Relevant Domains, Core Outcome Sets and Measurements for Implant Dentistry Clinical Trials: The ID-COSM International Consensus Report

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Data availability statement

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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Author contributions

Maurizio S. Tonetti conceived the work and drafted the final report based on the discussions and consensus development meetings. Maurizio S. Tonetti and Mariano Sanz co-chaired the process. Tord Berglundh, Elena Figuero, Lisa Heitz-Mayfiled, Hongchang Lai, Ronald Jung, Ian Needleman, Panos N. Papapanou, Mariano Sanz, Frank Schwarz and Maurizio Tonetti participated as members of the steering committee. Gustavo Avila-Ortiz, Francesco Cairo, Jan Derks, Filippo Graziani, Fernando Guerra, Irena Sailer, Ignacio Sanz-Sanchez, Junyu Shi, Daniel Thoma participated in the experts' committee together with the co-chairs and the steering committee. Mariano Sanz led the Delphi survey, and Ian Needleman the patient involvement part of the project. All co-authors participated in all stages of the consensus development process and critically reviewed the manuscript.

Running title: The ID-COSM Initiative Consensus

Abstract

Aim: Lack of consistently reported outcomes limits progress in evidence-based implant dentistry and quality of care. The objective of this initiative was to develop a core outcome set and measurements for implant dentistry clinical trials (ID-COSM).

Materials and methods: This COMET registered international initiative comprised 6 steps over 24 months: i) systematic reviews of outcomes reported in the last 10 years; ii) international patient focus groups; iii) a Delphi project with a broad range of stakeholders (care providers, clinical researchers, methodologists, patients and industry representatives); iv) expert group discussions organising the outcomes in domains using a theoretical framework and identifying the core-outcome sets; v) identification of valid measurement systems to capture the different domains; vi) final consensus and formal approval involving experts and patients. The methods were modified from the best practice approach following the OMERACT and COMET manuals.

Results: The systematic reviews and patient focus groups identified 754 (665 + 89, respectively) relevant outcome measures. After elimination of redundancies and duplicates, 111 were formally assessed in the Delphi project. By applying pre-specified filters, the Delphi process identified 22 essential outcomes. These were reduced to 14 after aggregating alternative assessments of the same features. The expert committee organised them into 4 core outcome areas: i) pathophysiology; ii) implant/prosthesis lifespan; iii) life impact; and iv) access to care. In each area, core outcomes were identified to capture both the benefits and harms of therapy. Mandatory outcome domains included: assessment of surgical morbidity and complications, peri-implant tissue health status, intervention-related adverse events, complication-free survival, and overall patient satisfaction and comfort. Outcomes deemed mandatory in specific circumstances comprised: function (mastication, speech, aesthetics, denture retention), quality of life, the effort for treatment and maintenance, and cost-effectiveness. Specialised core outcome sets were identified for bone and soft-tissue augmentation procedures. The validity of measurement instruments ranged from international consensus (peri-implant tissue health status) to early identification of important outcomes (patient-reported outcomes identified by the focus groups).

Conclusions: The ID-COSM initiative reached a consensus on a core set of mandatory outcomes for clinical trials in implant dentistry and/or soft tissue/bone augmentation. Adoption in future protocols and reporting on the respective domain areas by currently ongoing trials will contribute to improving evidence-informed implant dentistry and quality of care.

Keywords: Implant dentistry, core outcome set, outcome domain, clinical trials, consensus conference

Clinical relevance

Scientific rationale for the study: A standardised set of outcome measures in implant dentistry clinical trials is needed. These should cover broad domains to adequately capture the full spectrum of benefits and harms in implant dentistry, including outcomes relevant to people with lived experience of dental implants.

Principle findings: This international initiative identified four core areas and 11 mandatory outcome domains (ID-COSM) that should be included in the protocol and reporting of implant dentistry clinical trials. Specialised domains with additional mandatory outcomes were identified for bone and soft tissue augmentation trials (BA-COSM and STA-COSM).

Practical implications: Adopting the ID-COSM set of mandatory outcome domains will contribute to improving the evidence base of implant dentistry and lead to better-informed care.

1. Introduction

Outcome research is critically important to improving the quality of care. It comprises the accurate identification of the full spectrum of benefits and harms of interventions, the organisation of key features in domains and the identification of valid measurement instruments to capture them accurately. A core outcome set (COS) is an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care (COMET initiative –www.comet-initiative.org).

The 2012 European Federation of Periodontology workshop on implant dentistry research identified key areas for improvement in research design and reporting. Focusing on clinical research, the key recommendations included using high-quality randomised clinical trials to establish efficacy and reporting common outcome domains to adequately assess benefits and harms (Tonetti & Palmer, 2012). At the time, randomised clinical trials were rather infrequent in implant dentistry, but a dramatic increase in interventional research has been noted in recent years. A recent systematic analysis covering publications between 2005 and 2020 identified 1538 unique randomised clinical trials in this field. Of these, 238 were published in 2005-2010, 486 in 2011-2015, and 809 in 2016-2020 (Shi, Zhang, et al., 2022). In parallel to the increase in numbers, systematic reviews have also shown an improvement in the quality of reporting (Cairo, Sanz, Matesanz, Nieri, & Pagliaro, 2012; Lieber, Pandis, & Faggion, 2020; Shi, Zhang, et al., 2022).

Consolidation of these efforts into a systematic evidence base supporting the development of robust clinical practice guidelines in implant dentistry (Faggion et al., 2017), however, has been hampered by difficulties in synthesising research data in analyses. This is mainly due to the lack of consistently reported outcomes which results in the inability to perform meaningful meta-analyses in most of the published systematic reviews. Data from the five recent systematic reviews on implant dentistry clinical trial outcomes commissioned in the context of the Implant Dentistry Core Outcome Set and Measurements (ID-COSM) initiative (Avila-Ortiz, Couso-Queiruga, Pirc,

Chambrone, & Thoma, 2022; Derks et al., 2022; Messias, Karasan, Nicolau, Pjetursson, & Guerra, 2022; Sailer et al., 2022; Shi, Montero, et al., 2022) show an extensive list of reported outcomes. Additionally, the assessment of these outcomes was frequently based on different methodologies. Despite growing attention to patient-reported outcomes in dentistry, patient and public participation in the evidence-informed process has lagged behind other areas of medicine, partly due to the lack of patient associations focusing on aspects of oral health. Consequently, the patient perspective of what is important in assessing different treatments or the outcomes of clinical decision-making has yet to be systematically considered in oral health research and in implant dentistry.

In other areas of medicine, the above limitations have been addressed by defining core-outcome sets and measurement systems and involving patients and/or the public in the process. Pioneering work dating back more than 30 years in fields like rheumatoid arthritis led to the establishment of organisations focused on the development and refinement of core outcomes, such as the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT, (Tugwell & Boers, 1993)) in musculoskeletal diseases or the Core Outcome Measures in Effectiveness Trials (COMET), focused on the methodology across disciplines and diseases. Such work has been instrumental in improving the quality, and the clinical relevance of the evidence gathered in clinical trials and has effectively promoted outcome research in multiple disciplines.

This consensus report presents the first generation of standardised outcome domains and measurements for implant dentistry clinical research. It describes the process, the scientific evidence and the patient's perspectives informing the process, its rigorous methodology, and the agreed-upon core outcome areas and domains. It also provides a list of measurement instruments for capturing benefits and harms in the relevant domains.

2. Materials and methods

2.1 Protocol and registration

The present core outcome set and measurement development process was registered with COMET (No. 1765 accessible at https://comet-initiative.org/Studies/Details/1765). The protocol followed the COS-STAP statement (Kirkham et al., 2019), and the process followed modifications of the COS-STAD guidelines (Kirkham et al., 2016) and the COMET and OMERACT handbooks (Beaton, Maxwell, S, Shea, & Tugwell, 2021; Williamson et al., 2017).

2.2 Project outline

The project consisted of several elements: i) evidence-based reviews; ii) international patient focus groups; iii) a three-round Delphi process; iv) semi-structured expert group discussions; and v) a formal consensus meeting. It was carried out between November 2020 and October 2022. Figure 1 shows the overall organisation and timeline of the project and reports the number of involved stakeholders in all stages of the process. Throughout the process, all participants had the opportunity to review the material and propose amendments before moving to the next stage.

Figure 1.

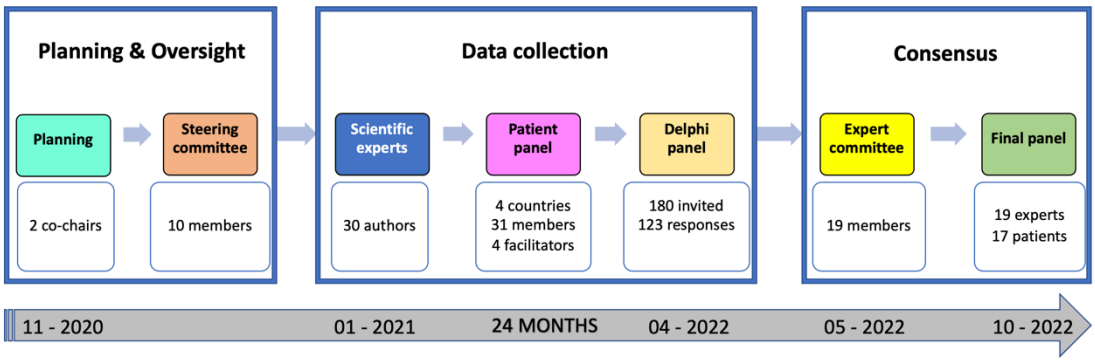

Figure 1 legend. Schematic representation of the different phases and levels of stakeholder representation over the 24 months of the ID-COSM project.

2.3 Systematic reviews

Five systematic reviews covering the main areas of clinical research in implant dentistry were commissioned to identify the outcomes used in publications from the 10-year period between 2011 and 2020. The five systematic reviews covered the following topics: i) single and partial tooth replacement (Sailer et al., 2022); ii) rehabilitation of full-arch edentulism (Messias et al., 2022); iii) prevention and treatment of peri-implant mucositis and peri-implantitis (Derks et al., 2022); iv) soft tissue augmentation (Avila-Ortiz et al., 2022); and v) bone augmentation trials (Shi, Montero, et al., 2022). All protocols were registered in PROSPERO.

2.4 People with lived experience

To gain an independent perspective of outcomes that matter to patients, 31 people with lived experience (PWLE) participated in four focus groups representing low-middle- (China & Malaysia) and high-income countries (Spain & UK) (Needleman et al. 2023). To avoid biased responses, participants were not provided with knowledge of outcomes collected in implant dentistry trials. Focus groups were conducted with a standardised methodology by trained facilitators and identified 34 candidate outcomes.

2.5 Delphi project

The outcomes identified in the systematic reviews and the patient focus groups were incorporated into an exercise using the Delphi methodology for gathering information from experts and other stakeholders (clinical trials specialists, methodologists, clinicians, PWLE, and industry representatives) (Sanz et al., 2023). Questionnaires were developed using these outcomes, which were completed in two rounds and incorporated individual feedback, group judgement and a final discussion to achieve the consensus through a structured unbiased assessment by multiple stakeholders. The DelphiManager software, developed and maintained by the COMET initiative,

was used to produce and later analyse the e-Delphi questionnaire. Participants were asked to score each outcome on a nine-point Likert scale and were offered the opportunity to add outcomes and comments as described (Williamson et al., 2017). One hundred eighty stakeholders were invited, of which 123 participated in the first and second rounds. Experts (N=19) and PWLE representatives (N=7) participated in the third Delphi round that used 3 filters to reduce the number of outcomes from 111 to 14. The first filter removed outcomes that did not receive a score of 7-9 (on a nine-point scale, with 1=least important and 9=most essential to include) by at least 70% of respondents or that received a score of 1-3 from 15% of respondents in the Delphi survey. The second filter excluded aspects of the PICO questions related to reporting on patient/population, intervention or comparison rather than outcomes. The third filter aggregated multiple ways to measure the same feature in a single outcome. At the end of the third round, experts and PWLE representatives were asked to anonymously rate each outcome as: i) essential for inclusion in the core set, ii) possible to be dropped, or iii) do not know. Detailed methods and results have been reported (Sanz et al., 2023).

2.6 Consensus Process

Experts met in person on June 15, 2022, for a one-day workshop in Copenhagen. Prior to the workshop, participants were trained in several online meetings: i) in best practice approaches to identify outcome domain areas covering benefits and harms according to the OMERACT approach (Beaton et al., 2021), and ii) in the development and use of the OMERACT "onion" concept to classify outcomes as mandatory in all trials, mandatory in specific circumstances, and important but optional. They also received a summary of the Delphi results. At the meeting, experts organised outcome domains according to a mindmap and agreed upon the definition and use of a specific tool – the ID-COSM onion (Figure 2) – and the format of specific outcome definition tables modified from the OMERACT manual (Table 1). The ID-COSM onion classifies relevant outcomes

into three layers: 1a) mandatory in all trials; 1b) mandatory in specific types of trials; 2) important but optional; and 3) research agenda items.

Figure 2. ID-COSM "onion"

Figure 2 legend. Illustration of the ID-COSM "onion" depicting the different layers in classifying outcomes: mandatory outcomes in all trials (core set to be reported in all clinical studies), outcomes mandatory in specific types of trials (expanded core set with additional mandatory outcomes), outcomes that are considered important but optional, and outcomes that belong to the research agenda. The latter category comprises areas that are currently under investigation and may provide outcomes for inclusion in the core set, once adequate development and validation has been completed.

Table 1. Domain and Measurement Definition Table Template

Core Area	Pathophysiology/life impact/lifespan/access to care
Broad Domain	General term of broad domain [e.g. pain impact]
Target Domain	The name given to this more specific domain [e.g. impact of pain in all realms of life], this is what is assessed
Working definition of target domain	Definition of the scope of the domain: what are the features that should be captured by the measurement instruments.
Measurements	Input: what needs to be measured and how to capture it (valid measurement tools)

Qualitative or literature support	Insert literature reference on outcome and measurement systems Insert input from patients/public focus group
Sources of variability in score	Identification of sources of variability or contextual factors

After the Copenhagen meeting, expert groups were assigned to draft the Outcome Domain and Measurement Definition Tables and specific ID-COSM onions for the multiple applications covered in the five systematic reviews. Definitions and drafts were discussed, and changes were agreed upon at an online expert meeting on September 21, 2022 that also included the decision to consolidate core outcome sets for single and partial tooth replacement, full-arch edentulism, and prevention and treatment of peri-implant mucositis and peri-implantitis. The group agreed that specialised outcome sets were necessary to capture outcomes of soft tissue and bone augmentation trials. Based on the result, working groups were tasked with the identification/definition of appropriate measurements to accurately reflect the core outcomes of interest. The identified measures were refined and agreed upon in an additional online expert meeting held on October 17, 2022. Lastly, core outcomes and measurements were discussed in a final online meeting with experts (N=19) and PWLE (N=17) and formally voted on using an anonymous online tool (Polls App for Teams, Microsoft, USA) on October 31, 2022. The strength of consensus was evaluated using the GRADE approach (German Association of the Scientific Medical Societies (AWMF), 2012). Throughout the process, also considering disruptions due to COVID-19, recordings and online power point presentations were made available to members of the panel who could not join a specific meeting.

3. Consensus Results

3.1 Core outcome areas and domains – implant dentistry trials

Outcomes identified in the Delphi survey and filtered through the third Delphi round (N=13) were organised into four core domain areas and aligned with a modification of the theoretical framework developed by the OMERACT group to organise core outcome sets: i) pathophysiology, ii) lifespan of the device/restoration, iii) life impact, and iv) access to care. In each core area, outcomes were grouped to reflect benefits and harms. Figure 3 shows the mindmap of core outcome areas and domains agreed upon by experts at the Copenhagen meeting. Regarding pathophysiology, benefits were captured in terms of improved function and comprised: i) mastication, ii) smiling/aesthetics, iii) speech, and denture retention. The main outcomes related to harms included surgical morbidity and complications and alterations of the tissue health status reflected by case diagnosis (health, peri-implant mucositis, peri-implantitis) and marginal bone level/loss. To capture the long-term benefits (lifespan) of tooth replacement with implants, complication-free survival was considered the most informative parameter. In contrast, technical complications and implant and prosthesis loss were used to describe harms. Life impact was identified as a core area with benefits captured by overall satisfaction with treatment and changes in quality of life, while harms were described by effort for treatment, oral hygiene and professional maintenance. Access to care was evaluated using health economic aspects including cost-effectiveness, affordability and the level of professional competence/experience necessary to ensure a good outcome.

Figure 3. ID-COSM Core Outcome Areas and Domains

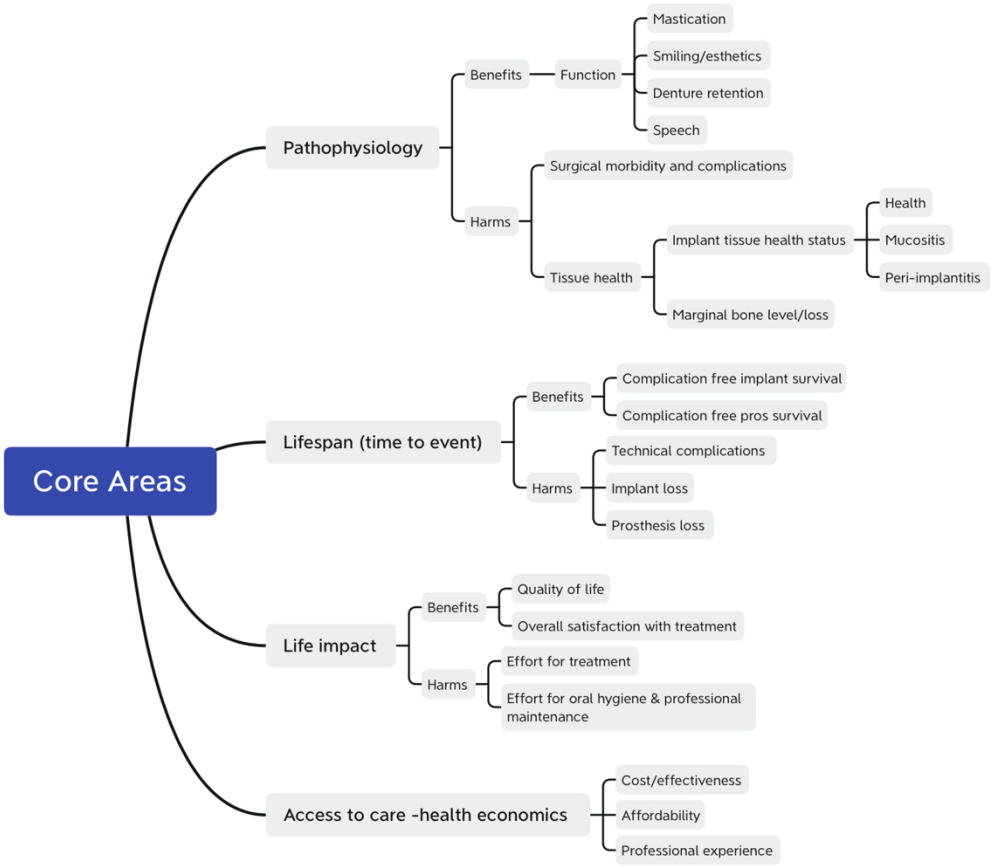

Figure 3 legend. Mindmap of the core outcomes areas and core outcome domains that should be captured in implant dentistry clinical trials. Each area needs to capture both benefits and harms.

3.2 Definition of core outcome domains and measurements – implant dentistry trials

To avoid ambiguity, the expert group defined the scope of each outcome domain in the different core areas using the template shown in Table 1.

The commissioned systematic reviews were used as the primary knowledge base to identify measurements that could discriminate the outcome domains of interest. These were complemented by a targeted evidence search, if necessary. The evidence generally needed more uniform and validated measures to precisely discriminate the outcomes of interest. In particular,

the consensus identified the existence of a large disparity in terms of the availability of validated tools to measure the different outcome domains. On one side of the spectrum, the assessment of tissue health status was performed using case definitions agreed upon in an international consensus conference (Berglundh et al., 2018). On the other, outcome domains with newly expanded scope, thanks to patient participation in this initiative, will require developing specific tools. The consensus group decided to maintain such outcomes within the core outcome set to emphasise their importance and the need to perform targeted research to develop and validate the necessary instruments. Specific assessment approaches were included in the domain definition and measurement tables (see below). Frequently, the selection of appropriate measurements is reported as an example. Investigators carefully considered each outcome's options to identify the best measurement instrument. The agreed description of each domain with its measurements is listed below.

3.2.1 Pathophysiology-benefits: Function

This domain's scope is assessing the functional benefit(s) of tooth replacement with implants. Based on the specific condition (population in PICO), the functional benefits include: i) masticatory function; ii) phonetics/speech; iii) aesthetics of the smile/ability to relate with others/self-worth; and/or iv) retention of a denture (Messias et al., 2022; Sailer et al., 2022). This domain includes both patient-reported and professionally assessed outcome measures

A. masticatory function (masticatory test, e.g. Schimmel test (Schimmel et al., 2015))
B. phonetics/speech (phonetic exam), or VAS (0-100), PROM
C. aesthetics of the smile/ability to relate with others/self-worth (VAS 0-100), PES/WES (Belser et al., 2009; Fürhauser et al., 2005)
D. retention of a denture (yes/no) or qualitative evaluation

3.2.2 Pathophysiology-harms: surgical morbidity and complications

This domain comprises early intervention-related adverse effects. It is defined as all harms and adverse events arising from surgical implant placement. These include (1) complications from the surgical placement of dental implants (e.g. failure to osseointegrate or early implant loss; injuries to adjacent structures; surgical wound failure, infection, swelling, post-operative pain, etc. Tonetti et al. 2004, Lang et al. 2007, Tonetti et al. 2017) and (2) complications associated with the temporary or definitive prostheses upon immediate implant loading after surgical placement.

The presence/absence of surgical complications encompasses both patient-reported outcomes and objective assessment. Evaluation of surgical complications should include the following:

A. **The number of days of total or partially impaired activity:** Total impaired activity: days that, in the patient's opinion, they could not perform their ordinary life activity, including work; Partially impaired activity: days that, according to the patient, they could only partially perform their everyday life activity, including work.
B. **Post-operative pain:** Patient-reported outcome: 100 mm visual analogue scale (VAS) or 5-point Likert scale – Use of pain control medications (number of tablets)
C. **Post-operative oedema/swelling**: Clinician-reported rating: 0=no visible oedema; 1=slight oedema (intraoral swelling in the surgical zone); 2=moderate oedema (extraoral swelling in the surgical area); 3=severe oedema (extraoral swelling extending the surgical site) and/or visible hematoma and ecchymosis.
D. **Surgical implant placement complications (reported dichotomously):** Intra-operative haemorrhage, ii) Injuries to adjacent structures (including teeth, nerves, maxillary sinus), iii) Injuries to nerves (self-reported sensory impairment); iv) Injuries to adjacent teeth (self-reported sensitivity/pain and/or radiographic evaluation), v) Implant displacement over the apical anatomic limit (maxillary sinus, sublingual space, submandibular space etc.)
E. **Post-operative implant placement complications (reported dichotomously):** Loss of

osseointegration (or failure to achieve osseointegration) or early implant failure (early implant loss); ii) Post-operative haemorrhage; iii) Wound dehiscence primary/ secondary (Wachtel et al. 2003), iv) Wound/Graft Infection.

F. **Post-operative complications related to prosthesis insertion (temporary or definitive) in immediate loading/temporisation cases:** Peri-implant soft tissue inflammation due to i) poor fit; ii) loss of retention of the prosthesis (screw loosening, partial de-cementation); iii) presence of remnants of submucosal luting cement following cementation of an implant-supported prosthesis; iv) Inability of the patient to obtain access to remove plaque from the prosthesis.

3.2.3 Pathophysiology-harms: peri-implant marginal tissue health status

Assessment of peri-implant tissue health status defines the presence of peri-implant mucositis, the presence of peri-implantitis according to established case definitions (2017 Workshop) and peri-implant health defined by the absence of either condition (Berglundh et al., 2018; Derks et al., 2022). These should include an assessment of the following parameters and specific reporting as follows:

A. **Bleeding on Probing (BOP)/Suppuration on Probing (SOP).** Tool: 0.5 mm diameter periodontal probe at 20-25 g. Assess: circumferentially. Measure in a dychotomous fashion (yes/no) and record at 4 or 6 sites per implant. Report the number/proportion of implants presenting with complete absence of BOP/SOP; the number/proportion of implants with limited extent of BOP (≤1 spot/implant - the presence of a single spot – not line or profuse bleeding– of bleeding on probing is considered acceptable); and the number/proportion of implants with extensive BOP (≥2 spots/implant or ≥1 site/implant with a line or profuse bleeding), and the number/proportion of implants with SOP.

B. **Probing pocket depth (PPD)** Tool: 0.5 mm diameter periodontal probe at 20-25 g.

Assess: circumferentially. Measure in mm and record at 4 or 6 sites per implant. Report mean of all sites, deepest site per implant and number/proportion of implants with PPD ≤5 mm.

C. **Marginal bone level (MBL)** Tool: intra-oral radiograph using the parallel technique with a standard holder. Assess and record: mesial and distal. Measure in mm from the implant platform. Also, assess and report examiner reproducibility and measurement error.

D. In studies with repeated assessments, assess and record **changes over time** for the parameters mentioned above. Report mean changes and number/proportion of implants presenting with changes of different magnitude (e.g. MBL change exceeding measurement error, MBL gain/loss >2 mm).

E. **Composite outcome** Concomitant absence of BOP (≤1 spot/implant), SOP, shallow PPD (≤5 mm) and absence of MBL loss. Report the number/proportion of implants/patients. Report: the number/proportion of implants/patients with health/peri-implant mucositis/peri-implantitis following the case definition.

3.2.4 Lifespan-benefits: Complication-free survival

It is defined as the time from completion of treatment (delivery of prosthesis) until the patient experiences the first complication requiring intervention. It is reported as a time-to-event analysis (months/years). The type and time of complication (event) should be fully reported in tabular format. It is understood that multiple Kaplan-Meier analyses will be required to accurately capture the spectrum of complications. For example, these will include biological complications (peri-implant mucositis, peri-implantitis), technical complications, and implant loss (Karlsson et al., 2018; Karlsson, Derks, Wennström, Petzold, & Berglundh, 2020). To capture multiple events occurring in the same case, an additional recurrence analysis may be considered (Cortellini, Buti, Pini Prato, &

Tonetti, 2017; Cortellini, Stalpers, Mollo, & Tonetti, 2020; Shi et al., 2021). In cases with multiple implants, separate analyses should be performed for implants and prostheses.

3.2.5 Lifespan-harms: Technical or intervention-related complications, Implant/Prosthesis loss

Technical complications and intervention-related adverse events occur after the insertion of the definitive prosthesis. This domain comprises adverse device events (implant, abutment and prosthetic components), screw loosening, decementation, fracture of prosthetic materials, etc., and should follow standard reporting for medical devices.

It is reported as the presence/absence of an adverse event as described in the working definition. It is expressed dichotomously or by validated rating scales (e.g. USPHS criteria (Naenni, Bindl, Sax, Hämmerle, & Sailer, 2015; Pol, Raghoebar, Cune, & Meijer, 2022)).

- **Implant/Prosthesis loss.**
- **Fixed Prostheses**: chipping, framework fracture, veneering fracture, abutment fracture, screw fracture, screw loosening, loss of retention, de-cementation.
- **Removable Prostheses**: fracture or dislodgement of matrix or bar, loss of retention of components, fracture of the prosthesis, relining/rebase, fracture/detachment of acrylic teeth, loosening of components (matrix, bar), wear of matrix, wear of acrylic teeth, replacement of acrylic teeth, discolouration.

They can be described as either minor (can be corrected in one appointment) or major (requires >1 appointment).

3.2.6 Life impact-benefits: quality of life

Oral health-related quality of life should be self-reported with a standard validated instrument sensitive to the specific condition. Examples of validated instruments include OHIP-49 (Slade &

Spencer, 1994), OHIP-14 (Slade, 1997), OHIP-20 / OHIP-EDENT (Allen & Locker, 2002), Dental impact on the daily living questionnaire (Leao & Sheiham, 1996), GOHAI (Atchison & Dolan, 1990). For some conditions, assessment of quality of life may require custom measures/intruments which are yet to be validated.

3.2.7 Life impact-benefits: overall satisfaction with treatment

This domain covers the overall level of patient satisfaction with the treatment received and comfort; it is a patient-reported outcome. Measures include patient-reported outcomes with a 100mm visual analogue scale (VAS) with defined questions and anchors (e.g. not at all satisfied – perfectly satisfied) or a 5-point Likert scale. In some conditions, validated, condition specific rating scales should be considered. Examples of validated standard instruments include the McGill Denture Satisfaction Instrument (Awad & Feine, 1998; de Grandmont et al., 1994; Feine et al., 1994), the Denture Satisfaction Questionnaire (DSQ) by Allen and McMillan (Allen & McMillan, 2002), the Patient Satisfaction Questionnaire (Layton & Walton, 2011) (Brennan, Houston, O'Sullivan, & O'Connell, 2010) (de Bruyn, Collaert, Lindén, & Björn, 1997; Komagamine, Kanazawa, Kaiba, Sato, & Minakuchi, 2014; Komagamine et al., 2012; Vermylen, Collaert, Lindén, Björn, & De Bruyn, 2003).

3.2.8 Life impact-harms: effort for treatment and maintenance

This domain covers the effort for treatment and maintenance from a patient perspective. The overall effort needed for treatment includes assessment of the duration (beginning to end), and total time effort (hours, number of appointments). It also includes the overall effort needed to maintain the result over time in terms of daily care (self-performed oral hygiene) and professional visits (supportive care). Examples of measurements include:

- Duration of treatment (months from beginning to end and number of appointments)
- Effort for maintenance in daily care (number and complexity of self-performed oral

hygiene sessions and related duration, PROM –VAS 0-100, e.g. “How difficult is it for you to clean your implant prosthesis?)

- Professional visits for supportive peri-implant care (number of professional visits/year).

3.2.9 Access to care: cost-effectiveness

Assessing this outcome requires an economic analysis comparing the relative cost and outcomes (effects) of different courses of action. One relies on the ratio of costs to gains in health. Health gains include improvement in clinical or professionally measured outcomes (such as esthetics and function), quality-adjusted life years, or quality-adjusted tooth/implant years). A cost-effectiveness analysis requires the assessment of direct plus indirect costs of treatment (time required to receive the treatment, including the absence from work and transportation and maintenance/treatment of complications) in relation to the benefit of treatment, i.e patient satisfaction with and longevity of treatment.

3.2.10 Access to care: affordability

Treatment affordability is an economic analysis comparing the relative cost and household resources. One relies on the ratio of costs to total household resources. It is measured as direct and indirect costs of treatment and supportive care in relation to the median income of the country/region. It has not been studied in implant dentistry clinical trials, but was considered essential among the relevant outcomes identified by the PWLE focus groups.

3.2.11 Access to care: professional experience/expertise

This domain covers the definition of the level of competence required for delivering an adequate level of care for a specific implant dentistry procedure. It relates to the level of care: primary care, specialist care, and tertiary care. It comprises an assessment of the qualifications of the clinician.

For example, clinician's specialist qualification (yes or no), number of years of clinical practice in implant dentistry, and number of implant-related procedures provided annually by the clinician. It parallels the data required by the CONSORT extension for non-pharmacological interventions. It has not been studied in implant dentistry clinical trials but was considered essential among the relevant outcomes identified by the PWLE focus groups.

3.3. Core Outcome Set for Implant Dentistry Clinical Trials – ID-COSM

Work by the expert group identified 11 core outcome domains (5 mandatory in all trials and 6 mandatory in specific circumstances/trial types) for use in implant dentistry clinical trials. The clinical trials evaluated to identify these core outcome domains encompassed a wide area of research involving implant treatment, including all surgical and restorative interventions associated with dental implant placement as well as the management of complications and diseases associated with dental implants. Trials evaluating soft tissue/bone augmentation procedures where dental implants were not placed were not included.

The agreed outcome domains are illustrated in Figure 4. The five outcome domains considered mandatory in all trials comprise the assessment of i) surgical morbidity and complications until definitive/final prosthesis delivery; ii) peri-implant tissue health status; iii) intervention-related adverse events; iv) complication-free survival; v) overall patient satisfaction and comfort. The definition of each outcome domain and its measurement instruments have been reported in the previous section.

Formal voting on the final set of ID-COSM core outcomes and measurements among experts and patients revealed unanimous consensus.

Figure 4. Core Outcome Set for Implant Dentistry Trials: ID-COSM Implant Dentistry

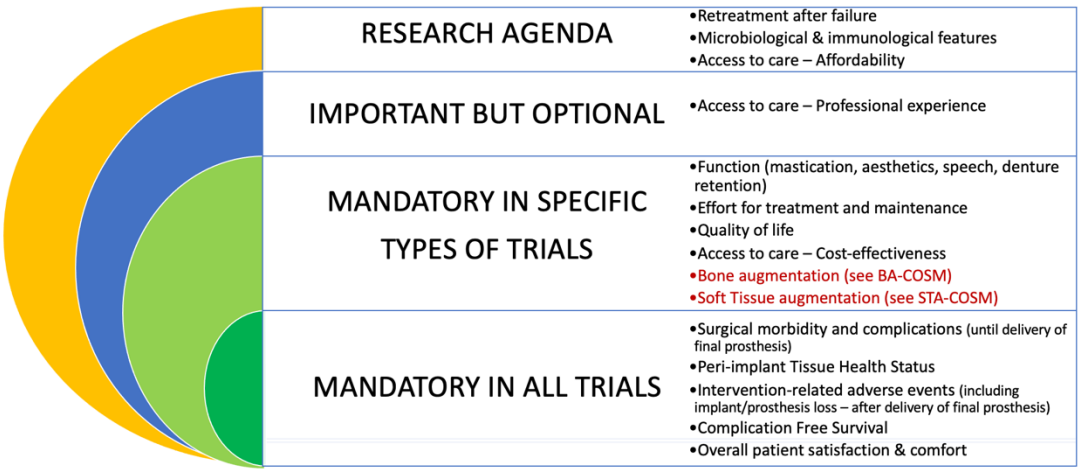

Figure 4 legend. Consensus of the core outcome domains inserted in the ID-COSM implant dentistry "onion". Five outcomes are considered mandatory in all trials, and 6 outcomes are considered mandatory in specific types of trials. Among the latter are the key pathophysiologic benefits of dental implant treatment: improving function. Appropriate functional benefit(s) should be selected based on the specific condition/population being treated. In red are specific outcomes mandatory for trials where the intervention involves bone (BA-COSM) or soft tissue augmentation (STA-COSM). For specifics about these outcomes, the reader is referred to Figures 5 and 6. Examples of the specific measures needed to capture ID-COSM implant dentistry outcomes are illustrated in the text.

Six outcome domains were considered mandatory in specific circumstances (types of trials or trials dealing with specific populations). Among these outcomes are the functional benefits of implant dentistry; these span from the improvement of mastication to improvements in aesthetics, smile, sense of self-worth, social interaction, speech and/or ability to retain a denture. The choice of capturing one or more of these functions depends upon the population/condition under study and the specifics of the intervention and comparison. Other aspects that should be considered for inclusion in a specific trial include i) measures of the effort required for treatment and maintenance of the implant and prosthesis (encompassing patient self-care and professional needs); ii) impact on measures of quality of life; and iii) cost-effectiveness assessments in trials where it is possible to estimate health economics. The panel of experts also agreed that in trials, in which the

intervention includes soft tissue and/or bone augmentation, specific outcomes are also mandatory and that specialised core outcome sets need to be applied to specifically enrich the set of mandatory outcome domains (please refer to the bone augmentation [BA-COSM] and the soft tissue augmentation [STA- COSM] core outcome sets, Figure 5b and 6b).

3.4 Definition of specialised core outcome domains – Bone Augmentation Trials (BA-COSM)

Figure 5A shows the mindmap of the specialised outcome domains identified for bone augmentation trials. The panel of experts recognised that bone augmentation could be part of the interventions in implant dentistry clinical trials or be assessed in specialised trials that do not include implant placement. In this context, the bone augmentation core outcome set and measurements (BA-COSM) domains can complement the general ID-COSM domains or be a stand-alone outcome set if implants are not placed within the trial.

Figure 5A. BA-COSM Core Outcome Areas and Domains for Bone Augmentation

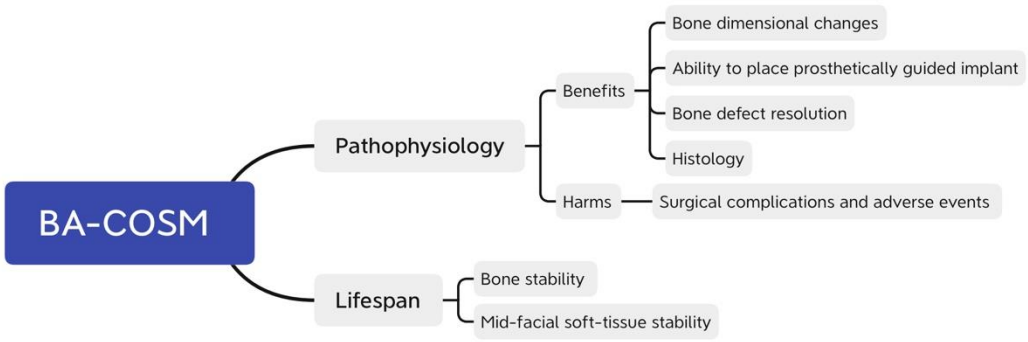

Figure 5A legend. Mindmap of the core outcomes areas and core outcome domains that should be captured in bone augmentation clinical trials.

Specific assessment approaches were included in the domain definition and measurement tables (see below). Frequently, the selection of appropriate measurements is reported as an example. Investigators shall carefully consider options while the necessary outcome research is conducted. The agreed description of each domain with its measurements follows.

3.4.1 Pathophysiology-benefits: bone dimensional changes

This domain area aims to identify changes in bone dimension (amount and rate of change) captured by linear or volumetric measurements to enable implant insertion in a prosthetically guided position with long-term complication-free survival of dental implants. Measurement examples include:

A. Clinical examination using a periodontal probe or a calliper with anatomic landmarks/stent as reference (Schwarz et al. 2018; Thoma et al. 2018).
B. 3D radiographic measurement: (a) superimposition of cone beam computer tomograms (CBCT) (Cesar et al. 2020); (b) measurement in CBCT with anatomy markers as references (Chiapasco et al. 2021; Abd-Elrahman et al. 2020); (c) volumetric change (Li et al. 2019).
C. 2D radiographic measurement of vertical changes: (a) measurement on panoramic radiographs with anatomy markers as references (Rammelsberg et al. 2015); (b) intra-oral radiographs using the parallel cone technique with a standard holder.

3.4.2 Pathophysiology-benefits: ability to place an implant

This domain area reports on the achievement of an adequate alveolar ridge for placing a properly dimensioned dental implant in the correct, prosthetically guided position with/without the need for additional grafting. The criteria are based on:

A. **In staged bone augmentation procedures** (alveolar ridge preservation, staged horizontal and/or vertical bone augmentation, staged soft-tissue augmentation) ability or not to place the implant in a prosthetically guided implant position with the endosteal portion of the implant completely in bone with more than 1-1.5 mm thickness on the buccal and oral aspect. Investigators should also report the need for additional bone augmentation based on the previous objective.

A. **In simultaneous approaches** (simultaneous horizontal and/or vertical bone

augmentation), the need of additional bone augmentation at re-entry if the previously exposed implant surface has not been completely surrounded by bone.

3.4.3 Pathophysiology-benefits: histology

This domain area reports on the biological healing characteristics of bone augmentation procedures. It comprises histology and functional tissue analyses. Histology reports on the fraction of newly formed bone, the soft tissue component (connective tissue/marrow spaces) and residual graft particles. Micro CT, immunohistochemistry (Keil 2021), and gene expression analyses (de Freitas et al. 2016) are frequently used to characterise the regenerated bone.

3.4.4 Pathophysiology-harms: surgical complications and adverse events

This domain area reports intervention-related surgical morbidity and adverse effects. It includes all harms and adverse events arising from bone augmentation procedures. It comprises complications associated with the placement of graft or bone augmentation devices (e.g. graft/device exposure, infection), injuries to adjacent structures, surgical wound failure, infection, swelling, and post-operative pain.

Presence /absence of surgical complications encompasses both patient-reported outcomes and objective assessment. Description of an adverse event is defined in the working definition. Evaluation of surgical complications must include:

A. **Number of days of total or partially impaired activity:** Total impaired activity: days that, in the patient's opinion, he/she could not perform his/her ordinary life activity, including work; Partially impaired activity: days that, according to the patient, he/she could only partially perform his/her ordinary life activity, including work. Report time to recovery.
B. **Post-operative pain:** Patient-reported outcome: 100 mm visual analogue scale (VAS) or 5-point Likert scale – Use of pain control medications.

C. **Post-operative oedema/swelling**: Clinician reported rating 0=no visible oedema; 1=slight oedema (intraoral swelling in the surgical zone); 2=moderate oedema (extraoral swelling in the surgical zone); 3=severe oedema (extraoral swelling extending the surgical zone) and/or visible hematoma and ecchymosis.

D. **Post-operative complications (reported dichotomously): i)** Post-operative haemorrhage; ii) Wound dehiscence primary/ secondary, iii) Wound/Graft/Device Infection.

E. **Wound failure:** Early wound healing index (Wachtel et al. 2003). Modified wound healing index.

3.4.5 Lifespan: bone stability

This domain area reports the stability of augmented alveolar bone volumes around an adequately dimensioned dental implant. Measurement examples include:

A. (Changes in) bone thickness in buccal and lingual surfaces assessed on CBCT
B. Percentage of resorbed bone volume versus initial (or augmented total) bone volume assessed on CBCT
C. Marginal bone level changes assessed on intraoral radiographs or panoramic radiographs
D. Percentage of resorbed bone height versus initial (or augmented total) bone height assessed on panoramic radiographs

Figure 5B shows the core outcome domains for bone augmentation trials identified by the experts and approved in the consensus. Formal voting on the final set of BA-COSM core outcomes and measurements among experts and patients obtained unanimous consensus.

Figure 5B. Core Outcome Set for Bone Augmentation Trials: BA-COSM

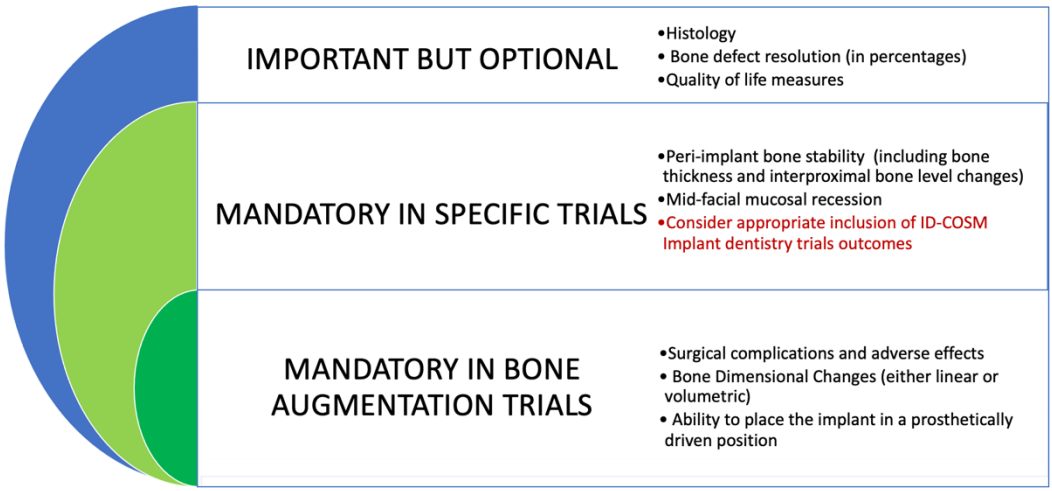

Figure 5B legend. Consensus on the core outcome domains inserted in the Bone Augmentation Core Outcome Set and Measurements (BA-COSM) "onion". 3 outcomes are considered mandatory in all trials, and 3 outcomes are considered mandatory in specific types of trials. In trials involving dental implants, the reader is referred to the need to include the general ID-COSM core outcome set (highlighted in red) and Figure 4. Examples of the specific measures needed to capture BA-COSM outcomes are detailed in the text.

Among mandatory outcomes in all bone augmentation trials, the consensus identified: i) assessment of surgical complications and adverse events, ii) dimensional bone changes, and iii) the ability to place the implant(s) in a prosthetically guided position. In specific types of trials, assessment of peri-implant bone stability and mid-facial mucosal recession were also considered mandatory (for this outcome domain, readers are referred to the STA-COSM). Finally, in bone augmentation trials involving implant placement, it is critical to refer to the general ID-COSM outcome set and include the relevant mandatory outcomes.

3.5 Definition of specialised core outcome domains – Soft Tissue Augmentation Trials (STA-COSM)

Figure 6A shows the mindmap of the specialised outcome domains identified for soft tissue augmentation. The consensus recognised that soft-tissue augmentation could be part of the interventions in implant dentistry clinical trials or be assessed in specialised trials that do not include implant placement. This area of research also includes the correction of soft tissue deformities around functioning dental implants. In this context, the soft-tissue augmentation core outcome set and measurements (STA-COSM) domains can complement the general ID-COSM domains or be a stand-alone outcome set, if implants are not placed within the trial.

Figure 6A. STA-COSM Core Outcome Areas and Domains for Soft-Tissue Augmentation

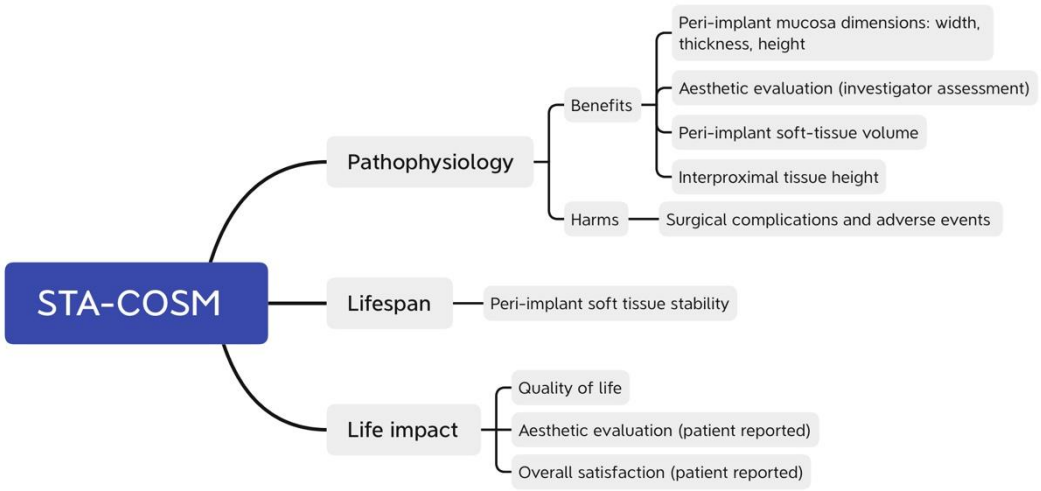

Figure 6A legend. Mindmap of the core outcomes areas and core outcome domains that should be captured in soft-tissue augmentation clinical trials.

Specific assessment approaches were included in the domain definition and measurement tables (see below). Frequently, the selection of appropriate measurements is reported as an example.

Investigators shall carefully consider options while the necessary outcome research is conducted. The agreed description of each domain with its measurements follows.

3.5.1 Pathophysiology-benefits: soft-tissue dimensions

This domain area aims to identify dimensional changes in the peri-implant mucosa in terms of width, thickness and height. It captures linear and profilometric changes in peri-implant soft-tissue dimensions over time following therapeutic intervention to achieve a desired clinical outcome (keratinised mucosa width, mucosal thickness and/or supracrestal tissue height gain) often to facilitate oral hygiene practice, protect the underlying bone and reduce the risk of peri-implant disease onset. Examples of relevant measurements are:

A. Keratinized mucosa width changes using a calibrated periodontal probe (Golmayo et al 2021).
B. Mucosal thickness changes via transmucosal horizontal probing using a piercing instrument (e.g., endodontic spreader) or with digital imaging analysis after superimposition of STL files or other advanced imaging methods (e.g., ultrasonography, Chan et al. 2018, Hutton et al. 2018, Cousu-Queiruga et al. 2021, Artzi et al. 2022,).
C. Supracrestal tissue height changes via transmucosal vertical probing using a piercing instrument or with digital imaging analysis after superimposition of STL files or other advanced imaging methods (e.g., ultrasonography, Puysis and Linkevicius 2015, Eghbali et al. 2016, Thoma et al. 2016, Zeltner et al. 2017, Chan et al. 2018,).

3.5.2 Pathophysiology-benefits: objective aesthetic assessment

This domain area includes the aesthetic assessment of the peri-implant mucosa by the investigator(s) following augmentation. It is performed using a standardised method (e.g., Pink

Esthetic Score [PES], Fürhauser et al. 2005) via direct or indirect assessment (Cooper et al. 2021, Cosyn et al. 2021).

3.5.3 Pathophysiology-benefits: mid-facial mucosal margin position

This domain area evaluates the position of the mid-facial mucosal margin. It reflects the ability to conceal the implant hardware below the tissue margin and, therefore, is related to soft-tissue esthetics. It measures the mid-facial mucosal margin position relative to a reproducible intraoral landmark (e.g., restorative interface, incisal edge) or a custom stent directly with a calibrated periodontal probe or indirectly with digital imaging assessments (e.g., standardised photographs or surface scans, Eghbali et al. 2018, Frizzera et al. 2019). Repeated measures provide estimates of stability/changes over time.

3.5.4 Pathophysiology-benefits: Peri-implant soft tissue volume

This domain area evaluates changes in peri-implant soft-tissue volume over time following augmentation procedures. Peri-implant soft tissue volume changes can be measured using standard tessellation language (STL) files obtained after intraoral scanning or extraoral scanning of models or other advanced imaging methods (e.g., STL and CBCT file superimposition or ultrasonography) using dedicated software (Eghbali et al. 2016, Zeltner et al. 2017, Naenni et al. 2021, Tavelli et al. 2021).

3.5.5 Pathophysiology-benefits: interproximal soft tissue height

This domain aims to assess changes in peri-implant interproximal soft tissue height dimensions over time following therapeutic intervention with augmentation purposes. Dimensional changes can be measured with an index (e.g. Jemt papilla score, Jemt 1997), measured directly with a

calibrated periodontal probe or indirectly with digital imaging analysis (e.g., standardised photographs or surface scans, Thoma et al. 2020).

3.5.6 Pathophysiology-harms: surgical morbidity and adverse events

This domain covers all harms and adverse events arising from soft-tissue augmentation. It comprises complications associated with the harvesting and placement of graft or soft-tissue augmentation devices (e.g. graft/device exposure, infection), injuries to adjacent structures, surgical wound dehiscence, postoperative infection, swelling, or pain.

The presence/absence of surgical complications encompasses both patient-reported outcomes and investigator assessment. The description of an adverse event is defined in the working definition. Evaluation of surgical complications must include:

A. **The number of days of total or partially impaired activity:** Total impaired activity: days that, in the patient's opinion, he/she could not perform his/her ordinary life activity, including work; Partially impaired activity: days that, according to the patient, he/she could only partially perform his/her ordinary life activity, including work.
B. **Post-operative pain:** Patient-reported outcome: 100 mm visual analogue scale (VAS) or 5-point Likert scale – Use of pain control medications.
C. **Intra-operative complications (reported dichotomously):** i) Intra-operative haemorrhage, ii) Injuries to adjacent structures (including bone, nerves, teeth, other; iii) If injuries to nerves occur: self-reported sensory impairment); iv) If injuries to adjacent teeth occur: self-reported sensitivity/pain and/or radiographic evaluation.
D. **Post-operative complications (reported dichotomously):** Post-operative haemorrhage; Wound dehiscence primary/ secondary; Wound/Graft/Device infection.
E. **Wound healing alterations:** Early wound healing index; Modified wound healing index (Wacthel et al. 2003).

3.5.7 Life impact-benefit: aesthetic and overall patient satisfaction

This domain covers patient-reported aesthetic outcomes and general satisfaction upon completion of therapy or at different follow-up intervals. They can be measured as:

A. Aesthetic satisfaction: 100 mm visual analogue scale (VAS) or 5-point Likert scale

B. Overall satisfaction: 100 mm visual analogue scale (VAS) or 5-point Likert scale

3.5.8 Life impact-benefit: quality of life

This domain reports the patient-reported impact of peri-implant soft tissue augmentation therapy on their quality of life. It is measured with oral health-related quality of life instruments (e.g., OHIP-14). Condition-specific instruments may be required for adequate sensitivity.

The specialised core outcomes identified by the experts and approved in the consensus in the Soft Tissue Augmentation Core Outcome Set and Measurements (STA-COSM) set are shown in Figure 6B. They cover conditions, in which soft tissue augmentation is performed before, during or after implant placement. Formal voting on the final set of core outcomes and measurements among experts and patients revealed unanimous consensus.

Figure 6B. Core Outcome Set for Soft Tissue Augmentation Trials: STA-COSM

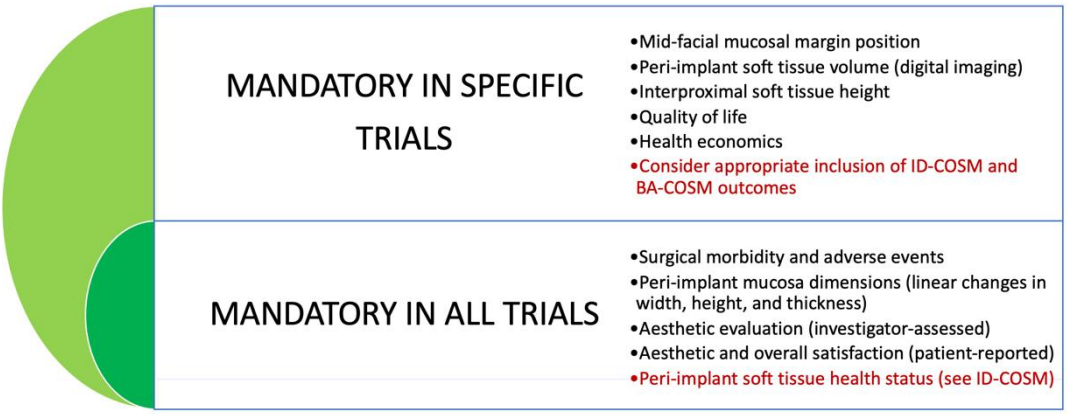

Figure 6b legend. Consensus of the core outcome domains inserted in the soft tissue augmentation core outcome set and measurements (STA-COSM) "onion". Five outcomes are considered mandatory in all trials, and 6 outcomes are considered mandatory in specific types of trials. For the outcomes necessary to capture the peri-implant soft-tissue health status, readers are referred to the appropriate section of the general ID-COSM. In trials involving dental implants, the reader is referred to the need to include the general ID-COSM core outcome set (Figure 4). If bone augmentation is part of the trial, the reader is referred to the BA-COSM (Figure 5). Outcomes highlighted in red indicate that they are part of another core outcome set. Examples of the specific measures needed to capture STA-COSM Soft Tissue Augmentation outcomes are detailed in the text.

Mandatory outcomes for trials involving soft tissue augmentation included the assessment of i) surgical morbidity and adverse events; ii) peri-implant mucosa dimensions; iii) objective professional aesthetic assessments; iv) subjective aesthetic assessments (patient-reported and professional evaluation); v) peri-implant soft-tissue health status following the ID-COSM criteria. In specific trials, mandatory outcomes may also comprise: i) mid-facial mucosal margin position; ii) peri-implant soft-tissue volume; iii) interproximal soft-tissue height (papilla height); iv) quality of life; v) health economics; and vi) relevant ID-COSM and/or BA-COSM outcomes.

4. Discussion

The objective of identifying a core-outcome set is to enrich clinical trials by providing a full picture of the benefits and harms of different interventions across all relevant areas and domains in the particular field of investigation. Importantly, it is a voluntary set of guidelines aimed at improving the relevance of clinical research. It is critical to emphasise that the current initiative, which focuses on clinical trials in implant dentistry, does not aim to standardise the primary outcome of individual trials. This selection should continue to be guided by the specific hypotheses of each trial. While the primary outcome will often be included in the mandatory outcomes in the ID-COSM set, investigators are free to add additional outcomes to capture the specific aims and benefits tested in their respective studies. However, the core outcome set is the minimum set of outcomes that should be consistently included across all reported trials.

The end product of this process is the definition of one general core set of outcomes (ID-COSM) and two specialised sets of outcomes applicable to bone and soft-tissue augmentation trials (BA-COSM and STA-COSM). The authors of this consensus debated the possibility of distilling outcomes into a single set. Still, they agreed that a single set would not adequately guide authors towards selecting core outcomes in many trials. The current structure refers investigators to the specialised outcome sets whenever bone or soft-tissue augmentation is incorporated into an implant dentistry trial. In particular instances, research may focus on developing better soft tissue and bone augmentation approaches and, on some occasions, may not involve the actual placement of dental implants within the course of the trial. In such trials, investigators should initiate the outcome selection from the specialised tools and enrich them with outcomes in the general ID-COSM domains, as appropriate.

This is the first systematic attempt to identify a core-outcome set for inclusion in implant dentistry research. Identification of core outcome sets in other areas of medicine has been an ongoing

process of maturation and improvement over several decades. This initial attempt in the field of implant dentistry will likely present shortcomings that require future modifications. Members of the steering committee and expert panels recognised the need to learn from best practice approaches and realised that the present document has limitations. They nevertheless recognised that introducing core outcome sets has great potential to improve clinical research in implant dentistry and clinical practice. A key strength of this project has been its inspiration by best practice approaches in applying a rigorous, inclusive and transparent process. Scientific evidence of outcomes used in clinical research in the latest ten years has been combined with an unbiased perspective provided by patients (PWLE) focus groups in the data collection step of the process. A broad collection of outcomes was compiled and subjected to a rigorous 3-round Delphi survey to identify essential outcomes using recognised a priori criteria to distil many outcomes into a manageable number of domains. Furthermore, the Delphi process was used to reach a wide constituency of stakeholders within the profession, patient population, and industry. Organising outcome domains into a theoretical framework is also a strength of the process.

An important limitation is a need for more valid and agreed-upon outcome measures to capture the multiple dimensions of benefits and harms of implant therapy. This is an area of priority for future development.

It is recognised that many studies are currently ongoing and that such studies may have included only some mandatory domains in their protocols. For these trials, the study outcomes should be reported following the logical structure of the core areas and essential domains identified in this project (see Figure 3-6). Missing mandatory outcomes should be highlighted in the trial materials and methods description.

Protocols for future trials should carefully consider the ID-COSM, BA-COSM, and STA-COSM mandatory domains (mandatory in all trials and mandatory in specific circumstances) as the current best-practice approach. It is strongly suggested that the trial protocol refers to the core sets

identified in this consensus report in the materials and methods section. The omission of a specific domain(s) should be explicitly acknowledged as a study limitation in the final publication(s). Limitations in terms of the validity of the instruments to accurately measure some of the outcomes are recognised. Nevertheless, implementing most of the domains included in the sets appears highly feasible.

The proposed core outcome sets for implant dentistry research should be periodically amended. An apparent challenge is a need for validated outcome measures/instruments to capture some mandatory domains, which are continuously refined as contemporary methodologies are being developed. Nevertheless, and because of the challenges with the present sets, implant dentistry outcome research should be encouraged.

5. Conclusions

The ID-COSM initiative agreed on the core areas and domains to capture benefits and harms in implant dentistry and soft tissue/bone augmentation clinical trials. It also identified a limited set of mandatory outcomes that should be assessed in all trials and additional mandatory outcomes that should be assessed under specific circumstances. It is recognised that evidence to support the use of specific measurement instruments is sometimes lacking and that outcome research in implant dentistry should be encouraged. Nevertheless, the panel of experts agreed that the ID-COSM, BA-COSM and STA-COSM should be implemented in the protocol of future clinical studies and utilised in the reporting of ongoing studies in implant dentistry.

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Table 1. Domain and Measurement Definition Table Template

Core Area	Pathophysiology/life impact/lifespan/access to care
Broad Domain	General term of broad domain [e.g. pain impact]
Target Domain	The name given to this more specific domain [e.g. impact of pain in all realms of life], this is what will be measured
Working definition of target domain	Definition of the scope of the domain: what are the features that should be captured by the measurement instruments.
Measurements	Input what needs to be measured and how to capture it (valid measurement tools)
Qualitative or literature support	Insert literature reference on outcome and measurement systems Insert input from patients/public focus group
Sources of variability in score	Please identify/think through sources of variability or contextual factors

Legend to Figures

Figure 1

Schematic representation of the different phases and levels of stakeholder representation over the 24 months of the ID-COSM project.

Figure 2

Illustration of the ID-COSM "onion" depicting the different layers in classifying outcomes: mandatory outcomes in all trials (core set to be reported in all clinical studies), outcomes mandatory in specific types of trials (expanded core set with additional mandatory outcomes), outcomes that are considered important but optional, and outcomes that belong to the research agenda. The latter category comprises areas that are currently under investigation and may provide outcomes for inclusion in the core set, once adequate development and validation has been completed.

Figure 3

Mindmap of the core outcomes areas and core outcome domains that should be captured in implant dentistry clinical trials. Each area needs to capture both benefits and harms.

Figure 4

Consensus of the core outcome domains inserted in the ID-COSM implant dentistry "onion". Five outcomes are considered mandatory in all trials, and 6 outcomes are considered mandatory in specific types of trials. Among the latter are the key pathophysiologic benefits of dental implant treatment: improving function. Appropriate functional benefit(s) should be selected based on the specific condition/population being treated. In red are specific outcomes mandatory for trials where the intervention involves bone (BA-COSM) or soft tissue augmentation (STA-COSM). For specifics about these outcomes, the reader is referred to Figures 5 and 6. Examples of the specific measures needed to capture ID-COSM implant dentistry outcomes are illustrated in the text.

Figure 5A

Mindmap of the core outcomes areas and core outcome domains that should be captured in bone augmentation clinical trials.

Figure 5B

Consensus on the core outcome domains inserted in the Bone Augmentation Core Outcome Set and Measurements (BA-COSM) "onion". 3 outcomes are considered mandatory in all trials, and 3 outcomes are

considered mandatory in specific types of trials. In trials involving dental implants, the reader is referred to the need to include the general ID-COSM core outcome set (highlighted in red) and Figure 4. Examples of the specific measures needed to capture BA-COSM outcomes are detailed in the text.

Figure 6A

Mindmap of the core outcomes areas and core outcome domains that should be captured in soft-tissue augmentation clinical trials.

Figure 6B

Consensus of the core outcome domains inserted in the soft tissue augmentation core outcome set and measurements (STA-COSM) "onion". Five outcomes are considered mandatory in all trials, and 6 outcomes are considered mandatory in specific types of trials. For the outcomes necessary to capture the peri-implant soft-tissue health status, readers are referred to the appropriate section of the general ID-COSM. In trials involving dental implants, the reader is referred to the need to include the general ID-COSM core outcome set (Figure 4). If bone augmentation is part of the trial, the reader is referred to the BA-COSM (Figure 5). Outcomes highlighted in red indicate that they are part of another core outcome set. Examples of the specific measures needed to capture STA-COSM Soft Tissue Augmentation outcomes are detailed in the text.

Figure 1.

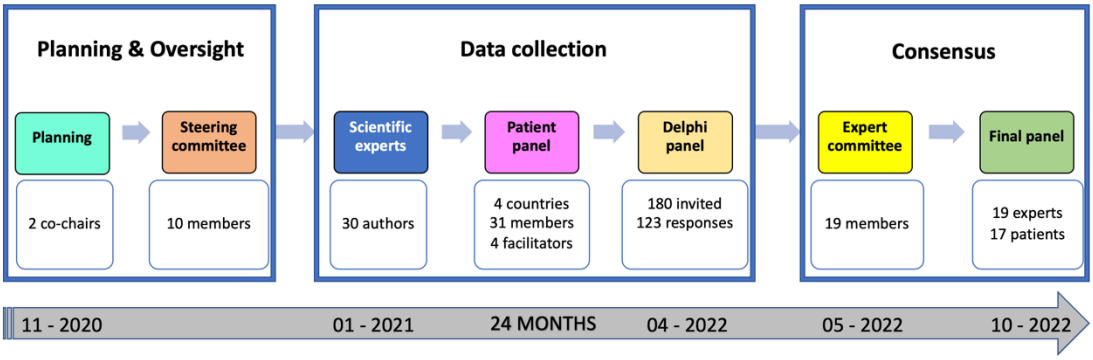

Figure 2.

Figure 3.

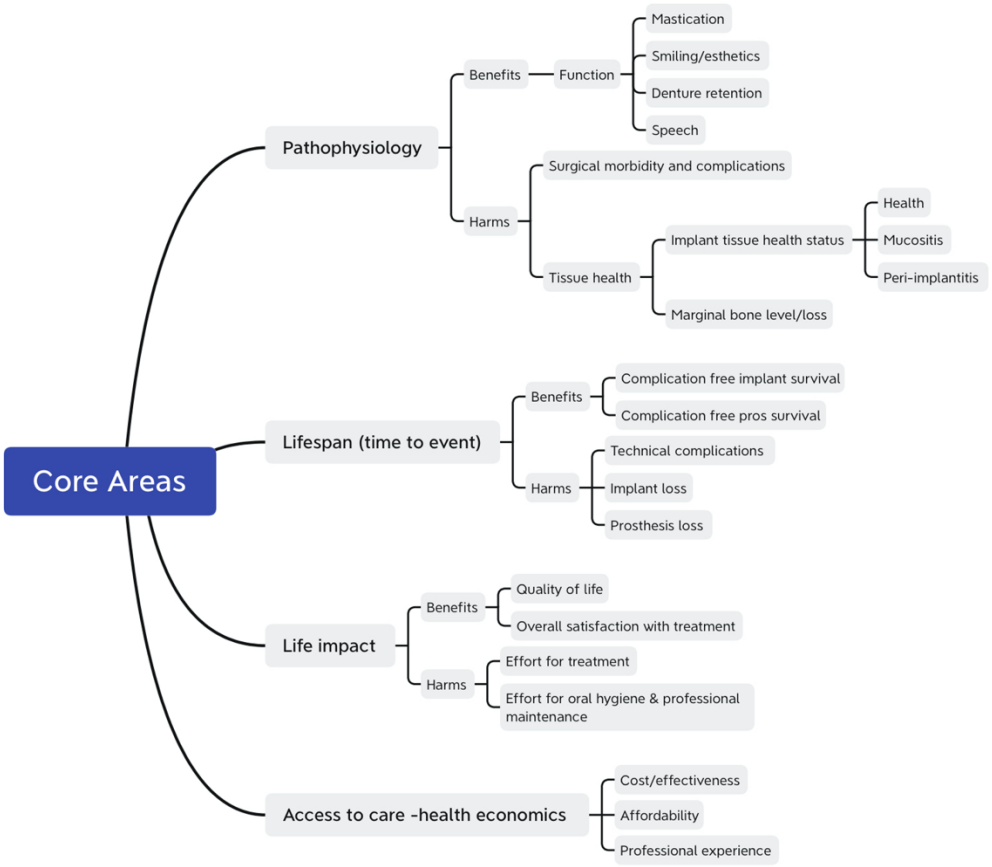
Core Areas
Pathophysiology
Benefits
Function
Mastication
Smiling/esthetics
Denture retention
Speech
Harms
Surgical morbidity and complications
Tissue health
Implant tissue health status
Health
Mucositis
Peri-implantitis
Marginal bone level/loss
Lifespan (time to event)
Benefits
Complication free implant survival
Complication free pros survival
Harms
Technical complications
Implant loss
Prosthesis loss
Life impact
Benefits
Quality of life
Overall satisfaction with treatment
Harms
Effort for treatment
Effort for oral hygiene & professional maintenance
Access to care -health economics
Cost/effectiveness
Affordability
Professional experience

Figure 4.

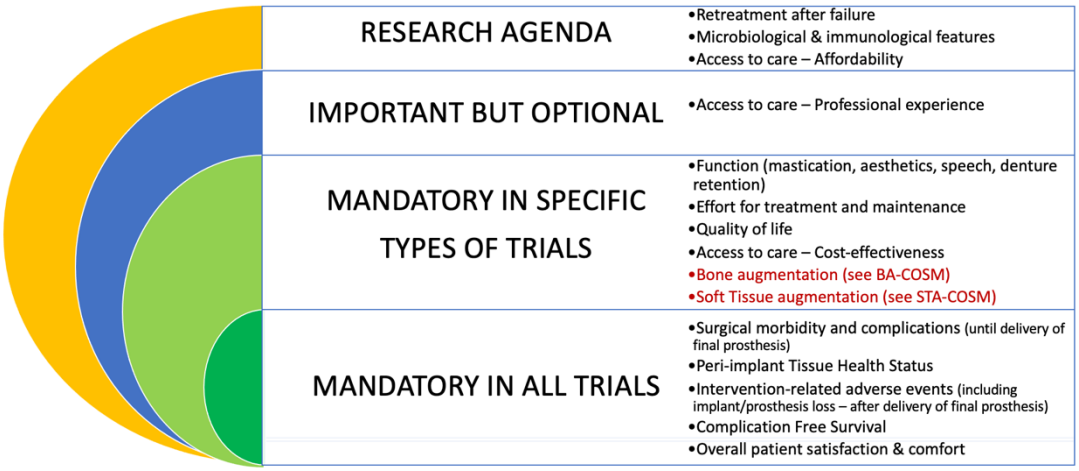
RESEARCH AGENDA
•Retreatment after failure
•Microbiological & immunological features
•Access to care – Affordability
IMPORTANT BUT OPTIONAL
•Access to care – Professional experience
MANDATORY IN SPECIFIC TYPES OF TRIALS
•Function (mastication, aesthetics, speech, denture retention)
•Effort for treatment and maintenance
•Quality of life
•Access to care – Cost-effectiveness
•Bone augmentation (see BA-COSM)
•Soft Tissue augmentation (see STA-COSM)
MANDATORY IN ALL TRIALS
•Surgical morbidity and complications (until delivery of final prosthesis)
•Peri-implant Tissue Health Status
•Intervention-related adverse events (including implant/prosthesis loss – after delivery of final prosthesis)
•Complication Free Survival
•Overall patient satisfaction & comfort

Figure 5A.

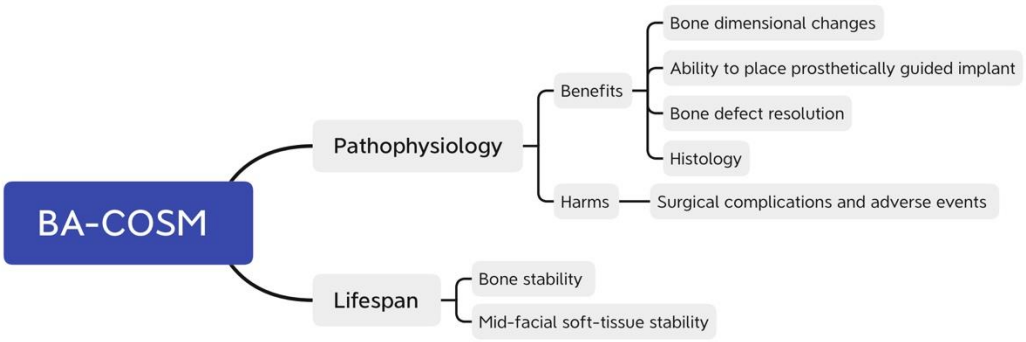

Figure 5B.

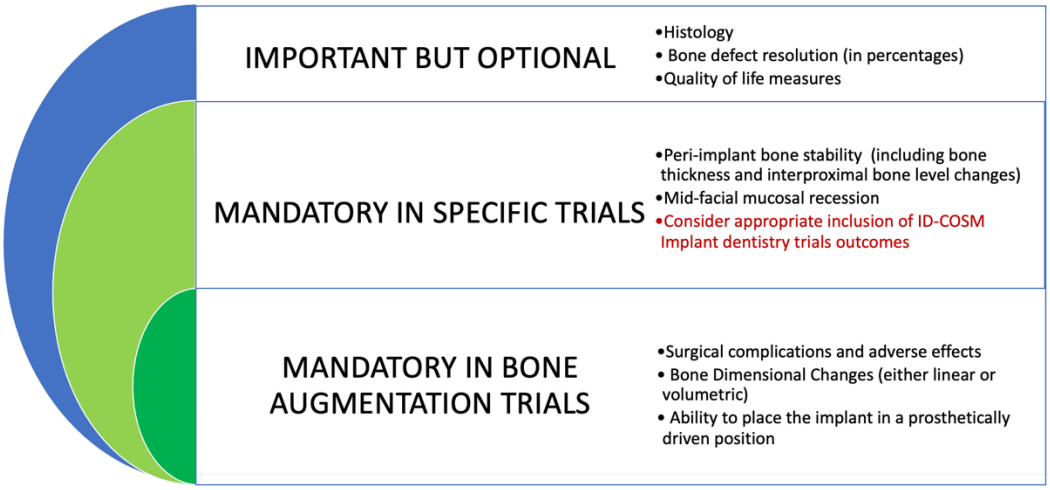

Figure 6A.

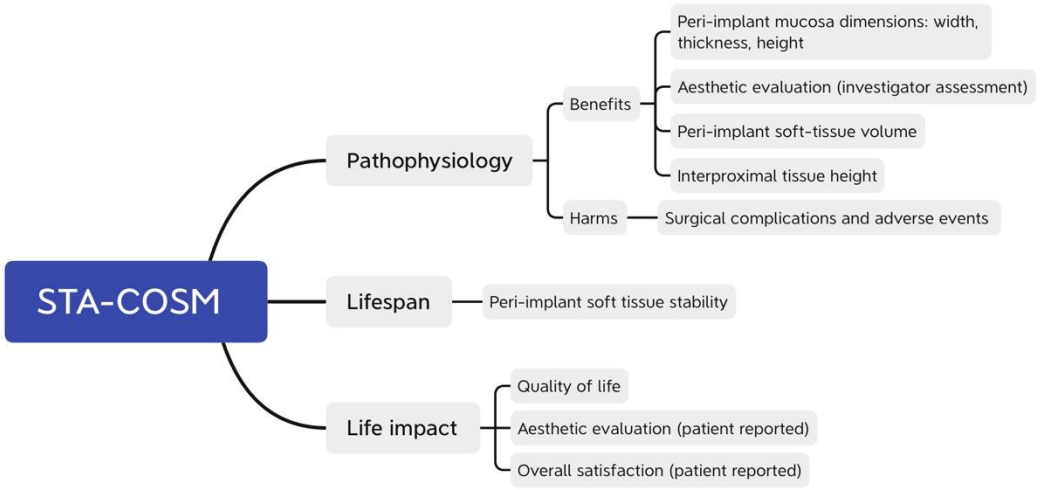

Figure 6B.