Identification and selection of attributes and levels

Step 1 Endpoints applied in benefit assessment N15-01: Systematic treatment of parodontopathies (considered as source for identifying attributes)

- Tooth loss
- Tooth mobility
- Pain
- Symptomatic gingivitis (Swelling, bleeding, suppuration on probing)
- Adverse events
- Health related quality of life if measured with validated Instruments (e.g. validated scales)
- Sufficiently valid surrogate attachment level as surrogate for tooth loss

Step 2 Literature review (considered as additional source for identifying attributes, and to specify levels)

An additional literature review was conducted primarily to identify levels for attributes and if necessary add potentially relevant attributes to the list of endpoints from the benefit assessment. Sources used in the review were clinical practice guidelines, systematic reviews on the epidemiology and course of disease, RCTs and observational studies investigating different treatment and follow-up care strategies. The following table summarizes the primary sources of information:

Topics	Sources
All potential attributes	Preliminary report plan benefit assessment N15-01
Relevant patient characteristics **(potential effect modifiers / subgroup analysis)**	Systematic Reviews: Smiley et al. / American Dental Association [1, 2]; Lee et al. [3]; Fritoli et al. [4]; Buset et al. [5, 6]; Rabelo et al. [7]; Canas et al. [8]; Eberhard et al. [9]; Mailoa et al. [10]; Vohra et al. [11]; Behdin et al. [12]; Bertl et al. [13]; Keestra et al. [14]; Newton et al. [15]; Monje et al. [16]; Fiorini et al. [17]
Tooth loss (quantification)	Lee et al. [3]; Bäumer et al. [18]; Eickholz et al. [19] Costa et al. [20, 21], Gilbert et al. [22], Hujoel et al. [23]
Quality of life	Review of different measument instruments for (oral-) health related quality of life Locker et al. [24] In particular the dimensions of the Oral Health Impact Profile Questionnaire were considered since this instrument is validated for the German context [25-27], Instruments are not specifically designed for periodontal disease
Side effects Especially related to the antibiotic therapy /Metronidazol, Metronidazol, Azithromycin, Clarithromycin, Moxifloxacin, Tetrazykline, Doxycyclin, Chlorhexidin	www.fachinfo.de (patient information leaflets for pharmaceutical products)

Results of review (including endpoints from benefit assessment and specifications of these)

- Attachment level
- Probing depth
- Gingival index
- Quality of life (or its separate dimensions)
- Gum bleeding (intensity and frequency)

- Pain (intensity and frequency)
- Hypersensitivity of teeth
- Halitosis
- Side effects of antibiotics: nervous system (e.g. gastro-intestinal disorder, dizziness, risk of antibiotic resistance)
- Tooth loss
- Fear of dentures
- Tooth mobility
- Problems with biting, chewing, speaking
- (Fear of) stigmatization
- Aesthetic consequences
- Hygiene measures patients have to complete
- Frequency of follow-up visits
- Out-of-pocket costs for patients (including mandatory dental scaling and follow-up care)

Step 3 Expert interviews with periodontologists (considered as additional source for identifying attributes, and to specify levels)

Primary symptoms reported by patients

E1: tooth mobility, but generally patients do not perceive symptoms and are referred to periodontal treatment because of dentist diagnosis

E2: patients report teeth become longer (which is due to gum recession), bleeding, tooth mobility, but usually patients are referred to periodontal treatment

E3: teeth become longer and unaesthetic, bleeding & pus, sometimes bleeding

Criteria applied for diagnosis

E1: radiographically visible bone loss, probing depth

E2: probing depth, attachment loss

E3: Attachment loss, bleeding on probing, probing depth

Treatment aim reported by patients

E1: preservation of teeth

E2: preservation of teeth is mentioned most often, reducing mobility of teeth, reducing inflammation is rarely mentioned

E3: patients do not want to look old, preservation of teeth

Do patients mention fear of losing teeth by themselves?

E1: Yes

E2: Yes, but usually this can only be achieved temporarily. Usually patients only realize they might lose teeth once a high attachment loss is present and teeth moved a lot.

E3: fear of financial consequences of tooth loss is often mentioned, fear of losing functions or needing

Frequency of follow-up visits

E1: every 3 months

E2: first follow-up visit after 6-12 weeks, afterwards depending on individual risk profile every 6 weeks, 3 months or 6 months

E3: every 2-12 months, depending on medical need and what is feasible for the patient

When does follow-up care end?

E1: When patient does not show up anymore.

E2: When patient does not show up anymore. We will not stop offering supportive periodontal therapy.

E3: When patient does not show up anymore. Usually patients attend a follow-up visit at least 1x per year.

What are typical symptoms after receiving therapy (Scaling and root planing)?

E1: If at all, patients report hypersensitive teeth.

E2: very few report wound pain, hypersensitive teeth are common

E3: Hypersensitivity of teeth

What are typical symptoms after receiving surgical therapy?

E1: Sensitivity and loss of gum

E2: wound pain, but this is rare; some patients do not dare to chew because of the stitches or patients feel uncomfortable with the stitches

E3: wound pain, gum problems, problems with chewing

Step 4 Patient interviews (considered as additional source for identifying attributes, and to specify levels)

Patients most frequently mentioned preventing tooth loss, preserving own teeth or preventing dentures as their primary treatment aims. In relation to this they stressed the difference between losing anterior or molar teeth, whereby loosing anterior teeth was considered worse in terms of effects on quality of life and wellbeing. Some also mentioned the reduction of symptoms as treatment aims. These symptoms included e.g. bone loss / gum loss, occasional gum bleeding or sensitive tooth necks. Patients also reported mobility of tooth as a late symptom. In their experience, a mobile tooth is associated with imminent tooth loss. Also, patients considered the aesthetic effects on teeth, especially the optical increase of teeth's length due to gum recession a very negative aspect of disease and treatment. For patients this implied looking "old" and "ugly" and stopped them from smiling. Patients reported high costs for treatment, follow-up care and re-treatment of up to 500 per year. Some patients recruited at the University Hospital Cologne reported that they intentionally choose to undergo treatment at there, since periodontal treatment was free of charge at the time of conducting the study. However, patients considered high costs as a preventive investment to avoid being in need of dentures, which would be much more costly. Overall, costs were the only aspect that might have prevented patients from undergoing therapy, since side effects (mainly related to anesthesia) were considered negligible. Similarly as with costs, patients considered attending regular follow-up visits important to prevent disease progression.

Step 5 Final selection of attributes and levels

Included disease and treatment aspects	
Disease and treatment aspect	**Reason for inclusion** (in the original working paper direct patient citations were used to illustrate relevance of these aspects)
Tooth loss	Tooth loss was the most frequently mentioned treatment goal and also included in the list of endpoints from the benefit assessment. The difference between molar and anterior teeth was not included as a separate attribute since therapies do not differentiate between these.
Hypersensitivity of teeth	Patients often report this as a symptom of disease or a negative consequence of treatment. It can be a symptom when gum recession already took place and tooth necks are exposed. Since the removal of plaque also leads to exposed tooth necks, treatment can also increase this complaint. This endpoints falls within the category of morbidity.
Gum bleeding (intensity and frequency)	Patients report to have occasional gum bleeding and considering this as a sign that something is wrong with their dental health. It signals an active phase of periodontal disease, but can be treated and reduced soon. Gum bleeding is included in the benefit assessment as one aspect of symptomatic gingivitis.
aesthetic consequence: "long teeth" due to gum recession"	Patients considered gum recession a relevant disease aspect since it leads to non-desirable outward appearance. They consider themselves looking older or ugly and sometimes even try to avoid smiling. This endpoint is not included in the benefit assessment, but considered an important implication of periodontal disease by patients.
Frequency of follow-up visits	Differences in effectiveness of different follow-up care regimes are
Out-of-pocket costs for patients (including mandatory professional plaque removal and follow-up care)	Patients reported out of pocket expenses ranging from none to around 500 Euro annually. Some patients choose to be treated at the University Hospital because of no fees.
Excluded disease and treatment aspects	
Disease and treatment aspect	**Reason for exclusion**
Attachmentlevel	The surrogate endpoint „Attachmentlevel" that was applied in the benefit assessment, as well as the diagnostic criteria probing depth, gingival / periodontal index were not considered in the preference analysis, since they are related to tooth loss. All are surrogate endpoints and patients are not familiar with most of them. Even though patients were aware that their dentists measures pocket depth during examinations, they were not aware of specific pockets depth and severity of disease or necessity of treatment.
Probing depth	
Gingival index / Periodontal index	
Quality of life (or its separate dimensions)	Only some aspects of quality of life were selected for inclusion since not all dimensions identified in quality of life instruments seemed to be relevant in periodontal disease.
Pain (intensity and frequency)	Is not reported as a typical symptom, neither by patients nor by periodontologists. Usually occurs if other dental diseases are present at the same time (e.g. abscess).

	Pain during treatment was excluded since all treatments can be provided with anesthesia and the experience of pain is restricted to shortly after treatment.
Halitosis	Is not considered a relevant symptom and rather perceived to be associated with other primary diseases or conditions (e.g. common cold, bad oral hygiene).
Side effects of antibiotics: nervous system (e.g. gastro-intestinal disorder, dizziness, risk of antibiotic resistance)	Usually patients only receive antibiotics, if they suffer from severe aggressive or treatment resistant periodontal disease or have other relevant comorbidities. Therefore patients usually have no experience with antibiotic treatment of periodontal disease and are also not familiar with the corresponding side effects.
Fear of dentures	Patients and periodontologist stated that loose teeth are related to loosing teeth soon and did not feel that really loose teeth could be saved. Receiving dentures is an immediate consequence of losing teeth.
Tooth mobility	
Problems with biting, chewing, speaking	Patients did not report this problem in relation to periodontal disease.
(fear of) stigmatisation	This is related to tooth loss as well as "long teeth" in the patients' perception.
Hygiene measures patients have to complete	This can be determined by patients themselves and is not related to dental treatments.

Level specification

Attribute	Selection of levels	Levels included in DCE
Tooth loss (within next 10 years)	The extent of tooth loss was estimated based on different types of studies (prospective controlled clinical trials or observational studies) and included patients from the general population (likely to have some tooth loss related to non-diagnosed periodontal disease) and patients with moderate or severe periodontal disease. [3, 19, 18, 20, 22, 23, 21, 28, 29]. A systematic review and meta-analysis Lee et al. 2015 conclude that on average 20 teeth need to be treated regularly for 5 years to save one tooth. Studies report a tooth loss ranging from 0 to 2 teeth over a period of 2 to 10.5 years [3]. The extent of tooth loss varied with disease severity, type of treatment and extent of patient compliance. Most studies did not only include periodontally diseased patients (e.g. only 20% of tooth loss in Costa et al.) and some did not specify the primary cause of tooth loss [20, 21]. Based on the studies and in accordance with the clinical experts consulted for this study, the levels for tooth lost were selected to range from 0 to 2 teeth over a period of 10 years. The time frame of 10 years was selected to provide integer numbers instead of eg percentages.	No tooth lost One tooth lost Two teeth lost
Symptoms and complaints	Patients reported for gum bleeding that it happens occasionally and with differing intensity. Neither frequency nor intensity could be linked to a particular risk factor patients were aware of. Patients knew that "long teeth" due to gum recession is a permanent symptom with very slow progression if periodontal disease is treated and regular dental hygiene is maintained. Sensitive tooth necks were also considered to be present permanently or with increasing intensity depending on e.g. consumption of cold / hot drinks and food. Through literature review, expert or patient interviews no specific values for frequency or intensity could be identified for any of the selected symptoms and complaints. Therefore these symptoms and complaints were summarised as one attribute with different categorical levels.	no complaints occasional gum bleeding "long teeth" due to gum recession sensitive tooth necks
Own costs for treatment, follow-up care and re-treatment per year	Costs ranged from 0 Euro up to 500 Euro of annual treatment costs reported by patients and price levels for dental scaling.	0 Euro per year 100 Euro per year 300 Euro per year 500 Euro per year
Frequency of follow-up visits	Levels were selected based on common frequencies of follow-up visits as identified through periodontist and patient interviews.	none necessary 2x per year 4x per year

This list of attributes and levels was consented with the IQWiG at meeting on 15th December 2015.

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