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Development of a Core Outcome Set For Use In Routine Orthodontic Clinical Trials

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Development of a Core Outcome Set For Use In Routine Orthodontic Clinical Trials

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Conclusions:
A bespoke, orthodontic core outcome set encompassing both clinician- and patient- focused outcomes was developed. Incorporating this is a first step into providing a more holistic assessment of the impact of treatment, while allowing for meaningful comparison and synthesis of results from individual trials.

- A core set of outcomes to include in routine orthodontic clinical trials has been developed using standardized methodology.
- The core outcome set encompasses both clinician- and patient- focused outcomes.
- These key outcomes should be tailored to individual orthodontic studies reflecting the diversity of orthodontic interventions and trial designs.
- The adoption and implementation of this standardised set of outcomes has the potential to improve the yield from future orthodontic research.

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Introduction

In the last few decades there has been a concerted effort to enhance the evidence underpinning healthcare decisions reflected in an increasing number of randomised controlled trials (RCTs) and systematic reviews (SR)[1]. The aim of such research is to help practitioners and patients improve the care process and ultimately therefore healthcare outcomes. In orthodontics, engagement with these 'gold standard' research methods has increased commensurately[2,3].

Information derived from RCTs is increasingly being used to aid decision-making in orthodontics, and the majority of comparative effectiveness systematic reviews and Cochrane reviews of orthodontic interventions incorporate evidence from RCTs in their meta-analyses[4]. The appropriate

selection, measurement and reporting of outcomes is therefore crucial in trial methodology. Specifically, the measurable change in key study outcomes should reflect the effects of the competing interventions; and consider the perspectives of both providers, consumers and funders of care, in order to comprehensively determine which intervention is the most beneficial. The value of using consistent outcomes is exemplified by pooling of data in meta-analyses permitting more precise effect estimates and more robust conclusions promoting better informed decisions based on best available evidence. Despite recent advances in research methodology, several issues persist across the research environment including orthodontic research. These include the heterogeneity in outcomes measured when evaluating similar interventions[5], the problem of outcome reporting bias that exists in clinical trials and systematic reviews of interventions[6,7] and the focus on measuring morphological effects of treatment, which may be more relevant to providers rather than patients[8].

Core outcome sets (COSs) have been introduced as one of a number of antidotes to these issues. Essentially, they represent an agreed, standardised set of outcomes that should be measured and reported in clinical trials of a specific condition or area of healthcare. They are regarded as a minimum that should be measured and should, therefore, not constrain innovation within research. It is suggested that use of a COS, would help to eliminate issues relating to outcome heterogeneity and reporting bias, while ensuring that wide-ranging perspectives are measured, thus enhancing the value of RCTs and systematic reviews[9].

Core outcome sets have been developed for a wide range of disease conditions, healthcare interventions and populations, such as adults and children[10]. As such, guidance on the development process is readily available[10,11]. Within dentistry, however, COS development remains in relative infancy with only a handful reported to date. These include COSs relating to traumatic dental injuries[12], pulp treatment for primary teeth[13], and periodontal therapy[14,15], although ongoing work on other dental COS projects is registered on the Core Outcome Measures in Effectiveness Trials (COMET) Initiative's database (www.comet-initiative.org)[16]. To date there is no established COS for orthodontic trials.

Inclusion of key stakeholders including researchers, clinicians, patients, public, policymakers and public health professionals is key to developing a meaningful consensus, with a recent review revealing that 77% of COS studies now report patient involvement[10]. However, qualitative methods

with patients or carers to assist with prioritization was previously reported in a very small number of studies (n=3) as a clear pre-determined part of COS development[17,18]. Although patients and carers participated in some COS studies to help elicit outcomes that may be important to them, the prioritization and consensus exercises were monopolized by health professionals[18]. Incorporating patient or carer views through qualitative research is certainly beneficial but does not guarantee that patients' perspectives will be echoed in the final COS, if the former are not part of the consensus processes.

Research to determine the most important and relevant outcomes to measure in trials of orthodontic treatment interventions, taking into account the perspectives of both patients and clinicians, is therefore necessary. The aim of the study was to identify a set of patient- and clinician-informed core outcomes for use in clinical trials of routine orthodontic treatment for non-cleft/orthognathic patients. The objectives were to identify outcomes that had been previously reported in contemporary trials of orthodontic treatment; to explore outcomes from the perspective of patients who were on an orthodontic treatment pathway; to prioritise outcomes of importance from the perspective of both health professionals and patients and to integrate their opinions into a holistic COS. The scope of this COS is aimed at paediatric and adult trials in primary or secondary care of routine orthodontic treatment involving either fixed, removable and/or functional appliances, but excluding cleft patients and those on an orthognathic treatment pathway.

Methods

The protocol for the study was previously published[19] with methods described briefly below. The study was registered on the COMET website (Registration number 785, www.comet-initiative.org/Studies/Details/785). Ethical approval including necessary amendments for the study were obtained from the NHS Health Research Authority (HRA) and the East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (REC reference 16/EE/0466). The study is reported in accordance with the Core Outcome Set-STAndards for Reporting (COS-STAR) guidelines[20].

Scoping Review

An overview of the different stages of the study to develop the COS is summarised in Figure 1. The first phase of the research involved a scoping literature review to identify previously used outcomes in contemporary orthodontic research involving orthodontic patients. Details regarding databases searched, inclusion/exclusion criteria, data extraction and trials retrieved have been published previously[5].

Qualitative research

Qualitative exploration of motives for having treatment, allied to views and expectations concerning orthodontic treatment was carried out concurrently by collecting data from adolescents at five different research sites- three secondary and two primary care centres across England providing National Health Service (NHS)-funded and private treatment. The research participants were at different stages of their orthodontic treatment pathway and were purposively recruited by the main researcher (XX). Focus groups and interviews were arranged in advance at a mutually suitable time and took place in non-clinical areas. Focus groups were stratified by age group (10-13 year-olds and 14-16 year-olds) and by orthodontic treatment stage (pre-treatment, mid-treatment and post-treatment). They were conducted with children with their parents/carers present, in accordance with research ethics guidance. Based on previous similar research work, a total sample size of approximately 25 to 35 participants was expected[21,22]. However, it was anticipated that the exact sample size could alter, if new opinions or themes ceased or continued to emerge, as qualitative samples are estimated pragmatically in order to achieve data saturation. One researcher (XX) conducted all interviews and focus groups after receiving formal training in qualitative research methodology, as well as informal training with the assistance of two experienced qualitative research members at different sites (XXX and XX). A second qualitative researcher (XXX) was also present in half the interviews and focus groups. Focus groups and interviews were semi-structured and based on a topic guide informed by the main research questions and the scoping review, but aimed to cover the major aspects of malocclusion and orthodontic treatment, as experienced by the research participants. The topic guide was piloted and updated as necessary. All interviews and discussions were audio-recorded using a digital sound recorder and field notes were recorded after each session. Data were transcribed verbatim following the interviews and analysed by two researchers (XX, XXX) using Framework Methodology[23] which is appropriate for applied health research[24]. Themes from the qualitative data were developed into outcomes and triangulated with those previously identified in the scoping review. All identified outcomes were categorised into

domains and discussed with members of the Study Advisory Group (SAG) consisting of orthodontic clinicians (n=4) and dental public health professionals (n=2) prior to being finalised. The SAG members reviewed and discussed each outcome and domain individually, and where necessary, duplicate or similarly-termed outcomes were re-arranged and re-grouped under one umbrella domain.

Delphi Consensus surveys

The Delphi consensus process involved rating of a list of outcomes over two separate electronic rounds by "experts". Experts in the Delphi process included orthodontic service users (orthodontic patients) and providers (general dental and orthodontic healthcare professionals), who were asked to rate outcomes on a 9-point scale of importance in accordance with the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) scale of 1- 9, with 1-3 marked 'not important', 4-6 marked 'important but not critical' and 7-9 marked 'critical'[25]. In the second round, the results of each stakeholder group were presented separately to participants for each outcome together with a reminder of their scores in round 1 and an opportunity to re-rate these. All outcomes were to be carried forward to the second round with an opportunity for stakeholders to suggest additional outcomes at the conclusion of Round 1. A bespoke electronic software produced the COMET Initiative (DelphiManager, UK) was used to administer the surveys (www.comet-initiative.org/delphimanager).

There is currently no accepted method for stipulating sample sizes in a Delphi process, therefore efforts were made to maximise response rates across stakeholder groups. Participants were recruited via an open invitation sent to the membership lists of the British Orthodontic Society, the European Federation of Orthodontic Specialists Association, through targeted blog posts on active orthodontic blogs (www.kevinobrienorthoblog.com, www.ukadultbraces.co.uk) and by purposive sampling of patients attending centres involved in the qualitative data collection. All participants were asked to provide their name and email address when directed to the link for the online survey, in order to register their responses. They were also asked if they had read through the study information sheet, which was available in a separate tab on the e-survey, and to declare their consent, although these responses were not conditional for taking part.

The number of rounds in a Delphi consensus process is not fixed and depends on the type of research questions and participants involved. In previous COS projects three or more Delphi rounds have been used[22,26] but in this study only two rounds were required. This was based on recommendations recently set out by COMET[11] supporting the use of multiple group feedback in round 2 in achieving greater consensus and less variability in item scoring across stakeholder groups negating the need for a third round[27]. A decision was, therefore, made by the SAG to deviate from the initial study protocol reducing from three to two rounds. Each round remained open for 10-12 weeks, with regular email reminders sent to those not having completed the round.

In each round of the Delphi survey, the proportion of each stakeholder group scoring outcomes as not important (scale response 1-3), important but not critical (scale response 4-6) and critical (scale response 7-9) was calculated. Consensus was was evaluated using a pre-defined definition of consensus :"consensus in" when $\geq$70% of participants had scored it as 7-9 across each stakeholder group and "consensus out" when <70% of participants had scored it 7-9 across each stakeholder group, in accordance with previous similar COS research[20,26]. If only one or two of the three stakeholder groups had >70% participants scoring an outcome as 7-9 this was considered as "no consensus". Possible response bias was evaluated to determine if those who did not respond in the second round had significantly different views form their peers who completed both rounds, by calculating average scores of individual outcomes amongst those who did and did not complete both rounds for each stakeholder group, in accordance with accepted COS methodological guidance[11].

Consensus meeting

A face-to-face consensus meeting was held with a small sample of UK-based participants who had completed both rounds of the Delphi and who responded to an invitation to take part. The consensus meeting was chaired by an independent facilitator and comprised of an overview of the study and presentation of results for each outcome in turn, grouped by those that had achieved the pre-determined definition of consensus "in", those that had "no" consensus and those that had been voted "out". Discussion of each outcome was followed by anonymous electronic scoring (Poll Everywhere) where necessary using the same 1-9 scale and the same definition of consensus. The list of outcomes voted "in" was discussed by the SAG and refined before a final report of the included outcomes within the COS was circulated to meeting participants.

Results

An overview of the study process is shown in Figure 1. Results from the scoping literature review have been published previously[6]. Briefly, outcomes were identified from 164 trials, with the most frequently measured being pain, periodontal health and tooth angulation/inclination changes and obvious disparity of outcome measurement tools within the studies.

Seven focus groups and sixteen qualitative interviews were carried out across the two primary care and three secondary care sites in England with a total of 35 participants (mean age 14.37 +/-1.23 years), who were due to commence (20%), were currently undergoing (49%) or had already completed orthodontic treatment (31%). Participants were commonly concerned about issues that centred on the dimensions of oral health-related quality of life (OHRQoL) with a desire to improve these with treatment. Five main themes: of dental appearance, function, social interactions, psychological and emotional well-being, and perception of long-term benefits were identified in relation to treatment outcomes, with an array of minor themes. All reported themes were converted into measurable outcomes following discussions with the SAG.

The list of outcomes elicited from these two stages was cross-referenced and refined into a final list of 34 outcomes grouped under 10 domains (Table 1). Lay explanations were also included for each term to ensure understanding by patients in younger age groups (Table 1).

The list of 34 outcomes was rated online in an e-Delphi survey, completed by 274 participants at the conclusion of Round 2 with an overall response rate of 58% involving 50 orthodontic patients, 28 general dentists and 196 orthodontic clinicians from 64 countries with most from the U.K. (22%) and the U.S. (20%) and the remaining countries each accounting for no more than 5% of participant responses. The number of outcomes reaching consensus within each stakeholder group in each round is shown in Table 2. Forty-five free text responses provided by participants in round 1 were reviewed and discussed by the SAG, but none represented new or additional outcomes; therefore, no additional outcomes were included in Round 2. At the conclusion of this round, 15 outcomes had reached the definition of “consensus in” and five outcomes had “no consensus”. The remaining 14 outcomes were scored as “consensus out” (Table 2). Responses between completers and non-completers were found to be very similar, with largest differences of less than two points on the response scale. With regards to the outcome of ‘impact on social interactions’, for which there was

a 1.8 difference in the response scale between the dentist group completers and non-completers, the orthodontist group reached consensus on the need for inclusion, whereas the patient group did not (Table 2); therefore, any change in scoring within the dentist group would not have changed the final classification of this outcome as "no consensus". The distribution of remaining outcome scores amongst completers and non-completers was within the range of one point, thus confirming that the views of non-completers were not extreme and that bias through attrition did not appear to be problematic.

Fourteen participants attended the consensus meeting of whom eight (4 patients and 4 healthcare professionals) were eligible to vote having completed both rounds of the Delphi survey (Figure 2). Each outcome was presented and discussed in turn by following the consensus matrix grouping. Six outcomes were re-scored on the day by participants, of which only one, "impact on emotions/feelings", scored as "critical" (7-9) across the stakeholders, thus reaching the definition of consensus "in". The remaining five outcomes were re-voted as "out". However, in the consensus meeting it was agreed that some outcomes, which patients were less familiar with, such as *root resorption* and *skeletal relationship,* would benefit from further discussion with the SAG regarding final inclusion in the COS. Following further discussions with the SAG and amalgamation of the 16 outcomes where appropriate, those meeting the definition of consensus and included in the final COS (n=7) were distilled (Table 3). These were categorised in four domains according to the taxonomy proposed by Dodd *et al* for COS developers[28] (Table 3). The seven included outcomes in the COS were impact of self-perceived aesthetics, alignment and/or occlusion, skeletal relationship, stability, breakages, adverse effects on teeth or tooth-supporting structures and patient-related adherence. These outcomes correspond to four outcome domains of perceived health status, clinical, adverse events and delivery of care (Table 3).

Discussion

The present study has produced a clinician and patient consensus recommendation about what outcomes should be measured in studies of routine non-cleft/non-surgical orthodontic treatment, with specific recommendations for utilising and reporting the COS.

Core Outcomes within Outcome Domains

In the adverse events domain, two outcomes were included: breakages and adverse effects on teeth or tooth-supporting structures. This derived from pooling of more specific outcomes relating to demineralisation, periodontal effects, and root resorption, so as not to restrict the scope and future applicability of the COS. However, a distinction needs to be made between operator and patient-related breakages, as the latter relates to patient adherence, which is measured under a different outcome domain. Therefore, breakages in this domain involve those which are assumed to be operator-induced, which would be relevant for studies investigating different bonding techniques, cements or bond strengths, such as those included in the Cochrane review of adhesives for fixed orthodontic brackets[29], as well as those involving potential fracture or failure of appliances or components such as temporary anchorage devices.

With regards to patient-related adherence, this was the only outcome included in the delivery of care domain derived from more specific outcomes, highlighting that it is integral for holistic evaluation of the process of treatment. Adherence can be measured both objectively and subjectively using clinician- derived measures or patient-reported outcome measures. In a previous orthodontic SR evaluating adherence with removable orthodontic appliance wear and adjuncts, however, it was found that subjective assessments resulted in an over-estimated duration of wear of appliances or adjuncts, with suboptimal levels of adherence reported overall[30]. Few interventional studies aiming to enhance and understand factors related to adherence have been performed, however, placing an onus for further research in this area.

In terms of the perceived health status domain, a composite outcome of impact of self-perceived aesthetics was included in the final COS. This evolved from the amalgamation of the 'self-perceived aesthetics' and 'impact on emotional well-being' outcomes, reflecting the possible impact of orthodontics on OHRQoL[31]. Outcomes relating to self-perceived aesthetics and its impact on social and emotional well-being were frequently reported as important by young patients during the qualitative interviews and focus groups. Despite this, impact on social well-being was not voted in by patient stakeholders (Table 2). A difference in age groups of participants in the Delphi consensus and qualitative interviews, could perhaps explain this finding. Equally, outcomes relating to OHRQoL domains have been rarely included in previous orthodontic trials, but orthodontists within the Delphi and consensus meeting sample consistently scored these outcomes as important (Table 2). It could be argued that with the increasing emphasis on measuring treatment effects from the

patient's perspective, as well as increasing need to justify treatment based on measurable benefits, clinicians and researchers are more aware of the potential impact of malocclusion and orthodontic treatment on OHRQoL, thus recognising the need for measuring this in future studies[32]. Further high-quality trials incorporating the use of appropriately selected PROMs to assess the impact of self-perceived aesthetics on patients' health status are, therefore, warranted.

Finally, in the clinical domain, skeletal relationship, alignment and/or occlusion and stability were included as core outcomes. All outcomes within this domain were unanimously perceived as important across all stakeholders. This was surprising given the lack of emphasis placed on these outcomes by young people during the qualitative interviews. Notwithstanding this, straightness of teeth and long-term effects were perceived to be important by them, as these would contribute to an "aesthetic smile". It is also conceivable that optimal alignment following orthodontics was taken for granted by the interviewees. Clinical measures already form the mainstay of outcomes measured in trials of orthodontic treatment[5,8]. It is, however, anticipated that not all outcomes might be relevant to a particular trial and discretion should be used when choosing which of these outcomes to measure in specific studies. This is particularly true for the clinical outcomes of stability and skeletal relationship, as well as in relation to studies incorporating phases of orthodontic treatment rather than the entire course of treatment.

Best Practice Recommendations for Implementing and Reporting the COS

Implementation and uptake of the COS in future orthodontic studies should lead to improved measurement and reporting of outcomes by streamlining research activities for trialists and, ultimately, improve outcomes for patients. However, several key factors should be considered in terms of implementing routine use of the COS and promoting its adoption in future orthodontic research. Given the uniqueness and longitudinal nature of orthodontic treatment in comparison to other one-off interventions or areas of healthcare, the following best practice recommendations are suggested for researchers conducting and reporting the orthodontic COS in future clinical trials. Specifically, we suggest the following:

- Clinical trials evaluating the effectiveness of interventions of non cleft/non-surgical orthodontic treatment should incorporate measurement and reporting of at least one

outcome category from each of the four outcome domains, as this will enable holistic assessments to be carried out and will contribute to the evaluation of COS activities in future research.

- It is anticipated that not all five core outcomes within the *Adverse effects/events* and *Clinical* domains will be relevant for all orthodontic trials. For instance, in a study considering the effectiveness of two different retention regimes, at least one outcome from each of the domains should be reported. This would suggest that from the *Adverse events* domain, breakages *or* adverse effects on teeth/teeth supporting structures are measured and from the *Clinical* domain, stability measures should be measured, although overlap with other clinical outcomes, particularly dental alignment is likely.
- Reasons for omission of the remaining outcomes should be justified and concisely reported where they are not considered relevant for inclusion.
- The remaining outcomes in the *Delivery of care* domain relating to patient-related adherence and *Perceived health status* domain associated with the impact of self-perceived aesthetics should still be measured and reported.
- Clinical trials evaluating effectiveness for the whole duration of orthodontic treatment should include each outcome from the final core outcome set, with the exception of stability. However, there is a paucity of such trials within orthodontics, with previous research highlighting that only a small proportion (8%) of studies over a four-year period evaluate outcomes based on the overall course of treatment[5]. Since longitudinal evaluation of some outcomes is necessary to yield meaningful results, the final COS domains and outcomes should apply as a minimum requirement for any orthodontic trial involving treatment periods of 3 months of more. Similar recommendations have been made in other COS projects across medicine. For example, in the COS developed by the OMERACT group, one outcome was only relevant for studies where the duration of follow up is greater than one year[32].
- Journal editors, reviewers and funding agencies should also encourage reporting of the COS for clinical trials meeting the above criteria. This will help raise awareness of the minimum set of outcomes without restricting the measurement of other potentially important outcomes.

Future Work

COS development projects typically aim to standardise "*what*" is measured in a specific condition or area of health, and subsequent consideration will be needed on "*how"* to measure these core outcomes and "*when"*. However, if COS users and stakeholders are to benefit from such research, it is important that COSs are disseminated appropriately so that they do not lead to research waste through poor uptake[11]. It is anticipated that measurement of the specific outcomes within these core domains can occur in different ways. Future research should be directed at developing, assessing and selecting the optimal methods for evaluating these core domains and outcomes in non-cleft/non-surgical orthodontic clinical trials, through rigorous methodology. Guidance on appropriate instrument selection is readily available through the COnsesus-based Standards for the selection of health Measurement INstruments (COSMIN) Initiative[33]. Considerable work will be required to achieve consensus by either streamlining existing tools or developing new approaches, as considerable heterogeneity in outcome measurement tools was exposed among previous orthodontic trials[5].

Further research evaluating optimal ways of engaging with young people and/or their parents/carers would also be beneficial to facilitate patient involvement in orthodontic research, as this was challenging in the present study. This could possibly involve the use of social media and other electronic means that are acceptable to young people.

Finally, an important part of COS development is the promotion and assessment of its uptake in subsequent primary research. Future empirical research findings should be monitored to evaluate endorsement of the proposed core outcomes. Further systematic and scoping reviews would therefore be valuable in assessing the uptake and indeed relevance of the developed orthodontic COS. To this end, researchers are also encouraged to register future trial protocols and share trial datasets in an effort to increase transparency of research methodology and findings, while facilitating data synthesis in future meta-analyses.

Strengths and Limitations

Established and rigorous methodology has been used in this project to develop a standardised minimum set of outcomes that will be meaningful for streamlining future orthodontic research activities. International consensus helps to promote uptake of the COS; the inclusion of an international pool of healthcare professionals in the Delphi surveys was, therefore, beneficial.

This is the also the first project within dentistry that has successfully integrated views of healthcare professionals and patients to develop a tailored COS echoing the views of both. While stakeholder involvement was good, the patient response rate to the Delphi survey was lower than expected, although similar numbers were included in consensus meetings in other COS projects[22,26]. A number of factors may have contributed to the low patient response rate, for example, the length of the survey, the method of delivery or the research questions and explanations but these were not evaluated. We were only able to include patients from the U.K. and the importance of outcomes to patients in other countries with different healthcare systems may differ. Nevertheless, targeted recruitment of patient participants ensured even attendance from both patients and healthcare professionals in the consensus meeting, helping to limit the risk of response bias or a more clinician-centric outcome set. It is acknowledged that development of a COS is a dynamic process. In accordance with previous COS development projects, the current COS may require refinement and revision in respect of outcomes and domains in the future with necessary adjustments to ensure it remains purposeful and relevant.

Conclusion

A consensus on the core outcome set domains and outcomes to include in non-cleft/non-surgical clinical trials of orthodontic treatment has been developed. The final set of seven core outcomes includes: impact of self-perceived aesthetics, alignment and/or occlusion, skeletal relationship and stability, patient-related adherence, breakages, and adverse effects on teeth or teeth-supporting structures. This core outcome set should be tailored to individual orthodontic studies reflecting the diversity of orthodontic interventions and trial designs. The adoption and implementation of this standardised set of outcome domains and categories has the potential to improve the yield from future orthodontic research.

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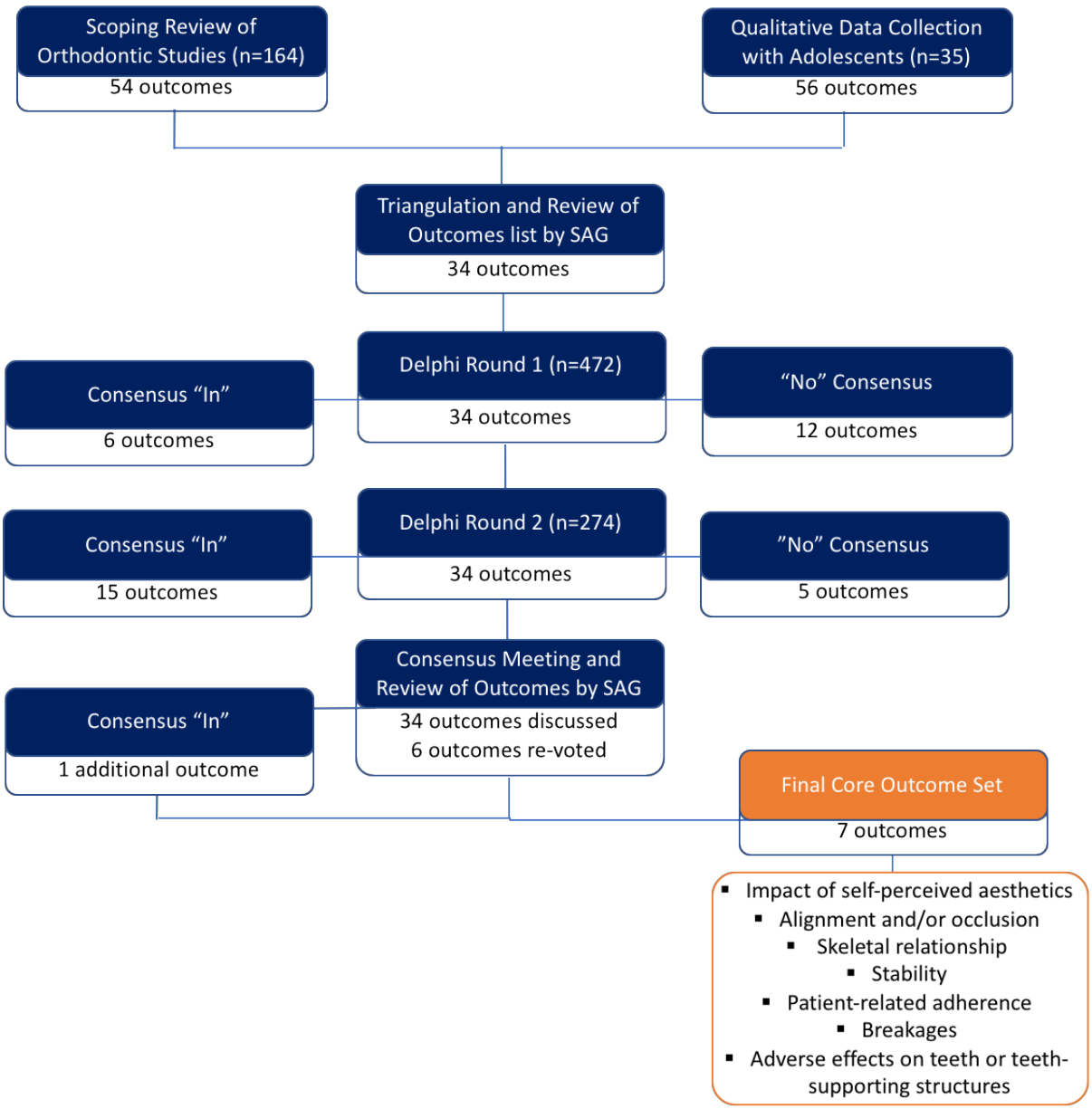

Figure 1. Overview of study design, identification and refinement of outcomes

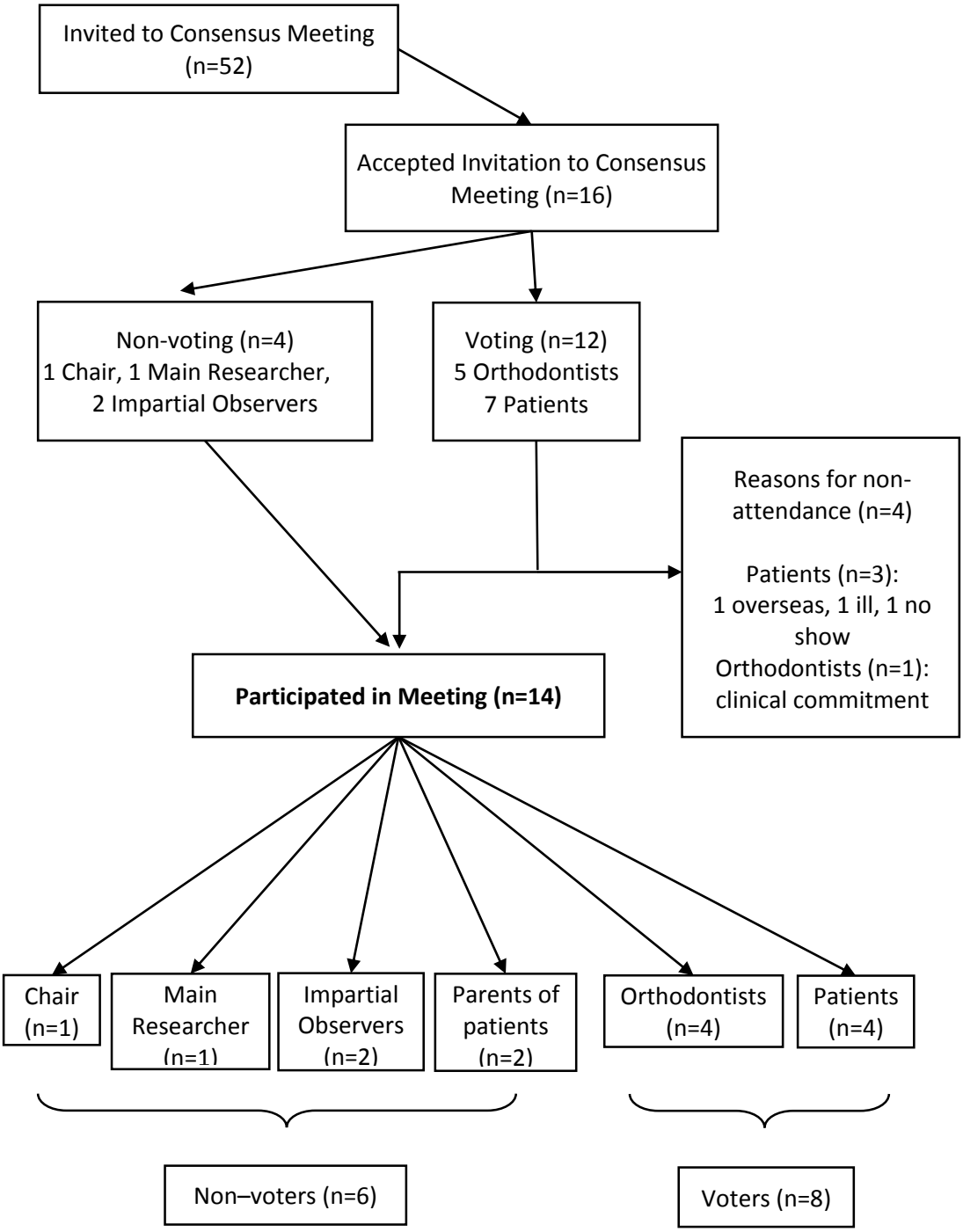

Figure 2. Flowchart of participants in the consensus meeting

Table 1. Final list of outcomes (n=34) under outcome domains (n=10) for ranking in the Delphi survey with definitions

Domain	Outcome	Lay description
Impact of appliance	Appliance weakness and/or failure	Brace not working as it should
	Pain	May hurt
	Irritation of lips and cheeks	May make the inside of your lips and cheeks sore
	Impact on hobbies and pastimes, including sports	May stop you from playing certain instruments and/or sports
Compliance	Appliance neglect including loss or breakages	Not looking after your brace causing them to break or losing them
	Wear/Use of appliance as directed by the orthodontist	Having to follow instructions so that the brace works properly
	Attendance	Having to attend to have braces checked regularly
Impact on oral health	Effect of marks on teeth	Make it more or less likely to have marks on teeth
	Effect on tooth decay	Make it more or less likely to have tooth decay or cavities on teeth
	Effect on gums	Make it more or less likely to have gum disease
	Dental trauma risk	Reduce the chance of your teeth being injured
	Effect on roots of teeth	Harm the roots of the teeth
Function	Chewing efficiency	How well you can chew
	Jaw joint health and movement	Opening and closing your mouth
	Airway volume and breathing	How you breathe
	Speech/speech assessment	How you speak
	Postural (head and neck) changes	Position of your head and neck
Hard tissues	Relationship of the jaws	How your top and bottom jaws meet
Soft tissues	Lip position	Position of top and/or bottom lip
	Lip thickness	How thick the top and/or bottom lip looks
Appearance	Appearance of face	How your face looks
	Appearance of teeth	How your teeth look
	Appearance of gums	How your gums look
Occlusal/Alignment	Straightness of teeth	How straight your teeth are
	Occlusion/overjet and overbite	The way your front teeth meet together
	Gaps between teeth	Having gaps between teeth
	Stability of outcome	Teeth moving back once you stop wearing a brace
	Slope of front teeth	How your front teeth are angled
Quality of life	Impact on emotions/feelings	How your teeth change the way you feel about yourself
	Impact on social interactions	How your teeth change the way you act when meeting and talking to people
Efficiency/ Cost-effectiveness	Cost to patient	How much the brace treatment costs you or your parents/carers
	Cost to health service	How much it costs to provide treatment
	Duration of stage of treatment	How long different stages of treatment will take
	Duration of overall treatment	How long brace treatment will take overall

Table 2. Changes in outcome scoring across stakeholder groups over the two Delphi rounds

Outcome Name	Round 1 (n=472)			Round 2 (n=274)		
	Outcome Scoring 7-9			Outcome Scoring 7-9		
	Orthodontists (n=325)	Dentists (n=45)	Patients (n=102)	Orthodontists (n=196)	Dentists (n=28)	Patients (n=50)
Appliance weakness and/or failure	82%	90%	66%	90%	89%	80%
Pain	49%	45%	41%	49%	50%	33%
Irritation of lips and cheeks	41%	31%	38%	38%	36%	37%
Impact on hobbies and pastimes, including sports	28%	24%	17%	22%	25%	14%
Appliance neglect including loss or breakages	84%	84%	60%	90%	89%	76%
Wear/Use of appliance as directed by the orthodontist	91%	90%	72%	96%	93%	90%
Attendance	79%	80%	78%	88%	79%	88%
Effect of marks on teeth	77%	79%	51%	84%	89%	79%
Effect on tooth decay	83%	91%	64%	89%	100%	79%
Effect on gums	71%	74%	65%	80%	86%	75%
Dental trauma risk	68%	57%	65%	76%	68%	77%
Effect on roots of teeth	74%	89%	65%	84%	100%	79%
Chewing efficiency	48%	45%	51%	44%	54%	58%
Jaw joint health/movement	57%	60%	50%	59%	68%	65%
Airway volume/breathing	38%	40%	59%	41%	46%	65%
Speech/speech assessment	36%	30%	44%	34%	29%	46%
Postural head/neck changes	26%	32%	42%	23%	25%	48%
Relationship of the jaws	77%	84%	64%	86%	86%	70%
Lip position	61%	58%	34%	63%	54%	38%
Lip thickness	37%	27%	26%	25%	25%	28%
Appearance of face	77%	71%	44%	87%	71%	60%
Appearance of teeth	89%	82%	66%	92%	86%	79%
Appearance of gums	69%	64%	59%	73%	64%	70%
Straightness of teeth	94%	87%	83%	96%	89%	89%
Occlusion including overjet and overbite	90%	84%	76%	92%	93%	89%
Gaps between teeth	77%	76%	78%	84%	82%	85%
Stability of outcome	88%	96%	80%	93%	96%	89%
Slope of front teeth	77%	71%	69%	85%	82%	79%
Impact on emotions/feelings	71%	69%	48%	78%	68%	53%
Impact on social interactions	70%	69%	45%	76%	61%	51%
Cost to patient	48%	47%	45%	44%	54%	51%
Cost to health service	42%	38%	43%	43%	50%	53%
Duration of treatment stage	47%	53%	42%	51%	46%	38%
Duration of overall treatment	61%	56%	42%	62%	57%	38%

Table 3. Final core outcome set with outcomes (n=7) categorized under four outcome domains

Outcome Domains	Provisional Core Outcome Set	Final Core Outcome Set
Adverse effects/events	Appliance failure /breakages (operator-related)	Breakages
	Demineralization/caries	Adverse effects on teeth or tooth-supporting structures
	Periodontal effects	
	Root resorption	
Clinical	Skeletal relationship	Skeletal relationship
	Straightness and slope of front teeth	Alignment and/or occlusion
	Gaps between teeth	
	Occlusion (overjet and overbite)	
	Stability (intra- / inter- arch)	Stability (intra- / inter- arch)
Delivery of care	Appliance neglect including loss or breakages (patient-related)	Patient-related adherence
	Wear/Use of appliance as directed by the orthodontist	
	Attendance	
Perceived health status	Self-perceived appearance of teeth	Impact of self-perceived aesthetics
	Impact on emotional well-being	