

Quality of Care for Salivary Gland Diseases




Author
Orlando Guntinas-Lichius

Affiliation
Department of Oto-Rhino-Laryngology, Head & Neck
Surgery, Jena University Hospital, Germany

Key words
Salivary glands, quality indicators, quality management,
clinical registry, evidence-based medicine, clinical guidelines

Bibliography
DOI <https://doi.org/10.1055/a-1012-9420>
Laryngo-Rhino-Otol 2020; 99: S319–S335
© Georg Thieme Verlag KG Stuttgart · New York
ISSN 0935-8943

Correspondence:
Univ.-Prof. Dr. med. Orlando Guntinas-Lichius
Department of Oto-Rhino-Laryngology
Jena University Hospital
Am Klinikum 1
07747 Jena
Germany
Tel.: +49 (0) 3641/9329301, Fax: +49 (0) 3641/9329302
orlando.guntinas@med.uni-jena.de

ABSTRACT

The treatment of salivary gland diseases represents an important segment of otorhinolaryngology. The individual otorhinolaryngologist might, however, see only a few cases per year from a large variety of salivary gland diseases. Surgical and endoscopic minimal-invasive therapy concepts play a key role. Therefore, gain of knowledge cannot only be provided by prospective clinical trials but also by meta-analyses and potentially also by registry data. Many reliable indicators are established to measure the function of a diseased salivary gland or the improvement of its function after therapy. In contrast, patient-reported outcome measures (PROMs) are not sufficiently developed. It has to be demanded that these indicators are consequently used in clinical trials. Perspectively, the same indicators could also be used for quality control for the outpatient and inpatient sector in clinical routine. The framework conditions for high-quality acquisition of knowledge are given by the otorhinolaryngology specialist medical training, the obligation of life-long continuous medical education, and certified salivary gland courses. Nevertheless, the specifications of quality standards for the treatment of patients with salivary gland diseases are not well formulated. In contrast to other disciplines also addressing salivary gland diseases, otorhinolaryngology ought to develop standards with high requirements of quality of care for salivary gland diseases.

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ABKÜRZUNGEN

AOK	Allgemeine Ortskrankenkasse
AWMF	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (Scientific Medical Societies in Germany)
CI	95% Confidence Interval
CODS	Clinical Oral Dryness Scale
COSS	Chronic Obstructive Sialadenitis Symptoms Score
CT	Computed Tomography
DEGAM	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (German Society of General and Family Medicine)
DEGUM	Deutschen Gesellschaft für Ultraschall in der Medizin e.V. (German Society of Ultrasound in Medicine)
DGHNOHC	Deutsche Gesellschaft für HNO-Heilkunde, Kopf- und Hals-Chirurgie (German Society of Oto-Rhino-Laryngology, Head & Neck Surgery)
DGMKG	Deutsche Gesellschaft für Mund-, Kiefer- und Gesichtschirurgie (German Society of Maxillofacial Surgery)
DQ	Drooling Quotient
DSFS	Drooling Severity and Frequency Scale
EBM	Evidence-based medicine
ENT	Ear, nose, throat
EORTC	European Organization for Research and Treatment of Cancer
ESGS	European Salivary Gland Society
ESSPRI	European League Against Rheumatism SS Patient-Reported Index
EXPeRT	European Cooperative Study Group for Pediatric Rare Tumors (
G-BA	Gemeinsamer Bundesausschluss (Federal Joint Committee)
GBI	Glasgow Benefit Inventory
HRQoL	15D health-related quality of life instrument
ICER	incremental cost-effectiveness ratio
ICF	International Classification of Functioning, Disability and Health
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KTQ	Kooperation für Transparenz und Qualität im Gesundheitswesen (Cooperation for Transparency and Quality in Healthcare)
MRI	Magnet Resonance Imaging
MSGS	Multidisciplinary Salivary Gland Society
NSQIP	National Surgical Quality Improvement Program
OR	Odds Ratio
POI-8	Parotidectomy-outcome-inventory-8
PROM	Patient-reported outcome measure
QALY	Quality-adjusted life year

QM	Quality management
QM-RL	Qualitätsmanagement-Richtlinie (quality management guideline)
QSR	Qualitätssicherung mit Routinedaten (quality management by means of routine data)
ROC	Receiver-Operating-Characteristic
RT	Radiotherapy
SF-8	Short-Form-8 Health Survey
SF-36	Short-Form-36 Health Survey
SGB	Sozialgesetzbuch (Social Security Code)
SSI	Sicca Symptoms Inventory
STEP	Seltene Tumorerkrankungen in der Pädiatrie (Rare Cancer Diseases in Pediatric Patients)
UWQOL	University of Washington Quality of Life
WIdO	Wissenschaftliches Institut der AOK (Scientific Institute of the AOK)
XI	Xerostomia Inventory
XQ	Xerostomia Questionnaire

1. Introduction

In his introduction of the motto of the Annual Meeting of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery, of 2020, Professor Andreas Dietz refers to a quotation of the US-American Institute of Medicine, National Academy of Sciences regarding the quality concept in the context of the treatment of ENT specific diseases. The quality of care is defined as “the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge”. Three important aspects are indicated for high-quality care. First, there is the healthcare service, i.e. the protagonists in healthcare systems such as ENT professionals, nurses, speech therapists but also the structure of the healthcare system itself. Then there are the patients and their desires regarding recovery. And third, the knowledge is mentioned, more concretely, the current professional knowledge. A major part of ENT specific care encompasses the treatment of salivary gland diseases. In the inpatient sector alone, the surgery rates for resections for example of benign salivary gland tumors alone amounted to 10.1 per 100 000 inhabitants between 2007 and 2011, and even for sialolithiasis to 2.1 per 100 000 inhabitants [1]. So an assessment of the quality of care is helpful also in this field of ENT specific diseases in order to further improve the treatment. With regard to diseases of the salivary glands and the quality of treatment, concrete questions have to be asked:

- Which preconditions and knowledge must ENT specialists, other people involved in the treatment, also other healthcare professional, and ENT departments have in order to assure an optimal care for patients suffering from salivary gland diseases?
- What are the patients’ desires regarding their recovery? This also leads to the aspect of the function of the salivary glands, the symptoms of diseases of the salivary glands as well as the adverse effects and complications of treatment. Generally, patients desire an alleviation or even the disappearance of the

► **Table 1** Possibilities of quality assurance in training and education regarding treatment of salivary gland diseases.

Instrument	Comment
ENT specialization	No detailed requirements. It is recommended that responsible teachers and trainers define internal competences that should be acquired.
Course on ENT specific knowledge	The current course provided in Germany also deal with salivary gland diseases; there are not requirements regarding the contents.
Test of ENT specialization	No detailed requirements. It is recommended that the examiner queries the knowledge about salivary gland diseases.
Course on salivary gland diseases	Certification by the State Chamber of Medicine and by the academy of the DGHNO should be present (or equivalent certification of international courses). It is recommended that certified salivary gland courses are attended in residency.
Course on head and neck ultrasound	Certification by DEGUM, State Chamber of Medicine, and the academy of the DGHNO should be present (or equivalent certification of international courses). Then the participants may be sure that ultrasound examination includes also the major salivary glands.
Manuals	Until now, there are no requirements for content-related quality. The current German manuals are based on knowledge about salivary glands summarized by experts in this field. The editors and sometimes external reviewers have checked the contents.
Medical literature	Journals with peer-review rely on a control of the contributions by reviewers. In German and English ENT journals articles, also review articles, are regularly found dealing with salivary gland diseases.

symptoms, possibly a restoration of the salivary gland function, certainly few adverse effects, and probably no complications due to the treatment.

- Which structures are already present that allow gains in knowledge regarding diseases of the salivary glands? What about the quality of the gain in knowledge? Is this knowledge included in guidelines? Where might be even a significant lack of evidence? To what extent are the patients' desires taken into account? Is the gain in knowledge implemented in the healthcare system?

In order to answer these questions, it is not sufficient to consider the treatment of diseases of the salivary glands according to the criteria of evidence-based medicine (EBM). EBM clarifies the validity of decision making and therapy of single diseases of the salivary glands. So this article deals with the basic conditions for service provision including the quality of training and education. Further it sheds more light to the functional loss in cases of diseases of the salivary glands because the quality of treatment must also be measured according to the degree of restoration of the possible functional loss. Therefore, also valid procedures will be described that allow measuring this functional loss and the consequences for the patients' quality of life. At the end of this article, also analyses regarding the cost-effectiveness are considered to complete the assessment; however, it must be mentioned that only few data are available on diseases of the salivary glands.

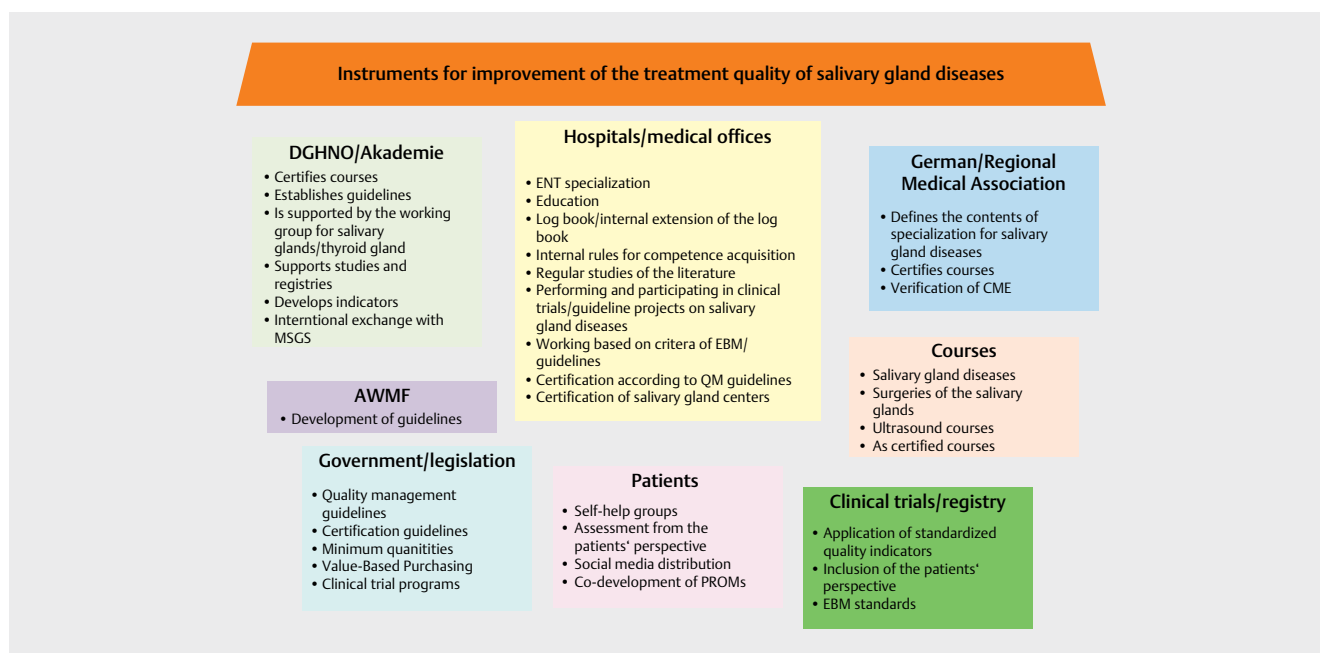
2. Training and Education

Tools of quality assurance in training and education in the context of salivary gland diseases are summarized in ► **Table 1**. The education guidelines for physicians (Weiterbildungsordnung für Ärzte) is a tool to control the treatment quality of salivary gland diseases. During the basic phase, the education guidelines of 2011 that are still valid require education regarding the identification and treatment of salivary gland diseases. At least 25 interventions of the sa-

livary glands and their excretory ducts are required during medical education. The chambers of medicine (Landesärztekammern) do not give specific statements about the type and extent of surgeries. Also the new medical education guidelines that have to be implemented in 2019 will not go more into detail. In comparison, for example the English ENT-specific curriculum describes the required knowledge in a very detailed way, however, regarding surgical interventions no concrete figures are mentioned. But the mastery of submandibulectomy and lateral parotidectomy is required (<https://www.gmc-uk.org/>). Beside this basic knowledge, the log-book for the European ENT specialization requires explicitly also knowledge of complication management, masses of the salivary glands, the correlation with facial nerve palsy, the European classification of salivary gland changes, and the classification of parotid surgery, immunological diseases, infections, salivary stones, and benign tumors. Surgical experience includes – without mentioning concrete figures – the performance under specialists' supervision of interventions of the submandibular gland and the excretory ducts, interventional sialendoscopy as well as assistance in the context of parotidectomy including reconstruction techniques ([http://orluems.com/gestor/upload/LOGBOOK %20REVISED %20FINAL %202018.pdf](http://orluems.com/gestor/upload/LOGBOOK%20REVISED%20FINAL%202018.pdf)) (► **Fig. 1**).

In the education catalogue of maxillofacial surgery, salivary gland surgery is not explicitly mentioned. 100 septic surgeries are requested and as an example the removal of salivary stones is listed. In summary, it may be confirmed that the requirements in the ENT specific education guidelines are only poorly detailed. The quality control is subject to the physician who is responsible for the education without further defining quality criteria. However, this is true for most areas of the medical education guidelines and is not specific for the education regarding the treatment of salivary gland diseases.

Beside the internal specialization, also courses are offered. In the German speaking countries, several education offers can be found in 2019, among others in Erlangen, Jena, Cologne, Munich,



► **Fig. 1** Instruments for improvement of the treatment quality of salivary gland diseases. Most structures and tools already exist and interact. There are also ideas for future elements (e.g. Value-based Purchasing programs) or requirements (e.g. standardized quality indicators). AWMF = Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften; CME = Continuous Medical Education; EBM = Evidence-based medicine; MSGS = Multidisciplinary Salivary Gland Society; PROM = Patient-reported outcome measure.

or Vienna. These courses teach current knowledge about salivary gland diseases, mostly focusing on surgery and also with live demonstration of surgical interventions as well as practical exercises with models and preparations. The German Academy for Oto-Rhino-Laryngology, Head and Neck Surgery (Deutsche Akademie für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie) provides the possibility to certify a course. Two reviewers, i.e. experts in their field, evaluate the contents and prepare a decision for the presidium of the academy. At the occasion of the annual meeting of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie, DGHNOHC), the Akademie provides in 2019 (and certainly also in 2020) two central courses on salivary gland diseases. The quality of the contents is evaluated by the presidium and the approval is granted.

Written criteria for the assessment of courses on salivary glands are not available. During the annual meeting, always sessions on most recent knowledge about salivary gland diseases take place that contribute to continuous medical education. Internationally, the Multidisciplinary Salivary Gland Society (MSGS since 2019, formerly European Salivary Gland Society [ESGS]) arranges scientific sessions on salivary gland diseases in the context of international meetings and also organizes the International Salivary Gland Congress where the most recent knowledge on salivary gland diseases is exchanged every 5 years.

Meanwhile two courses could be established for the German ENT specialization exam where the basic knowledge on salivary gland diseases is repeated. The contents are freely determined by the lecturers.

The section of head and neck of the German Society of Ultrasound in Medicine (Deutsche Gesellschaft für Ultraschall in der Me-

dizin, DEGUM) has defined quality standards for ultrasound examinations of the head and neck area (<https://www.degum.de/sektionen/kopf-hals.html>). In the DEGUM courses, ultrasound examination of the major salivary glands is taught in the module about sonography of the salivary glands. It does not only include examinations in cases of tumors but also ultrasound of infectious diseases and ultrasound-controlled interventions of the salivary glands. Knowledge about ultrasound of salivary gland diseases is taught in three consecutive courses. In order to acquire also the billing permission of the Association of Statutory Health Insurance Physicians (Kassenärztliche Vereinigung), a certificate confirming 200 sonographies of the cervical soft parts is necessary without the need to prove specific examinations of the salivary glands.

Another important source for education and training are ENT specific manuals. Experts decide about the contents regarding salivary gland diseases. For example, the current ENT surgery manual published by Rettinger et al. dedicates an own chapter to surgeries of the salivary glands [2]. Quality standards regarding the contents do not exist. Beside the classic scientific literature that undergo a quality control by a review process in peer-reviewed journals German and English ENT journals regularly provide review articles on salivary gland diseases. These review articles are also peer-reviewed, and reflect expert opinions, but mostly no higher evidence level.

In summary, this means that the quality of education and training regarding salivary gland diseases is mostly in the responsibility of experts of this field. In this area, only few consented quality requirements exist up to now.

3. Structural Preconditions, Quality Management, and Certification

According to § 137 SGB V (Book V of the German Social Security Code, Sozialgesetzbuch), every hospital approved based on § 108 SGB V has to have an internal quality management. In this context, the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) has written a quality management guideline (Qualitätsmanagement-Richtlinie Krankenhäuser, QM-RL) which was published in the Federal Gazette (Bundesanzeiger, BAnz AT 16.04.2014 B4). Here, only the basic elements of quality management are described. Single disciplines or even surgical interventions are not mentioned. Even if no obligation to certification exists, numerous hospitals have certified their quality management system for example based on the regulations that are specifically developed for the healthcare system entitled “Kooperation für Transparenz und Qualität im Gesundheitswesen“ (KTQ; Cooperation for transparency and quality in healthcare) or based on the cross-sectoral quality norm of ISO 9001 [3]. The contents for otorhinolaryngology (hospitals or offices) are not defined and thus neither for salivary gland diseases. The author’s ENT department is certified according to DIN EN ISO 9001. The quality management system contains detailed descriptions, not only in terms of organization, e.g. process of the consultation regarding salivary gland diseases, but also with regard to the workflows of the single diseases. In this way, graduated diagnostics and therapy steps for Sjögren disease may be retrieved by each staff member at any time on every hospital computer. Even if there are no regulatory obligations, an ENT department may use the (inevitable) certification in order to standardize the treatment of salivary gland diseases in the own department in a transparent and always available way.

Another interesting element is quality assurance by means of routine data (Qualitätssicherung mit Routinedaten, QSR, <http://qs-mit-routinedaten.de/>). This project of the AOK tries to measure the treatment quality of a hospital based on anonymized account data of hospitals and basic data of the AOK. The scientific institute of the AOK (WIdO) in its QSR procedure performed a panel procedure in 2015 in terms of a re-development of quality indicators for the service area of surgery of benign thyroid gland diseases. Based on data of the accounting period of 2008–2010 and the complications documented up to one year after discharge, recommendations have been developed for indicators of the internal reporting of complications (http://www.qualitaetssicherung-mit-routinedaten.de/imperia/md/qs/methoden/wido_qsr_abschlussbericht_schilddruesenoperation.pdf). The QSR methods might also be applied for frequently observed salivary gland surgeries. Such evaluations on complications have not yet been performed.

At the end of 2019, there will be 57 head and neck cancer centers in Germany that are certified based on the certification guidelines of German Cancer Society (Deutsche Krebsgesellschaft). In the data entry form, malignomas of the salivary glands were not explicitly assessed until 2018 but now they are included. A particular expertise for these relatively rare head and neck tumors is not required for certification. Furthermore, numerous ENT departments have established salivary gland centers. This term is neither defined nor protected. Generally, it means the organization of a special consultation for salivary gland diseases. The idea behind the

foundation of a center is also to provide patients with an interdisciplinary treatment in a department that is specialized in the treatment of salivary gland diseases, e.g. the interdisciplinary treatment of patients suffering from advanced Sjögren disease by rheumatologists and ENT specialists in one place at the same time. Such an institution is currently not known in Germany. Structured interdisciplinary cooperation is only observed for malignomas of the salivary glands in the context of tumor boards and in guideline creation.

Also the European Organization for Research and Treatment of Cancer (EORTC) wants to establish more QM programs for head and neck surgeons that participate in EORTC trials. In the current EORTC trial, the number of surgeries per year and the treatment outcomes (R0 resection, number of removed lymph nodes in the context of neck dissections etc.) must amount to at least 1 420 [4]. For EORTC trials about salivary gland tumors, currently not such quality standards are defined.

Already in 2008, the American College of Surgeons started the National Surgical Quality Improvement Program (NSQIP) [5]. Based on the collected data, the NSQIP risk calculator was developed [6]. After entry of several risk-associated variables, this calculator calculates the risk of postoperative complications (<https://riskcalculator.facs.org/RiskCalculator/>). Entering for example lateral parotidectomy in an otherwise healthy female patient younger than 65 years, the risk for severe complications amounts to 1.2% in the first 30 days after surgery. In cases of a comorbid female patient with insulin-dependent diabetes, the risk increases to 5.5%. The otherwise healthy patient undergoing total parotidectomy with neck dissection has a risk of 11.1%. In this way, the results of the own hospital may be compared with risk calculations and thus, referring to these parameters, the own treatment quality may be assessed.

In summary, this means that there are not specific regulatory standards for German ENT departments or offices regarding the treatment of salivary gland diseases. On the other hand, certification would generally allow a good frame for standardization of the treatment and the introduction of quality indicators for successful treatment of salivary gland diseases. It would already be positive if salivary gland malignomas and parameters such as extent of surgery, resection status, and dimension of neck dissection were documented in certified head and neck cancer centers.

4. Saliva Production in Salivary Gland Diseases

One basic parameter for the treatment quality is the preservation and/or the restoration of the salivary gland function by the treatment. The salivary glands produce about half a liter of saliva per day [7]. The functional consequences of a reduced salivation are swallowing disorders, disturbed tasting, susceptibility for oral infections and caries. The sequelae of reduced salivation on the immunologic function of the saliva have not been fundamentally investigated.

The result of too low salivation is a dry mouth. This must be distinguished from xerostomia that describes the subjective perception of the dry mouth and hyposalivation that means the reduced salivation rate [8–12]. The typically recommended clinical method

for examination is sialometry as quantitative examination of the unstimulated and stimulated overall flow rate [13]. Dry mouth is expected as of an unstimulated flow rate of <0.1 ml/min or a stimulated flow rate of 0.7 ml/min [14, 15]. In order to collect saliva, a dental roll is placed under the tongue (for examination of the submandibular gland) and one roll for each cheek pouch (for examination of the parotid gland) and left there for 5 min. Then, the rolls are weighed [16]. The correlation between a reduced flow rate and the subjective perception of dry mouth is poor [8, 14, 17, 18]. Even in healthy individuals, the salivation rate shows a high intra- as well as interindividual variability [19]. So it is recommended to additionally apply other parameters beside direct measurement of the salivation. It is not surprising that there is a lack of papers systematically comparing the measurements of saliva production and the measurements of the quality of life (see below) [13].

Although salivation is the major function of the salivary glands, only few papers are available that objectively investigate the salivation after therapy of salivary gland diseases. Most data are provided for the evaluation of therapies of Sjögren syndrome. For example treatment with pilocarpine leads to a significant improvement of the salivation rate in patients suffering from Sjögren syndrome [20].

A recently published systematic review on salivation after surgery of the parotid gland or the submandibular gland could only identify eight prospective trials (from 1993–2016) [21]. Six of them examined patients after surgery of the submandibular gland by means of the sputum method and two trials investigated the function after surgery of the parotid gland by means of Lashley cups that are placed over the excretory duct (Stenon duct) and thus only collect saliva from the parotid gland. Six trials reached the evidence level 4 and only two studies evidence level 2. The analytic methods were very inhomogeneous (used stimulus, evaluation of the results, investigation period). Only one out of these eight trials also included sialometric examinations regarding saliva composition: sodium, potassium, and amylase did not show any differences before and after surgery [22]. Three studies that used salivary gland scintigraphy for objective assessment of the salivary gland function were not included in the systematic reviews because of methodical deficits [23–25]. The authors of the systematic reviews take the view that salivary gland scintigraphy cannot be recommended for functional examination because the radiation exposure is disproportionate [21].

In contrast, drooling describes pathologic hypersalivation. Beside the measurement of the salivation rate, the drooling quotient (DQ) has been established as semi-quantitative procedure [26]. Every 15 seconds over 10 min (i.e. 40 measurements) it is registered if new saliva is found on the lips which is expressed as quotient per 40 observations. In studies, often the number of patients with a reduction of the DQ of 50% is used as outcome measure [16].

Clinical measurements of salivation are not difficult to perform and they measure directly the most important function of the salivary glands. So in terms of better evaluation of the treatment quality it would be desirable if the quantitative salivation rate was used more frequently as outcome parameter after therapy of salivary gland diseases.

5. Further Symptoms of Salivary Gland Diseases as well as Side Effects and Complications of Therapy

Furthermore, other symptoms of salivary gland diseases such as swelling, inflammation, or pain are clearly more unspecific and thus less appropriate as parameters of specific quality control. In cases of diseases of the salivary glands that are associated with pains, this parameter is important and is assessed by all commonly used quality of life questionnaires (see below). A reduction of the saliva secretion as possible side effect not only of the disease but also of the therapy has already been mentioned. In the context of pharmaceutical therapy of salivary gland diseases, the side effects of the drugs are in the focus. Since these side effects are usually not salivary gland-specific, they are not further discussed here. For example, dysphagia may develop as rare adverse effect of botulinum toxin treatment of patients with drooling as well as in every other botulinum toxin treatment of the head and neck. For quality evaluation, drug-specific assessment instruments should be considered in these cases [27].

The significant and rare complications of sialendoscopy are duct injuries (about 0.5%), facial nerve palsy (single case reports), damage of the lingual nerve/reduced sensitivity (0.5–1%), postoperative sialoceles (0.5–1.7%), fistula development (no clear data), scarring or strictures of the duct system (1–4%) as well as missing therapy success (persistent sialolithiasis, insufficient dilation of the stenosis) [28, 29]. Already today, these complications are regularly documented in trials on the success of sialendoscopy (see below).

With regard to quality assessment, mainly complications of salivary gland surgery are relevant. The risk of transient facial nerve palsy amounts to up to 40% and the one of permanent facial nerve palsy to about 4% with an increased risk in cases of large tumors, chronic parotitis as indication, and malignant tumors [30]. Further complications influencing the quality of life are gustatory sweating (Frey's syndrome) in 3–15% of the cases, depending on the measurement method, and fistula development or sialocela in 1–25% [31–36]. Other complications such as pains, sensitivity disorders in the surgery site, changed outer appearance, and dry mouth may also significantly influence the quality of life, however, these symptoms have only been investigated in few systematic trials (see below).

6. Patients' Desires Regarding Treatment of Salivary Gland Diseases

Investigations on the patients' perspective with regard to salivary gland diseases or surgeries of the salivary glands are not available. This is mainly due to the fact that these diseases are only rarely observed and the group with severe sequelae of the disease is too small for many of the diseases. The largest group should be represented in self-help groups of Sjögren syndrome (e.g. <https://www.sjoegrensyndrom.de>). This self-help group has defined demands for research: procedures for early diagnosis of Sjögren syndrome and causal therapies should be developed. In Germany, patients suffering from salivary gland malignomas have no own self-help group. These patients are at best organized in self-help networks such as the Head and Neck Cancer Foundation (Kopf-Hals-Tumorstiftung) or Head, Neck,

► **Table 2** Examples for Patient-reported outcome measures (PROMs) that are applied to describe the preservation of the function and the quality of life in salivary gland diseases and their therapy.

Instrument	Comment
Short-Form-36 Health Survey (SF-36)	Disease-unspecific tool. It allows a comparison with other diseases and the normal population. Validated in German.
Short-Form-8 Health Survey (SF-8)	Short form of the SF-36. Validated in German.
15D health-related quality of life (HRQoL) instrument	A general tool that focuses more on the sensory function than the SF-36.
International Classification of Functioning, Disability and Health (ICF) Items	General classification of the WHO to describe the functionality of the patients. Disorders of the salivary gland function may be assessed (functions b5104). Validated in German.
EORTC QLQ-C30	This questionnaire was actually meant for general surveys of cancer patients. Thus, different cancer diseases may be compared. Questions about salivary gland function are not contained, neither directly nor indirectly. Validated in German.
EORTC-QLQ-H&N35	This questionnaire was conceived for patients with malignant head and neck tumors. Questions about dry mouth and its consequences are contained. It allows comparing patients with salivary gland malignomas with other head and neck malignomas. A revised version called EORTC-QLQ-HN43. Validated in German.
University of Washington Quality of Life Questionnaire (UWQOL)	Similar to EORTC-QLQ-H&N35. Saliva is one domain.
Glasgow Benefit Inventory (GBI)	It is conceived for single measurement after specific surgical or conservative therapy. Validated in German.
Chronic Obstructive Sialadenitis Symptoms (COSS) Score	COSS is a specific questionnaire to retrieve information about symptoms of sialadenitis.
Xerostomia Questionnaire (XQ)	XQ assessed information about dry mouth, pain, gustatory loss, and swallowing disorders.
Xerostomia Inventory (XI)	XI is similar to XQ and seems to allow a differentiation to the Burning-Mouth Syndrome.
Clinical Oral Dryness Scale (CODS)	In the proper sense, it is no PROM because the treating physician is involved and standardized examination findings are classified.
Dryness domain des European League Against Rheumatism SS Patient-Reported Index (ESSPRI)	ESSPRI is a specific instrument to assess the complaints in cases of Sjögren syndrome.
Sicca Symptoms Inventory (SSI)	COSS is a specific questionnaire to assess the Sicca symptoms.
Drizzling Severity and Frequency Scale (DSFS)	DSFS is a specific instrument to assess the severity and incidence of drooling; it is meant for asking parents of affected children.
Parotidectomy Outcome Inventory 8 (POI-8)	POI-8 is the only established, specific questionnaire on complaints after surgery of the parotid gland. Validated in German.

and Oral Cancer (Kopf-Hals-Mund-Krebs). In Facebook, there are English-speaking forums such as Parotid People that explicitly address patients with salivary gland tumors. Generally, the wishes of patients who suffer from ENT specific diseases are poorly investigated. It is a rather new scientific field to systematically assess the patients' perspectives. There are only very few systematic analyses up to now regarding the wishes and preferences, and only for patients with head and neck cancer [37–39]. The conclusion may be drawn that there is a significant deficit in this field. Good quality of care should take into account the wishes of patients with salivary gland diseases – but the wishes have to be known.

7. Patient-reported Outcome Measures (PROMs)

To measure the health-related quality of life in cases of salivary gland diseases, up to now mostly general questionnaires on the quality of life have been applied in retrospective cohort studies [40–44]. An overview of the used PROMs is given in ► **Table 2**.

7.1 Quality of life after surgery of salivary gland tumors

Hereby, in-house developed, non-validated questionnaires [40–42] were used as well as the EORTC QLQ-C30 and EORTC-QLQ-H&N35 questionnaires that have been developed for malignant cancer diseases [43, 45, 46]. When using general questionnaires or tools that were developed for malignant tumors, the result is always that the quality of life is high (mostly preoperative data are missing). If such questionnaires are used, typically at least one year after surgery no significant impairment of the quality of life can be found, probably they are observed due to clinically relevant Frey's syndrome [45]. Patients with malignant tumors have a poorer quality of life after surgical treatment compared to patients with benign salivary gland tumors [47]. However, this is not due to the surgery itself but to the more radical therapy including adjuvant radiotherapy. The difference must be made with regard to surveys of patients with salivary gland malignomas. Specific instruments for the survey of patients with salivary gland malignomas are not available. If the above-mentioned questionnaires are used in the context of malignant

cancer diseases or others such as the University of Washington Quality of Life (UWQOL), it is less the circumstance of malignant salivary gland disease that has an impact on the reduced quality of life; if at all, it is an associated facial nerve palsy [48].

Up to now, only one single disease-specific measurement instrument is available for patients with salivary gland tumors. This instrument has been exclusively conceived for the assessment of the quality of life after parotidectomy. The tool called Parotidectomy Outcome Inventory 8 (POI-8) is able to reliably and validly measure the health-related quality of life in adults after parotidectomy in cases of benign diseases of the parotid gland [49]. POI-8 asks questions about pains, sensitivity disorders, and scarring in the surgery field, about the appearance with facial nerve palsy, the loss of glandular tissue, gustatory sweating, dry mouth, and the fear of revision surgery. The questions are based on a survey of experts who defined the symptoms with regard to the patients' quality of life. Patients were not involved in the conception of POI-8. Recently, 30 Indian patients with benign salivary gland tumors were examined 6 months after parotidectomy by means of a non-validated English version of the POI-8. Absolutely, the quality of life was high with ≥ 80 (of a maximum score of 100 points in all subscales) and slightly better quality of life after lateral in comparison to total parotidectomy [50]. Also a German article with 196 patients revealed that all POI subscales were always > 80 after different parotid surgeries (with highly various postoperative follow-up periods). After lateral parotidectomy, the POI subscale of sensitivity disorders was lower than after more circumscribed interventions of the parotid gland, while more unspecific questionnaires such as EORTC QLQ-C30 and EORTC QLQ-H&N35 did not reveal any differences [51]. Recently, the POI-8 was applied in a German multi-center prospective surgical trial on long-term effects after lateral parotidectomy [52]. This tool could show in 130 patients that two years after surgery scarring, xerostomia, and also the fear of revision surgery deteriorate the patients' quality of life.

7.2 Quality of life after sialendoscopy

The quality of life of 46 patients after sialendoscopy was investigated with the general quality of life instrument called Short-Form-36 Health Survey (SF-36) [53]. Absolute values were not presented so that the quality of life cannot be estimated, chronically persisting symptoms were associated with poorer quality of life in the section of physical aspects. Using the Glasgow Benefit Inventory (GBI), a questionnaire about the general assessment of a surgical intervention [54], an average improvement of the GBI of 31 points could be observed after interventional sialendoscopy in 54 patients [55]. Another publication with 130 Danish patients revealed an average GBI of 13.4; mainly patients with sialolithiasis and patients undergoing sialendoscopy of the parotid gland benefited from the procedure [56]. A comparable improvement of the GBI is also found in retrodisplacement of Wharton's duct in children with drooling. A recent trial assessed the quality of life after sialendoscopy 3 and 12 months after intervention in 260 patients by means of the general 15D HRQoL questionnaire [57]. For 74 patients, also preoperative data were available, which is a noteworthy particularity. Preoperatively, patients reveal lower values compared to a normal cohort in the dimensions of "distress" and especially in "discomfort and symptoms", in other dimensions not. The dimensions of "distress" and

"discomfort and symptoms" recover to a normal level within 3 months.

So if general questionnaires are applied for measurement of the quality of life, first it needs to be stated that the quality of life is not considerably limited. Quite another result appears when measuring the disease-specific quality of life. Recently, a specific questionnaire was developed for the evaluation of sialendoscopy, i.e. the Chronic Obstructive Sialadenitis Symptoms (COSS) Score [58]. 66 patients filled out the questionnaire containing 20 items that refer to sialadenitis-related complaints. Retrospectively, the patients were also asked about the improvement of the complaints after sialendoscopy. So it was not a survey performed before and after treatment. Patients with obstructive sialadenitis of the parotid gland had a higher COSS score (poorer quality of life) compared to patients with diseases of the submandibular gland. Patients with sialolithiasis had a lower COSS score than patients with obstruction without sialoliths. 60 % reported healing by sialendoscopy and had the lowest COSS score. At the same time, also the general questionnaire of SF-8 was filled out. The changes could not be discriminated in contrast to the COSS scores. The COSS score was also applied in a prospective trial in 40 patients with pre- and postoperative measurement after 3 months [59]. It could be confirmed that the score after sialendoscopy was significantly reduced. Patients suffering from diseases of the submandibular gland and sialolithiasis benefited more from the intervention. Furthermore, the SF-8 could not assess the change of the quality of life after sialendoscopy. In further 19 patients with mere duct stenoses and also in 80 patients (29 with long-term follow-up up to one year) of a prospective trial, the improvements were lower, the quality of life improved least in proximal stenoses [60–62]. For analysis of the treatment outcomes after sialendoscopy in patients with radio-iodine therapy-induced xerostomia, the Xerostomia Questionnaire (XQ) and the Xerostomia Inventory (XI) were applied pre- and 3 months postoperatively as two PROMs that have been developed primarily for assessment of xerostomia [63–65]. Six patients who underwent interventional sialendoscopy showed a significant improvement of the quality of life compared to 6 patients without sialendoscopy, while the findings of salivary gland scintigraphy did not improve [65].

7.3 Quality of life after treatment of xerostomia

Xerostomia plays a major role in Sjögren syndrome and other autoimmune diseases. Easily applicable are the already mentioned Xerostomia Inventory (XI), the Clinical Oral Dryness Scale (CODS), or the Dryness Domain of the European League Against Rheumatism SS Patient-Reported Index (ESSPRI) [63, 66–68]. The CODS and in a limited way also the ESSPRI, but apparently not the XI, seem to well correlate with the objectively measured salivation rate [69]. The Sicca Symptoms Inventory (SSI) focuses on the sicca symptoms and allows good discrimination of patients with primary Sjögren syndrome of other diseases [70].

7.4 Quality of life after treatment of drooling

Regarding the conservative management of salivary gland diseases, investigations about the quality of life in cases of drooling are available based on The International Classification of Functioning, Disability, and Health (ICF) [16]. With this instrument, a maximum

improvement of the quality of life can be revealed 8 weeks after botulinum toxin injection into the parotid and the submandibular glands. Since drooling may also affect children, the questionnaires are often conceived in that way that relatives may be asked. So these tools are not necessarily “patient-reported” but also “care-taker-reported”. Reliable specific instruments for measuring the drooling-associated quality of life that seem to better assess the impairment by the disease than the Drooling Quotient (DQ, see above) are for example the Drooling Impact Scale or the Drooling Severity and Frequency Scale (DSFS) [19, 26, 71–73].

In summary, it may be stated that it is meanwhile obvious to apply specific PROMs for evaluation of conservative procedures for example in the context of treatment of Sjögren syndrome or drooling. For assessment of the treatment outcome after sialendoscopy, first instruments have been developed that should now be applied. For salivary gland surgery, there is currently only one tool, i.e. the POI-8 for assessment of surgeries of the parotid gland. It is recommended to use the POI-8 regularly in trials about parotid surgery.

8. Quality of Scientific Knowledge Gain Based on Evidence Criteria

Regarding the quality of knowledge gain, the criteria of evidence-based medicine are suitable. Looking for prospective clinical phase-III-trials on salivary gland diseases in PubMed, 20 hits can be retrieved. Actually, phase-III-trials that are relevant for ENT specialists are only found with regard to the effect of different radiotherapy concepts for salivary gland protection on the salivary gland function (e.g. [74]). If phase-I/II-trials are included, the number of results still amounts to less than 30. In the last years, some phase-I/II-trials were published with patient numbers of about 30–60 patients undergoing treatment of non-resectable or distantly metastasized salivary gland malignomas, in particular with regard to the application of new medications for targeted antibody therapy for aggressive salivary gland malignomas (e.g. [75–78]). Fortunately, the number of prospective trials on diagnostic and surgical procedures has increased in the last years and also the one of meta-analyses. However, only very few Cochrane reviews are available. It is important to be conscious about the limitations of meta-analyses. Also the meta-analyses quoted here have different quality levels with regard for example to a publication bias, study heterogeneity, or sensitivity analyses [79].

8.1 Evidence-based data on diagnostics

The significance of fine needle aspiration cytology is still controversially discussed, although meanwhile a series of meta-analyses has been published. In a large analysis of 71 trials with 6,964 patients (prevalence of malignant tumors of 25%), the area under the ROC curve for differentiation of benign and malignant tumors amounted to 0.96 (95% confidence interval [CI] = 0.94–0.97) [80]. The summed sensitivity amounted to 0.81 (CI = 0.76–0.83). The specificity was 0.97 (CI = 0.96–0.98). The positive likelihood ratio amounted to 28.6 (CI = 20.5–39.8). The negative likelihood ratio was 0.21 (CI = 0.17–0.25). The positive predictive value was 0.90 and the negative predictive value amounted to 0.94. One problem

was the wide dispersion of the results between the single trials, i.e. the accuracy of fine needle aspiration cytology was high in some place; however, in others it was insufficient. This aspect is confirmed by two recent papers from 2016 and 2019 that emphasize again that the outcomes under sonographic control are better [81, 82].

In recent times, needle biopsy has become more and more popular, especially in centers that do not provide fine needle cytology. Up to now, only few observational studies are available and already one meta-analysis. This meta-analysis includes 10 trials with a total of 1 315 needle biopsies. The pooled sensitivity amounted to 0.94 (CI = 0.92–0.96). The specificity was 0.98 (CI = 0.97–0.99). The area under the ROC curve for the differentiation of benign and malignant tumors amounted to 0.98 (CI = 0.97–0.99) [83]. The positive likelihood ratio was 43 (CI = 10–191); negative likelihood ratio 0.08 (CI = 0.05–0.12). Also in the context of needle biopsy, a relevant variability of the quality of the outcomes between the trials was observed; and also here an ultrasound-guided procedure improved the quality. It is important to mention that hematomas and also temporary facial nerve palsy are described more frequently after needle biopsy.

8.2 Evidence-based data on sialendoscopy

One first large meta-analysis on interventional sialendoscopy in the context of obstructive sialadenitis included 29 trials published until October 2010 with a total of 1 213 adult patients. It already revealed a pooled success rate for all patients of 0.87 (CI = 0.83–0.89) and of 0.93 (CI = 0.89–0.96) for the subgroup of 374 patients who underwent combined interventions [84]. Another meta-analysis on obstructive sialadenitis included patients until April 2014. The pooled success rate with application of sialendoscopy alone amounted to 0.76 (CI = 0.71–0.82) for 40 trials with 2 654 patients and to 0.91 (CI = 0.88–0.94) for 23 trials with 1 480 patients with combined interventions. The complication rate amounted to 4.6% [85]. A meta-analysis including trials until March 2015 could identify 10 trials with 148 patients who underwent combined transfacial-endoscopic surgery of sialoliths of the parotid gland [29]. The pooled rate of calculi removal amounted to 0.99 (CI = 0.97–1.00), to 0.97 (CI = 0.93–0.99) for improvement of symptoms, to 1.00 (CI = 0.99–1.00) for preservation of the gland, and to 0.06 (CI = 0.01–0.15) for complications. Also for sialendoscopy in children, already meta-analyses have been published. Regarding the treatment of juvenile recurrent parotitis, the pooled success rate for no further parotitis episodes of 7 trials with 120 patients amounted to 0.73 (CI = 0.64–0.82). The pooled success rate for no further sialendoscopy was 0.87 (CI = 0.81–0.93). Severe complications were not observed [86]. Another meta-analysis investigated sialendoscopy in 323 children who were included in 17 trials with multiple diseases (69% of juvenile parotitis, 15% of sialolithiasis). A success rate was not calculated. Based on the average pooled follow-up period of 18 months, the rate of recurrent complaints amounted to 14.5% [87]. The success rates were highest for the treatment of sialolithiasis, in adults, and with the necessity of combined interventions. Significantly less data are available for pediatric patients compared to adults.

8.3 Evidence-based data on surgical therapy: parotidectomy and extracapsular dissection

In order to prepare patients for surgery after indication of salivary gland surgery for surgery, there are no specific examinations or recommendations for salivary gland interventions to minimize perioperative risks. Even if perioperative quality assurance is not new as research field, there are only few ENT specific requirements. In otorhinolaryngology, and thus also for salivary gland surgery, for example the British NICE recommendations for perioperative risk assessment and patient preparation may be used, as well as the US-American recommendations of the National Surgical Quality Improvement Program (NSQIP) or the recommendations of the German Society of Anesthesiology (Deutsche Gesellschaft für Anästhesiologie) [88, 89].

Even if parotidectomy is a surgical procedure that has been established for a long time, there are less than 20 prospective clinical trials on parotidectomy with more than 50 included patients (only these will be considered more in detail) and less than 10 trials that are registered in acknowledged study registries. Regarding extracapsular dissection, no registered prospective clinical trial was available until April 2019. Fortunately, the Workgroup of Salivary Gland and Thyroid Diseases of the DGHNO (Arbeitsgemeinschaft Speicheldrüsen- und Schilddrüsenerkrankungen) has assumed the urgent task to support prospective trials on parotid surgery. Thus, a multicenter trial with 130 patients could show that the sternocleidomastoid muscle flap is not suitable to reduce Frey's syndrome [90]. Another study could confirm that the preservation of the posterior branch of the great auricular nerve contributes relevantly to the preservation of the sensitivity in the surgery site [91, 92]. Recently it could be shown that on the long term this sensitivity loss is the most important impairment from the patients' perspective two years after surgery [52]. So it should be a major objective of surgery to preserve at least the posterior branch of the great auricular nerve. It is not clear, to what extent this recommendation is observed. First results of a second prospective multicenter trial with 148 patients were published afterwards. While the extent of exposing the facial nerve has no effect on the perioperative complication rate, it could be revealed that a more extensive exposure is associated with a higher risk of facial nerve dysfunction 12 months later [93].

The extracapsular dissection, in particular in cases of pleomorphic adenomas, was assessed in several meta-analyses. One first large meta-analysis from 2012 with 1 882 patients (9 trials from 1979 to 2011) showed a lower rate of temporary facial nerve palsy compared to lateral parotidectomy (odds ratio [OR] 0.256; CI=0.174–0.377), but no difference with regard to persistent facial nerve palsy (OR 0.878; CI=0.282–2.730). Also the recurrence rate was similar (OR 0.557; CI=0.271–1.1147) [94]. Another meta-analysis investigated already 3 194 patients from 14 trials until the beginning of 2015 with identical results as well as a recent meta-analysis including trials published until the end of 2018 with 1 641 patients [95, 96]. Another meta-analysis with 1 152 patients – however, it remains unclear how 123 trials could meet the inclusion criteria – revealed a higher recurrence rate for lateral parotidectomy without performing a direct statistical comparison [97]. Another meta-analysis investigated the recurrence rate of pleomorphic adenomas after extracapsular dissection not only with lateral parotidectomy but also with total parotidectomy. The recur-

rence rates for all procedures amounted to 1–2% (CI=1.14%). Overall, the recurrence rate was low for all procedures [98]. Unfortunately, in the mentioned trials the recurrence rates were not correlated with the follow-up period which only rarely exceeded 10 years. In general, the median follow-up period remained unclear in most of the included trials.

8.4 Evidence-based data on facial nerve management

One single large randomized trial was performed on the technique of facial nerve preparation and could not find any difference between anterograde and retrograde preparation [99]. This aspect is also confirmed by a recent meta-analysis including 8 trials with 770 parotidectomies [100]. Supported by the Workgroup of Salivary Gland and Thyroid Diseases, another prospective trial with 100 parotidectomies revealed that facial nerve monitoring reduced the duration of surgery in a teaching hospital without an increase of complications [101]. Furthermore, a meta-analysis elaborated that the facial nerve monitoring in the context of parotidectomy reduces the risk at least of temporary facial nerve palsy [102] which is also confirmed by a recent randomized study (\pm monitoring) [103]. For a long time already it is evident that a regular postoperative application of prednisolone is not effective in postoperative facial nerve palsy after parotidectomy with preservation of the facial nerve [104]. Also the perioperative prophylaxis with dexamethasone does not seem to be suitable to reduce the rate of postoperative facial nerve palsies after parotidectomy which was shown in a prospective randomized trial with 49 patients [105]. In a prospective trial with 79 patients suffering from facial nerve palsy after lateral parotidectomy, the recovery rates in a group of patients with typical mimic exercises at home were similar to the one with physiotherapeutically supervised exercises [106].

8.5 Evidence-based data on drug-related non-oncologic therapy procedures

Interestingly, in 2018 the IQWiG performed an effect assessment on behalf of the G-BA regarding the application of glycopyrronium bromide for treatment of sialorrhea in children and adolescents older than 3 years with chronic neurological disorders. Up to then, there was not approved medication for these symptoms in children so this might be the only effect assessment (dossier assessment A18–22) for salivary gland diseases. The IQWiG stated that none of the three trials on this topic implemented the suitable alternative therapy defined by the G-BA as best supportive care. Thus there was no hint for an additional benefit of glycopyrronium bromide compared to the suitable alternative therapy [107–109]. Finally, however, the G-BA acknowledged a non-quantifiable additional benefit and thus the approval. Since mid-2018, based on data of a phase-III-trial, also incobotulinumtoxinA is approved for the treatment of sialorrhea in adults with neurodegenerative diseases [110]. The approval in Germany is expected for 2019. Recommendations on the treatment with glycopyrronium bromide and botulinum toxin are also found in the ENT-specific guideline on hypersalivation (see below).

There are only five Cochrane reviews about the treatment of salivary gland diseases and they all deal with medication procedures. So until now no drug-related therapy for salivary gland protection

► **Table 3** Significant AWMF guidelines that deal with salivary gland diseases.

Guideline	Comment
Hypersalivation (S2k, No. 017–075)	Coordinated by the DGHNO. Revised in September 2018. Meanwhile, recommendations are given at least for drug-related therapy of hypersalivation based on trials with high evidence level.
Obstructive sialadenitis (S2k, No. 017–025)	Coordinated by the DGHNO. Revision started in 2018. Surgical procedures and in particular sialendoscopy are in the focus. For this procedure, meanwhile at least suitable meta-analyses are available that are included in the recommendations of the guideline.
Antibiotic therapy of infections of the head and neck (S2, No. 017/066)	Coordinated by the DGHNO. Revision started in 2018. The described principles also apply for antibiotic therapy of bacterial salivary gland inflammations.
Diagnostics and therapy of salivary gland tumors of the head (S3, No. 007–1020L)	Coordinated by the DGMKG and DGHNO. The elaboration of the guideline will start in 2019.
Cancer of the oral cavity (S3, 007–1000L)	Coordinated by the DGMKG. For prevention of irradiation-due damage of the salivary gland function, the possible application of pilocarpine is recommended.
Earache (S2k, Nr. 053/009)	Coordinated by the DEGAM. The focus is placed on differential diagnosis of sialolithiasis of the parotid and submandibular glands.
Non-purulent CNS infections of the brain and spinal cord in children and adolescents (S1, No. 022/004)	Coordinated by the Society for Neuro-Pediatrics (Gesellschaft für Neuropädiatrie). The differential diagnosis of mumps is focused.
Caries prophylaxis for permanent teeth (S2k, No. 083/021)	Coordinated by the German Society for Tooth Preservation (Deutsche Gesellschaft für Zahnerhaltung). The prophylactic effect of salivary stimulation against the development and progression of caries is focused.
Idiopathic facial nerve palsy (S2k, No. 030–013)	Coordinated by the German Society of Neurology (Deutsche Gesellschaft für Neurologie). The focus is placed on the differential diagnosis of facial nerve palsy caused by a parotid tumor.
Diagnostics and therapy of eating disorders (S3, No. 051–026)	Coordinated by the German Society for Pediatric and Adolescent Psychiatrics (Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie). The significance of the typical salivary gland hypertrophy is described.

and prevention of postradiogenic xerostomia can be recommended [111]. Neither can pilocarpine be recommended for treatment of already occurred postradiogenic xerostomia [112]. According to the criteria for Cochrane reviews, there is no medication for therapy of Frey's syndrome that may be recommended due to the lack of randomized studies [113]. Also for drug-related treatment of drooling in pediatric patients, not recommendations could be given in 2012 [114], neither for the symptomatic treatment of hypersalivation in cases of amyotrophic lateral sclerosis [115]. Meanwhile, this may be considered as obsolete – as described above. In this chapter, also trials on antibiotic therapy of acute bacterial sialadenitis might be expected. However, no prospective studies are available. So, the general recommendations of the AWMF guideline on antibiotic treatment of infections of the head and neck are mentioned (see ► **Table 3**).

9. Investigations About Cost-Effectiveness

There are only few detailed trials about the cost-effectiveness and none that calculates on the basis of the German DRG system. Based on a literature research for calculation of the treatment costs of sialendoscopy with radioiodine induced sialadenitis, a US-American trial could show that sialendoscopy is only cost-effective when it is applied as initial procedure for further therapy planning, prior to ultrasound (by radiologists), MRI or CT sialography, because sialendoscopy often allows immediate therapy decision without further imaging [116]. In a prospective Finnish trial with 270 patients who underwent sialendoscopy between 2014 and 2016, higher thera-

py costs in cases of sialolithiasis were associated with a better gain of quality of life compared to other indications; however, the data were not correlated as for example for calculation of a quality adjusted life year [57]. In a US-American study, sialendoscopy was particularly cost-efficient for removal of intraparotid calculi in the context of a transfacial approach, i.e. when the calculus could not be reached via Stenon's duct and alternatively only parotidectomy was possible [117]. A retrospective US-American study with 46 patients who underwent surgery in a period of 4 years (i.e. 11.5 surgeries per year which makes clear the limitations of the study) showed that the duration of surgery and hospitalization after extracapsular dissection were shorter and thus the costs were lower compared to lateral parotidectomy [118]. There is only one study published until now that does not assess the cost-effectiveness on a monetary level but with a patient-related measure of effectiveness, which is the prevention of Frey's syndrome after parotidectomy. The implantation of fat was more cost-effective than the use of acellular dermis [119, 120]. Cost-effectiveness analyses do not belong to the main expertise of ENT specialists. Where more treatment options seem to be medically equivalent, more such observations would be welcome in cooperation with economists.

10. Implementation of Current Knowledge in Guidelines

Currently, there are only two guidelines of the AWMF referring to salivary gland diseases that have been created coordinated by the DGHNO (an overview about AWMF guidelines with reference to sa-

► **Table 4** The most important recommendations of the British guideline about the treatment of salivary gland tumors [126]. Simple expert opinions are specifically marked.

- Ultrasound guided fine needle aspiration cytology is recommended for all salivary tumors and cytology should be reported by an expert histopathologist.
- Adjuvant radiotherapy following surgery is recommended for all malignant submandibular tumors except in cases of small, low-grade tumors that have been completely excised.
- For benign parotid tumors complete excision of the tumor should be performed and offers good cure rates.
- In the event of intra-operative tumor spillage, most cases need long-term follow-up for clinical observation only. (Expert opinion: These should be raised in the multidisciplinary team to discuss the merits of adjuvant RT. *).
- As a general principle, if the facial nerve function is normal pre-operatively then every attempt to preserve facial nerve function should be made during parotidectomy and if the facial nerve is divided intra-operatively then immediate microsurgical repair (with an interposition nerve graft if required) should be considered.
- Neck dissection is recommended in all cases of malignant parotid tumors except for low-grade small tumors.
- In cases of mucoepidermoid carcinoma, the histologic grade is an important factor correlating to outcome and should be considered when planning treatment.
- Adjuvant RT should be considered in high grade or large tumors or in cases where there is incomplete or close resection margin.
- Where malignant parotid tumors lie in close proximity to the facial nerve there should be a low threshold for adjuvant RT.
- Adjuvant RT should be prescribed on the basis of clinical factors in addition to histology and grade, e. g. stage, pre-operative facial weakness, positive margins, peri-neural invasion and extracapsular spread.

* In Great Britain, other than in Germany, for example also radiotherapy is frequently applied for recurrent pleomorphic adenomas.

► **Table 5** Proposals for specific * quality indicators regarding the quality of treatment of salivary gland diseases or as target criteria in clinical trials and registries.

Indicator	Comment
Function/deficit	
Salivation rate	Objective parameter of the salivary gland function for the parotid and submandibular glands. In all trials on diseases of these glands, the unstimulated and stimulated flow rate should be measured.
Drooling quotient	Semi-quantitative procedure for measurement of drooling.
Pain scale	At least for diseases with relevant pain to be assessed by means of questionnaires on the quality of life or Likert/Rating scale.
Extent of surgery	In cases of parotid surgery, e. g. based on the proposal of the <i>European Salivary Gland Society</i> [136].
Complications	Standardized assessment of the most important complications of surgical procedures: facial nerve palsy by grading Frey's syndrome by means of minor test, appearance and sensitivity disorders at least by means of Likert/Rating scale. Assessment of the mortality and in cases of inpatient treatment of the 30-days readmission rate.
Adherence to guidelines	Where guidelines are available, their observance should be assessed.
Patient-reported outcome measures (PROMs) * *	
Parotidectomy-outcome-inventory-8 (POI-8)	Specific instrument for parotid surgery, which should be applied in clinical trials.
Chronic Obstructive Sialadenitis Symptoms Score (COSS)	To be applied in obstructive sialadenitis, validation of the German version is required.
Xerostomia Questionnaire (XQ) or Xerostomia Inventory (XI)	In cases of xerostomia-associated diseases, validation of a German version is required.
Sicca Symptoms Inventory	In the context of xerostomia-associated diseases, validation of a German version is required.
Drooling Severity and Frequency Scale (DSFS)	In cases of drooling-associated diseases, validation of a German version is required.
Indicators to be developed	
Further PROMs	For the assessment of patient-related outcomes for diseases/surgery of the submandibular gland.

* unspecific indicators (e. g. pains, duration of surgery, readmission rate), that might be suitable to be measured, are not mentioned here. * * more details on PROMs are found in ► **Table 2**.

lary gland diseases is found in ► **Table 3**). The S2k guideline on hypersalivation (AWMF No. 017–075) was revised in September 2018. The particularities of frequently necessary interdisciplinary treatment are described including recommendations for the approach. In particular standards for ENT-specific swallowing tests are defined. It is relevant for ENT physicians that recommendations are given on the rather rare surgical therapy, especially the gradual medication therapy of hypersalivation with glycopyrrrolates and botulinum toxin [108, 121–125]. Still in 2019, the approval of incobotulinumtoxinA for this indication is expected which will allow further standardization of the therapy for ENT specialists. Until 2019, the S2k guideline on obstructive sialadenitis (AWMF No. 017–025) will be revised. This guideline was an important step to define treatment standards for the therapy of sialolithiasis and salivary duct obstruction in other diseases regarding the increasing distribution of sialendoscopy. Algorithms for conservative therapy, oral surgery, and the application of sialendoscopy were developed and also the significance of ultrasound of the salivary glands was emphasized as important tool for ENT specialists. A relevant step for quality assurance is the implementation of the S3 guideline on diagnostics and therapy of salivary gland tumors of the head. The creation of the guideline will be started together with the German Society of Maxillofacial Surgery (Deutsche Gesellschaft für Mund-, Kiefer- und Gesichtschirurgie, DGMKG) in 2019.

For the first time in 2016, a national multidisciplinary guideline on the treatment of salivary gland tumors was presented in Great Britain [126]. This guideline is the most detailed guideline regarding the treatment of salivary gland tumors up to now. The recommendations differentiate between evidence-based recommendations and recommendations based on clinical experience. Details on the evidence level are not explained. The key aspects of the British guideline are summarized in ► **Table 4**.

11. CONCLUSION

How can the initially asked questions be answered? ENT specialists and other healthcare professionals treating patients with salivary gland diseases have to acquire specific knowledge. By means of the official specialization and the obligation of lifelong continuous medical education, ENT physicians prove their qualification. Specifically defined requirements for the treatment of salivary gland diseases are not determined. The desires of patients suffering from salivary gland disorders with regard to their disease are not sufficiently known in order to define quality objectives. The function of the salivary glands is well-known and salivation as most important function can be easily measured. The symptoms of the different diseases as well as the consequences and possible complications of the treatment are well described. This leads to a multitude of options to further improve the treatment quality of salivary gland diseases. Some proposals are summarized in ► **Table 5**.

11.1 Possibility of disease registries

Some salivary gland diseases do not occur very often and the surgical therapy, on the other hand, plays a major role in many salivary gland diseases. So there will be no randomized controlled trials in several areas. Beside the gain in knowledge by means of meta-analyses, registries might play an important role. For example in the Netherlands and also in Denmark, national registries are established for pathology findings. This fact allowed recently a Dutch analysis of 3,506 pleomorphic adenomas. The 20-years-recurrence rate amounted to 6.7 % with a median interval until the first recurrence of 7 years. Malignant transformation was observed in 0.15 % of the cases (3.2 % in recurrences) [127]. In Denmark, the recurrence rate of 5,497 patients amounted to 2.9 % from 1985–2010; malignant transformation was found in 3.3 % of the tumors [128]. Only based on the registry structure it was possibly in Denmark to calculate the incidence of sialolithiasis (7.3 per 100 000) [129]. This makes clear which powerful analyses might be performed based on registries. With regard to malignant salivary gland tumors, the national cancer registry in Germany is more than overdue. The DGHNO currently tries to transform the clinical salivary gland registry of Erlangen – with coordinated by Prof. Iro, Professor and Chairman of the ENT Department in Erlangen – into a national registry. For pediatric malignant tumors of the salivary glands, there is already today the possibility to register in the STEP registry of pediatric oncologists (<http://www.seltene-tumoren.de/>) and thus also the European registration in the European Cooperative Study Group for Pediatric Rare Tumors (EXPeRT; <https://www.raretumors-children.eu/>). Only in this way, epidemiologic questions may be answered appropriately, for example to exclude, which was shown in Finnish data, that the use of mobile phones is not associated with the development of salivary gland tumors [130]. There is no need to limit such registries to Germany. In times of Big Data, multinational registries on molecular phenotyping are necessary like for example the Sjögren Big Data Consortium [131, 132].

11.2 Outlook

This article shows that it is still a long way until it is worth thinking about Value-Based Purchasing programs in the context of salivary gland diseases [133]. Financing systems of this kind are still in an early stage in Germany and should be tested in other fields where for example in the USA (e.g. in hip endoprosthetics) already sufficient experience is found [134]. Remuneration concepts including Public Reporting, Pay for Reporting, Pay for Performance might probably also be established for surgery of salivary gland tumors. Concepts and process indicators (see ► **Table 5**) would generally be available [135].

Acknowledgement

The author want to thank Dr. Maria Grosheva and Dr. Jovanna Thielker for carefully reading the text and for giving valuable comments.

Conflict of Interest

There is no conflict of interest.

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