological, ethical as well as practical questions concerning primary therapeutic research using different methods of observational studies.

Background

In April 1997, at the German cancer research centre in Heidelberg a conference took place under the title of 'Nonrandomized Comparative Clinical Studies'. This conference was organised by U. Abel and A. Koch, who also published an accompanying conference volume [1]. It was the first conference of its kind and served as a model for our event.

Comparative observational studies, in particular nonrandomised studies, are necessary for various reasons. For example, if the effect is very strong, a controlled randomised trial (CRT) might be less important. In addition, CRTs are unsuitable for rare effects (i.e. adverse effects) or effects which take a very long time to show up. If patients and/or therapists have strong preferences, CRTs are impossible.

If a random allocation of patients to different treatment groups is not possible, what are the alternatives? What are the best options

for the clinical trial researcher to choose, both in design and analysis? Sometimes, instead of choosing between randomisation and nonrandomisation, the alternative is to allow for both random allocation as well as allocation based on preferences.

If the patient allocation for different treatment groups is not based on randomisation, there might be serious imbalances in the groups relating to baseline factors, known prognostic factors and known or unknown confounders. In this symposium these challenges were addressed and some methods were discussed to minimise the selection bias through study design as well as through subsequent statistical analysis.

This problem arises now and then within the context of complementary medicine, since in this setting either patient or therapist, or both, very often have strong treatment preferences. In addition, in many complementary therapy fields, the patient-therapist relationship is thought to be an important factor in therapeutic concepts. However, randomisation hinders this relationship, and for this reason cannot be applied, if one accepts appropriate standards for respective complementary interventions.

Local Planning Group

Renatus Ziegler (chair) and Corina Caminada (conference secretary), Society for Cancer Research, Arlesheim, Switzerland.

Scientific Planning Group

Renatus Ziegler (chair), Society for Cancer Research, Arlesheim, Switzerland; Wilhelm Gaus, Department of Biometry and Medical Documentation, University of Ulm, Germany; Peter Heusser, University Hospital, Berne, Switzerland; Franz Porzsolt, Clinical Economics, University of Ulm, Germany.

Inviting Institutions

Department of Biometry and Medical Documentation, University of Ulm, Germany; Institut Hiscia, Society for Cancer Research, Arlesheim, Switzerland; Institute for Complementary Medicine (KIKOM), University Hospital, Berne, Switzerland.

Sponsors for the Conference and the Proceedings

Society for Cancer Research, Arlesheim, Switzerland; Weleda AG, Arlesheim, Switzerland; Dr. Hauschka Stiftung, Bad Boll/Eckwälden, Germany; Stiftung Helixor, Rosenfeld, Germany; Gesellschaft für Biologische Krebsabwehr e.V., Heidelberg, Germany; Carl und Veronica Carstens Stiftung, Essen, Germany; Dr. Willmar Schwabe Arzneimittel, Karlsruhe, Germany.

Talks

Introduction and Overview

W. Gaus (Ulm): Randomised Trials versus Observational Studies: Is the Comparative Observational Study a Poor Compromise or a Perfect Synthesis?

General Considerations: Terminology and Classification of Research Designs

R. Ziegler (Arlesheim): Basic Elements of the Structure of Therapeutic Research.

B. Reeves (London): A Framework for Classifying Study Designs to Evaluate Health Care Interventions.

Methodology

R. Huber (Freiburg), M. Rostock: Double Blind Randomised Controlled Trials and Observational Studies in Research into the Effectiveness of Therapeutic Interventions within Complementary and Alternative Medicine: The Clinician's Perspective.

M. Müller (Winterthur): As Randomised as Possible.

T. Ostermann (Herdecke): The Use of Inter-Rater-Agreement and Subjective Probabilities for Therapeutic Outcome in Clinical Research: Potentials, Pitfalls and Limitations.

Levels of Evidence

A. Burls (Birmingham): Levels of Evidence.

Prospective Comparative Cohort Studies with Prior Starting Point
B. Schneider (Hannover): Use of Propensity Score for Adjustment of Treatment Groups in Comparative Cohort Studies.

P.R. Bock (Rümlingen), W.E. Friedel, J. Hanisch, M. Karasmann, B. Schneider: Retrolective Comparative Cohort Studies with Parallel Group Design for Evaluation of Efficacy and Safety of Drugs with 'Established Use': Experience from the Investigation of Long-Term European Mistletoe Treatment in Addition to Conventional Oncologic Therapy in Primary, Non-Metastatic Breast Carcinoma.

Clinical Methodology and Examples

W. Weidenhammer (München), K. Linde, D. Melchart: Treatment Outcomes in Patients with Migraine – An Ex-Post-Facto Comparison of Two In-Patient Facilities.

C. Güthlin (Freiburg), H. Walach: What do Historical Controls Contribute to the Evaluation of Effects?

M. Habs (Karlsruhe): The Prospective, Comparative Cohort Study and Its Contribution to the Benefit Evaluation of Therapeutic Options as Illustrated by Heart Failure Treatment with and without Hawthorn Special Extract WS 1442.

F. Porzsolt (Ulm), R. Ziegler, W. Gaus, E. Pöppel: Model Based on Three Components of Therapeutic Interventions.

A. Lowy (Bern): Second-Line Chemotherapy in Lung Cancer – a Population-Based Prospective Cohort Study.

Evaluating and Reporting Non-Randomised Studies

B. Reeves (London): Reasons for Caution when Evaluating Health Care Interventions Using Nonrandomised Study Designs.

Workshops

F. Porzsolt, A. Burls: Levels of Evidence.

B. Reeves, W. Gaus: Guidelines for Reporting Observational Studies.

References

- 1 Abel U, Koch A: Nonrandomized Comparative Clinical Studies. Düsseldorf, Symposium, 1998.