Evaluation of Multicenter Registry Data

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ABSTRACT

A registry actively documents and standardizes patient data on pre-defined questions. The term „registry“ emphasizes the data-holding aspect with the aim of describing epidemiological relationships and differences, supporting quality assurance and improvement, as well as clinical research. Evaluation of efficacy in the medical care routine, monitoring of patient safety as well as economic evaluation and minimum quantity research are further tasks of registries. Patients and reporting institutions determine the quality of registries through completeness and high data validity. This must be taken into account when designing, financing, and operating a registry. The analysis of potentially confounding or effect modifying variables is of significant importance for the evaluation of multi-center data from registries. Regular feedback to reporting institutions, patient information, public announcements and scientific publications as well as compliance with data protection regulations increase the transparency of the register. Otorhinolaryngology has few points of contact with registries. An exception is the integration into the cancer registry and the newborn hearing screening registry, which is currently under construction. The great variety of measurable outcome parameters in otorhinolaryngology, such as in otology, phoniatrics, rhinology, allergology, etc., forms the basis for various potential registries. Clinical questions, prevention measures, quality assurance, healthcare research and recommendations for health policy would be scientifically sound and evidence-based.

Contents

ABBREVIATIONS

ADSR	Arbeitsgemeinschaft Deutschsprachiger Schlaganfall-Register (Workgroup of German Stroke Registries)
ATLS	Advanced Trauma Life Support
BDSG	Bundesdatenschutzgesetz (Federal Data Protection Act)
CI	Cochlea implantation
CIO	Chief Information Officer
DDR	Deutschen Demokratischen Republik (German Democratic Republic)
DGHNO	Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie (German Society of Otorhinolaryngology, Head and Neck Surgery)
DNVF	Deutsches Netzwerk Versorgungsforschung
DSGVO	Datenschutz-Grundverordnung (General Data Protection Regulation)
EDC	Electronic Data Capture
FAST	Focused Assessment with Sonography for Trauma
GEKID	Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V. (German Society for Epidemiologicl Cancer Registries)
GKR	Gemeinsames Krebsregister (Common Cancer Registry)
IACR	International Association of Cancer Registries
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Healthcare)
IT	Information technology
KFRG	Krebsfrüherkennungs- und -registergesetz (Cancer Screening and Registry Act)
MTP	Monosyllable, Trochee, Polysyllable
RCT	Randomized controlled trial
SGB	Sozialgesetzbuch (Social Security Law)
TR-DGU	TraumaRegister der Deutschen Gesellschaft für Unfallchirurgie (Trauma Registry of the German Society for Trauma Surgery)
ZfKD	Zentrum für Krebsregisterdaten (Center for Cancer Registry Data)

1. Introduction

In medical research, diverse study types exist that are classified into primary and secondary research. In the context of secondary research, already existing research results are summarized in review articles and meta-analyses. Primary research, however, where trials are conducted, are subdivided into three main focuses of basic medical research, clinical, and epidemiological research [1]. Epidemiological trials analyze the distribution and temporal change of the incidence of diseases as well as their origins. In analogy to clinical trials, experimental and observational studies are differentiated in epidemiology [2, 3]. Epidemiological observational studies can be further categorized into cohort studies (follow-up studies), case control studies, cross-sectional studies, ecological studies, and descriptions with registry data. Healthcare research is a subdomain of healthcare system research that is included in the limit area of clinical and epidemiological research, public health research, and health economics. The German Network of Healthcare Research (DNVF, Deutsches Netzwerk Versorgungsforschung, http://www.dnvf.de) currently consists of 52 professional societies and 37 scientific institutes and research consortiums. One exception is the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (DGHNO, Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie), which does not belong to the member societies. The objective of the interdisciplinary network is the methodical, content-related, and institutional development of healthcare research and the elaboration of common strategies. The DNVF defines registries (etymology: lat. registrum – directory, inventory, list, registry) as a possibly active, standardized documentation of observation units about previously determined questions that may be expanded in the further course, for which a precise correlation to the target population may be described transparently [4]. Active, standardized documentation means that data assessment is performed prospectively by staff belonging to the registry or specifically entitled. A high level of standardization of all applied methods (data assessment, data entry, evaluation, reporting) is expected. Observation units are single persons (patients or healthy subjects), groups (persons, treatment institutions such as hospitals), or other entities (e. g. biomaterial). All observation units of the registry emerge from the so-called source population that has to be precisely characterized (e. g. based on the region, basic disease, therapeutic measures, age, gender, period, exposition etc.). The group about which a statement should be found is called target population. Ideally, the source population of the re-

gistry is identical to the target population in the sense of external validity (representativeness) [4, 5]. Registries have to be differentiated from cohorts and randomized clinical trials (RCTs). RCTs are experiments comparing diagnostic or therapeutic interventions with a control procedure regarding a specifically selected patient group in a highly standardized environment. RCTs are the gold standard for evidence of effectiveness and safety of innovative therapies [6]. A cohort is a representative cross-section of subjects, e. g. birth cohort, school enrolment cohort, or a cohort that is representative for the entire population. These cohorts allow investigating the development of diseases, differences between sick and healthy subjects as well as people with and without risk factors [7]. The largest and best-known cohort study is the Framingham Heart Study that since 1948 performs a systematic examination of the population of the town of Framingham (Massachusetts, USA) with regard to origins and risks or coronary heart disease and arteriosclerosis [8].

The term of "registry" emphasizes the data conserving aspect while cohort studies are focused on knowledge gain. Registries include subjects with a certain disease, such as for example midfacial fractures, or with a particular healthcare situation, e. g. cochlea implantation (CI). The objective is a nearly complete or at least representative image of the total population. Hence, a registry reflects the effectiveness of an intervention of routine healthcare provision [9, 10]. Another difference between cohort and registry is the implementation of data assessment: a registry contains information and knowledge from regular patient healthcare without performing interventions. In contrast, cohort studies only conduct the research project under controlled conditions, own research staff, and defined investigators.

2. Objective of Registries

The objective of registries is the scientific assessment and analysis of healthcare provision and the health status of the population. Disease-, product-, quality-, and population-based registries may display the healthcare reality and its changes.

2.1. Description of epidemiological correlations and differences

Epidemiological, population-related registries are the most central data basis for incidence, regional distribution, and temporal development of certain diseases in the population (e. g. epidemiological cancer registries). In this way, prevalence, incidence, or distribution and course of diseases are characterized, possible causes of diseases are investigated, and the risk factors influencing the disease as well as regional differences and temporal changes are identified [11].

2.2. Support of quality management and improvement

In Germany, quality management has a central significance due to legal requirements anchored in the 5th Book of the Social Security Law (SGB V) [12]. The objective of the evaluations is the assessment and comparing description of indicators that are directly or indirectly correlated with the quality of healthcare. These comparisons allow conclusions regarding differences in the healthcare situation (treatment quality, overuse, underuse, and misuse of healthcare services) and evaluation of the quality of diagnostics and therapy with reference to guideline-based treatment.

2.3. Support of clinical research

Registries support clinical research by observing and evaluating the effectiveness, safety, efficiency in the healthcare routine. Registry data may serve as basis for clinical research: beside generating hypotheses and planning case numbers, registries can be used as sampling frame [4]. Moreover, hybrid designs (RCTs plus registry) – also the combination of experimental and observing investigations – provide the possibility of complementary addition by embedding a small group of homogenous patients in a larger patient group in which the effectiveness can also be measured in the healthcare routine [13].

2.4. Evaluation and monitoring of patient safety and effectiveness in healthcare provision

Due to their mostly high numbers of cases and long duration, registries present the possibility to assess the occurrence of rare and/or delayed results, complications, and/or drug interactions up to product defects in a statistically valid and significant way. In addition, there is the option to achieve evidence on the safety within patient groups that usually do not participate in clinical trials. Those include pregnant women, children, older people, but also severely/mildly sick individuals and/or patients with comorbidities/multimorbidity or accompanying medication [14, 15].

2.5. Economic evaluation

Evidence on the effectiveness and efficiency of interventions can be found by means of registries. One example is the utilization of certain medical services by patients. In addition, registries provide health-economic data on specific interventions over a longer period that otherwise could only be roughly estimated because of missing evidence. The assumption of guideline-based therapy is another example [16].

2.6. Minimum quantities

A possible correlation between the number of surgeries performed in a hospital and the mortality after the intervention was revealed for the first time in the US American literature 20 years ago. The mortality in hospitals performing a high number of certain interventions was lower than in those with low quantities [17, 18]. In Germany, the principle of self-management is applicable. The government provides the legal conditions and tasks; the insured and financially contributing parties as well as the service providers, however, organize themselves in associations that are self-responsible for medical care of the population [19]. According to the SGB V, a catalogue of predictable services shall be established. Hereby, the quality of the treatment outcome depends particularly on the quantity of the performed service. The Institute for Quality and Efficiency in Healthcare (IQWiG) has already performed regression-analytic calculations for coronary surgery and knee arthroplasty (www.iqwig.de). By analyzing the healthcare quality in dependence of the frequency of interventions, registries may contribute relevantly to the establishment of evidence-based minimum quantities.

3. Registry Development

Registries are different with regard to their form, their assessment methods and tools. Specific questions and objectives are an essential basis for the development of registries. Beside financial, staff-related, and time resources of the research institution, the knowledge of structural and processual conditions of national and regional healthcare systems as well as legal and regulatory requirements have to be exactly defined. The registry protocol documents the results of single steps according to internationally acknowledged guidelines [20–22] and describes in detail all single phases of the procedure [4].

3.1. Planning phase

Beside the definition of the question, the objective of the registry for clinical research has to be clarified in the planning phase. The data assessed in the registry can be classified into the categories of patient, treatment, outcome, and general conditions. The characteristics that have to be analyzed should be target values, interesting influencing parameters, potentially disturbing factors (confounder/effect modifier), or data required for administration. Inclusion and exclusion criteria define the source population and the evaluation collective. Often, registries are planned for large collectives. In the sense of a reflected use of resources, the basic principles of sample size estimate should be taken into consideration. The assessment procedure has to be defined with regard to type and number of evaluation centers, reporting channels (paper-based, electronic, automated interfaces) as well as the duration and organization of follow-up. Competence and responsibility referring to organization, conduction, quality management, statistics, reporting, and publication have to be determined previously. Secure financing of the registry presents a relevant part of planning because it is essential for the later operation of the registry. Besides financing by national public sponsors, foundations, cost bearers, or federal states, generally also financing by industrial enterprises can be imagined. Financing of existing registers will be elucidated in the paragraphs on the respective registries.

3.2. Draft phase

In the draft phase, the variables elaborated in the planning phase have to be implemented in a logic data model. Essential variables or characteristics have to be differentiated from less relevant ones because with higher data variety the risk of incomplete and invalid datasets increases. The definition of indispensable core data elements ensures a complete minimum dataset for all patients. Possibly resulting disregard of certain variables may cause problems for later evaluation. The creation of respective assessment documents and forms (electronic, paper-based), the definition of pseudonyms for pseudonymized storage as well as the retention of identifiable data (registry central, registration centers, trustees) have to be discussed. Data management serves for systematic organization, quality assurance, and validation of registry data. To achieve a possibly high recruitment rate, the inclusion of registry participants over several levels/healthcare pathways (e. g. hospitals, practices, pharmacies) may be suitable. In order to realize a target sample size with voluntary participation of patients and/or registry subjects, well-planned strategies are essential for recruiting and sustainable motivation.

3.3. Implementation phase

Main objectives in the implementation phase are the renting of rooms, acquisition of staff, purchase of hardware, realization of online applications, and contracting with the assessment centers. The onset of the registry operation starts as soon as the assessment centers are ready for recruiting and the registry central disposes of the infrastructure and functions to include inscriptions.

4. Technical Organization of a Registry

The following different levels with clear interfaces to support the sustainability of the registry are defined for the conception of the registry management [4].

4.1. Hardware

A registry should dispose of 2 servers. While the first server provides the productive environment, the second one secures an identical environment for the case of the first server's failure.

4.2. Software

The selection of the appropriate software for systematic assessment is an elementary aspect. The so-called remote data entry is a computer-based system for data entry from the distance that is conceived for the assessment of electronic data. If the registry pursued a defined reporting strategy similar to clinical trials, electronic data capture (EDC) systems may be considered. However, if the registry intends patient-accompanying documentation, a system with realization of electronic health records is suitable [23].

4.3. IT management

Information technology management (IT management) should be conducted by a chief information officer (CIO) with specific expertise regarding management and operation of computer-based application systems in healthcare.

4.4. Registry operations

The main tasks of registry operations encompass the creation and maintenance of assessment and presentation forms, user administration, data control, verification and correction, providing trainings, dunning, archiving as well as generating regular reports.

4.5. Management

The management board represents the registry and requires a close connection to the bearer. High levels of identification and experience with the specific objectives of the registry are essential.

5. Evaluation

During the evaluation process of primary data, the application of mathematical-statistical methods does not differ from other scientific investigations. Because of the complex data structure, registries with repeated prospective data assessment (follow-up) and inclusion via multiple institutions (multicenter) often require particular multivariate methods of analysis.

5.1. Description

The primary work of a registry encompasses the socio-demographic and clinical characterization (baseline description) as well as its treatment and outcome. Hints to statistical precision or uncertainty of the results should be contained in the descriptive analyses, preferably in form of confidence intervals. The data quality should be presented transparently by mentioning type, frequency, and outcome of necessary queries, statements on data concordance (congruence of registry and original data), and plausibility (consistency of registry data) [24].

5.2. Methods for adjustment

Statistical results of group-comparing analyses can be biased by confounding or effect modifying variables with unequal structures of the observed groups. Potentially existing structural inequalities can be balanced by means of various control and/or adjustment procedures [25–30].

5.2.1. Stratification/subgroup analyses

Stratification is defined as the classification of the registry collective based on at least one potentially confounding or effect modifying variable in subgroups. Consequently, regarding the stratification variables, the subgroups are equivalent or homogenous. A rapidly growing number of subgroups and thus the increasing probability for incidental findings with at the same time reduced power setting is a problem in the context of this type of analysis.

5.2.2. Matching

Matching characterizes a procedure to form groups that are homogenous in at least one potentially confounding or effect modifying variable. The comparability of the groups increases with higher numbers of matching criteria. However, the identification rate decreases for identical group members so that the analysis can only be performed in a subsample of comparable group members. A balanced number of matching criteria and size of the matched control group is essential.

5.2.3. Propensity Score

The propensity score is a statistical matching technique in order to control systematic differences or biases between comparison groups so that the affiliation probability to one group may be given.

5.2.4. Standardization

The subsequent adaptation of the result of stratified groups regarding a potentially confounding or effect modifying variable with an identical stratified comparison population is defined as standardization.

5.2.5. Multivariate modeling

Multivariate models allow the simultaneous definition of the relationship between group and outcome. Potentially confounding or effect modifying variables may be integrated in theoretically unlimited numbers as so-called co-variates (statistical control, risk adjustment). Their effect on the outcome is then quantified in a statistically correct way (effect adjustment).

5.3. Modeling of longitudinal data structures

In the context of evaluation of repeatedly assessed data, the dependence between multiple assessments (follow-ups) has to be checked with statistical models for repeated measurements or time-to-event models.

5.4. Adjustment for multiple statistical testing

The control of the type 1 error probability should be performed by respective adjustment procedures, e. g. Bonferroni correction, in cases of repeated interim evaluation or statistical test between several registry groups.

5.5. Control of cluster effects

Potential effects regarding reporting institutions such as hospitals vs. practices or institutions with high or low reporting should be controlled by multi-level models (e. g. hierarchic linear models) in registries with multicenter reporting structure.

5.6. Data mining

Data mining means the systematic application of statistical methods and procedures of pattern recognition on registry data with the aim of identifying new interconnections and trends of previously unknown correlations, independently from a hypothesis.

6. Reporting

Regular and current communication of the registry findings to all interest groups is highly relevant. Feedback on the registry process optimizes the motivation of the reporting institution as well as of the patients [4].

6.1. Feedback to reporting institutions

Regular feedback to the single reporting institutions should contain the quantity and quality of the provided data. Furthermore, the interest situation with contents-related evaluations together with “benchmarking” of the providing institutions should allow a structured, indicator-related comparison of the performance. The therapeutic behavior of involved reporting institutions can be influenced by feedback in the course of registry operation.

6.2. Patient information

If the evaluations of the registry lead to potentially relevant findings for the individual patient, this information can be forwarded to the reporting institutions involving also the ethical commission or to the patient even including a trustee based on preliminary regulations.

6.3. Public reports

Fundamental evaluation results of registries should be made available to the public in a suitable way. In order to adequately answer questions on risk stratification, the evaluation of the results to be published should involve the target groups (e. g. patient organizations).

6.4. Scientific results

After checking and evaluating, relevant registry data should be made available to science in form of congress contributions, publications, and annual reports. If interested scientists need registry data, an application should be submitted to the registry describing the aim of the investigation. According to the definition of type and extent of the data as well as rights and obligations of the data recipient, they are provided with an offline access.

7. Data Protection, Legal and Ethical Aspects

7.1. Data protection

On May 25, 2018, the European General Data Protection Regulation (GDPR) as well as the new German Federal Data Protection Act (Bundesdatenschutzgesetz, BDSG), and far-reaching modifications of the data protection regulations of the 10th book of the Social Security Law (SGB) became effective [31]. The new data protection act protects registry participants towards inadmissible processing or publishing of personal data and preserves the right of informal autonomy. Data protection regulations are mainly determined by the possible identification of a certain person based on transferred and stored data. The following steps of data management are differentiated [4]:

7.1.1. Clear text storage

Medical data allowing direct conclusion on the identity of the person in clear text may only be stored exclusively with the patients' written consent.

7.1.2. Anonymization

Data stored in an anonymized way can no longer be decoded and thus do not allow a direct relation to the patient. Personal data are highly protected in the context of anonymization. An essential disadvantage of this data storage system, however, is that data fusion from several sources or at different times (follow-ups) becomes impossible.

7.1.3. Pseudonymization

In the context of pseudonymization, names and other identification characteristics are replaced by a clear code (pseudonym), which impedes identification or at least makes it difficult. Personally identifiable data are generally separated from medical data. In contrast to anonymized storage, decoding is possible. After verification based on data protection regulations, subsequent merging of the data is possible. Pseudonymization, which must be consented by the patients, is often a scientifically justified and necessary way to strike the balance between clear text storage with open data and anonymization.

7.2. Data protection concept

All aspects regarding data protection have to be presented to the respective state data protection commissioner in form of a data protection concept. This data protection concept should contain the basic principles of registry development (see chapter 3) with particular focus on the objectives, the expected benefit, patient information, and consent. Furthermore, data on anonymization/pseudonymization and data transmission as well as data storage and management must be displayed.

7.3. Patient information and consent

After sound information, enrolled patients have to give their written consent. This consent is composed based on short and understandable patient information and the declaration of the consent. Patient information should focus on the following aspects:

- Title of the registry
- Objective, purpose, and possible benefit of the registry
- Duration and process of participation
- Possible risks
- Data on data protection and user group
- Voluntary character of participation vs. legal obligation of reporting
- Option of revocation
- If applicable, remuneration/reimbursement
- Data on legal status and responsible body
- Contact data for possible questions

7.4. Ethical aspects

The early integration of the ethical commission for registry development is recommended. The primary objective of the ethical commission is the consulting service for involved physicians regarding the registry. An informal query to the responsible ethical commission with presentation of the data protection concept and the description of the scientific question of the registry is often sufficient. Hereby, the focus is placed on data protection aspects in the context of collecting and assessing registry data. It is recommended to initially apply for an ethical vote in one of the participating centers and to include the required modifications regarding the design of the registry. The positive vote of one center generally facilitates the decision for the ethical commissions of other participating registry centers.

In general, for the evaluation of the ethical commission, structured application forms are necessary that are locally different and defined by the statues of the respective ethical commission. They always contain a synopsis of the project plan, patient information, and an informed consent with data protection declaration. If data are assessed in children, the people who have custody of the child receive particular information and declarations of informed consent.

The later use of ethically perfect data fosters confidence in patients as well as in possible sponsors and supporters of the registry.

8. Existing Registries

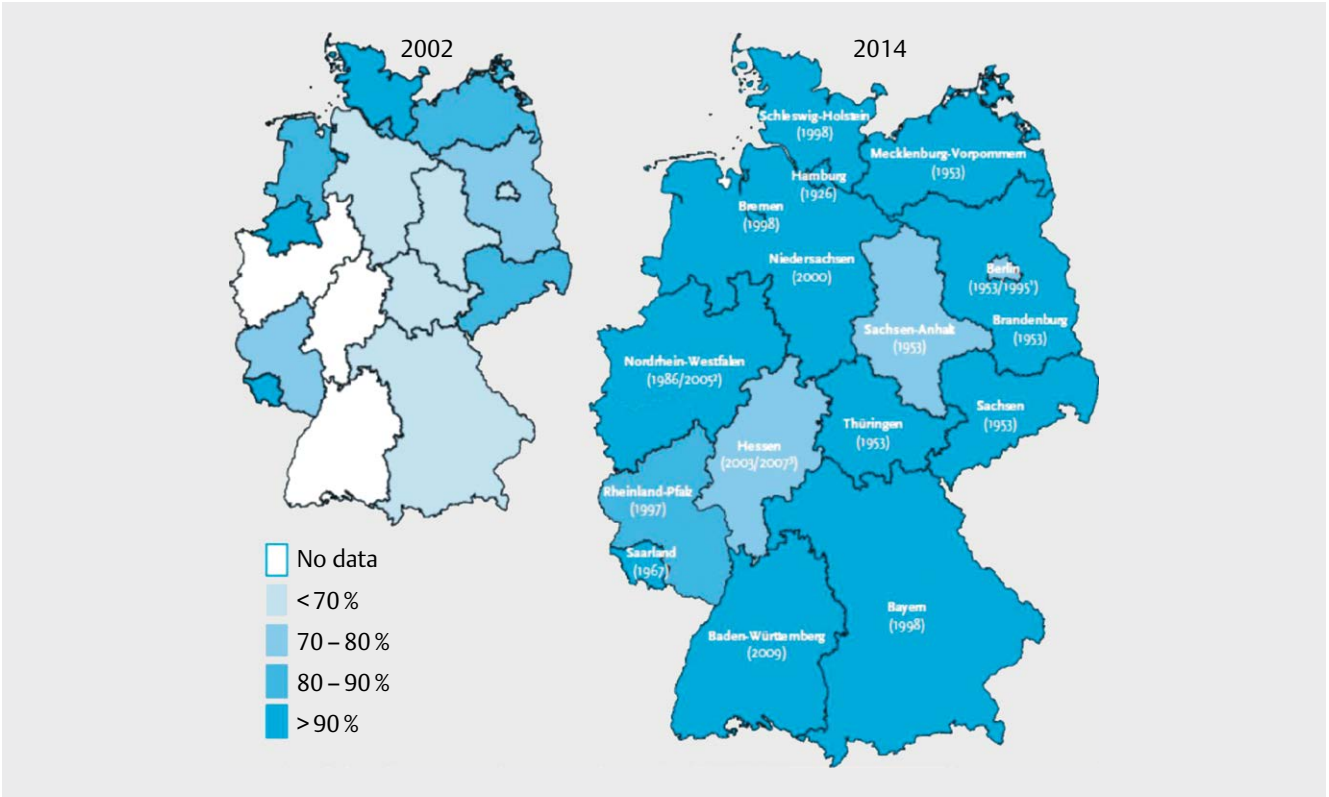
Despite their increasing significance and growing appreciation, the knowledge about existing registries is rather low [32]. A systematic overview about registries is currently not available. The knowledge about closed, open, or planned registries is mainly based on incidence, personal knowledge, publications in scientific and non-scientific journals, or online research. This lack leads to parallel developments of projects, impedes translation of knowledge from registries into research and healthcare provision, makes active contact of potential study centers and subjects with registries rather difficult, and impedes the exchange between experts of the registry operators [5]. The following registries will be described more in detail:

- Cancer
- Trauma
- Stroke
- Medical technology
- Newborn hearing screening
- Orphan diseases
- EudraCT

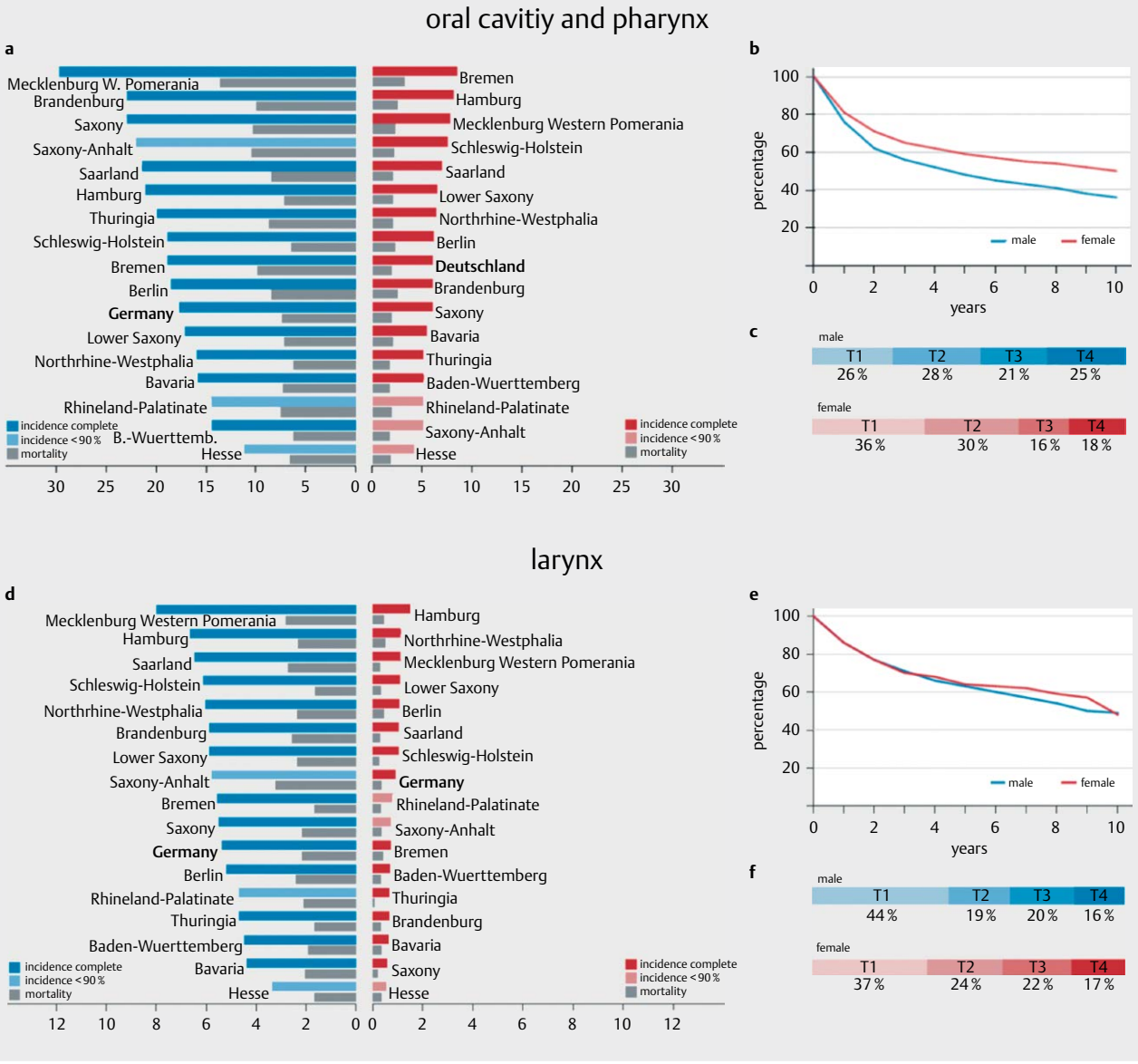
8.1. Cancer registry

The aim of the cancer registry is the systematic assessment and analysis of malignant neoplasms including lymphoma and leukemia. The difference is made between epidemiological and clinical cancer registries. Epidemiological cancer registries include the occurrence of specific cancer diseases in a defined region. Clinical cancer registries aim at improving cancer therapy by detailed data assessment of disease and therapy. In Germany, the registration of cancer diseases is regulated in federal state acts with different lengths of tradition. In 1926, the worldwide first regional cancer registry was established in Hamburg. Since 1953, the National Cancer Registry of the German Democratic Republic (Nationales Krebsregister der Deutschen Demokratischen Republik) exists, which continues since 1992 as the Common Cancer Registry (Gemeinsames Krebsregister, GKR) of Berlin, Brandenburg, Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt, and Thuringia. The cancer registry of the Saarland exists since 1967. With introduction of a cancer registry in Baden-Württemberg as last federal state in Germany in 2009, the Center for Cancer Registry Data (Zentrum für Krebsregisterdaten, ZfKD) was established at the Robert Koch Institute (▶ **Fig. 1**). "Cancer in Germany" (Krebs in Deutschland) appears every 2 years as common publication of the ZfKD and the Society of Epidemiological Cancer Registries in Germany (Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V., GEKID) [33]. The most significant epidemiological parameters as well as current trends are described for 27 different cancer entities. According to this publication, in Germany 476,120 newly diagnosed cancer patients were registered in 2014; in 2018, 493,600 are expected. In this context, ENT specific tumors are classified into the subgroups of "Oral cavity and pharynx" and "Larynx". In 2014, 12,830 patients developed tumors of the oral cavity and the pharynx (9,130 male and 3,700 female subjects) and 3,500 patients developed laryngeal cancer (2,980 male and 520 female individuals). All tumors of the upper aerodigestive tract show a difference regarding the incidence and the federal state (30 tumors of the oral cavity and the pharynx per 100,000 in Mecklenburg-Vorpommern vs. 11 per 100,000 in Hessen in males and 8 tumors of the larynx per 100,000 in Mecklenburg-Vorpommern vs. 3.3 per 100,000 in Hessen). The reason is seen in a significantly higher consumption of alcohol and tobacco (▶ **Fig. 2a** and **d**). In female patients, tumors of the oral cavity and the pharynx have a higher relative 5-year survival rate with 59 % compared to 48 % in males (▶ **Fig. 2b**). In more than 1/3 of the female patients, tumors of the oral cavity and the pharynx are diagnosed in an early stage (T1), however, in males this rate amounts to only one out of four (▶ **Fig. 2c**). The relative 5-year survival rates of male laryngeal cancer patients (63 %) and females (64 %) are not significantly different (▶ **Fig. 2e**). With 44 %, a higher percentage of early tumor stages (T1) at the time of diagnosis is achieved for male patients compared to females with 37 % (▶ **Fig. 2f**).

Since the introduction of the Cancer Screening and Registry Act (Krebsfrüherkennungs- und -registergesetz, KFRG) adopted in April 2013, the clinical cancer registration in Germany is reimbursed at 90 % by the statutory health insurances, the remaining part is paid by the federal state governments. For financing of epidemiological



▶ **Fig. 1** Development of the estimated comprehensiveness of epidemiological cancer registries of the single federal states in Germany from 2002 to 2014. Quelle: Gemeinsame Publikation des Zentrums für Krebsregisterdaten und der Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V. Krebs in Deutschland für 2013/2014. 11. Ausgabe. Robert Koch-Institut, Berlin 2017 [rerif].



▶ **Fig. 2** Assessed, age-standardized rates of newly diagnosed diseases and mortality in the federal states according to the gender per 100,000; categorized into tumors of the oral cavity and pharynx **a** as well as tumors of the larynx **d**. The relative survival rate up to 10 years after first diagnosis of tumors of the oral cavity and the pharynx is significantly higher in females than in males **b**; for tumors of the larynx, the difference of the relative survival rates in males and females is not significant **e**. The distributions of the T stages at the time of first diagnosis are displayed in for tumors of the oral cavity and the pharynx and in for tumors of the larynx. Quelle: Gemeinsame Publikation des Zentrums für Krebsregisterdaten und der Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V. Krebs in Deutschland für 2013/2014. 11. Ausgabe. Robert Koch-Institut, Berlin 2017 [rerif].

federal state registries, exclusively the respective federal state governments are responsible. The Center for Cancer Registry Data of the Robert Koch Institute is paid by federal funds.

In 1966, the single cancer registries of different nations and regions formed the International Association of Cancer Registries (IACR) with its head office in Lyon/France [34]. In analogy to the publication on cancer in Germany [33], the World Cancer Reports of 2014 classified head and neck cancer into cancer of the oral cavity and the pharynx as well as laryngeal cancer. In 2012, the number of worldwide newly diagnosed cancer diseases is estimated to 529,000 for tumors of the oral cavity and the pharynx as well as 157,000 for laryngeal carcinomas. The highest incidence for tumors of the oral cavity and the pharynx is found in Papua New Guinea, Bangladesh, Hungary, India, and Sri Lanka; laryngeal carcinomas are mostly found in East Europe, Kazakhstan, and the Caribbean.

8.2. Trauma registry

The Trauma Registry of the German Society for Trauma Surgery (TraumaRegister – Deutsche Gesellschaft für Unfallchirurgie, TR-DGU) is an association of 675 trauma hospitals in Germany, Austria, Switzerland, and Belgium. Inclusion criterion of the TR-DGU is the admission of patients via shock room with subsequent intensive care. The most important parameters for the TR-DGU are the morta-

lity, the duration of hospitalization, and the health condition or the disability degree at the time of discharge. The objective of the TR-DGU is to predict the survival prognosis already at the time of admission for every patient based on the injury pattern and severity. The basic cohort of the registry consists of more than 240,000 patients who were treated during the last 10 years (2008–2017). In 2017, 29,396 patients were registered in the TR-DGU. The mean age amounted to 51.6 years; 70 % were male and the mortality prognosis was 10.1 %. Until 2017, more than 330 scientific articles have been published out of the TR-DGU that clearly influenced the medical treatment of severely injured people. This includes the reduced volume loading in the preclinical first-aid support, ultrasound of thorax and abdomen (Focused Assessment with Sonography for Trauma, FAST), the introduction of whole-body computed tomography in the shock room, the standardized training concept (Advanced Trauma Life Support, ATLS) as well as the early treatment of injury-related coagulation disorders [35].

8.3. Stroke registry

The Workgroup of German Stroke Registries (Arbeitsgemeinschaft Deutschsprachiger Schlaganfall-Register, ADSR) is a consortium of the regional stroke registries of Baden-Württemberg, Bavaria, Berlin, Erlangen, Hamburg, Hessen, Nordrhein, Northwestern Germany, Rheinland-Pfalz, and Schleswig-Holstein for the assessment of standardized data on stroke. An association of the single registries to one large stroke registry has not been realized up to now [36].

8.4. Medical technology registry

In the field of medical technology, 101 registries are found in Europe. The sections of cardiology (heart pacemaker and coronary stents) (n = 38), arthroplasty (n = 29), and breast implants (n = 9) are the leading ones [37].

For cochlea implants, only the Swiss Cochlea Implant Registry exists in Europe. It was founded in 1992 by five Swiss CI centers and since 1977 it comprises 3,096 implantations (▶ **Table 1**) [38]. Audiological speech test conditions for children (monosyllable, trochee, polysyllable [MTP] test) as well as for adolescents and adults (Freiburg monosyllable test) were defined in a common workgroup of the five CI hospitals in Switzerland. 67 % of the children reached discriminations between 80 and 100 % in the MTP test; more than half of the adult CI patients had a word understanding of more than 50 %.

8.5. Newborn hearing screening

The universal newborn hearing screening was introduced nationwide in 2009; since September 2016 it is part of the directive for children (Kinderrichtlinie, §§ 47–57) [39]. The final report on the evaluation of the newborn hearing screening of 2011/2012 dated January 15, 2017, showed that in 2012 a newborn hearing screening could be documented in 82.4 % (554,578) of the children. Significant differences between the single federal states could be observed. While in Baden-Württemberg 42.8 % and Niedersachsen 37.9 % of the newborns were not examined, the percentage of non-examined newborns amounted to 0.2 % in Mecklenburg-Vorpommern and to 0.7 % in Sachsen-Anhalt. In 3.7 % of the children with conspicuous screening result, a hearing disorder was diagnosed; in 56.2 % hearing disorder could be excluded, and in 40.1 % no final result was documented ("lost to follow-up"). The prevalence of a bilateral, permanent, congenital hearing disorder was estimated to 1.3:1,000 newborns based on present data. Up to 7 % of the children with diagnosed hearing disorder had an inconspicuous screening. In 2012, the sensitivity amounted to 95.1 %, the specificity to 97.1 %, and the positive-predictive value to 6.2 % [40].

▶ **Table 1** Age distribution and number of cochlear implantations of the Swiss cochlea implant registry.

	0–3 Jahre	3–12 Jahre	12–18 Jahre	18–65 Jahre	>65 Jahre	
Gesamt	534	675	201	1282	404	3096
bilateral	183	183	43	206	25	640

8.6. Registry of orphan diseases

Most registries exist for orphan diseases, since clinical trials are rather difficult to conduct. Currently, there are 846 registries of different quality with various objectives and concepts [41].

8.7. EudraCT – Registry for clinical trials

EudraCT (European Union Drug Regulatory Authorities Clinical Trials) is a registry for clinical drug studies conducted in the European Union. It exists since 2004. EudraCT is operated by the European Drug Agency and used for approval and monitoring of clinical trials by the drug authorities of the member states.

The EudraCT registry was established to increase the transparency of clinical trials conducted in the EU and to improve the security for study participants by better monitoring. The legal basis for its structure is article 11 of the directive 2001/20/EG for application of good clinical practice (GCP). GCP defines for Germany that the approval may only be applied for when a planned clinical trial has been registered in EudraCT. The registry is active since May 1, 2004, and as of October 2018 more than 55,355 trials have been registered [42].

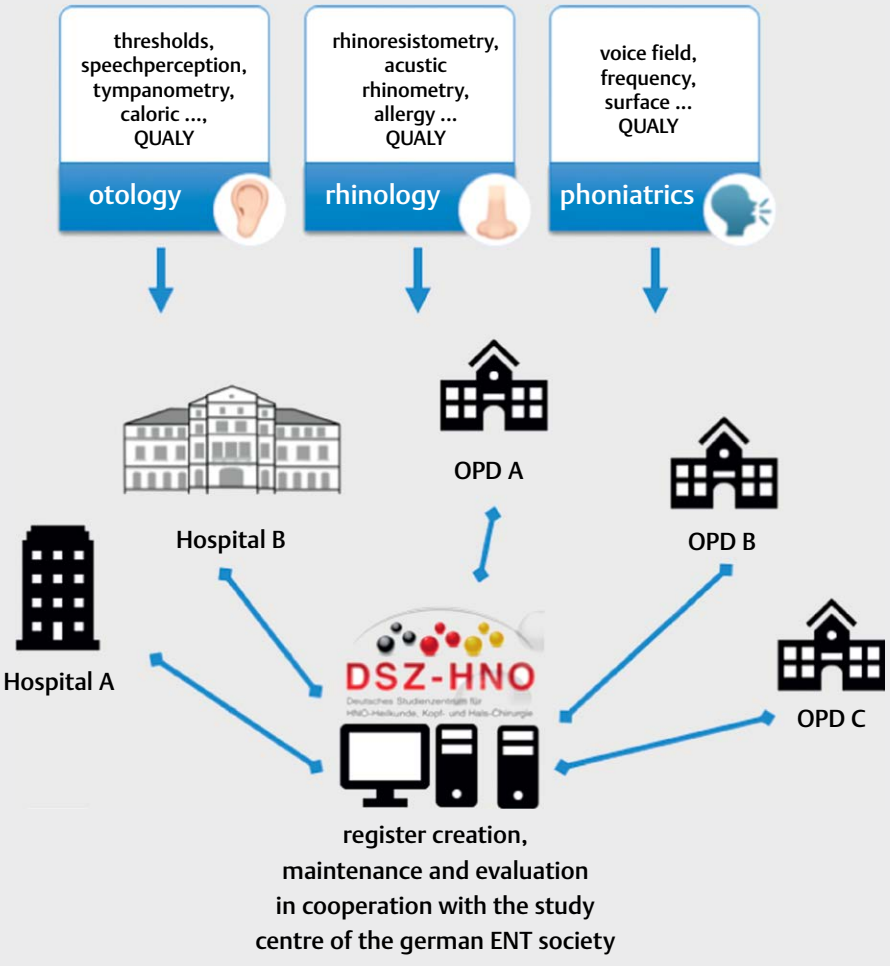
9. Outlook

The application and utilization possibilities of registries are manifold. Physicians in hospitals, private practices, and research, scientists, and medical associations use registries as basis for preventive measures, clinical questions, quality management, healthcare research, and politics. Up to now, oto-rhino-laryngology is not significantly involved in the work of registries. This is reflected by the fact that the DGHNO is the only medical professional society that is not member of the DNVF. The membership and active participation of the DGHNO in the DNVF is an objective that should be pursued as soon as possible.

In Germany, the section of ENT specific oncology is sufficiently represented by the cancer registry. The systematic registration of the newborn hearing screening is currently further developed. A drastic reduction of the non-examined newborns in all federal states as well as the improved quality of data assessment is necessary to avoid that newborns with relevant hearing disorder are not identified.

The white paper on cochlea implantation [43] that has been established by the presidency of the DGHNO in April 2018 contains recommendations on the structure, organization, equipment, qualification, and quality management in the treatment of patients with CI in Germany. The treatment of patients with high-grade congenital or acquired hearing impairment or deafness is a complex process that is only successful with the support of audiological, pedagogical, technical, and medical expertise within a cochlea implanting institution. The process of CI includes the preoperative care and consultation, implantation, postoperative basic and consecutive therapy as well as life-long follow-up. Failures in the CI treating process lead to missing or insufficient hearing and speech development of affected children, an insufficient quality of the outcome, reduction of the quality of life, loss or lacking recovery of socialization and ability to work as well as medical complications. The white paper on cochlea implantation is meant to be a future basis for certification of cochlea implanting institutions as well as the foundation of a national CI registry. The data collection of the CI registry is subdivided into the following 9 data blocks.

1. Basic data (treating institution, patient ID, pseudonym, date of birth, gender, mother language)
2. Preoperative audiometry (audiogram [500, 1000, 2000, 4000 Hz]; Freiburg test for numbers; Freiburg test for monosyllables [65, 80, 100 dB SPL])
3. Preoperative hearing history (hearing loss since birth, childhood, adolescence, adulthood, hearing loss/deafness in years [0–1, 1–5, 5–10, 10–20, >20]; use of hearing aids with CI)
4. Implantation (date of implantation; implant manufacturer; serial number)
5. Surgery (date of surgery; primary/revision surgery; electrode insertion [round window, cochleostomy]; insertion depth [partial, complete]; radiological control [conventional X-ray Stenvers, CBT, CT scan])
6. CI-related complications (malposition of the electrode requiring revision; facial paresis; inpatient admission; meningitis; death)
7. Use of CI and progress of rehabilitation (patient presented for follow-up; duration of CI use [in hours per day] based on patient's report/data logging; current rehabilitation status [basic therapy, consecutive therapy, follow-up])
8. Postoperative audiometry (time after CI in months; audiogram without CI; use of acoustic components/EAS; contralateral side in cases of residual hearing occluded/masked; Freiburg



▶ **Fig. 3** Possibilities of implementation of registries in the discipline of otorhinolaryngology.

monosyllables test with CI at 65 dB SPL; sentence tests [OlSa, GöSa, HSM] in silence or in noise)
9. Quality of life (modified/translated "Nijmegen Cochlear Implant Questionnaire" [NCIQ])

Due to the assessment of multiple parameters in nearly all aspects of the discipline, otorhinolaryngology presents excellent preconditions for implementation of registries. Completeness, comprehensiveness, and high data validity significantly determine the quality of registries. The basis is the positive vote and acceptance of the registry by patients as well as reporting institutions. This has to be taken into consideration when planning and developing registries. In otology, numerous subjective and objective audiological test procedures exist. If test parameters were standardized, e. g. the conduction of the Freiburg speech understanding at 65 and 80 dB, the implementation of registries for the topics of "chronic otitis media", "active middle ear implants", "sudden hearing loss", or "vestibular schwannoma" could be imagined. Also the systematic registration of vertigo with vestibular genesis, allergology, rhinology, and phoniatrics are a basis for prevention and therapy. Especially those established, standardized, and entirely digitally and metrically stored measurements allow the creation of registries in a unique way (▶ **Fig. 3**).

With the historic background and the long tradition of our discipline with all its manifold therapeutic procedures that are partly applied since long time and often even in an unmodified way, the scientific evidence-based confirmation and verification by means of registries is an unparalleled chance for the further development of otorhinolaryngology.

Conflict of Interest

The author states that there is no conflict of interests.

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