Health Services Research and Health Economy – Quality Care Training in Gynaecology, with Focus On Gynaecological Oncology

Versorgungsforschung und Gesundheitsökonomie – Arbeitsgeschwister in der Frauenheilkunde mit Schwerpunkt gynäkologische Onkologie

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Abstract

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In the era of cost increases and reduced resources in the German healthcare system, the value of health services research and health economics is increasing more and more. Health services research attempts to develop concepts for the most effective ways to organise, manage, finance and deliver high-quality care and evaluates the implementation of these concepts with regard to daily routine conditions. Goals are the assessment of benefits and the economic advantages and disadvantages of new and established diagnostic methods, drugs and vaccines. Regarding these goals, it is clear that health services research goes hand in hand with health economics, which evaluates the benefits of diagnostic and therapeutic procedures in relation to the costs. Both scientific fields have focus principally on gynaecology and particularly on gynaecological oncology in Germany, as can be seen by numerous publications. These present several advantages compared with clinical trials - they uncover gaps in health care, question the material, staffing and consequently the financial resources required and they allow the estimation of value and the comparison of different innovations to identify the best options for our patients.

Zusammenfassung

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Im Zeitalter der Kostensteigerung und reduzierten Ressourcen im deutschen Gesundheitswesen gewinnen Versorgungsforschung und Gesundheitsökonomie immer mehr an Wert. Versorgungsforschung ist die Entwicklung von Versorgungskonzepten, deren Umsetzung begleitend erforscht und unter Alltagsbedingungen evaluiert wird. Ziele der Versorgungsforschung sind u. a. die Bewertung des Nutzens wie auch der ökonomischen Vor- und Nachteile neuer diagnostischer Methoden und neuer, und auch langjährig eingesetzter Arzneimittel und Impfstoffe. Dementsprechend wird deutlich, dass dieses Hand in Hand mit der Gesundheitsökonomie einhergeht, welche die Kosten von diagnostischen und therapeutischen Maßnahmen mit dem jeweiligen Nutzen in Relation bringt. In Deutschland haben beide Forschungsbereiche vor allem einen Schwerpunkt in der Frauenheilkunde bzw. insbesondere in der gynäkologischen Onkologie, was durch zahlreiche Publikationen belegt wird. Diese haben im Vergleich zu klinischen Studien deutliche Vorteile - sie decken Lücken in der Versorgung auf, hinterfragen die notwendigen materiellen und personellen und somit auch finanziellen Ressourcen und ermöglichen erst die Ermittlung des Wertes und somit den Vergleich unterschiedlicher Innovationen, um die beste Option für Ratsuchende und Patientinnen zu identifizieren.

Introduction



After years of serious neglect of health services research and health economics in Germany, interest in these areas is currently undergoing a considerable upturn.

Health services research projects and studies and analyses of health economics are being increasingly undertaken as a result of the structural changes in the healthcare system as well as growing financial pressures, since healthcare costs have risen exponentially in recent years. With regard to these healthcare costs, Germany is one of the highest-spending countries in the world [1]. Whereas healthcare expenditure stood at \in 206.6 billion in 1999, the money spent on the German healthcare system had jumped to \in 263.2 billion by 2008 (\circ Fig. 1) [2].

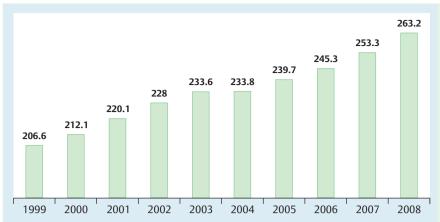


Fig. 1 Development of healthcare costs in Germany (nominal) in billion Euros [2].

Both processes are also keen to answer many other scientific questions, such as the comparison of the effectiveness and side effects of diagnostic and therapeutic procedures in real care situations outside clinical studies with strictly regulated inclusion criteria, the significance of new procedures for the entire population, and finding answers to professional policy issues, such as the evaluation of future structural and personal responsibility within professionals' own disciplines.

In light of the numerous possibilities and the high value of these two scientific methods of investigation, it is particularly pleasing that they focus on women's health in Germany. The intention of this paper is to chart this development. Consequently, our specialist field is one of the front runners in health services research and health economics in the German healthcare system.

Why Examine Health Economics and Health Services Research Together?

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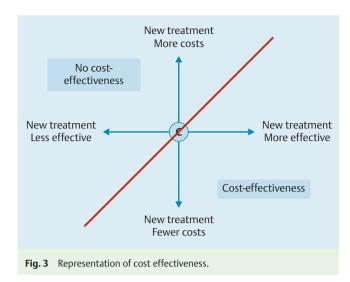
At this point the first task at this point is to clarify the definition of these two methods. Health services research itself is a subfield of healthcare system research, which relates to the microlevel of the healthcare system and, in particular, to hospitals, GP surgeries or individual technologies in healthcare [3]. It particularly focuses on patient care, i.e. medical as well as psycho-social care, and on healthcare which includes prevention and health promotion. Health services research develops care concepts, researches their implementation and evaluates them under everyday conditions. The objectives of health services research include the evaluation of benefits as well as a comparison of the economic advantages and disadvantages of new diagnostic methods as well as of new and existing drugs and vaccines. At this point, it

becomes clear that health services research needs to include health economics.

Health economics is an interdisciplinary science which focuses on the production, distribution and consumption of scarce healthcare commodities in the healthcare system and therefore brings together elements of health sciences and economics [4]. This has arisen from the need to bring the costs of a procedure in line with its benefits. In many cases, we know the cost of a diagnostic procedure or treatment, but not the value of this healthcare service. The healthcare system needs to be managed, however, not on the basis of costs, but on the value of the service. Also, there are usually several options available. The difficulty lies in the fact that there are not enough financial resources to support all options. As a result, an evaluation of the costs in relation to the benefits needs to be carried out using a health economics decision model, which can be regarded as part of health services research [5]. Essentially, all models are decision models (Fig. 2). The best established models are the cost/effectiveness analysis (i.e. determination of the costs for an additional year of life, for example), the cost/benefits analysis (i.e. the costs incurred are offset against the resources required, with lifetime being expressed in monetary terms, for instance) and the cost/useful value analysis (i.e. the determination of costs taking into account quality of life, e.g. quality-adjusted life years [QALYs]). The models or the results of the analyses are intended to facilitate objective decisions regarding a means of offering better-quality healthcare services and to do so with the least possible consumption of resources. Comparable innovations can be depicted on a chart and assessed accordingly (Fig. 3).

Analysis	Comparison	With
Cost effectiveness analysis (CEA)	Resources consumed in monetary units	Clinical effect
Cost-utility analysis (CUA)	Resources consumed in monetary units	Quality of life gained
Cost-benefit analysis (CBA)	Resources consumed in monetary units	Resources saved or gained in monetary units

Fig. 2 Overview of health economics evaluations.



Examples of Health Services Research and Health Economics in the German Healthcare System From the Perspective of Gynaecology and Obstetrics

Care with consideration of staffing resources and ongoing training

Adequate education, advanced training and ongoing training are essential for safeguarding future clinical competence [6] and are based on the following definitions: education means the dissemination of skills and knowledge required to carry out the profession, i.e. study. Advanced training is taken to mean the expansion and renewal of knowledge, skills and abilities following the initial training phase, i.e. further specialist training. Ongoing training means the furthering of qualifications in occupations that require continuing training, for instance after reaching the consultant level [7]. The concern is that dwindling economic resources in hospitals, along with the dissatisfaction amongst clinicians with these working conditions, are leading to cutbacks in clinical education, advanced and ongoing training - with the resulting lack of qualified specialists. The flood of doctors at the end of the last millennium changed directly at the start of the new millennium into a shortage. The reasons cited for this include increasing numbers of graduates going abroad and entering other professions. At the moment, the number of places available for advanced clinical training is frustrated by a shortage of interns seeking advanced training [8]. There is no shortage of advanced training places, but only a small number of doctors and specialists are interested in these.

Education, advanced training and ongoing training therefore need to be made more appealing. These are based essentially on the parameters which also depend on adequate financing: a good working environment, good, supervised dissemination of advanced training content, and adequate remuneration.

By contrast, Germany has numerous problems, forcing specialists to increasingly focus on this issue in the context of health service research. One example is the new working time directive, which has led to a shortage of doctors on day shifts and therefore to a shortening by 250 days of the actual time spent on day shifts across the entire advanced training phase [7]. As a result, the opportunities to acquire skills in a practical setting have considerably diminished. The operational catalogue of advanced training has also shrunk, lowering the demand for practical qualifications.

The increasing administrative duties – one third of the time spent at work is spent at a desk - considerably hampers advanced training. Ongoing training courses, which cannot replace clinical experience and therefore, according to the definition set out above, cannot replace advanced training, are also being called into question [7]. Advanced training must also needs be affordable in the future. A study in Switzerland from 2002 calculated the costs of training specialists at around 60 000 Swiss Francs per intern and year [9]. This correlates with other data, according to which a five-year advanced training course costs 300 000 Swiss Francs (around € 240000) per individual [10]. As clinical advanced training in Switzerland is comparable with that in Germany, this can be taken as a guideline for further training costs in Germany. An examination of the distribution of advanced training in hospitals reveals a rather uneven picture. All hospitals receive the same diagnostic-related case (DRG) per-case flat rates. Consequently, hospitals without advanced training and therefore without the associated costs must be labelled as over-financed, while hospitals which offer increased advance training are under-financed and therefore at a competitive disadvantage [6]. There are many possible solutions. The German Association of Gynaecology and Obstetrics (DGGG e.V.) has already begun restructuring its advanced and ongoing training. Advanced training courses will now include practical modules in which participants will learn not only techniques, but also the entire spectrum of knowledge from indication to aftercare and follow-up.

In the context of limited staffing resources in hospitals, improved teaching may also be assisted by new concepts, such as the integration of structured practical teaching (skills training) based on suitable obstetric and gynaecological models delivered by specially-trained student trainers (peer teachers) [11]. Verification of the skills learned can be as a formative theory/practical examination ("mini-OSCE"). This type of concept, however, needs to be supported and evaluated in the context of health services research. Frobenius et al. [12] compared skills training with classical training from lecturers in an experiment involving 139 students. After examination of the learned content, it was found that teaching by specially-trained student peers is just as effective for communicating the principles of fundamental practical skills as teaching by lecturers - with the bonus of reduced clinical staffing costs. This is certainly applicable to clinical advanced training also. In a prospective study, for example, a three-month laparoscopy training course was evaluated on the basis of four training models [13]. An evaluation of the exercises carried out was performed before the study commenced and after the training phase. The uni-variant and multi-variant analysis showed that a structured laparoscopy training course can achieve a learning success using models independently of the level of training and surgical experience and would be a useful tool in clinical training. In relation to ongoing training also, after completion of training to become a specialist, there are concepts whose content has been evaluated in comparison with international concepts. One example of note at this juncture is the established curriculum for the training of certified breast surgeons of the German Working Group for Aesthetic, Plastic and Restorative Operational Procedures in Gynaecology (AWO-gyn) [14]. This encompasses not only the mastery of operating techniques, but also a comprehensive knowledge of the interdisciplinary treatment of patients with breast cancer. It also needs to be borne in mind that increasing operative specialisation is associated with the outcome [15-17]. Skinner et al. [16] compared the results of oncological and general surgeons based on a group of 29666 patients with breast

cancer, for example. In this case, specialisation and treatment by an oncological surgeon showed a 23% higher overall survival rate (RR 0.77 [95% 0.67–0.88]; p < 0.0001). This leads indirectly to the conclusion that an evaluated curriculum for specialisation represents a cost-effective measure from the perspective of the health-care economy as well in terms of the improvement of the quality of the outcome and the reduction of follow-on costs due to avoided recurrences/metastases [15].

A further urgent problem in advanced clinical training is the distribution by gender. While the number of female students is constantly rising – over 60% in the 2009/2010 winter semester – the number is falling in the higher echelons of universities and hospitals [18]. Only eight per cent of consultants' positions are held by women, and in surgical disciplines this figure is even lower. This problem is particularly acute in relation to gynaecology. In this discipline, women take 77% of all university advanced training places, but hold only 34% of managerial positions or 4% of the consultants' positions [18]. In a survey carried out by the DGGG involving 1037 responses, the cause was revealed to be the lack of scope for harmonising family and work life (e.g. due to lack of child care). Consequently, the majority of female clinicians prefer to work in general practice [18]. The problem for the future can be predicted accordingly; if more and more women are working in gynaecology, but are not holding the senior clinicians' roles in hospitals, there will be a lack of experienced surgeons and sufficiently comprehensive care will be at risk.

The fact is that education, advanced training and ongoing training in our discipline needs to be improved and stepped up, as we shall otherwise be faced with a huge lack of specialists – both in terms of numbers and in terms of quality. Besides the campaigning of the professional association for better funding new, resource-saving concepts for communicating knowledge and skills need to be developed and evaluated in the context of health services research.

Oncological care and quality assurance

In the field of oncological care and quality assurance much has changed in recent years. These changes, such as care in certified structures, an expansion of quality assurance measures, the development of guidelines, etc. will continue to make great strides in the immediate future.

Below, these changes will be explained using the example of patients with breast cancer to show which changes are transferrable to the structures of other organ entities.

Although the incidence of breast cancer has risen significantly in the last few decades and continues to do so, mortality rates have fallen. This can only be convincinly presented, however, if data from clinical and epidemiological cancer registers are made available and sufficient levels of follow-up are possible, as patients can be lost to follow-up, especially those in remission, and therefore this may indicate a poorer quality of treatment and not in fact reflect reality [19]. Consequently, causes for these developments can be analysed and positive influencing factors stepped up – this is a significant, if not in fact the most important, aspect of health services research.

Data from the German cancer register, the Robert Koch Institute and the German Statistics Office indicate that the incidence of breast cancer has risen by 50% between 1980 and 2004 [20]. According to the latest estimate, the annual number of women developing the disease in the last 10 years has risen from 50000 in 1995 to 57000 in 2004 (**Fig. 4**). The use of hormone replacement therapy in recent years and improved early detection are

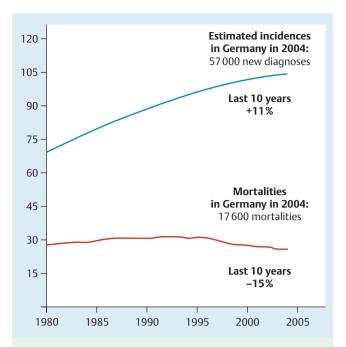


Fig. 4 Incidence of and mortality from breast cancer, trend from 1980 to 2004, number of diagnoses and deaths in 2004 [20].

regarded as possible reasons for the upward trend. By contrast, mortality has fallen over the last decade by 15%. The five-year survival rate rose from 73% in 1998-1992 to 80% with the initial diagnosis in 1998–2002, presumably due to the earlier detection of tumours while still small and primarily due to improved adjuvant therapy [21]. Further progress is expected by the establishment of certified organ cancer centres [22-24], the implementation and consistent use of guidelines [25], the use of targeted therapies [26], early detection via mammography with suitable quality assurance [27] and the identification of new and prognostic markers [28]. This will only be measurable, however, if the implementation of these new structures and innovations is accompanied by health services research-related projects. In a retrospective cohort study involving a total of 3976 patients with a primary breast carcinoma diagnosed between 2001 and 2005, Wöckel et al. showed that only 2063 patients had been treated completely in accordance with guidelines [25]. The variable "guideline-compliant treatment" had a significant influence on recurrence-free survival and overall survival (p = 0.001)(Fig. 5). As the number of deviations from the guidelines rose, the overall survival rate fell (p = 0.0001). Guideline-compliant treatment, however, also requires compliance on the part of the patient. The patient needs to play her part in every recommended treatment option. Consequently, the adequate communication of information and shared decision-making are essential. A health services study by the University of Cologne involving 3733 patients from 51 breast cancer centres also showed that, for the most part, this functions well from the patients' perspective, but that there is potential for improvement in terms of information going beyond medical treatment, as well as the active inclusion of patients in the treatment process by the physicians treating them [29]. Patients are also the most important factor when it comes to establishing certified centres. An awareness of the role – as well as the presence – of a certified centre is a key requirement for their implementation. This can be evaluated

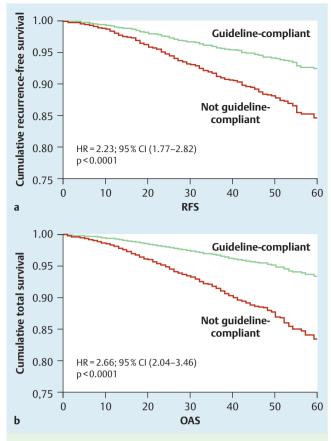


Fig. 5a and **b** Kaplan-Meier curves on **a** recurrence-free and **b** overall survival for guideline-compliant vs. non-compliant treatment, adjusted for tumour size, node status, grading and age [25].

through health services research. In a study involving 1073 patients, no fewer than 78.2% of the patients at a breast centre were familiar with the definition of a certified centre [22]. Compared to obstetric patients, receiving treatment in a specialist centre was seven times more important for oncology patients – a highly significant figure.

A further reduction in mortality, as well as optimisation of the care of oncology patients, can be expected from the introduction of the National Cancer Plan (Fig. 6) [6,30–32]. The underlying reason for the National Cancer Plan, initiated by the German Ministry of Health, German Cancer Society (Deutsche Krebsgesellschaft e.V. [DKG]), German Cancer Aid (Deutsche Krebshilfe e.V. [DKH]) and the Working Group of German Tumour Centres (Arbeitsgemeinschaft Deutscher Tumorzentren e.V. [ADT]), is the ongoing high number of new diagnoses of and deaths from cancer in Germany. In view of the high incidence of breast cancer, this subject plays a key role in shaping the care of women with cancer and therefore the National Cancer Plan. Areas of focus in this context include the further development of oncology care in certified structures, along with a clear definition of these (Fig. 7) and guideline-compliant therapy. The objective here is to define organ-specific (such as the breast or ovary) but also multi-organ (such as psycho-oncology, supportive measures, palliative medicine and pain management) approaches in order to implement transparent standards of care and also to further develop existing guidelines. An informative oncology quality reporting system is also being promoted for service providers, de-





Fig. 7 Definition of cancer centres [32].

cision makers and patients, with particular support for clinical cancer registers. Adequate documentation systems will ensure a high quality of documentation and data, which on the one hand will relieve the pressure on certified organ cancer centres which expend considerable staffing resources to achieve the figures required in the survey sheets and which, on the other hand, will comprehensively stratify the progress of the disease not only in terms of mortality, but also in terms of such parameters as recurrence and metastatic disease. Proving the benefit of certified structures based on outcome quality will enable a determination of the cost effectiveness of these structures and funding then requested on the basis of adequate data. Until now there has been no definitive evidence that a certified breast centre is able to achieve a better outcome quality independently of other influencing factors or propose an independent parameter for the prognosis of breast cancer. It is here that health services research can help. Recently, the highly significant proof of mortality figures in relation to an improvement in mortality figures was published in Middle Franconia [33]. The data from 3940 patients with breast cancer from three certified centres and 18 further

non-certified treatment units was examined with the help of the Erlangen-Nuremberg Tumour Centre to determine whether care in a certified breast centre offers a better survival prognosis. The data showed that patients treated in a certified breast centre had a 30% better overall survival rate after four years – regardless of the tumour characteristics or other patient characteristics, such as age.

Aftercare is an important topic, not least in relation to oncology care. The optimisation of aftercare, in particular compliance with participation in recommended investigatory procedures, remains a challenge [34]. Health services research can also help here [28]. A Canadian study randomised patients with breast cancer to routine aftercare or an intensive programme comprising a half-hour educational session, a patient's version of the aftercare recommendations, brochures and information on how to obtain further support [35]. In the control group, higher QALYs were achieved (1.42 vs. 1.41); this was also achieved with reduced costs compared to the intervention arm. The probability of cost effectiveness of the intervention arm was 27% in the case of \$ 50 000 per QALY. This means that the more intensive system was definitely not cost effective and therefore cannot be recommended. These data emphasise the need for health economics evaluations for the case of more intensive support programmes, as not every approach is necessarily effective.

Drug therapy

Drug therapies in particular are associated with enormous costs and are therefore ideal for health economics evaluations. The costs of drugs rose, for example, from € 19.2 billion in 1999 to € 32.4 billion in 2009. The financial pressure is also underscored by the new law on the restructuring of the medicines market (AMNOG) [36]. Oncology preparations, such as anti-hormone treatments, chemotherapies, targeted therapies and supportive medications, account for a significant part of these costs. For these, there are usually numerous study outcomes serving as the basis for guidelines and recommendations [37–39]. Rarely, however, are these integrated into health services research and health economics, although this could be of considerable benefit [40]. As an example, we mention drug therapy for patients with breast cancer.

One key element of health economics considerations concerns the endocrine therapies employed in adjuvant therapy for patients with hormone receptor-positive breast cancer [40]. The age-standardised incidence of breast cancer has risen since the 1980s by around 50% [41]. Current calculations indicate a fiveyear prevalence of 249 600 women. The five-year prevalence of all women with breast cancer over the age of 50, i.e. generally post-menopausal women, is 193 000 women [41]. Assuming that 71.5% of these are hormone receptor-positive [42], treatment with aromatase inhibitors will potentially affect 137 995 women in Germany. This corresponds to nearly half a per cent of the female population over the age of 20. In view of the high proportion of women and taking account of the long duration of endocrine therapy (at least five years and including extended adjuvants up to 10 years), it is perfectly understandable that the benefits of endocrine therapy need to be weighed against the risks and costs from the perspective of the healthcare system [43]. The benefits of aromatase inhibitor therapy are well documented and are also supported by current publications, such as the effectiveness of letrozole in accordance with the results of the BIG 1-98 study [44]. Health economics is useful for weighing advantages and costs, including quality of life, in the equation. In

2007 the Health Technology Assessment (HTA) programme published a meta-analysis of the available economic analyses of the aromatase inhibitors letrozole, anastrozole and exemestane compared with tamoxifen. The HTA, which is part of the National Institute for Health Research (NIHR), provides the data in support of decisions made by NICE. The cost effectiveness of aromatase inhibitors was between £ 21000 and £ 32000 per OALY for upfront therapy, £ 10000 for extended adjuvant therapy with letrozole, and £ 20 000 for switch or sequential therapy. Aromatase inhibitors were consequently evaluated as cost-effective therapy. This is also reflected in the prescribing behaviour in Germany. In a survey from 2009 involving 74 clinicians whose organisations treated a total of 31 000 breast cancer patients a year, the proportion of post-menopausal women receiving adjuvant therapy with an aromatase inhibitor at the time of the survey was 74% [46]. In this case, up-front therapy was the first choice, followed by sequential therapy (40%). Regional differences were only slight. A further German health services research analysis investigated the incidence of adverse gynaecological and surgical interventions in treatment with anastrozole, compared with tamoxifen [47,48]. A significantly higher incidence of gynaecological events was found with tamoxifen (34.2 vs. 20.5%, p < 0.0001). This resulted in an increase in diagnostic and surgical procedures and a four-fold increase in hysterectomies with tamoxifen (p < 0.0001) and thus underscores the cost-effectiveness of aromatase inhibi-

Endocrine therapies are only as good as the manner in which they are used. As a result, investigating compliance with drug therapies is an important element of health services research. Non-adherence, i.e. the consumption of less than 80% of the planned dose, and non-persistence, i.e. the premature discontinuation of endocrine therapy as a result of poor compliance, lead to a significant reduction in the overall survival rate (HR = 1.26 vs. HR = 1.49) [49]. Only 40–60% of patients complete endocrine therapy as planned. Predictors for the discontinuation of endocrine therapy include a younger (<50 years) and older (≥75 years) stage of life, breast-conserving treatment (vs. mastectomy), the prescription of smaller package sizes, a higher contribution (especially among older patients) and the existence of comorbidities (≥2). During follow-up therapy, a detailed investigation of the issue of compliance with endocrine therapies is required, bearing in mind the predictors described above, while possible reasons for early discontinuation, e.g. side effects, need to be discussed [34]. Compliance also needs to be improved by prescribing larger package sizes as well as a reduction in contributions from patients with chronic diseases through cost bearers which, given the possible economic damage caused by follow-on costs, are marginal for the company involved.

One major deficit for health economics analyses is the lack of data in respect of costs in metastasis situations, which can generally only be estimated. Chastek et al. [50] investigated the costs of post-menopausal women with a hormone receptor-positive breast cancer who had metastases. Using a retrospective health economics analysis, 1202 women were identified with a median age of 58.9 years. Before commencing chemotherapy, the mean costs were \$ 79139 \pm \$ 121489 per year (year 1: \$54725, year 2: \$73107 and year 3: \$84200). After chemotherapy was initiated, the mean costs were \$132786 \pm \$117635 (year 1: \$92639, year 2: \$148228 and year 3: \$176163). The highest costs occurred in the outpatient sector. It is clear that endocrine therapies must be given priority as long as possible and wherever

available – not just in light of the quality of life they bring, but also in view of their relevance to the health economy.

A significant rise in costs is also seen with the increasing use of targeted therapies. The focus is on the treatment of Her2/neupositive tumours. The development of targeted therapies for patients with a triple-negative breast cancer is also of scientific interest [26]. An interesting meta-analysis of 75 pharmaco-economic studies of targeted therapies (e.g. monoclonal antibodies and tyrosine kinase inhibitors) has been published on this subject [51]. The studies, which were financed by pharmaceutical companies, showed a significantly more frequent cost-effective result (87 vs. 48%, p=0.001). Even the alleged conflicts of interests of the authors were associated with a positive outcome (78 vs. 43%, p=0.007). As with all types of studies, it is necessary to examine the funding of the project, even in the case of health economics studies.

Whereas modern supportive therapies may in some cases be associated with high costs, the prevention of side effects, along with their associated cost-intensive management, can save resources. The personalisation of supportive therapy, for example anti-emetics, may also increase its cost effectiveness. In a German study, 66 patients undergoing a total of 190 cycles of chemotherapy were given anti-emetic therapy adapted to the cytostatic drugs' emetogenic potential or therapy based on an algorithm taking account of individual risk factors (such as age, gender, history of hyperemesis gravidarum, etc.) [52]. The personalised algorithm demonstrated a significant advantage in relation to complete freedom from nausea (76% vs. 55%, p = 0.035). A cost saving of 78.8% was also achieved, emphasising the significant potential of health service research.

Surgical treatment

Health services research and health economics evaluations focus on structural issues or drug therapies which are mostly, by their very nature, very cost-intensive. This is also apparent from the new law on prescribing drugs (AMNOG), which particularly deals with the approval of drug therapies [36]. Research into surgical treatment tends to be neglected. This is regrettable, as major surgical procedures require the provision of high levels of personnel and material resources and enormous potential exists for optimising cost effectiveness. Internationally, interesting work is being carried out in this field. In a multi-centre, randomised study involving 21 Dutch hospitals, laparoscopic hysterectomy (TLH) was compared with open abdominal hysterectomy (TAH) in relation to complication rates and the associated costs in 283 patients with endometrial adenocarcinoma of the uterus (stage I) or complex atypical hyperplasia [53]. The TLH had a lower complication rate (2.7%) than the TAH (4.3%), which other studies also confirm [54]. The costs of a TLH were € 3453 and the costs of a TAH €3577. The authors calculated a cost saving of €3700 per additional complication-free patient when a TLH is carried out instead of a TAH. On this basis, they concluded that the TLH was a safe and, in particular, cost-effective option for patients with early-stage endometrial carcinoma from the perspective of the healthcare industry.

Health economics studies are also available from Germany. Schem et al., for example, investigated whether the G-DRG revenues for vaginal, abdominal and laparoscopic hysterectomy (HE) are sufficient to cover costs [55]. In this case, not only were personnel and material costs taken into account, but the services of other institutions were also documented and included into the calculation. 79 hysterectomies, performed from 2005 to 2007,

were taken into consideration. The staffing costs alone accounted for one third of the total costs. In the evaluation, the vaginal approach offered the highest level of cost effectiveness from the DRG system's perspective. Although the inpatient stay was shorter for laparoscopic operations (5.33 days vs. 7.47 days for vaginal hysterectomy and 8.59 days for abdominal hysterectomy), this was compensated by the higher costs associated with the longer operation. Added to this are the costs of procedure-specific, specialist endoscopic instruments (e.g. manipulators and morcellators) and case-related accessories. In this case "high-tech" and "high-cost" are both to the benefit of the patient [56]. From an ethical perspective, laparoscopy is associated with the least physical trauma, the lowest level of analgesia consumption and the shorter inpatient stay and can therefore not be rejected [54,57, 58]. The results of the health services research underscore the need for more adequate and more appropriate remuneration and a fair representation of minimally-invasive procedures. If one raises the question of fairness in the DRG system from the point of view of the extent to which the higher outlay for more patient-friendly (since they are minimally invasive) procedures is covered, the problem only really becomes apparent when one compares the reimbursement price for a hysterectomy (N21Z) of €3380.57 with that of an organ-preserving myoma nucleation procedure, which is frequently more surgically intensive, of €2992.44. At least it must be established that the DRG system does not a priori encourage organ-preserving procedures [56]. As the length of the inpatient stay following surgical treatment for patients with breast cancer is continuously decreasing, more patients are treated as outpatients and major, radical surgical procedures are increasingly tending towards breast-conserving therapies with sentinel node biopsies. The question of costs therefore also becomes relevant in the treatment of patients with breast cancer. Possibilities have to be developed for achieving cost coverage or an actual earning situation while delivering the best possible care. Process management and interface optimisation are key concepts in this field which are being applied in the context of interdisciplinary clinical treatment pathways. Even given the often pessimistic attitude of practising clinicians towards quality management, proof of their effectiveness needs to be provided. The interdisciplinary breast care centre at the Charité Hospital in Berlin has examined this issue and, by implementing a treatment pathway, achieved a reduction in overall case costs of 23.4% [59].

In order to allow further cost effectiveness analyses of surgical techniques which are essential both in terms of financial viability and in terms of allowing a comparison of different methods to be carried out, as elaborated above consideration will also need to be given in future to investigating the associated quality of life. These go without saying in clinical studies on drug treatments and are required to calculate quality-adjusted years of life, for example. Unfortunately there are only a few isolated studies available on this issue [60].

Therapy in reproductive medicine

Therapy in reproductive medicine is particularly affected by the financial aspects of healthcare. With the law on the modernisation of legal health insurance (GKV-Modernisierungsgesetz – GMG), the regulations that applied until then to artificial insemination were changed to the clear disadvantage of couples wanting children [61]. As well as a limit to a maximum of three cycles of treatment and the definition of a lower as well as an upper age limit of eligibility for in vitro fertilisation paid for by the health

insurance scheme, lawmakers have also decreed that couples must bear 50% of the cost of the treatment themselves. Compared with 2002, during which 87 044 cycles of treatment were carried out, this number rose in 2003 with the announcement of the forthcoming revision of the legal framework to 105854 ("anticipatory effect"), falling to 59448 in the year in which the GMG came into force, as confirmed by the data from the German IVF register [62]. These changes to the care of couples wanting children, with their dwindling case numbers, will have far-reaching consequences for our profession. In the 1960s and 70s, Germany played a leading role internationally in gynaecological endocrinology [63]. Currently, however, the specialised study of endocrinology, reproductive medicine and andrology at universities is dropping, as these disciplines are unable to offer job security and prospects for the future. Thanks to increasing survival rates for oncological diseases and continual advances in reproductive medicine over recent years, however, the field of fertility protection in cancer offers a wide variety of opportunities for dedicated scientists with the establishment of new techniques enabling patients who have undergone cancer therapy and, in some cases, aggressive surgical interventions and even ovary-toxic malignancy therapy, to realise their wish to have children. Examples of this include the establishment of trachelectomy in patients with early cervical cancer, as well as the introduction of ovarian cryo-conservation. Both methods were inconceivable years ago and in under appropriate circumstances represented an oncologically arguable breakthrough in reproductive medicine offering the opportunity to initiate a pregnancy after the conclusion of primary therapy. Such examples of success are closely linked to university-based structures, as these are the only institutions having an infrastructure suitable for the development and practical implementation of theoretical hypotheses. Close cooperation between various disciplines, in particular the close collaboration between oncology and reproductive medicine concerning the nature and time window until commencing cancer treatment, on the one hand, and the feasibility of various fertility-protecting measures, on the other hand, are essential. And not least, the needs of the patients affected are ultimately the deciding factor for determining the type of treatment they receive. As fertility protection measures such as the cryo-conservation of oocytes or ovarian tissue are generally not covered by health insurance schemes, a decision also needs to be made on the financial burdens associated with these procedures [64]. However, the first pregnancy in Germany following successful ovarian re-transplantation, which was performed in the Gynaecology Department of the University Hospital of Erlangen, has shown that focused, consistent work can be rewarded. The spectrum of fertility-protecting measures continues to grow, and the indications encompass an ever-broadening area of oncology. Disciplines such as internal medicine, paediatrics and surgery have long since had to consider these issues also, as they are increasingly faced with the same questions.

The provision of fertility-protecting measures for young patients is currently not part of the certification criteria for organ cancer centres. As the bundling of expertise from various focal areas increases in oncology centres and the achievement of corresponding case numbers furnishes proof of the efficacy of individual procedures, figures will emerge which may also reflect the discipline of fertility protection in a certified centre. However, not every centre will be able to maintain this type of infrastructure. On the one hand, health services research can open up new pathways by developing cooperation models. On the other hand, this

type of service requires commensurate counter-funding, which may not be passed on to the patient. The wishes of young couples also need to be borne in mind on our way towards comprehensive care in a certified centre.

Given the continuous decrease in the number of university-based reproductive medicine centres, Germany is at risk of being downgraded to the status of a "scientifically developing country" in this field. Legal obligations restricting the activities of scientists in this field in Germany also mean that research is virtually impossible and appears unappealing, since the legal framework in Germany is highly unlikely to create competitive conditions on the international market for high-ranking, scientific publications. Added to this is the fact that 75% of reproductive medicine patients are now treated in general practices, while networking concepts between universities and practices are generally lacking. As well as research, advanced and ongoing training are in great jeopardy. Consequently, a clear definition of goals in health services research needs to be developed along with suitable concepts for networking and cooperation. These must then be implemented and evaluated on the basis of the extent to which the duty of care is met, but also on the basis of research opportunities. Reproductive medicine is also currently facing numerous ethical questions (pre-implantation screening, single embryo transfer, heterologous insemination, oocyte donation) [65]. Only health services research can pursue these questions and answer them expediently.

Pursuing this point further, health economics can also be of great benefit. If one examines the cost-effectiveness of reproductive medicine, it is reasonable to call for financial support for couples wanting children. Solely from the perspective of health economics, artificial insemination is arguably the most cost-effective medical treatment available. Based on the transparent costs for artificial insemination, each child represents an increase of at least 60 quality-adjusted life years and, in view of the child's subsequent working potential, represents a considerable contribution to the gross social product.

Summary for implementation in practice

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This paper underscores the importance of health services research and health economics for and in our discipline. Gynaecology is the front-runner in this and makes significant contributions to German healthcare. Research on health care and health economics also furnishes proof of the benefits of new methods and drug therapies and reveals gaps in funding and therefore indicate the data still required for targeted treatments in order that care structures and therapies can be maintained and more effectively supported in the future.

Conflict of Interest



None.

References

- 1 *Lux MP, Beckmann MW.* Klinische Ökonomie in der gynäkologischen Onkologie. FHA 2008; 2: 35–41
- 2 Federal Statistics Office Wiesbaden, 2010
- 3 Health services research. http://de.wikipedia.org/wiki/Versorgungsforschung; last access: 29.9.2011
- 4 Health economics, http://de.wikipedia.org/wiki/Gesundheitsoekonomie: last access: 29.9.2011

- 5 Porzsolt F. Klinische Ökonomik. Die ökonomische Bewertung von Gesundheitsleistungen aus der Sicht des Patienten. In: Porzsolt F, Williams AR, Kaplan RM, Hrsg. Klinische Ökonomik. Effektivität und Effizienz von Gesundheitsleistungen. Landsberg: Ecomed; 2003: 17–40
- 6 Beckmann MW, Bader W, Bechtold I et al. Finanzierung und finanzielle Probleme von Leistungen und Strukturen im Fachgebiet Gynäkologie und Geburtshilfe im Jahr 2011 allgemeine Aspekte und geburtshilfliche Versorgung. II. Artikel der Finanzierungskommission der DGGG e. V. Teil I. Geburtsh Frauenheilk 2011; 71: 367–380
- 7 *Costa SD.* Medical training and residency programs: current caveats. Geburtsh Frauenheilk 2009; 69: 1065–1070
- 8 Bücking BJ. Ärztliche Weiterbildung im Spiegel veränderter Ordnungspolitischer Rahmenbedingungen. Dissertation. Westfälische Wilhelms-Universität Münster; 2009. http://miami.uni-muenster.de/ servlets/DerivateServlet/Derivate-5270/diss_buecking.pdf; last access: 13 11 2009
- 9 Studer P. Kosten der Weiterbildung. VSAO-Journal 2003; 4/5: 20-23
- 10 Dubach P, Spycher S. Vorstudie zur Erhebung der Kosten der ärztlichen Weiterbildung im Auftrag des VSAO. BASS, 12/2006. http://www.buerobass.ch/pdf/2006/VSAO_Vorstudie_Schlussbericht.pdf; last access: 27.12.2006
- 11 Frobenius W, Nicolaisen-Murmann K, Junger J et al. Optimization of a practical course in gynecology and obstetrics based on current considerations for medical teaching. Geburtsh Frauenheilk 2009; 69: 517–524
- 12 Frobenius W, Ganslandt T, Junger J et al. Effectivity of peer teaching for gynecological and obstetrical skills training. Geburtsh Frauenheilk 2009; 69: 848–855
- 13 Polterauer S, Grimm C, Hanzal E et al. Surgical skills training results of a prospective trial. Geburtsh Frauenheilk 2010: 70: 990–993
- 14 Dieterich M, Dieterich H, Nestle-Kramling C et al. Certification of breast surgeons in Germany – AWO-gyn curriculum in an international comparison. Geburtsh Frauenheilk 2009; 69: 987–991
- 15 Beckmann MW, Bani MR, Löhberg CR et al. Are certified breast centers cost-effective? Breast Care 2009; 4: 245–250
- 16 Skinner KA, Helsper JT, Deapen D et al. Breast cancer: do specialists make a difference? Ann Surg Oncol 2003; 10: 606–615
- 17 Hillner BE, Smith TJ, Desch CE. Hospital and physician volume or specialization and outcomes in cancer treatment: importance in quality of cancer care. J Clin Oncol 2000; 18: 2327–2340
- 18 Hancke K, Toth B, Kreienberg R. Umfrage: Karriere und Familie unmöglich? Dtsch Arztebl 2011; 108: A-2148/B-1819/C-1801
- 19 Karn T, Holtrich U, Ruckhaberle E et al. Methodical bias of retrospective follow-up investigations and impact on the collection of quality assurance data. Geburtsh Frauenheilk 2010; 70: 41–46
- 20 Katalinic A. Breast cancer: declining mortality despite its increasing incidence. Geburtsh Frauenheilk 2009; 69: 237–239
- 21 Kaufmann M, Rody A. Breast cancer: reduced mortality by early detection and adjuvant therapy. Geburtsh Frauenheilk 2009; 69: 218–232
- 22 Lux MP, Fasching PA, Bani MR et al. Marketing of breast and perinatal centers. Are patients familiar with the product "specialized centers and certification"? Geburtsh Frauenheilk 2009; 69: 321–327
- 23 Lux MP, Fasching PA, Schrauder M et al. The age of centers: the influence of establishing specialized centers on patients' choice of hospital. Arch Gynecol Obstet 2011; 283: 559–568
- 24 Lux MP, Hildebrandt T, Bani MR et al. Gesundheitsökonomische Aspekte und finanzielle Probleme in den zertifizierten Strukturen des Fachgebietes. Gynäkologe 2011; 44: 816–826
- 25 Wöckel A, Varga D, Kurzeder C et al. Guideline adherence in primary breast cancer. Geburtsh Frauenheilk 2009; 69: 611–616
- 26 Liedtke C, Wolf MK, Kiesel L. New concepts for targeted systemic therapy in breast cancer. Geburtsh Frauenheilk 2010; 70: 625–633
- 27 Pfandzelter R, Wulfing U, Boedeker B et al. Diagnostic image quality of mammograms in German outpatient medical care. Geburtsh Frauenheilk 2010; 70: 998–1005
- 28 Kümmel S, Kolberg HC, Lüftner D et al. Mammakarzinom 2011 Neue Aspekte. Geburtsh Frauenheilk 2011; 71: 939–953
- 29 Steffen P, Kowalski C, Scheibler F et al. Patient information and shared decision-making for postoperative women with newly diagnosed breast cancer. Results of a patient survey in North Rhine-Westphalian breast centers. Geburtsh Frauenheilk 2009; 69: 1005–1011
- 30 Beckmann MW. Nationaler Krebsplan des Bundesministeriums für Gesundheit Strategieplan der Deutschen Krebsgesellschaft. Frauenheilkunde up2date 2009; 5: 323–329

- 31 Beckmann MW, Lux MP. Brustzentren im Nationalen Krebsplan: Versorgung, Leitlinien und Dokumentation. Senologie 2011; 8: 97–98
- 32 Bundesministerium des Bundes. *Nationaler Krebsplan*. http://www.bmg.bund.de/cln_169/nn_1168248/SharedDocs/Standardartikel/DE/AZ/N/Glossarbegriff-Nationaler-Krebsplan.html#doc1632822body Text14; last access: 26.2.2010
- 33 Beckmann MW, Brucker C, Hanf V et al. Quality assured health care in certified breast centers and improvement of prognosis of breast cancer patients. Onkologie 2011; 34: 362–367
- 34 Lux MP, Scharl A. Nachsorge Mammakarzinom. In: Kommission Mamma (represented by Anton Scharl), Arbeitsgemeinschaft Gynäkologische Onkologie e.V., Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e.V., Deutsche Krebsgesellschaft e.V., Hrsg. Aktuelle Empfehlungen zur Therapie primärer und fortgeschrittener Mammakarzinome State of the Art 2011. Munich: W. Zuckschwerdt Verlag; 2011: 179–197
- 35 Coyle D, Grunfeld E, Coyle K et al. Cost-effectiveness of a survivorship care plan for breast cancer survivors. J Clin Oncol 2011; 29 (Suppl.): Abstr 6082
- 36 Bundesministerium für Gesundheit. Gesetz zur Neuordnung des Arzneimittelmarktes (AMNOG). 21.12.2010. http://www.bmg.bund.de/krankenversicherung/arzneimittelversorgung/amnog/amnog.html; last access: 21.12.2010
- 37 Kommission Mamma (vertreten durch Anton Scharl), Arbeitsgemeinschaft Gynäkologische Onkologie e.V., Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e.V., Deutsche Krebsgesellschaft e.V. Aktuelle Empfehlungen zur Therapie primärer und fortgeschrittener Mammakarzinome – State of the Art 2011. Munich: W. Zuckschwerdt Verlag; 2011
- 38 Beckmann MW, Blohmer JU, Costa SD et al. Zurich consensus: German expert opinion on the St. Gallen votes on 15 March 2009 (11th international conference at St. Gallen: primary therapy of early breast cancer) 2009 St. Gallen conference: primary therapy of early breast cancer opinion among German experts (Zurich 2009). Geburtsh Frauenheilk 2009; 69: 377–383
- 39 Kreienberg R, Kopp I, Albert U et al. Interdisziplinäre S3-Leitlinie Diagnostik, Therapie und Nachsorge beim Mammakarzinom. Munich: Zuckschwerdt Verlag; 2008
- 40 Lux MP, Reichelt C, Karnon J et al. Cost-benefit analysis of endocrine therapy in the adjuvant setting for postmenopausal patients with hormone receptor-positive breast carcinoma, based on survival data and future prices for generic drugs in the context of the German healthcare system. Breast Care 2011; 6: 381–389
- 41 Robert Koch-Institut. Verbreitung von Krebserkrankungen in Deutschland. Entwicklung der Prävalenzen zwischen 1990 und 2010. Beiträge zur Gesundheitsberichterstattung des Bundes. Berlin: Westkreuz-Druckerei; 2010: 77–82
- 42 Brown SB, Mallon EA, Edwards J et al. Is the biology of breast cancer changing? A study of hormone receptor status 1984–1986 and 1996–1997. Br J Cancer 2009; 100: 807–810
- 43 Fasching PA, Fehm T, Janni W et al. Breast cancer therapy a state of the art review. Geburtsh Frauenheilk 2010; 70: 875–886
- 44 Regan MM, Neven P, Giobbie-Hurder A et al.; for the members of the BIG 1-98 Collaborative Group and the International Breast Cancer Study Group (IBCSG). Assessment of letrozole and tamoxifen alone and in sequence for postmenopausal women with steroid hormone receptorpositive breast cancer: the BIG 1-98 randomised clinical trial at 8-1 years median follow-up. Lancet Oncol 2011; 12: 1101–1108
- 45 *Hind D, Ward S, De Negris E et al.* Hormonal therapies for early breast cancer: a systematic review and economic evaluation. Health Technol Assess 2007; 11: iii–iv, ix–xi, 1–134
- 46 *Lueftner D, Schelenz C, Possinger K.* Prescription pattern of aromatase inhibitors for the adjuvant endocrine therapy of breast cancer a current survey of opinion leaders in Germany. Geburtsh Frauenheilk 2009; 69: 1012–1019
- 47 Forbes JF, Cuzick J, Buzdar A; Arimidex, Tamoxifen, Alone or in Combination (ATAC) Trialists' Group. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. Lancet Oncol 2008; 9: 45–53
- 48 Distler W, Canzler U, Duffy SR et al. Undesirable gynaecological and operative interventions during treatment of breast cancer with anastrozole and tamoxifen. Geburtsh Frauenheilk 2010; 70: 57–61

- 49 Hershman DL, Shao T, Kushi LH et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. Breast Cancer Res Treat 2010; 126: 529–537
- 50 Chastek B, Gao S, O'Malley C et al. Health care costs incurred by postmenopausal women with hormone-positive breast cancer following the initial diagnosis of metastasis. Cancer Res 2010; 70 (24 Suppl.): 156 s
- 51 Nearchou AD, Valachis A, Polyzos NP et al. Conflict of interest in economic analyses of targeted therapies in oncology. J Clin Oncol 2011; 29 (Suppl.): Abstr. 6120
- 52 Rosenhahn A, Camara O, Runnebaum IB et al. Effectiveness and costs of an individualized therapy for the treatment of cytostatic-induced emesis. Geburtsh Frauenheilk 2009; 69: 401–405
- 53 *Mourits MJ, Bijen CJ, Vermeulen KM et al.* Laparoscopic hysterectomy versus abdominal hysterectomy in early-stage endometrial cancer. J Clin Oncol 2010; 28 (Suppl.): 15 s
- 54 Mueller A, Boosz A, Koch M et al. The Hohl instrument for optimizing total laparoscopic hysterectomy: results of more than 500 procedures in a university training center. Arch Gynecol Obstet 2011; DOI: 10.1007/S004-011-1905-y
- 55 Schem C, Bauerschlag DO, Gravert C et al. Economic aspects of abdominopelvic surgery in times of limited case-based compensation. Geburtsh Frauenheilk 2010; 70: 574–579
- 56 Beckmann MW, Bader W, Bechtold I et al. Finanzierung und finanzielle Probleme von Leistungen und Strukturen im Fachgebiet Gynäkologie und Geburtshilfe im Jahr 2011 DRG-System und stationäre Versorgung inklusive Urogynäkologie und benigner wie auch maligner gynäkologischer Operationen. II. Artikel der Finanzierungskommission der DGGG e.V. Teil II. Geburtsh Frauenheilk 2011; 71: 497–510
- 57 Mueller A, Oppelt P, Ackermann S et al. The Hohl instrument for optimizing total laparoscopic hysterectomy procedures. J Minim Invasive Gynecol 2005; 12: 432–435

- 58 Mueller A, Thiel F, Lermann J et al. Feasibility and safety of total laparoscopic hysterectomy (TLH) using the Hohl instrument in nonobese and obese women. J Obstet Gynaecol Res 2010; 36: 159–164
- 59 *Richter-Ehrenstein C, Schneider A, Kramer M et al.* A clinical pathway in breast cancer surgery: pathway monitoring and impact. Geburtsh Frauenheilk 2009; 69: 617–622
- 60 Henkel AK, Strittmatter HJ. Quality of life after conventional axillary lymph node dissection compared to sentinel node biopsy in breast-sparing therapy for breast cancer. Geburtsh Frauenheilk 2010; 70: 127–133
- 61 Hilland U. Gesundheitsökonomische Aspekte und finanzielle Probleme in der Endokrinologie und Fortpflanzungsmedizin. Gynäkologe 2011; 44: 801–804
- 62 Bühler K, Bals-Pratsch M, Kupka MS; Board of Trustees. DIR Annual 2009. J Reproduktionsmed Endokrinol 2010; 7: 470–497
- 63 *Diedrich K, Strowitzki T, Kentenich H.* Position paper current state of reproductive medicine in Germany. Geburtsh Frauenheilk 2010; 70: 355–360
- 64 von Wolff M, Montag M, Dittrich R et al. Fertilitätsprotektion bei Frauen. Geburtsh Frauenheilk 2010; 70: R85–R100
- 65 *Maio G*. Reproductive medicine: medical service or market driven? Geburtsh Frauenheilk 2010; 70: 24–29

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