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RoBDEMAT: A risk of bias tool and guideline to support reporting of pre-clinical dental materials research and assessment of systematic reviews

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ABSTRACT

Objectives: To develop a risk of bias tool for pre-clinical dental materials research studies that aims to support reporting of future investigations and improve assessment in systematic reviews.
Methods: A four-stage process following EQUATOR network recommendations was followed, which included project launch, literature review, Delphi process and the tool finalization. With the support of the European Federation of Conservative Dentistry (EFCD) and the Dental Materials Group of the International Association for Dental Research (DMG-IADR), a total of 26 expert stakeholders were included in the development and Delphi vote of the initial proposal. The proposal was built using data gathered from the literature review stage. During

this stage, recent systematic reviews featuring dental materials research, and risk of bias tools found in the literature were comprehensively scanned for bias sources. The experts thus reached a consensus for the items, domains and judgement related to the tool, allowing a detailed guide for each item and corresponding signalling questions.

Results: The tool features nine items in total, spread between 4 domains, pertaining to the following types of bias: bias related to planning and allocation (D1), specimen preparation (D2), outcome assessment (D3) and data treatment and outcome reporting (D4). RoBDEMAT, as presented, features signalling questions and a guide that can be used for RoB judgement. Its use as a checklist is preferred over a final summary score.

Conclusion: RoBDEMAT is the first risk of bias tool for pre-clinical dental materials research, supported and developed by a broad group of expert stakeholders in the field, validating its future use.

Clinical significance: This new tool will contribute the study field by improving the scientific quality and rigour of dental materials research studies and their systematic reviews. Such studies are the foundation and support of future clinical research and evidence-based decisions.

1. Introduction

Recently, there has been an increasing demand for evidence-based guidelines to support clinical decisions [1,2]. Such guidelines are usually informed by clinical data and, in most cases, their synthesis, which is presented mainly in the form of systematic reviews and meta-analyses [3,4]. More recently, systematic reviews for non-clinical data, including laboratory studies (such as biological, physical and chemical property studies performed in materials/samples), have been conducted [5]. Given that a firm foundation of laboratory data may allow more targeted clinical research and possibly facilitate omitting animal research, systematic reviews of such data are justified [5,6].

In dentistry, articles presenting laboratory-generated data are very common, since less costs, time and resources are needed for this type of research in opposition to what may be required in clinical studies. Also, laboratory data provides good indication on how biomaterials perform, which are the subject of extensive research in dentistry. Studies on dental materials and their various properties are abundant, e.g., to screen for novel materials and formulations, but also to compare them against existing standards or to predict clinical success (within certain limitations of such predictions) [7,8]. However, systematic errors, or bias, during laboratory study conduction or during their reporting, are common. Examples include selection bias due to poor randomization of samples, questionable reproducibility of specimen treatment and methods or insufficient statistical detail, among others [9–12]. Yet no clear bias reduction checklists exist for such data collection. Calls for improving the quality of planning, undertaking and reporting *in vitro* research have been raised in the past [2].

Furthermore, a risk of bias (RoB) tool is especially important to conduct a systematic review, where a rigorous step-by-step procedure must be followed, involving several items and stages. One of these steps is the quality assessment of the individual included studies [13,14], i.e., the delineation of the studies' risk of bias, that gauges the internal validity of each study and the overall body of evidence [14,15]. Risk of bias tools can be checklists, items, or scales [16]. For randomized controlled trials, the Cochrane risk of bias tool (RoB 2) is the most up-to-date tool presently used [17,18], while many other tools are available, accounting for the specific needs of different study types [19,20]. However, none exist for laboratory studies. Without the use of RoB tools, there is a great risk of including studies with concerning flaws in the methodology which will hamper the reliability of the conclusions that are reached [15].

The central issue is that poor reporting is commonly seen in dental material laboratory studies, which does not allow correct reproducibility or critical appraisal. Since materials researchers do not have a clear guideline on how to report, a RoB tool specifically defined and consented will be extremely useful to improve reporting and to reduce bias. Moreover, authors of existing systematic reviews in this field either devised their own risk of bias tool or adapted existing tools that are not specific for these types of studies [12,21]. Recommendations have outlined that the risk of bias tools should be specific to the study design, and

this specific tool does not yet exist. Thus, this RoB tool will also support the conduction of systematic reviews of materials research.

Therefore, the present study aimed to develop a RoB assessment tool for laboratory studies on dental materials, and to validate the tool by a broad group of expert stakeholders. The resulting tool should be used as a guideline for reporting pre-clinical research of dental materials studies, as a critical appraisal tool for such studies and also in systematic reviews that assess the risk of bias of studies investigating dental material properties, *in vitro*. This allows the correct identification of systematic errors in such studies. Users will include researchers and clinicians involved in evidence-based dentistry, dental materials experts, researchers involved in systematic reviews and meta-analysis of dental materials and laboratory studies, guidelines and guidance developers, journal editors and reviewers.

2. Materials and methods

2.1. Project methodology

The EQUATOR Network stages and checklist for developing reporting guidelines in healthcare were adapted and followed to systematize the design of a quality assessment tool [23]. The present project consisted of four stages, which are shown in Fig. 1.

2.1.1. Stage I – project launch

The project launch was in September 2020 and involved a core team [A.D. – Portugal/United Kingdom, and F.S. – Germany] responsible for planning and setting out the methodology to develop the RoB tool.

2.1.2. Stage II – literature Review

After the project launch, it was pertinent to conduct two distinct review phases for Stage II of the tool development. The first review was conducted to create a list of the RoB tools used in recent systematic reviews (last five years) concerning dental materials. This review would help map the sources of bias that are being used by current systematic review teams. The second review was to determine existing RoB tools developed for use, in all types of research studies. This would further help define a baseline framework from which our own tool was developed.

For the literature review (first phase), a comprehensive and systematic search, following the latest PRISMA 2020 guidelines [22] was conducted in PubMed/Medline, Scopus and EMBASE, with controlled and free keywords (search strategy shown in Table 1), to identify systematic reviews. Without language restrictions, peer-reviewed systematic reviews of laboratory studies on dental materials published between 2015 and 2021 (last 5-year period) were included (Fig. 2). Additional references were also found through hand searching. The last search was conducted on June 8th, 2021. Data extraction was carried out in the identified systematic reviews, with data selected and exported to a Microsoft Excel Spreadsheet (v. 16.35, Microsoft, Boston, MA, USA). The data extracted were the RoB tool/instrument used to perform the quality

assessment, specifically a list of the individual sources of bias used by the authors to classify each study.

A second review was aimed to identify existing RoB tools in the literature, with RoB tools for basic research (e.g., animal studies), interventional research and observational research being screened across the literature. The same databases were searched as described above. Additionally, methodological checklists for *in vitro* studies such as the modified CONSORT developed by Faggion (2012) [2] were also considered at this stage, to aid the development of the tool. The relevant criteria were grouped in domains from the existing tools, and the most relevant domains for *in vitro* studies of dental materials were tailored and included in a preliminary form sheet, by two reviewers (A.D. and F. S) working independently. Each criterion was screened for applicability to assess bias in *in vitro* studies of dental materials. The team also proposed new criteria and/or domains that were not identified in any of the existing tools found or used in the literature and added for voting.

2.1.3. Stages III and IV – Delphi and finalization of the tool

A preliminary RoB criteria list was formulated, considering the sources of bias identified from existing RoB tools found or from systematic reviews of *in vitro* studies of dental materials also by reviewing methodological checklists. Members of the International Association for Dental Research – Dental Materials Group (IADR-DMG) and the European Federation of Conservative Dentistry (EFCD) board were invited to participate. The EFCD and IADR-DMG approved and supported the initiative and process. A meeting was held with the president of the EFCD and the IADR-DMG before the Delphi round. In addition, experts

Table 1
Strategy used for the systematic search in the three databases.

Database	Search strategy
PubMed/ Medline	(systematic review OR meta-analysis) AND dental AND properties AND (compatibility OR toxicity OR polymerization OR antibacterial OR remineralization OR bond* OR adhes*)
Scopus	TITLE-ABS-KEY ((("systematic review") OR ("meta-analysis")) AND (dental) AND (properties)) AND (("compatibility") OR ("toxicity") OR ("polymerization") OR ("mechanical") OR ("antibacterial") OR ("remineralization") OR (bond*) OR (adhes*) OR ("mechanical"))
EMBASE	(systematic review OR meta-analysis) AND dental AND properties AND ("compatibility" OR "toxicity" OR "polymerization" OR "antibacterial" OR remineralization OR bond* OR adhes*)

and key opinion leaders who were not associated with the two associations were identified and invited to participate. These additional experts were selected based on their scientific expertise in dental materials.

The resulting expert panel, consisted of 26 experts - EFCD (44%), IADR-DMG (40%), and additional experts (16%), from 14 different countries and 3 continents. These stakeholders were known experts in dental materials research, with extensive experience in conducting laboratory pre-clinical studies in this field, but voters also included experts in research methodology (J.T. and F.S.). They were invited to vote on the tool acronym (name of the tool), domains, criteria/sources of bias, and choices of response types. Moreover, to improve the tool's applicability, signalling questions were defined. Each section contained
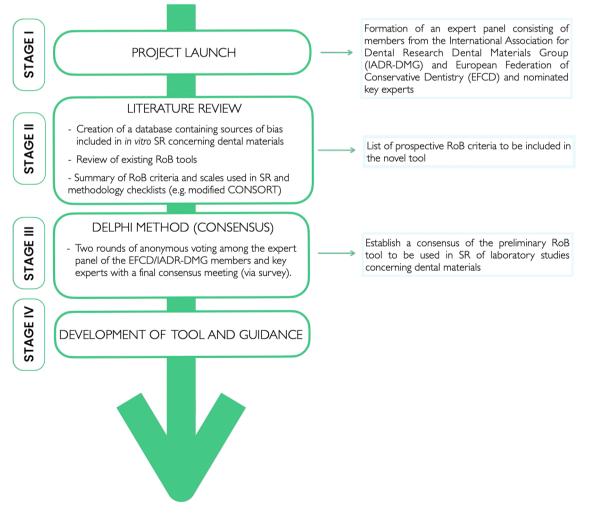

Fig. 1. Stages involved in the development of the novel RoB tool (RoBDEMAT).

an introductory text to provide background and explanation. The survey was written in English. The 26 participants participated in the voting of the domains and items featured in RoBDEMAT. The Delphi technique allows a stepwise approach to reach a consensus after an initial discussion via e-mail messages and virtual meetings. It provided a systematic and comprehensive approach for the development of the tool. During the Delphi round, several suggestions and comments were made to improve the domains and items listed in each domain, used by the team core members (A.D. and F.S.) to improve the clarity of the resulting tool.

A Google Forms survey was used for voting, which was carried out over a period of ten weeks (20th December 2020– 1st of March 2021). The survey contained seven distinct sections with several different answer formats, such as multiple-choice and a 5-point Likert scale from "strongly disagree" to "strongly agree". Feedback was also encouraged in the comments sections for each item.

The threshold for consensus for the Delphi was set at 70% and agreement was considered for answer types "agree" or "strongly agree". The survey and the voting results can be freely accessed via the GitHub platform (https://github.com/ahsdelgado/RoBDEMAT).

The resulting manuscript reflects the consensus recommendations set out by all the experts who developed the present tool.

2.1.4. Reliability analysis

A subset of the stakeholders (3) was randomly chosen to serve as independent assessors, allowing the measurement of the inter-rater reliability (IRR) and test re-test reliability. The guidance table and the judging scale was provided and seven laboratory studies in the dental materials research arena were used as test papers and independently assessed by the three reviewers. Kappa (κ) statistics was used to evaluate IRR for each domain of bias. The scale for agreement was judged as poor (0), slight (0.1 - 0.2), fair (0.21 - 0.4), moderate (0.41 - 0.6), substantial (0.61 - 0.8), or near perfect (0.81 - 0.99).

3. Results

3.1. Literature review stage

From the systematic search and flowchart method, 28 systematic reviews were retrieved. These were used as a sample to screen for sources of bias that are being included in the RoB assessment of dental materials studies. Key results are shown in Table 2. Such bias items were considered for the development of the tool, outlined in 3.2.

Table 2

Key sources of bias found in the RoB assessment included in the retrieved systematic reviews, grouped by frequency.

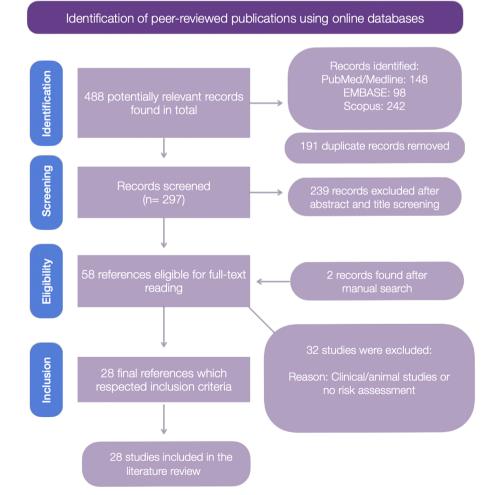| SOURCES OF BIAS	FREQUENCY
Randomization of samples	75% (21/28)
Sample size calculation	71% (20/28)
Sample preparation by the same operator	50% (14/28)
Materials used according to information supplied by the manufacturer	46% (13/28)
Presence of a positive or negative control group	36% (10/28)
Appropriate statistical analysis	25% (7/28)
Correct outcome measurement and reporting	14% (4/28)

Fig. 2. PRISMA flowchart for the systematic search followed in Stage II of the EQUATOR stages.

Existing RoB tools for clinical research were used as models, such as RoB 2 Cochrane Tool for randomized controlled trials, RoBANS tool for non-randomized studies, validated by Cochrane, or the RoB In Non-randomized Studies - of Interventions (ROBINS-I) tool. Other tools for animal research were also used as sources for bias items, such as the Stroke Therapy Academic Industry Roundtable (STAIR), The Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMARADES), Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) or the OHAT RoB Rating Tool for Human and Animal Studies.

3.2. The RoBDEMAT tool outline

The final RoBDEMAT tool contains four different domains: bias related to planning and allocation (D1), specimen preparation (D2), outcome assessment (D3) and data treatment and outcome reporting (D4; Table 3), and nine items pertaining to different sources of bias within the domains (Table 4), along with signalling questions and a guide that can be used for RoB judgement. The choice of four domains, was accomplished by taking into account the stages and domains identified in the clinical/animal RoB tools identified and used in 3.1.

The assessment with this tool should be undertaken by two reviewers, working independently after calibration and, when necessary, adjustments can be implemented for each systematic review. An individual RoBDEMAT should be completed for each laboratory study included in the systematic review. Disagreements should be resolved by seeking a third reviewer through discussion.

3.3. Judgement

Each signalling question should be answered as either "sufficiently reported/adequate", "insufficiently reported", "not reported/not adequate" or "not applicable". In domains such as bias in specimen preparation, outcome assessment or reporting of outcomes, experts may answer feel the need to answer with "adequate" or "not adequate". Answering "sufficiently reported" will indicate that the paper under

evaluation correctly reports the item being judged, whereas "insufficiently reported" would indicate that not enough details were given. Finally, judging as "not reported" indicates that no detail or explanation was given. Although this judgement is based on reporting and not directly on methodological quality, the absence of sufficient details can raise bias concerns. When details are not given, there may also be an unclear risk of bias, as there is not enough information to judge. This is why judging as "adequate" or "not adequate" may prove very useful, as reporting the item alone does not necessarily eliminate bias potential. Generating a summary RoB score is therefore also not recommended as this would require the attribution of weights to different domains which is highly subjective and difficult to justify [14,23]. The attribution of bias potential and summary score can be misleading Thus, in line with other authors that criticized summary scores, the present work recommends the application of a checklist, which provides relevant information as to what was done in the laboratory studies, what was reported and if it was done adequately, using the answer scale mentioned above, shown in a table format. This comes in replacement of a final, often times subjective, judgment score.

3.4. Reliability analysis

The results for the Cohen's kappa statistics are shown in Table 5 and the test re-test results are shown in Table 6. Three questions obtained perfect or near perfect agreement among raters, while only two questions scored a fair agreement (3.1 and 4.1). Test re-test scores gave very good intra-class correlation coefficients.

4. Discussion

It is important to propose a systematic tool to assess and evaluate the quality of *in vitro* studies concerning dental materials research, since currently there are no tools to accomplish this. Several different RoB tools have been developed over the years, covering clinical trials, interventional studies, analytical and case series studies, pre-clinical animal studies or qualitative studies, but to our knowledge no RoB assessment tools exist for this type of laboratory bench studies [24]. Furthermore, in what concerns systematic reviews, pooling results from different studies may jeopardize the credibility of the review or meta-analysis outcome, whenever the methodological risk assessment of each study is not adequately conducted [25]. For this reason, RoBDEMAT was developed to provide an organized, systematic approach to evaluate RoB of dental materials research studies. The development phase was undertaken according to similar studies that recently developed RoB tools. The development of these recent tools also featured a review stage and a Delphi process stage within a systematized, step-by-step approach, to achieve a final, consented tool [26–28].

The present tool was designed to assist researchers and authors, journal editors, reviewers, systematic review teams and readers to evaluate the methodological quality of dental materials studies. In fact, systematic reviews of dental material studies from pre-clinical laboratory data are frequently published in current literature [19].

The clinical RoB model tools retrieved in the search helped to categorize the domains that were chosen and voted for inclusion in RoBDEMAT. These tools, mentioned in 3.1, followed a general domain outline that could be divided into three main sections: before the study, or pre-intervention phase, during the study or intervention phase, and after the study or reporting phase [29,30]. The four domains chosen for this study also followed this general outline, as D1 and D2 can be included in the pre-intervention phase, D3 can be regarded as the intervention phase and D4, the reporting phase, after laboratory phase completion.

The systematic search, which was part of the review stage during the development, identified several systematic reviews that had similar sources of bias within their RoB assessments. The most prevalent sources of bias screened were the correct randomization of samples (75%),

Table 3
Domains (D1-D4) discussed, approved, and included in the RoBDEMAT tool along with their description.

Domain name		Description
D1	Bias in planning and allocation	In this domain, reviewers are expected to assess the bias arising from planning the study and allocating samples/specimens. Bias in this domain directly influences the experimental design and it relates to the presence of a control group, proper sample allocation (randomization, concealment) and sample size determination.
D2	Bias in sample/specimen preparation	In this domain, reviewers should evaluate if the researcher minimized bias during sample/specimen preparation and/or replication/repetition. This domain evaluates whether the preparation of the samples/specimens and materials used was standardized whenever possible.
D3	Bias in outcome assessment	Relates to bias arising from the testing procedures and assessment. This domain deals with whether the tests/assays carried out were appropriate to meet the objective(s) of the study and whether bias could have been introduced during testing.
D4	Bias in data treatment and outcome reporting	The last domain deals with bias arising from statistical treatment of data and its reporting. In this domain, reviewers should judge the statistical analysis undertaken in the study and whether the outcomes previously set by the study authors were correctly reported, without missing relevant data.

Table 4
Sources of bias within each domain and signalling questions, assisting the classification of the RoB from each source.

	Sources of bias	Signalling question(s)	Guidance
D1	**(1.1) Control group**	Did the study employ one or more control groups (positive or negative or existing standard) in its experimental design?	Control groups are critical to the experimental design. Studies should be assessed for an adequate control group which can be a positive or negative control or an existing standard. Control groups will vary by study topic. Some studies will require more than one control group and reviewers should use their judgement to classify the presence of control groups as "insufficiently reported" if more control groups are needed. Otherwise, they should be marked as "sufficiently reported" or "not reported", respectively.
	(1.2) Randomization of samples	Was randomization adequately carried out and reported?	Randomization is important in samples whose nature implies intervariability (i.e., teeth). Reviewers should assess whether samples were randomized, and their allocation was concealed appropriately. Randomization may be conducted using computer generated sequences, random number attribution tables, shuffling envelopes, or cards. Studies that only mention "teeth were randomly allocated" but fail to give details of the randomization process should be marked as "insufficiently reported". Otherwise, they should be marked as "sufficiently reported", when it was adequately carried out, or "not reported", if not.
	(1.3) Sample size rationale and reporting	Did the study provide a rationale and justification for the sample size chosen or feature an *a priori* power analysis?	Explanation of sample size rationale is critical to dental materials research. Authors are required to justify the rationale for the sample size of their study. This rationale may lie in existing defined standard sample sizes (i.e. ADM guidelines or ISO standards) or a sample size estimation. Post-hoc power analyses are not recommended, but *a priori* analyses are highly recommended. In any case, a transparent explanation for the chosen sample size as well as its estimation needs to be provided. To judge this item as "sufficiently reported", authors should have referred to accepted standards, or should have explained the expected effect size and power level as well as the software used for calculation. The expected effect size should be justified based on a pilot study or previously published studies. Otherwise, studies should be marked as "insufficiently reported" or "not reported", respectively.
D2	**(2.1) Standardization of samples and materials**	Were samples and material choice/employment standardized according to the aim of the study?	Reviewers should assess how standardized samples and materials were employed across groups (e.g., different shades of composites being used). If a non-carious teeth study model is adopted, authors should explicitly mention the use and randomization of sound teeth (free of restorations and other defects). Reviewers are expected to judge whether manufacturers' recommendations were followed for materials (whenever this is applicable to the study design). Studies which involve light-curing (photopolymerisation) of samples must report correct irradiance output, wavelength and tip distance to sample. Reviewers should also assess whether sources and composition of materials are correctly reported. If these details are incomplete or non-existent, they should be marked as "insufficiently reported" or "not reported".
	(2.2) Identical experimental conditions across groups	Were the storage, experimental or treatment conditions standardized across samples and materials?	Reviewers should assess whether identical conditions were provided for different experimental groups. Factors such as temperature, humidity, time and equipment settings are expected to be identical and controlled, and indications that suggest otherwise should raise concerns. Authors should specifically indicate storage conditions (solution source, concentration, time) and storage/ageing solution or other reagent preparation methods, to enable reproducibility. Studies that fail to give sufficient information should be marked as "insufficiently reported" or "not reported".
D3	**(3.1) Adequate and standardized testing procedures and outcomes**	Were testing procedures and outcome(s) measure(s) explained or defined in sufficient detail to allow reproducibility and critical appraisal?	Reviewers should assess whether the chosen test or test procedure (including equipment or instruments) was adequately described to allow critical appraisal and replication, if needed. Any outcomes and outcome measures should be defined properly to allow interpretation and, if needed, comparison or pooling across studies. Careful consideration should be given to testing procedures being standardized. ADM guidelines or ISO/ASTM standards should be used if applicable and in line with the research question.
	(3.2) Blinding of the test operator	Was the test operator blinded to the different experimental groups?	If applicable to the study design, test operators should be blinded to the different experimental groups under testing, and reviewers should appraise this blinding step.
D4	**(4.1) Statistical analysis**	Was the statistical analysis adequate and reported in sufficient detail?	Reviewers should assess if the chosen descriptive and analytical statistical approach was adequate to the yielded data and the study aims. This relates to the scale of data (continuous, ordinal, nominal) but also its distribution (e.g. reporting of means or median values or choice of the appropriate statistical test depending on skewness). Specific study design factors (e.g., factorial design, repeated measures at time points) should be appropriately reported and reflected. The software used for statistical evaluation and the applied level of significance should be reported. If relevant information is missing, reviewers should judge whether the study merits "insufficiently reported" or "not reported".
	(4.2) Reporting study outcomes	Are all relevant outcome data, expected to be reported, available in sufficient detail?	Reviewers should assess whether the reported outcomes of a study are complete and in line with what could be expected or has been defined as planned outcomes by the researcher before conducting the study, but also if outcomes are reported in sufficient detail for a full appraisal. Reviewers will

Table 4 (*continued*)

Sources of bias	Signalling question(s)	Guidance
		evaluate if relevant outcome data is missing or incomplete (e.g., are bond strength data reported alongside failure mode data), and if outcome reporting is sufficiently detailed (e.g., measures of precision like confidence intervals or standard errors are expected to be reported if applicable).

ADM guidelines: Academy of Dental Materials; ISO/ASTM standards: International Organization for Standardization/American Society for Testing and Materials standards.

sample size calculation reporting (71%) and judgment whether a single operator performing the sample preparation (50%). Correct sample randomization and concealment can be seen in virtually all RoB tools devoted to clinical and animal research. Flaws that condition sample selection will translate into a direct assault of the internal validity of the study [31]. Thus, this item is crucial and had to be included in the present tool. For instance, allocating perfectly sound teeth to certain experimental groups while allocating others that may have structural defects, to other materials, can completely bias the results of the study.

Sample size calculation may also be critical to materials research as it can compromise the confidence in the results, when it is arbitrarily chosen without appropriate rationale. It is especially important in certain studies, such as ones where mechanical properties are tested, which are subject to random material flaws during sample preparation and testing [32]. Common practice to solve this is to recommend larger sample sizes [33]. Sample size relates to precision rather than directly to bias. However, limitations in sample size affect the credibility of the results. Thus, having this item listed in the checklist table will provide an informative indication that contributes to the total risk of bias an individual study may have, as agreed by all in this consensus. Turning to the following item, mentioning "a single operator performing the sample preparation", RoBDEMAT included this in Domain D2, where standardization of samples and materials is expected and evaluated. In this item, the tool states that no differences should exist, and identical conditions must be met across all samples that are equal. This domain also included other sources identified in the systematic reviews, such as the manufacturer's recommendations for material use (46%). As pointed out by Darvell (2021) [34], manufacturer recommendations, when detailed, are an important piece to provide reproducibility of laboratory studies. Researchers need to have detailed information to understand how things were performed "in order to assess, analyse and use the information". Likewise, Price (2018) pointed out issues in replicability and reproducibility in studies that involve light-curing of dental resins [35]. He advocated that studies featuring light-curing must indicate radiance exposure and characteristics of the light received by the resin specimens (wavelength and tip distance). This has been included as part of D2 (2.1) within our RoB tool.

Less prevalent among the items retrieved from the systematic reviews, but still extremely important, are the presence of a control group (36%) or items related to the correct reporting of statistical analysis (25%) and outcomes (14%). Firstly, studies without control groups are

of limited value as there is no standard or reference to compare to, especially in the case of materials research [36]. In what concerns statistical reporting, it is observable that papers featuring incomplete or is poorer statistical reporting are generally s lower quality publications that tend to avoid critique during the peer review process [37], raising substantial bias risk towards its results.

As previously stated, RoB tools should be specific to the study design. For example, in terms of randomization carried out in a randomized controlled clinical trial, the purpose is to distribute the confounding variables more evenly, between different groups [38]. To achieve this, the subjects are typically put in random order, which are logically listed or in blocks. Nonetheless, in practice of some laboratory-based methods, such randomization scheme might not be scientifically meaningful because the bias from the method itself has not been controlled. In a simpler term, the error (bias) from the method may be much larger than the error minimised from randomisation of samples, in certain chemical or mechanical tests where selection bias is not as meaningful. Given a certain method that is validated, such randomization can only provide an assurance about robustness [39].

Existing RoB tools contain between 5 and 13 items [18]. The proposed RoBDEMAT tool has a total of 9 items, which falls within the average range seen in the literature. In fact, it is considered alike other successful tools which report a total of 10 items [40]. When it comes to RoB items, simpler checklists are preferred in comparison to a large number of items, which also justifies our number. Furthermore, domain-based tools, such as RoBDEMAT, are often preferred to simple scales or checklists [41]. This categorization of sources of bias improves systematization and it is found in gold-standard tools such as RoB 2 [30].

Considering the IRR and test re-test results, it was possible to obtain fairly consistent agreement scores. Even though lower agreement was seen in some of the items within Domains 3 and Domains 4, it is important to reiterate that this risk of bias tool will be typically employed by a group of reviewers (2+) and disagreements are expected - they should be resolved by consensus. In fact, this risk of bias tool has been applied to a recent peer-reviewed systematic review [42], which contributes to its validity.

The development of this tool will allow future systematic reviews to incorporate such risk of bias measurement that meets the high standards of *in vitro* dental research. In addition, it will establish a standard to which we can evaluate whether there is an under- or over-estimation of the results (i.e., level of trust) in each primary study included in the

Table 5
Reliability analysis showing inter-rater reliability and test re-test scores (Cohen's k).

IRR	Cohen's k (n=7)	SE	Interpretation
1.1	0.76	0.17	Substantial
1.2	1.00	-	Perfect
1.3	0.61	0.15	Substantial
2.1	0.41	0.32	Moderate
2.2	0.83	0.11	Near perfect
3.1	0.37	0.21	Fair
3.2	1.00	-	Perfect
4.1	0.24	0.11	Fair
4.2	0.43	0.19	Moderate

Table 6
Test-re test results showing intra-rater reliability at different time points, evaluated through intraclass correlation coefficient.

Test Re-Test	Intraclass correlation	CI 95%
1.1	1.00	-
1.2	1.00	-
1.3	0.80	0.28 – 0.96
2.1	1.00	-
2.2	1.00	-
3.1	0.68	-0.16 – 0,94
3.2	1.00	-
4.1	0.80	0.28 – 0.96
4.2	1.00	-

review process. Consequently, it is possible to avoid being misled to an inference, or conclusion, that does not reflect a true populational estimate.

The limitations of this study should also be addressed. The number of experts included in the discussion and designing the tool was limited and it may not cover the full spectrum of dental materials from which systematic reviews can be made. Nevertheless, a multidisciplinary team of experts was gathered, strengthening the feedback and resulting tool. Additionally, the expertise of two societies (EFCD and IADR-DMG) was provided and had direct involvement in the study, and other bodies provided input and evaluated the tool, assisting on the development of the final tool and list of items [43]. Considering that other RoB tools, such as the Cochrane RoB (RoB 2), underwent updates in the course of its use and application, which is always beneficial, the present tool will be open to future updates to enhance its scientific quality and to fit its forthcoming needs. The well-defined EQUATOR stages and Delphi process allowed a comprehensive and detailed approach to devise a user-friendly tool that can also be considered methodologically sound, as it followed a similar methodology to other tools developed recently [27].

5. Conclusion

This article reports a novel risk of bias tool – RoBDEMAT – developed by a broad panel of international and multidisciplinary dental materials expert stakeholders, within the field of dental materials, to assess the quality of laboratory dental materials studies. This tool will serve to significantly improve reporting of dental materials studies, by assessing their quality in a systematic and transparent manner, while also being used as a tool for systematic reviews that plan to include such studies.

CRediT Author Statement

We declare that all the authors involved substantially contributed to the study and manuscript draft and revision.

CRediT authorship contribution statement

António HS Delgado: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing. **Salvatore Sauro:** Conceptualization, Methodology, Validation, Formal analysis, Writing – review & editing. **Adriano F. Lima:** Methodology, Validation, Writing – review & editing. **Alessandro D. Loguercio:** Methodology, Validation, Writing – review & editing. **Alvaro Della Bona:** Methodology, Validation, Writing – review & editing. **Annalisa Mazzoni:** Methodology, Validation, Writing – review & editing. **Fabricio Mezzomo Collares:** Methodology, Validation, Writing – review & editing. **Frode Staxrud:** Methodology, Validation, Writing – review & editing. **Jack Ferracane:** Methodology, Validation, Writing – review & editing. **James Tsoi:** Methodology, Validation, Writing – review & editing. **Julia Amato:** Methodology, Validation, Writing – review & editing. **Klaus W. Neuhaus:** Methodology, Validation, Writing – review & editing. **Laura Ceballos:** Methodology, Validation, Writing – review & editing. **Lorenzo Breschi:** Methodology, Validation, Writing – review & editing. **Matthias Hannig:** Methodology, Validation, Writing – review & editing. **Mary Anne Melo:** Methodology, Validation, Writing – review & editing. **Mutlu Özcan:** Methodology, Validation, Writing – review & editing. **Nicola Scotti:** Methodology, Validation, Writing – review & editing. **Niek Opdam:** Methodology, Validation, Writing – review & editing. **Satoshi Yamaguchi:** Methodology, Validation, Writing – review & editing. **Sebastian Paris:** Methodology, Validation, Writing – review & editing. **Lezize Sebnem Turkun:** Methodology, Validation, Writing – review & editing. **Sophie Doméjean:** Methodology, Validation, Writing – review & editing. **Vinicius Rosa:** Methodology, Validation, Writing – review & editing. **William Palin:** Methodology, Validation, Writing – review & editing. **Falk Schwendicke:** Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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