Valorisation

The work of the thesis gained extensive insight into the using of evidence of multiple study designs in systematic reviews. A review of a comprehensive literature showed a tendency that nonrandomized studies should be conducted and integrated in systematic reviews to complement available randomized controlled trials or replace lacking those trials. The risk of presenting uncertain results without knowing for sure the direction and magnitude of the effect holds true for both nonrandomized and randomized controlled trials. The consideration of registry analyses and case reports can be very helpful to draw attention to possible dangerous and life-threatening events beyond the scope of a randomized controlled trial. Ethical concerns may prevent trials with a random allocation of patients to treatment groups. Health-related quality of life may vary considerably if the treatment options are characterized by varying degrees of invasiveness. In this case, reluctance of patients and physicians alike to participate in randomization corroborates the consideration of alternative approaches. The work showed the importance of using multiple study designs in systematic reviews and provided many examples. A decision tree was constructed to facilitate the choosing of study designs for particular research questions, as shown below. Length of follow-up, frequency of events, and type of outcomes were the main decision points. It was ensured that the preset pathways retain sufficient flexibility to consider ethical and practical issues as well as unavailable best evidence. The appropriateness of the pathways of the decision tree was confirmed by backtracing four systematic reviews. The theory-based algorithm proved to be useful in various practical situations and helped to choose the appropriate study designs for inclusion in each tested systematic review.
Follow up

Events

Outcomes

Design labels

Practical

Switch

RCT/CCT may be chosen if less serious discomfort etc expected
Observational if data for discomfort etc is scarce
RCT: best choice for all outcome categories

Ethical concerns may arise against experimental allocation
RCT: best choice for disease and discomfort etc
RCT: high costs for death and disease but may be appropriate for discomfort etc

All study designs

Follow up

Short

Rare

Death

Disease

Discomfort

Disability

Dissatisfaction

Frequent:

Death

Disease

Discomfort

Disability

Dissatisfaction

RCT

CCT

Long

Rare

Death

Disease

Discomfort

Disability

Dissatisfaction

Frequent

RCT

Nested case contr

Cohort study

Case control

Case series

Case report

Registry analysis
Relevance

The use of multiple study designs in systematic reviews clearly showed that various study designs increased the information that should be considered in decision-making. The impact of the extra information may not be foreseen very well. The extra information may complement the best available evidence based on randomized controlled trials by adding new important data and by opening the horizon to bring attention to issues that may be overlooked but are nevertheless pertinent to health care. Sometimes information from multiple study designs can induce prudence in those who decide about an acclaimed new intervention. For example, randomized controlled trials may not be the typical study design to provide sufficient evidence for market withdrawals.

Target groups

The algorithm is foreseen to function as a tool helping to bring seminal features of a systematic review to the attention of anyone who is planning to conduct a systematic review. This includes persons working in organizations or institutes that prepare health technology assessment reports, evidence reports, or systematic reviews on health care interventions. It helps to reorientate oneself to major features of the studies eligible for an evaluation of a health care intervention. This is not meant to add a new regulation, but the benefit is the provision of awareness of the value of different study designs in systematic reviews. The intention is to provide a guide that might be used fully or partially by persons who are going to prepare a systematic review. While conducting a systematic review, it may be important at an early time point to identify the relevant and the most appropriate study designs necessary to find answers for a variety of pre-specified outcomes. It might also be of interest for persons who evaluate the quality of systematic reviews and might want to check whether all study relevant designs have indeed been considered. This may include individual physicians who intend to make evidence-based decisions on the treatment of their patients, although it will not be easy for busy clinicians to do so. It should also include persons with positions on a more collective level of evidence synthesis, such as scientists of academic institutions and members of guideline committees who critically assess the published evidence on various health care interventions, and staff of governmental administrations that make political decisions on the reimbursement of public health care services.