Methods for health economic evaluation of complex interventions in healthcare: current practice, challenges and guidance for future research

Methoden zur gesundheitsökonomischen Evaluation komplexer Interventionen in der Gesundheitsversorgung: aktuelle Praxis, Herausforderungen und Weiterentwicklungsbedarf

Authors

Nadja Chernyak[1, 2, 3], Damon Mohebbi[1, 2], Adrienne Alayli[4, 5], Johann Behrens[6], Helene Eckhardt[7], Cornelia Henschke[8], Rolf Holle[9], Nadja Kairies-Schwarz[1], Sebastian Liersch[10], Ralph Möhler[1], Dirk Müller[4], Anja Neumann[11], Markus Vomhof[1, 2, 3], Ingrid Zechmeister-Koss[12], Juliane Köberlein-Neu[13], Andrea Icks[1, 2, 3]

Affiliations

1 Institute for Health Services Research and Health Economics, Centre for Health and Society, Medical Faculty and University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany
2 Institute for Health Services Research and Health Economics, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany
3 German Center for Diabetes Research, Partner Düsseldorf, München-Neuherberg, Germany
4 Institute of Health Economics and Clinical Epidemiology, University of Cologne, University Hospital of Cologne, Cologne, Germany
5 Clinic of General Pediatrics, Neonatology and Pediatric Cardiology, Heinrich-Heine-University, University Hospital of Düsseldorf, Düsseldorf, Germany
6 Institute of Health and Nursing Science, Martin Luther University of Halle-Wittenberg, Halle, Germany
7 Department of Health Care Management, Faculty Economics and Management, Technische Universität Berlin, Berlin, Germany
8 Department of Health Care Management, Berlin Center for Health Economics Research, Technische Universität Berlin, Berlin, Germany
9 Institute for Medical Information Processing, Biometry, and Epidemiology, Ludwig Maximilian University Hospital, Ludwig-Maximilians-University Munich, Munich, Germany
10 AOK North East, Potsdam, Germany
11 Institute of Health Services Management and Research in the School of Economics and Business Administration, University of Duisburg-Essen, Essen, Germany
12 Austrian Institute of Health Technology Assessment, Wien, Austria
13 BUW Competence Centre for Health Management and Public Health, Faculty of Management and Economics, Schumpeter School of Business and Economics, University of Wuppertal, Wuppertal, Germany

Keywords

Health economic evaluation, Complex interventions, MRC framework

Schlüsselwörter

Gesundheitsökonomische Evaluation, Komplexe Interventionen, MRC Framework

received 18.10.2024
accepted after revision 30.12.2024
accepted manuscript online 31.03.2025
published online 2025

Bibliography
Gesundheitswesen
DOI 10.1055/a-2569-9765
ISSN 0941-3790

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

Correspondence
Prof. Andrea Icks
Heinrich Heine Universität Düsseldorf
Funktionsbereich Public Health
Moorenstraße 5
40225 Düesseldorf
Germany
andrea.icks@uni-duesseldorf.de

ABSTRACT

Health economic methods can support the development and evaluation of new healthcare interventions by generating data on the resources used and relating these to a defined benefit. However, the standard methodology of health economic evaluation that is usually used does not do justice to the high degree of complexity of interventions in healthcare. As a result, there is a lack of decision-relevant information, for example, on the preferences of the target group, on spillover effects on the part of carers, or on implementation costs and the role of different contexts in the implementation of interventions into routine care. The UK Medical Research Council's (MRC) standard-setting framework for complex interventions therefore emphasises the need to incorporate health economic aspects more strongly into all phases of the development and evaluation of complex interventions. To make this possible, the MRC's recommendations for expanding and adapting the standard methodology of health economic evaluation must be concretised and supplemented. Building on already established methodological procedures, recommendations should be developed and proposals for necessary further research formulated.

ZUSAMMENFASSUNG

Gesundheitsökonomische Methoden können die Entwicklung und Evaluation von neuen Versorgungskonzepten unterstützen, indem sie Daten zu eingesetzten Ressourcen genieren und diese ins Verhältnis zu einem definierten Nutzen setzen. Die meist angewendete Standardmethodik der gesundheitsökonomischen Evaluation wird dabei jedoch dem hohen Komplexitätsgrad von Interventionen in der Gesundheitsversorgung nicht gerecht. Dadurch fehlen entscheidungsrelevante Informationen, beispielsweise zu Präferenzen der Zielgruppe, zu Spillover-Effekten auf Seiten pflegender Angehöriger, oder zu Implementierungskosten und der Rolle unterschiedlicher Kontexte bei der Überführung von Interventionen in die Regelversorgung. Das Standard setzende Rahmenwerk des britischen Medical Research Councils (MRC) für komplexe Interventionen betont daher die Notwendigkeit, gesundheitsökonomische Aspekte stärker in alle Phasen der Entwicklung und Evaluation komplexer versorgungsbezogener Interventionen einzubeziehen. Um dies zu ermöglichen müssen die Empfehlungen des MRC zur Erweiterung und Anpassung der Standardmethodik der gesundheitsökonomischen Evaluation konkretisiert und ergänzt werden. Aufbauend auf bereits etablierten methodischen Verfahren sollen hierzu Empfehlungen entwickelt sowie Vorschläge für erforderliche weitere Forschung formuliert werden.

Complex interventions in healthcare and approaches to their development and evaluation

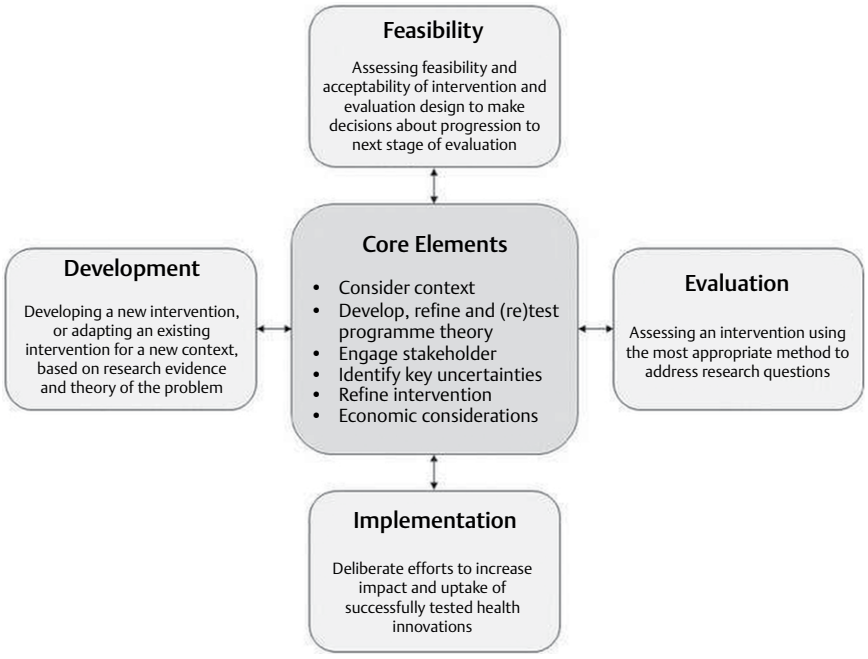
Healthcare concepts are characterised by a high degree of complexity [1–4]. The UK Medical Research Council (MRC) has commissioned a prominent framework for the methodology of developing and evaluating complex interventions in healthcare, first published in 2000. In 2008, a highly influential revision followed [3], and in 2021, an updated version was published [5]. According to the current MRC framework, the degree of complexity arises from the characteristics of the intervention itself, the context in which an intervention is implemented, and the interaction between these two. A similar perspective is held by the Throughput Model, often referenced in healthcare research in German-speaking countries, applied by Schrappe and Pfaff [6].

The MRC framework divides the development and evaluation of complex interventions into four phases: development or identification of the intervention, feasibility, evaluation, and implementation (▶ **Fig. 1**). Research on complex interventions can take place along these phases. All phases of complex intervention research should align with six "core elements": consideration of context; development, refinement, and (re)testing of programme theory; stakeholder engagement; identification of key uncertainties; refinement of the intervention; and economic considerations.

Health economic evaluation of complex interventions in healthcare

In the healthcare system, health economic evaluation refers to a range of different evaluation methods, including cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis [7]. These evaluation methods compare both the costs and effects of two or more interventions. The goal is to determine whether a specific intervention is cost-effective (efficient) compared to another. In addition, budget-impact analyses are employed to examine the financial effects of different healthcare concepts on the expenditure patterns of a given healthcare system [8].

Health economic evaluation has developed as a pragmatic, decision-relevant method of quantitative evaluation of interventions, providing insights in a specific context (e. g., within a specific effectiveness study) for a particular decision-making level (e. g., macro, meso, or micro level). Decision-making bodies in Europe, Australia, and Canada have incorporated cost-effectiveness analyses into



▶ **Fig. 1** MRC Framework for the Development and Evaluation of Complex Interventions (Data from [5]).

their processes for evaluating health technologies (health technology assessment, HTA) to make decisions about cost coverage [9]. Health technologies, beyond pharmaceuticals and medical devices, also include procedures and models of care or service delivery. While most international guidelines for health economic evaluation appear to be more general, they were originally designed for the evaluation of pharmaceuticals, as other types of health technologies and care concepts are often not subject to mandatory cost-effectiveness evaluation [10–12].

In health services research in Germany, increasing attention is being paid to evidence surrounding the cost-effectiveness of interventions. This is particularly evident in the fact that health economic evaluations are increasingly welcomed or even required by funding bodies, such as the Innovation Committee of the Federal Joint Committee (G-BA), as a component in study protocols for evaluating new care concepts. However, the question arises as to whether the commonly applied standard methodology for health economic evaluation adequately addresses the often very high complexity of new care models and provides sufficient information to fully account for economic aspects.

The suitability of standard health economic methodologies for the evaluation of complex interventions is also discussed in the international literature in various contexts. Adaptations of methodological approaches or further development towards new methods are being called for [13–21].

Some challenges identified in this context are outlined in the following overview.

CHALLENGES IN HEALTH ECONOMIC EVALUATION OF COMPLEX INTERVENTIONS

- Heterogeneity of intervention participants (e. g., regarding age, gender, socioeconomic status, health status)
- Heterogeneity of intervention components (e. g., due to (context-specific) adaptations of the intervention)
- Multiple outcomes (e. g., at the level of patients, professionals, organisations, and systems)
- Incomplete identification of relevant costs (e. g., direct medical, direct non-medical, indirect costs from the perspective of different stakeholders and societal sectors)
- Spillover effects beyond the intervention participants (e. g., on caregivers, family members, institutions)
- (Causal) attribution of outcomes and costs to interventions
- Generalisability, implementation issues (e. g., due to contextual differences)
- Timing of the evaluation of (newly introduced) services or programmes
- Identification and inclusion of uncertainties

In the most recent update of the MRC framework for the development and evaluation of complex interventions [5], greater attention has been given to health economic analyses compared to earlier versions. The importance of considering health economic evaluation in all phases of intervention research is emphasised. In particular, it is proposed to systematically incorporate decision

modelling and value of information (VOI) analysis when prioritising research questions and optimising research design. These formal methods were developed in the field of economic evaluation. Moreover, the MRC framework suggests that health economic evaluation should, more than before, also generate explanatory findings, such as the impact of different intervention implementations on costs. This can be achieved by integrating methodological approaches from other areas, such as realist research.

The updated MRC framework provides specific guidance on how health economic evaluation should be considered and designed in particular phases of the development and evaluation of a complex intervention. However, it does not include recommendations for the application of specific methods or how to address challenges in their use.

Implications for methodological advancement

Integration of health economic evaluation into the development and evaluation of complex interventions

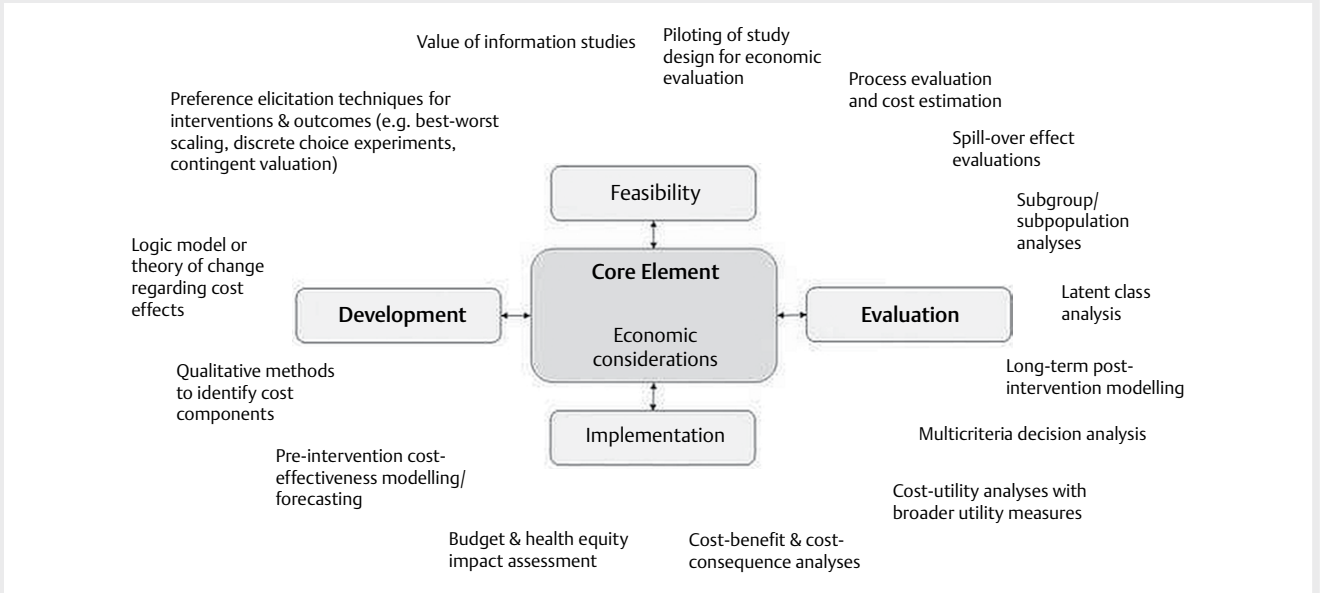
The impetus set by the new MRC framework underscores the need to develop additional recommendations for its methodological realisation, particularly regarding how health economic evaluation can be continuously integrated throughout the entire lifecycle of the development and evaluation of complex interventions. ▶ **Fig. 2** presents a selection of health economic methods from the extensive repertoire that can, in some cases iteratively, be applied in the different phases of complex intervention research – from development to feasibility testing, evaluation, and implementation. These methods provide a starting point to address the challenges outlined in the overview. In the *development phase*, decision-analytic pre-intervention modelling can be used to determine the potential cost-effectiveness of the planned intervention. In the *development and feasibility phases*, the identification of relevant cost and benefit components from various perspectives can be achieved, for instance, by employing qualitative methods. These identified benefit components can then be prioritised using quantitative methods of preference elicitation such as Best-Worst Scaling (BWS) or Discrete Choice Experiments (DCE).

Based on these insights, the necessary measurement instruments can be selected or newly developed if required. In the *evaluation phase*, a cost-consequence analysis (CCA) could be conducted alongside or as an alternative to a cost-effectiveness analysis (CEA) or cost-utility analysis (CUA) to present intervention effects at different levels in a non-aggregated manner. In the *implementation phase* of a complex intervention, health economic evaluation methods can be employed to re-assess the cost-effectiveness of a care model as it is expanded geographically and/or institutionally anchored. Additionally, in this phase, it is crucial to conduct health economic evaluations of the implementation strategies used for a care concept.

Methodological paper on health economic evaluation of complex interventions

The working group "Health Economics" of the German Network for Health Services Research (Deutsches Netzwerk Versorgungsforschung, DNVF), in collaboration with the sections "Methodology" and "Public Health" of the Evidence-Based Medicine Network (Netzwerk Evidenzbasierte Medizin, EbM-Netzwerk) and the committee "Economic Evaluation and Decision-Making" of the German Society for Health Economics (Deutsche Gesellschaft für Gesundheitsökonomie, dggö), is currently developing a methodological paper that addresses the challenges mentioned in the overview and the methods outlined in ▶ **Fig. 2**.

On the one hand, it demonstrates how already established methodological approaches to the health economic evaluation of complex interventions can be applied. On the other hand, it identifies areas where further methodological research is needed. The



▶ **Fig. 2** Core Health Economic Elements for Complex Intervention Research.

aims are twofold: first, to improve consistency and quality in the implementation of health economic evaluations in the development and evaluation of future complex interventions; and second, to provide guidance for research funding focused on methodological development or advancement.

Acknowledgements

We would like to thank all those involved in the "Health Economics" working group of the German Network Health Service Research (DNVF), the "Methodology" and "Public Health" departments of the "German Network for Evidence-based Medicine" (EbM-Network), and the Committee on "Economic Evaluation and Decision-Making" of the German Association for Health Economics (dggö) for their valuable discussions.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Campbell M, Fitzpatrick R, Haines A et al. Framework for design and evaluation of complex interventions to improve health. BMJ 2000; 321: 694–696. DOI: 10.1136/bmj.321.7262.694

[2] Campbell NC, Murray E, Darbyshire J et al. Designing and evaluating complex interventions to improve health care. BMJ 2007; 334: 455–459. DOI: 10.1136/bmj.39108.379965.BE

[3] Craig P, Dieppe P, Macintyre S et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008; 337: a1655. DOI: 10.1136/bmj.a1655

[4] Datta J, Petticrew M Challenges to evaluating complex interventions: a content analysis of published papers. BMC Public Health.2013: 13: 568. DOI: 10.1186/1471-2458-13-568Alayli-Goebbels AF, Evers SM, Alexeeva D et al. A review of economic evaluations of behavior change interventions: setting an agenda for research methods and practice. J Public Health (Oxf) 2014; 36: 336–344. DOI: 10.1093/pubmed/fdt080

[5] Skivington K, Matthews L, Simpson SA et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ 2021; 374: n2061. DOI: 10.1136/bmj.n2061

[6] Schrappe M, Pfaff H. Versorgungsforschung vor neuen Herausforderungen: Konsequenzen für Definition und Konzept. Gesundheitswesen 2016; 78: 689–694. DOI: 10.1055/s-0042-116230

[7] Drummond MF, Sculpher MJ, Claxton K et al. Methods for the economic evaluation of health care programmes. 4. Aufl. Oxford: Oxford university press; 2015

[8] Yagudina RI, Kulikov AU, Serpik VG et al. Concept of Combining Cost-Effectiveness Analysis and Budget Impact Analysis in Health Care Decision-Making. Value Health Reg Issues 2017; 13: 61–66. DOI: 10.1016/j.vhri.2017.07.006

[9] Sanders GD, Neumann PJ, Basu A et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. JAMA 2016; 316: 1093–1103. DOI: 10.1001/jama.2016.12195

[10] Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. JAMA 2003; 290: 1624–1632. DOI: 10.1001/jama.290.12.1624

[11] Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs – same or different? Value Health 2009; 12: 402–404. DOI: 10.1111/j.1524-4733.2008.00476_1.x

[12] Meacock RL. Economic evaluation of changes to the organisation and delivery of health services: methods and applications [Dissertation]. Manchester: The University of Manchester; 2017

[13] Weatherly H, Drummond M, Claxton K et al. Methods for assessing the cost-effectiveness of public health interventions: Key challenges and recommendations. Health Policy 2009; 93: 85–92. DOI: 10.1016/j.healthpol.2009.07.012

[14] Alayli-Goebbels AF, Evers SM, Alexeeva D et al. A review of economic evaluations of behavior change interventions: setting an agenda for research methods and practice. J Public Health (Oxf) 2014; 36: 336–344. DOI: 10.1093/pubmed/fdt080

[15] Rogowski W, Payne K, Schnell-Inderst P et al. Concepts of 'personalization' in personalized medicine: implications for economic evaluation. Pharmacoeconomics 2015; 33: 49–59. DOI: 10.1007/s40273-014-0211-5

[16] Anderson R, Hardwick R. Realism and resources: Towards more explanatory economic evaluation. Evaluation (Lond) 2016; 22: 323–341. DOI: 10.1177/1356389016652742

[17] Tsiachristas A, Stein KV, Evers S et al. Performing Economic Evaluation of Integrated Care: Highway to Hell or Stairway to Heaven? Int J of Integr Care 2016; 16: 3. DOI: 10.5334/ijic.2472

[18] Bojke L, Schmitt L, Lomas J et al. Economic Evaluation of Environmental Interventions: Reflections on Methodological Challenges and Developments. Int J Environ Res Public Health 2018; 15: S 1–9. DOI: 10.3390/ijerph15112459

[19] Meacock R. Methods for the economic evaluation of changes to the organisation and delivery of health services: principal challenges and recommendations. Health Econ Policy Law 2019; 14: 119–134. DOI: 10.1017/S1744133118000063

[20] Madan J, Bruce Kumar M, Taegtmeyer M, Barasa E et al. Seep-CI: A Structured Economic Evaluation Process for Complex Health System Interventions? Int J Environ Res Public Health 2020; 17: 6780–6891. DOI: 10.3390/ijerph17186780

[21] Gomes M, Murray E, Raftery J. Economic Evaluation of Digital Health Interventions: Methodological Issues and Recommendations for Practice. Pharmacoeconomics 2022; 40: 367–378. DOI: 10.1007/s40273-022-01130-0

This article is part of the DNVF Special Iissue "Health Care Research and Implementation"