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Who is the fastest?

Global competition in product and process innovation.

What are the success factors?

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«Who is the fastest?»

Global competition in product and process innovation.

What are the success factors?

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Introduction

In research- and knowledge-intensive industries, innovation is one of the keys to strengthening a company's position in the field of international competition. Innovations emerge in complex networks, in which various stakeholders interact in an interdisciplinary and collective process with many feedback loops [1;2]. To be successful, not only the sub-systems (including science/ education, industry, supply/demand) need to be effective, but the subsystems, too, must be optimally interconnected. Rather than individual factors or stakeholders, it is the interaction and networking of high-performing subsystems and their participants that determine a company's capacity to innovate. This means that, in order to strengthen international competitiveness, continuing improvements of location factors in the field of both supply and demand are necessary, combined with the interaction of all those concerned along the value-added chain [3;4].

Healthcare has always depended on innovations, as well as being driven by them. This is true, whether we are talking about new products, services, processes or structures. Elaborate structures are in place to develop and evaluate new products and processes and introduce them into the market. These include the public funding of basic research, public-private partnerships in applied research, the regulation, implementation and monitoring of clinical trials, the appraisal of innovations for marketing authorisation and reimbursement, as well as knowledge transfer from research into clinical practice.

This paper analyses the location factors for the following three subsystems of the health innovation system:

- clinical research as the intermediate step between basic research and market entry
- the appraisal of innovations for routine introduction through health technology assessment as a means to link the demand of the healthcare systems with the supply of new technologies
- the provision of innovative healthcare services as a process that matches the needs of patients with the best technology that the healthcare system can offer.

1. Development of innovations

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Clinical research is the most costly phase of the development of pharmaceuticals. Clinical trials are required to test the safety and efficacy of new drugs. This information is used to complete the application for marketing authorisation. Besides their significance for the manufacturer of a new drug, clinical trials offer patients who are waiting for new treatment options the opportunity to access new treatments which are not yet provided in regular care. Furthermore, clinical research creates employment for highly qualified personnel. Clinical research is a prerequisite to dealing with health-related challenges like the ageing population, widespread illnesses, and inequality in health [5].

The guidelines for clinical drug research are, to a large extent, internationally harmonised and legally codified, principally under the regulations of good clinical practice (GCP). However, other framework conditions, such as the details of ethical reviews of applications for clinical trials, the co-financing of clinical research by industry and public budgets or the availability of well-educated personnel and sufficient numbers of study participants, can be influenced by national policy-making and differ from country to country.

Different approaches are used to improve the performance of national clinical research systems. The following examples highlight different priorities in the many factors of clinical research systems which need critical attention.

For example, in the UK two institutions steer the R&D for healthcare products. The Medical Research Council (MRC) focuses on basic sciences, whereas the National Institute for Health Research (NIHR) covers clinical and applied research and supports research networks. A review of the health research system called for improvements in cooperation between MRC and NIHR [6;7]. A new «Efficacy and Mechanism Evaluation (EME) Programme» has therefore been established linking programmes scheduled for development with the Health Technology Assessment Programme of the NIHR. This approach aims at translating innovations from research into interventions more quickly [7;8].

In Sweden, finding highly qualified researchers and offering them suitable working conditions are seen as key factors. In addition, there are demands for the prioritisation of research activities and increased cooperation on the part of stakeholders, as well as improvements in the quality of research, the recruitment of researchers and the financing of research [5]. Sweden has therefore implemented a system for the prioritisation of research issues which involves not only researchers and funding organisations, but also external stakeholder groups and lay people [9].

Similarly to the UK, the USA supports regional or community-level structures for the recruitment of patients for clinical studies. For this, new ways must be found to collect data and changes must be made in study protocols using modern information technology. There is also a need for innovative models of cooperation between research institutes and patient organisations [10].

Clinical research is the phase within the innovation process which consumes most resources. It is highly regulated, but offers big opportunities for manufacturers, researchers, clinicians and patients

Internationally, different approaches are used to more strongly relate clinical research with basic research and application

Clinical research is not optimally linked with other subsystems of medical innovation

Even within the clinical research subsystems, national solutions vary enormously, reflecting different traditions and different ways of healthcare provision. However, this confirms that a single best way to organise clinical research does not exist, given the heterogeneity of the underlying healthcare systems. Clinical research is not optimally linked with other subsystems of medical innovation. Government-driven programmes for translational research try to overcome the disintegration on the R&D side «from bench to bedside» [11]. For the early access of patients to new drugs, i.e. the linking of clinical trials to healthcare provision, the UK government plans a programme to subsidize selected new treatments to be used for three years without requiring a positive technology appraisal from the UK's NICE, so that additional clinical data can be collected [12]. A major concern remains the «information/prescription gap», i.e. the suboptimal use of knowledge from research in clinical practice [13].

In the transition of a new technology from clinical research to application, safety requirements have to be balanced against the usefulness of early access to the treatment

In the early phases of biotechnological R&D, policy mixes that support both the scientific base and commercial activities correlate with higher performance levels. In addition, it is beneficial to implement instruments that stimulate generic research as well as instruments which are specific to biotechnology [14]. The German example of how to implement the EU Clinical Trials Directive shows that countries do not have to reduce safety requirements in order to implement an innovation-friendly regulatory framework. Clinical trial regulations should allow for sufficient flexibility to adapt to emerging risks of new technologies, so that the pre-emptive safety hurdles need not be prohibitive to innovation, although the individual assessment of a specific trial's risks demands high competencies for sponsors, regulatory agencies and clinical researchers. Easy access of patients to clinical studies facilitates the early completion of clinical trials, to the benefit of all the patients waiting for innovative treatments, as well as the sponsors and researchers. This is fostered by strong regional connections between research centres and healthcare providers, e.g. among many clinical research centres in the UK [15].

2. Introduction of innovations into regular healthcare

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Innovations have to be assessed at many points and by many stakeholders all along their way from basic research to the patient. Depending on the stage of development and the stakeholders concerned, the different aspects of costs and benefits may bear an influence on decision-making. Among the scenarios for appraisal are the manufacturer's decision as to whether the product's potential turnover justifies the high investments for clinical research, and the judgement of governmental bodies as to whether a product's efficacy, safety and quality justify marketing authorisation. A critical factor which largely defines the size of a new product's market is whether the costs will be reimbursed through public health insurance schemes or public health systems. In order to make such resource allocation decisions, health insurance companies and public administrations are informed by health technology assessment (HTA) [16].

The beneficial influence of HTA in improving the evidence base for medical treatment is generally acknowledged. With its contribution to the reimbursement decision as a «gate» to the most relevant markets, HTA plays an important role in the shaping of technical changes in healthcare. However, it is unclear whether the existing public HTA activities function in a transparent and efficient manner [17;18].

In most industrialised countries, HTA is being used as a basis for reimbursement decisions, and to some extent clinical decision-making as well. Whereas HTA generally has a broad scope of issues to analyze, many HTAs adopt a pragmatic approach that focuses on a subset of the elements of HTA, such as clinical effectiveness and cost-effectiveness. «Traditional» HTA has a clear focus on health outcomes, sometimes complemented by cost or efficiency considerations and specific resource allocation decisions [16]. The broader aspects of HTA, such as ethical, social, legal, and organizational considerations, as well as other system-related aspects of the diffusion of technology (many of which are relevant for patients or legislators rather than clinicians and funders), may still be considered in the assessment. However, they are often not addressed so explicitly and are less likely to be evidence-based [19;20]. The focus on costs and health outcomes, however, might result in the under-utilization of new health technologies [4]. From the perspective of the funders (e.g. health insurance companies), restricting the scope of an HTA bears the risk of suboptimal decisions based on a restricted view of benefits [21].

According to the OECD Health Project on new and emerging health-related technologies, gaps caused by the lack of sound evidence hamper good policy-making related to emerging health technologies. Both the processes and the type of information sought for decision-making need to be modified to take into account the special challenges of emerging technologies [17]. In order to facilitate the progress of promising ideas through the critical steps and generate the missing data, regulators are beginning to re-think their role in the innovation process. This involves moving from a strictly gate-keeping role based on evaluating the evidence for new technologies to a more collaborative or

Innovations are assessed from different perspectives, both formally and informally, at transitions from one phase to another

Thematic scope and methods of Health Technology Assessment are not yet finally determined

A lack of sound evidence hampers decision-making and sometimes access to new therapies

Public agencies change their role from gate-keepers to supporters of innovation

facilitative role. This new policy orientation has taken concrete shape in programmes such as the NIH's Roadmap [22] with its commitment to translational research, the FDA's Critical Path initiative [23], EMEA's Road Map strategy [24], the Innovative Medicines Initiative in Europe [25], and further support in the field of translational research as a bridge between basic research and clinical development [26]. National initiatives complement the generation of better data on emerging healthcare technologies, e.g. the UK Clinical Research Collaboration [27] and the new health research structures in the United Kingdom, as well as processes including an earlier HTA intervention in the drug development process [6], or the health research within the German Hightech Strategy for R&D [28].

HTA must orientate itself more strongly towards the users

An important trend in the assessment of innovative healthcare technologies is the broader involvement of the users, as the use and dissemination of HTA reports by patients, healthcare professionals (HCPs) and other specific groups could help to broaden the debate about controversial health technologies and lead to more pragmatic decisions [29-31]. Although patients' preferences are not systematically included in the quantitative analysis of new technologies, patients, consumers or citizens are to some extent involved in reimbursement decisions, e.g. in consumer councils [32]. In an approach including training for and intensive interaction with consumers to enable their involvement in all phases of HTA, Oliver et al. [33] found a great readiness to participate and unique contributions were made by the consumers to the HTA programme.

New models of Health Technology Assessment are tested in order to guarantee the earliest possible access to promising methods

Despite these encouraging steps, the role of HTA in the innovation process is far from clear. Severe gaps exist in the evidence that would be needed to support the many decisions that stakeholders must make about emerging healthcare technologies [34]. On the other hand, duplicate assessments are made and existing evidence is insufficiently used [32]. All this hampers the smooth functioning of the healthcare innovation system. In addition to the generation of evidence at an early stage, some countries grant reimbursement for technologies which are sorely needed, but for which the cost-benefit ratio is still unclear, only under certain circumstances, e.g. only in hospital settings or specialized centres or only in combination with additional research to improve the evidence base. Such schemes are called «coverage with evidence development» [35] and are used in many countries, such as the UK, France and the Netherlands. Other instruments to ensure patients' early access to the medicines they need and manufacturers' access to public healthcare markets with technologies whose cost-effectiveness is not yet fully established include reductions in the cost of reimbursement, as is the case in the UK, or schemes where the risk of treatment failure is borne by the manufacturer [36]. Manufacturers, on the other hand, have become more open to discussing reimbursement issues with the relevant agencies and funders [37]. Moreover, instruments such as Constructive Technology Assessment, which help to shape new technologies along with the users' needs are also at hand [38;39].

With sufficient control over product safety and informed consent by patients to undergo a treatment with only modest evidence of effectiveness, such

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strategies can improve healthcare and keep markets attractive enough to encourage innovations. The greater the flexibility of regulators, funders and users in promoting early market access of the instruments mentioned and the greater the responsiveness of manufacturers to the specific needs of patients and other users, the faster the evidence gaps can be closed and patients can benefit from healthcare innovations.

3. Innovative healthcare services

Far-reaching changes in the health system are necessary to cope with today's megatrends

While healthcare systems in the industrialised countries are generally very strong in the treatment of acute illnesses, their effectiveness in maintaining health and preventing the spread of diseases is at least questionable, although keeping the population healthy is vital in periods of demographic change or when faced with the spread of chronic diseases and growing healthcare costs. Far-reaching changes are needed in order to maintain and improve the health of the population and to make health systems more sustainable. Such changes can only partly be brought about by incremental innovation [40]. Changes in epidemiology and in the needs of society will always require substantial efforts in R&D and the stepwise adjustment of procedures and regulations. There is already a huge body of evidence on good practice for health, but it is not implemented in our societies, meaning that decisions in individual cases or on health policy in general are not sufficiently evidence-based. This phenomenon is known as the «knowledge-to-practice gap» [41], the «knowledge-behaviour gap» [42] or as the «evidence-to-practice gap» [43]. It needs to be addressed urgently in order to make more efficient use of existing knowledge and increase preparedness for the coming challenges.

The health system needs self-responsible users, who should be optimally supported

Even governments have only limited direct influence on the structure and performance of their health systems [44]. Governments can thus often only assume the role of enablers of innovation. Who, then, should be in charge of guiding innovation processes? Particularly in the healthcare field, users are acquiring increasing importance thanks to the increased availability of information and their often-requested self-responsibility and growing out-of-pocket payments. Health is no longer a product generated by HCPs but, rather, it is being co-produced by citizens or patients with the support of the HCPs [45;46].

Stronger self-responsibility for individuals or even a healthcare system that builds on the autonomy of the users has a number of prerequisites. The relationship between HCPs and patients needs to change radically [47]. Models of participatory or shared decision-making between HCPs and patients are already being explored. The acquisition of practical skills by both sides is not sufficient and changes in self-image and role definitions, both of HCPs and patients, are required for implementation [48].

Areas in particular need of innovation are: active participation, investments in health, transparency, orientation towards outcomes, sustainability, integration, subsidiarity and more societal benefit

Citizens and patients must be enabled to make optimal use of the available information and services. Besides the «readability» of the health systems, which includes services that are understandable and easy to manage and which make sense in the view of the users [49], patients must be trained to acquire sufficient competence to use the services according to their wants and needs [50]. A basis for this should be the psychological concepts of self-efficacy expectation and a sense of coherence, which help citizens to protect their health [51].

Factors and concrete steps to facilitate and empower changes in the health systems have been developed at the «MetaForum Innovation in the health system». They include a shift in paradigms from disease-oriented to health-maintaining

and health-promoting strategies, autonomy of the users, the principle of health in all policies, and eight areas in particularly urgent need of innovation. These are: increase in active participation, investment in health, transparency, result-orientation, sustainability, integration and subsidiarity, as well as higher economic and societal benefit [52].

It is assumed that stronger consumer involvement would lead to a far more efficient healthcare economy and better health outcomes for the committed and empowered patients of the future [53]. However, besides somewhat extended patient involvement in some decision-making committees and in clinical practice, the structures for negotiating interests and requirements between the different stakeholder groups are by no means sufficient to reflect the changing roles and requirements. Healthcare systems are strongly separated from other fields of action in society (education, economy), although these should play an important role in the adjustment of health systems to society's needs through fundamental innovation processes.

**The health systems need
fundamental innovations**

Three theses about competition for healthcare innovation

The short review of three subsystems of the healthcare innovation system showed that vital links between these fields of action are missing, thus hampering efficient and targeted innovation processes. In some countries, attempts are being made to overcome this situation and gain relative superiority in international competition, but their scope is limited to specific details of the network of stakeholders only.

Beyond the broadly accepted principles of innovation, attitudes towards the following three theses will shape future discussions about innovations in the field of health and will influence in the longer term the competitiveness of healthcare innovation:

1. The improvement of people's health, even in Western European countries, requires fundamental changes in the public health systems

Although it is broadly accepted that healthcare for certain diseases should be improved and that innovative products and treatment processes are needed to achieve this, it is unclear how fundamental the changes in our health systems should be. While the protagonists of the existing structures believe that only incremental changes are necessary and the stakeholders' roles and organisational structures should generally remain the same («incremental innovation of healthcare»), others believe that it is necessary to fundamentally rethink and reorganise healthcare in order to cope with the megatrends of demographic change, chronic illness, rising healthcare expenditure, changing lifestyles etc. («radical innovation of healthcare»). Orientation towards health instead of disease, user autonomy and health in all policies would be such fundamental changes, including totally new roles for patients and healthcare professionals and radically new business models beyond outpatient and hospital-based healthcare.

2. The innovation of innovation processes themselves will have to go much further than we thought

A change of perspective from supply-orientation to users' needs and preferences is not only necessary in the provision of healthcare, but also in the development of innovations. Actually, innovation clusters in general only involve researchers and manufacturers, with only marginal consideration being given to the regulatory aspects of marketing authorisation and reimbursement, conditions for introduction into daily healthcare and consumers' or patients' preferences. Where informed consumers are well aware of their needs and choices, new products and processes can only be successful if they are developed with a focus on the user («user innovation»). Evidence about an innovation's costs and benefits from the different perspectives of the stakeholder groups must be used far more efficiently, and new ways of carrying out and using research are required.

3. Empowerment of citizens and patients as keepers of their health is the key to more efficient healthcare innovation

Innovation in the field of healthcare requires greater coordination of the different subsystems (e.g. basic and clinical research with the markets). Here, the guiding principle should be the needs of the citizens, clients and patients because, through insurance premiums, taxes and out-of-pocket expenditures, these groups are the funders of all health products and services. Without their understanding, agreement to prescriptions and active co-production of their health, the provision of healthcare will remain inefficient. A system that is determined by the health of well-informed and empowered citizens instead of the traditional structures of policy-making, financing and service provision will be far more able to innovate and to adapt to the needs of the individual and society. This will require substantial re-allocation of resources towards health-maintenance and health promotion, radical changes in the role of healthcare professionals from a patriarchal to a serving and supporting function, and (through democratic procedures) shifting the power of decision from the experts to those directly concerned.

References

1. Breschi S, Malerba F. Sectoral innovation systems: Technological regimes, Schumpeterian dynamics, and spatial boundaries. In: Edquist C, editor. *Systems of Innovation: Technology, institutions and organisations*. London: Pinter; 1997.
2. Malerba F. Sectoral systems of innovation and production. *Research Policy* 2002; 32:247-264.
3. Nusser M, Wydra S, Hartig J, Gaisser S. *Forschungs- und wissensintensive Branchen: Optionen zur Stärkung ihrer internationalen Wettbewerbsfähigkeit*. Berlin: Büro für Technikfolgen-Abschätzung beim Deutschen Bundestag, 2007.
4. The OECD Health Project: *Health Technology and Decision Making*. Paris: OECD, 2005.
5. Stendahl, Olle. *Världsklass! Åtgärdsplan för den kliniska forskningen*. 14-2-2008; cited 13-4-2008. Available from: http://www.regeringen.se/download/3881eb4a.pdf?major=1&minor=97905&cn=attachmentPublDuplicator_0_attachment
6. Cooksey D. *A review of UK health research funding*. London: HMSO, 2006.
7. NIHR. *Efficacy and Mechanism Evaluation (EME) programme*. 2008; cited 19-8-2008. Available from: <http://www.eme.ac.uk/>
8. Walley T, Thakker RV. *Developments for funding clinical research in the UK*. *Lancet* 2008; 372(9638):518-519.
9. Clavisi O, Gruen R, Bragge P, Tavender E. *A systematic method of identifying and prioritising research questions*. *Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen* 2008; 102:16.
10. National Institutes of Health. *NIH Roadmap for Medical Research – Re-engineering the Clinical Research Enterprise*. 24-10-2008; cited 24-11-2008. Available from: <http://nihroadmap.nih.gov/clinicalresearch/index.asp>
11. Adams JU. *Building the bridge from bench to bedside*. *Nat Rev Drug Discov* 2008; 7(6):463-464.
12. Hughes B. *Defining innovation*. *Nat Rev Drug Discov* 2009; 8(9):683-684.
13. Boissel J-P, Amsellem E. *Bridging the gap between therapeutic research results and physician prescribing decisions: knowledge transfer, a prerequisite to knowledge translation*. *Eur J Clin Pharmacol* 2004; 60:609-616.
14. Enzing C, Reiß T. *The Effectiveness of Biotechnology Policies in Europe*. *International Journal of Biotechnology* 2008; 10(4):327-340.
15. Bührlen B, Vollmar HC. *Biomedizinische Innovationen und klinische Forschung – Wettbewerbs- und Regulierungsfragen*. Abschlussbericht. Berlin: Büro für Technikfolgen-Abschätzung beim Deutschen Bundestag, 2009.
16. Drummond MF, Schwartz JS, Jönsson B, Luce BR, Neumann PJ, Siebert U et al. *Key principles for the improved conduct of health technology assessments for resource allocation decisions*. *International Journal of Technology Assessment in Health Care* 2008; 24(03):244-258.
17. The OECD Health Project: *Towards High-Performing Health Systems*. Paris: OECD, 2004.
18. Packer C, Simpson S, Stevens A. *International diffusion of new health technologies: A ten-country analysis of six health technologies*. *International Journal of Technology Assessment in Health Care* 2006; 22(04):419-428.
19. Hutton J, Trueman P, Facey K. *Harmonization of evidence requirements for health technology assessment in reimbursement decision making*. *International Journal of Technology Assessment in Health Care* 2008; 24(04):511-517.
20. Johri M, Lehoux P. *The Great Escape? Prospects for Regulating Access to Technology Through Health Technology Assessment*. *International Journal of Technology Assessment in Health Care* 2003; 19(1):179-193.
21. Jönsson B. *Ten arguments for a societal perspective in the economic evaluation of medical innovations*. *The European Journal of health economics* 2009; 10(4):357-359.
22. Zerhouni E. *The NIH Roadmap*. *Science* 2003; 302(5642):63-72.
23. US Department of Health and Human Services. *Food and Drug Administration. Innovation or stagnation: challenge and opportunity on the critical path to new medical products*. Washington, DC: US Food and Drug Administration, 2004.
24. European Medicines Agency. *The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future*. London: EMEA, 2005.
25. Innovative Medicines Initiative. *The Innovative Medicines Initiative (IMI) strategic research agenda: Creating biomedical R&D leadership for Europe to benefit patients and society*. Brussels: IMI, 2008.
26. Office of Strategic Coordination (OSC). *Re-engineering the Clinical Research Enterprise*. 24-10-2008; cited 15-12-2008. Available from: <http://nihroadmap.nih.gov/clinicalresearch/index.asp>
27. UK Clinical Research Collaboration (UKCRC). *What is the UKCRC?* 10-3-2008; cited 24-5-2009. Available from: <http://www.ukcrc.org/aboutus/whatistheukcrc.aspx>
28. Bundesministerium für Bildung und Forschung. *Forschung und Innovation für Deutschland - Bilanz und Perspektive*. Berlin: BMBF, 2009.
29. Fattal J, Lehoux P. *Health technology assessment use and dissemination by patient and consumer groups: Why and how?* *International Journal of Technology Assessment in Health Care* 2008; 24(04):473-480.
30. FitzGibbon F, Brown A, Meenan BJ. *Assessment of User Perspectives of Cardiac Point of Care Technologies in Chest Pain Diagnosis*. *Proceedings of the 29th Annual International Conference of the IEEE EMBS*, August 23-26, 2007, Lyon, France 2007;1762-1765.
31. Royle J, Oliver S. *Consumer involvement in the health technology assessment program*. *International Journal of Technology Assessment in Health Care* 2004; 20(4):493-497.

32. Sorenson C, Drummond M, Kanavos P. Ensuring value for money in health care – The role of health technology assessment in the European Union. Copenhagen: European Observatory on Health Systems and Policies, 2008.
33. Oliver S, Milne R, Bradburn J, Buchanan P, Kerridge L, Walley T et al. Involving consumers in a needs-led research programme: a pilot project. *Health Expect* 2001; 4(1):18-28.
34. Bührlen B. Innovation im Gesundheitssystem: Akteure und Ziele in der Gesundheitswirtschaft. In: Goldschmidt AJW, Hilbert J, editors. *Gesundheitswirtschaft in Deutschland – Die Zukunftsbranche*. Wegscheid: Wikom; 2009. p. 744-759.
35. Hutton J, Trueman P, Henshall C. Coverage with Evidence Development: An examination of conceptual and policy issues. *International Journal of Technology Assessment in Health Care* 2007; 23(04):425-432.
36. de Brantes F, D'Andrea G, Rosenthal MB. Should Health Care Come With A Warranty? *Health Aff* 2009; 28(4):w678-w687.
37. Hughes B. Payers growing influence on R&D decision making. *Nat Rev Drug Discov* 2008; 7(11):876-878.
38. Douma KFL, Karsenberg K, Hummel MJM, Bueno-de-Mesquita JM, van Harten WH. Methodology of constructive technology assessment in health care. *International Journal of Technology Assessment in Health Care* 2007; 23(2):162-168.
39. Hummel MJM, van Rossum W, Verkerke GJ, Rakhorst G. Assessing medical technologies in development. A new paradigm of medical technology assessment. *International Journal of Technology Assessment in Health Care* 2000; 16(4):1214-1219.
40. Christensen CM, Grossman JH, Hwang J. *The Innovator's Prescription - A Disruptive Solution for Health Care*. New York, NY: McGraw-Hill, 2009.
41. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W et al. Lost in knowledge translation: time for a map? *J Contin Educ Health Prof* 2006; 26(1):13-24.
42. Kennedy T, Regehr G, Rosenfield J, Roberts SW, Lingard L. Exploring the gap between knowledge and behaviour: a qualitative study of clinician action following an educational intervention. *Acad Med* 2004; 79(5):386-393.
43. Lang ES, Wyer PC, Haynes RB. Knowledge translation: closing the evidence-to-practice gap. *Ann Emerg Med* 2007; 49(3):355-363.
44. Hurst J. Performance measurement and improvement in OECD health systems: Overview of issues and challenges. In: Smith P, editor. *Measuring Up: Improving Health System Performance in OECD Countries*. Paris: OECD; 2002. p. 35-54.
45. Kickbusch I. Die gesellschaftliche Innovationsdynamik für Gesundheit. In: Bührlen B, Kickbusch I, editors. *Innovationssystem Gesundheit: Ziele und Nutzen von Gesundheitsinnovationen*. Stuttgart: Fraunhofer IRB; 2008. p. 49-62.
46. Kickbusch I. Policy Innovations for Health. In: Kickbusch I, editor. *Policy Innovation for Health*. New York: Springer; 2009. p. 1-21.
47. Gray M. Making the future of healthcare. *Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen* 2008; 102(4):231-233.
48. Scheibler F, Loh A. Therapeutische Effekte mit partizipativer Entscheidungsfindung – Ein Blick über die Studienlage. In: Klusen N, Fließgarten A, Nebling T, editors. *Informiert und selbstbestimmt – Der mündige Bürger als mündiger Patient*. Baden-Baden: Nomos; 2009. p. 66-79.
49. Großkinsky S. Der Patient als Subjekt in der Gesundheitsversorgung - Perspektive der Salutogenese. In: Klusen N, Fließgarten A, Nebling T, editors. *Informiert und selbstbestimmt – Der mündige Bürger als mündiger Patient*. Baden-Baden: Nomos; 2009. p. 17-33.
50. Nagel G. Patientenkompetenz im Gesundheitswesen der Schweiz am Beispiel der Onkologie. In: Klusen N, Fließgarten A, Nebling T, editors. *Informiert und selbstbestimmt – Der mündige Bürger als mündiger Patient*. Baden-Baden: Nomos; 2009. p. 97-108.
51. Bengel J, Belz-Merk M. Subjektive Gesundheitskonzepte. In: Schwarzer R, editor. *Gesundheitspsychologie*. Göttingen: Hogrefe; 1990. p. 105-115.
52. Bührlen, Bernhard and Kickbusch, Ilona. *Innovations for more health - Concluding document for the MetaForum «Innovation in Healthcare» 2007-2009*. 24-8-2009; cited 24-8-2009. Available from: <http://www.metaforum-innovation.de>
53. Mulley AG. The role of the Patient in Medical Decision Making and Management: An American Perspective. In: Klusen N, Fließgarten A, Nebling T, editors. *Informiert und selbstbestimmt – Der mündige Bürger als mündiger Patient*. Baden-Baden: Nomos; 2009. p. 109-120.



