Indexing, reporting and identification of time-to-event survival analyses in the dental literature

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ABSTRACT: Indexing, reporting and identification of time-to-event survival analyses in the dental literature

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Objective: This research explored how time-to-event dental articles were indexed and reported, and sought solutions to help improve the reporting and identification of these articles, so that they could be more easily found and used to inform practice and research.

Methods: Articles reporting time-to-event dental outcomes in humans were identified from the 50 dental journals with the highest impact factor for 2008. These were handsearched, identifying ‘case’ articles (n=95), active controls (likely false positives, n=91), and passive controls (other true negatives, n=6796). The medical subject headings (MESH) that had been assigned to the articles in MEDLINE, and words used in titles and abstracts describing time-to-events were compared between the ‘cases’ and controls. Time-to-event words and figures within articles were also sought, and reporting quality was assessed. Search strategies to identify time-to-event articles were developed, using indexing terms and free-text words. An independent cohort of articles was used to validate the search strategies, consisting of 148 time-to-event articles handsearched from 6514 articles in the 50 dental journals with the highest impact factor for 2012. The findings of the research were used to draft guidance to improve reporting, which was circulated amongst 78 stakeholder experts for comment, and modified.

Results: MeSH indexing of time-to-event analyses was inconsistent and inaccurate, author descriptions in abstracts and titles varied, and the quality of time-to-event reporting and graphics in the body of those articles was poor. The burden faced by someone wishing to find and use these articles was considered high. Sensitive, precise and optimized electronic search strategies were developed and validated with sensitivities up to 92% and precisions up to 93%. The draft guidance attracted comment from 46 experts across 15 countries, with approximately 90% of the 130 comments accepted into the revised version. The importance of good quality reporting was endorsed, and there was high interest in commending the guidance to authors, reviewers, and training dental specialists.

Conclusions: This research programme explored how time-to-event dental articles were reported, and used those findings to suggest solutions that would help to improve the identification and use of these data, reducing research waste.

LONG ABSTRACT: Indexing, reporting and identification of time-to-event survival analyses in the dental literature

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Background:

Time-to-event analyses are regularly used to report dental outcomes, but, "surviving" inanimate objects differ conceptually from surviving humans. I hypothesized that this nuance would affect how research was described and indexed, and thus affect retrieval yields when these research articles are sought in bibliographic databases. My pilot research (published in a dissertation submitted for partial fulfillment of the degree of Master of Science in Evidence Based Health-Care at the University of Oxford in 2011) indicated that identification of time-to-event dental articles was difficult, resulting in research waste in this field.

Objective:

The research for this DPhil explored how time-to-event dental articles were indexed and reported, and sought solutions to help improve the quality of reporting and the identification of the relevant articles, so that these could be more easily found and used to inform practice and research.

Specific objectives were determined for each section in this programme of research. The introductory chapter summarised the way the thesis explored its overall aim and individual objectives, and explains why this programme of research is relevant to decision making in dentistry. These objectives were:

1. Identification of articles published in the dental literature to facilitate assessment of studies reporting time-to-event dental data
2. Assessment of the allocation of MEDLINE Medical Subject Headings (MeSH) to articles reporting time-to-event dental data
3. Identification of the words and phrases that authors had used to describe time-to-event dental data
4. Reviewing the quality of reporting of methods, results and graphics of dental articles containing time-to-event data
5. Reviewing of the "burden of the problem" of indexing and reporting time-to-event dental data
6. Development and validation of electronic search strategies to identify time-to-event dental data

7. Development and review of a guidance document for reporting time-to-event dental survival analyses

Methods:

The aims, objectives and structure of this thesis were summarized in an introductory chapter, and the possible impact of the findings was explored in the context of dental decision-making.

Articles reporting time-to-event dental outcomes in humans were identified as a starting point, providing information on what can be considered the “burden” of the problem, equivalent to the “burden of disease” when considering health care more generally. In this context, this refers to the “burden” of poor reporting or inaccurate indexing of dental survival analyses and the challenges this causes for people who wish to use the relevant articles for practice or research. The 50 dental journals with the highest impact factor for 2008 were systematically handsearched, identifying included ‘case’ articles, active controls (likely false positives), and passive controls (other true negatives). A single reviewer completed article screening twice, and two independent reviewers completed eligibility assessments.

Bibliographic databases allocate indexing terms to articles to classify details about the research. These terms are selected from a standardised vocabulary, such as the medical subject headings (MeSH) in MEDLINE. I assessed which MeSH were allocated to articles that reported time-to-event outcomes, and contrasted these with the two control groups. Terms that related to (1) time-to-event statistical techniques, (2) time-to-event prosthesis outcomes, or (3) the conduct of research over time were identified and extracted manually from the included ‘case’ and active control articles. Relevant MeSH were extracted as they were identified, and were not determined prior to review of the records. When these terms had been identified, I checked whether these had been used for the 6769 passive controls. I analysed the accuracy of, and differences in allocation of the terms between the included ‘case’, active and passive control groups.

I explored the words authors used in the titles and abstracts of the time-to-event ‘case’ articles, and whether articles in the control groups also used these words. The 95 included ‘case’ and 91 active control articles were read and this identified 43 English words that the authors had used in their title, aim and abstract, which indicated that dental outcomes were studied over time. These words were then sought in the same sections in the 6796 passive controls. The 43 words were divided into six groups. Group 1 related to time-to-event statistics, groups 2 to 4 indicated that an outcome was studied over time, group 5 indicated that an outcome was studied, and group 6 related to time. Differences in use of words among the three types of article were analysed for groups 1 to 4, and between the ‘cases ‘and active controls for groups 5 and 6.

The quality of reporting of the articles that used time-to-event analyses to report dental treatment outcomes was explored by considering words used to describe survival in the methods and results sections of the included ‘case’ and active controls. I also assessed the use and reporting quality of life tables and survival curves, and the use and reporting quality of time-to-event statistical methods. Two investigators independently assessed subjective criteria (using the kappa statistic to analyse agreement), and one investigator completed all other assessments. I considered survival curves and life tables that included all graphic quality measures to be of high quality, and graphics that included all measures except for the standard error or confidence interval to be of acceptable quality. Articles that reported all quality measures regarding the statistical tests in the methods of the article were considered to be of high quality, while those that reported the type of survival statistic and summary figure only were considered to be of acceptable quality.

Following these assessments of 6955 articles, I explored the overall findings and reviewed the severity of the reporting burden. This identified some ways to reduce the impact that the reporting burden may have on identifying and utilizing studies with time-to-event dental data. The solutions were aimed at guiding the writing of such articles, so that reporting was more transparent, and identifying the time-to-event articles. I used the results from the first section of this research to develop search strategies and draft the reporting guidance, which were then assessed in the second phase of this research.

I used two independent article cohorts containing time-to-event articles to develop and then validate sensitive, specific and precise search strategies for MEDLINE (Ovid). Descriptive words and indexing terms were determined objectively from the 2008 article cohort, and used to construct the electronic search strategies. The performances were then tested in an independent validation dataset, and sensitivity, precision and number needed to read (NNR) were calculated. The validation dataset was identified through an additional systematic handsearch of articles published in the 50 dental journals with the highest impact factor from the year 2012. The 6514 articles were identified and classified as those reporting dental treatments in humans with time-to-event statistics (n=148) and all other articles (n=6366).

To conclude this DPhil research, I developed a guidance document to improve reporting transparency of time-to-event articles in dentistry, drawing on my earlier research. The draft guidance, including a proposed checklist, tables and figures, explanatory document and background information were sent to 78 experts in 19 countries by email. Over 60% of those invited to participate had published time-to-event related articles. Over 85% of experts were from the field of prosthodontics. Their feedback was used to modify the document, which is presented in this thesis.

Finally, I reviewed my research in the context of the existing literature, and explored the implications of the research findings on clinical practice and future research.

Results:

The systematic handsearch of the 50 dental journals from 2008 identified 95 articles reporting the survival of dental prostheses in humans with time-to-event statistics (which formed the included ‘case’ articles) and 91 without time-to-event statistics (active ‘control’ articles), as well as all other articles that did not report studies of the survival of dental prostheses (passive ‘control’ articles, n=6796). In total, 6955 articles were checked and categorised. Screening was completed by a single reviewer twice, with the second search undertaken six months after the first (Kappa was 0.92). Eligibility was assessed by two independent reviewers (Kappa was 0.86). The included ‘case’ articles were the true positives, those definitely reporting time-to-event outcomes of dental prostheses in humans over time. The active ‘controls’ reported such outcomes, but without time-to-event statistics. These active controls were the most likely to be false positives in electronic searching, which is why they were categorised separately from the other true negative articles, the passive controls. Thereafter, details contained within these 6955 articles were used to inform how the research was indexed and reported.

The time-to-event 'case' articles had been allocated seventeen different outcome-, statistic- and time-related MeSH. The most frequently allocated MeSH for the included 'case' articles and active controls were 'Dental restoration failure' (77%, 52%) and 'Treatment outcome' (54%, 48%). The use of at least one outcome MeSH was similar between the 'cases' and active controls (86%, 77%), but significantly greater than in the passive controls (10%, P<0.001). Significantly more included 'case' articles were allocated at least one statistical MeSH when compared to the active or passive controls (67%, 15%, 1% P<0.001). Sixty-nine included 'case' articles specifically used Kaplan-Meier or life table analyses, but only 42% (n=29) were indexed as such. Significantly more included 'case' articles were allocated at least one time-related MeSH compared to the active controls (92%, 79%, P=0.02), and to the passive controls (22%, P<0.001). Therefore, the allocation of MeSH to time-to-event dental articles in MEDLINE was sometimes inaccurate and inconsistent. Regarding one of the three groups of indexing terms studied, statistical MeSH were omitted from 30% of the included 'case' articles and incorrectly allocated to 15% of active controls. Such errors will adversely impact search accuracy.

Turning to the words used by authors in their titles and abstracts, the included 'case' articles used group 1 (statistical technique) and group 2 (statistical terms) more frequently in their abstracts than the active and passive controls (group 1: 35%, 2%, 0.37%, P<0.001 and group 2: 31%, 1%, 0.06%, P<0.001). The 'cases' and active controls used group 3 (quasi-statistical terms) equally, but significantly more often than the passive controls (82%, 78%, 3.21%, P<0.001). In the aims, use of target words in groups 1, 2, 3, 4, 5 and 6 was similar for 'cases' and active controls (P values 0.10 to 0.59), but less frequent for groups 1, 2, 3 and 4 in the passive controls (P values <0.001). In the titles of the 'cases' and active controls, group 2 terms were not used, groups 1, 3, 4 and 5 were used with a similar frequency (P values 0.15 to 0.96), and group 6 were used in significantly greater number of included 'case' articles (54%, 30%, P=0.001). When compared with the titles of passive controls, use of group 2 and 3 terms was significantly less frequent (P values <0.001). Across the abstracts, aims and titles of the passive controls, terms in groups 5 and 6 were not assessed. Overall, there was great variation in the words used by authors to describe dental time-to-event outcomes. Specifically, two-thirds of the included 'case' articles did not use words in the title or abstract highlighting "how" (time-to-event statistic) the research was conducted; and other articles in the cohort at times also used these words. Such variation will adversely impact search accuracy.

When I reviewed the reporting of time-to-event methods and results in the body of the article, words describing dental outcomes "over time" were much more common in the included 'case' compared with the active control articles (77%, 3%, P<0.001). Non-specific use of "rate" was common across both groups. Life tables and survival curves were used by 39% and 48% of the time-to-event articles respectively, and use of at least one of these graphics was common (82% of articles). Construction quality was generally poor, with no life table or survival curve achieving a high quality standard, and only 21% and 28% achieving an acceptable quality standard, respectively. Time-to-event statistical reporting was also poor in a substantial minority of articles, with 3% achieving a high quality standard and 59% achieving an acceptable quality standard. The survival statistic, summary figure and standard error were reported in 76%, 95%, and 20% of time-to-event articles. I found that important details were regularly omitted from both statistical descriptions and survival figures, making the overall quality of reporting poor.

The afore-mentioned assessments revealed that MeSH indexing of time-to-event dental data was inconsistent and inaccurate, that author descriptions of research in their abstracts and titles varied greatly, and that construction of survival graphics and reporting quality of survival-outcomes in the body of those articles was poor. Errors in indexing and poor reporting quality meant that dental survival articles would not be readily identified when sought electronically by a MeSH or text word search, and these failures to identify relevant material may be compounded by the poor reporting quality in those that are found. The level of research waste could be high. To develop ways to reduce the burden of this problem, I directed further research towards developing electronic search strategies to improve article identification, and proposing guidelines to improve the reporting quality.

I developed sensitive, precise and optimized search strategies from an objective list of search terms to identify time-to-event articles in the dental literature. The performances of the sensitive (92% sensitivity, 14% precision, 7.11 NNR), precise (93% precision, 10% sensitivity, NNR 1.07) and optimized filters (83% sensitivity, 24% precision, 4.13 NNR) were independently validated in the 2012 article cohort. The construction and validation cohorts contained different journal titles and publication years, enhancing the generalizability of the results.

After developing a document containing guidance for the reporting of time-to-event dental outcomes, I sought feedback from 78 experts. Of these, 55 acknowledged receipt, 46 completed feedback, 9 initial responders did not continue, and there were 23 were non-responders. Feedback was received across 14 domains such as title, abstract, checklist, example figures and 9 themes such as endorsement of the importance of the guidance, editorial recommendations and suggestions for additions. Out of the 130 comments received, I used approximately 90% to modify the guidance. The feedback also showed that a range of participants wished to commend the document to authors submitting manuscripts, reviewers of those manuscripts, and dentists in specialty training programmes. The final proposed guidance included an explanatory document and abbreviated checklist; lists of MeSH and words that may be used to describe the research; as well as examples of life tables, survival curves and abstracts.

<u>Implications:</u>

The findings of this research are the result of assessing approximately 14,000 dental articles published in high impact dental journals in 2008 and 2012, and input from the 46 professionals from 15 countries who had knowledge of time-to-event dental articles, who provided feedback on the draft guidance.

There is a significant reporting burden affecting time-to-event dental survival analyses that would adversely impact on accurate article identification, and mean that many of those that are found would be difficult to understand. The level of research waste could be high.

The proposed search strategy will help identify articles that had already been published by overcoming some of the reporting shortcomings; and implementing the reporting guidance will improve the reporting quality, such that articles become easier to find and simpler to understand once identified. This will reduce waste in the time-to-event dental research by improving its identification and use.

Post-doctoral research will involve validation and dissemination of the guidance and search strategy. Validation of the search strategy across other fields reporting time-to-event articles, and validation of the guidance document for use in dentistry can be undertaken. Dissemination of the search strategies and the guidance document through publication, lecturing, submission of conference abstracts, and endorsement by university courses and key dental journals can be sought.

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1.0 BACKGROUND

Pilot research indicated that identification of time-to-event dental articles was difficult, resulting in research waste in this field.

1.1 THESIS AIMS

This programme of research sought to explore how time-to-event dental articles were indexed and reported, and to see what might be done to improve this so that studies with time-to-event dental data were not lost in the literature.

1.2 THESIS OBJECTIVES

1. Identification of articles published in the dental literature to facilitate assessment of studies reporting time-to-event dental data
2. Assessment of the allocation of MEDLINE Medical Subject Headings (MeSH) to articles reporting time-to-event dental data
3. Identification of the words and phrases that authors had used to describe time-to-event dental data
4. Reviewing the quality of reporting of methods, results and graphics of dental articles containing time-to-event data
5. Reviewing of the “burden of the problem” of indexing and reporting time-to-event dental data
6. Development and validation of electronic search strategies to identify time-to-event dental data

7. Development and review of a guidance document for reporting time-to-event dental survival analyses

1.3 Thesis structure

Chapter 2 will report how articles regarding time-to-event dental outcomes in humans were identified to facilitate this programme of research. To achieve this, a contained cohort of articles was identified, and classified into three groups. The included ‘case’ articles are the true positives, those definitely reporting time-to-event outcomes of dental prostheses in humans over time. The active “controls” reported such outcomes, but without time-to-event statistics. These active controls are the most likely false positives, and were identified separately to all other true negative articles, the passive controls.

People indexing articles for databases such as MEDLINE use a standardised vocabulary, such as the medical subject headings (MeSH) to classify details about the research. Chapter 3 will assess what MeSH were allocated to articles that reported time-to-event outcomes, and contrast these with the two control groups. Time-to-event research concerns time-dependent outcomes. Such outcomes have three things in common: the outcome, time and time-related statistic. Therefore, my assessment of the MeSH sought those terms that indicated an outcome had been explored, over time, and analysed with a time-to-event statistic.

Chapter 4 will review what words authors used in the titles and abstracts of the time-to-event ‘case’ articles, and then whether these words were used by articles in the control groups. Therefore, this assessment sought whether words indicated an outcome had been studied, over time, and analysed with time-to-event statistics.

It is important that all scientific articles are reported clearly and with transparency, allowing those seeking information to make full use of the research findings. Therefore, chapter 5 will review how the time-to-event methods and results were reported in the body of the article. The words used by authors to describe the statistical methods and to report those results were identified. Also, the articles were reviewed to identify whether life tables or survival curves had been used, and to then assess how they had been constructed. The quality of reporting in the methods and results, and the quality of construction of the survival figures was assessed.

Following this assessment of time-to-event dental articles, Chapter 6 will summarise the information gathered thus far by this programme of research and presented in the preceding chapters. The chapter aims to review the severity of the reporting burden at the moment, and then explore what might be done to reduce this so that studies with time-to-event dental data do not remain lost in the literature. The solutions offered will be aimed at identifying the time-to-event articles, and guiding the writing of such articles so that reporting is transparent.

Chapter 7 relates to identification of time-to-event articles. Two independent article cohorts containing time-to-event articles were used to develop and then validate sensitive, specific and precise search strategies to identify such articles. The MeSH used by indexers and the descriptive words used by authors were tallied for the initial article cohort, and used to develop the search strategies. Following the methods outlined in chapter 2, a validation article cohort was sought from a different publication year. This validation cohort was used to assess the performance of the proposed search strategies.

Chapter 8 focuses on developing a guidance document to improve reporting transparency of time-to-event articles in dentistry. The results from the research presented in the initial chapters of this thesis were used to inform a guidance document. Feedback on this was sought from a group of experts known to have knowledge about time-to-event reporting in dentistry, and the resultant information was used to modify the final proposal.

This programme of research has been developed to explore how dental articles that contain time-to-event data are reported, and to use these findings to inform recommendations improving researchers' ability to identify and then use these studies. This research seeks to reduce waste in the field of time-to-event dental survival analyses, by making it easier to find and making it easier to use.

1.4 THESIS CONTEXT

Time-to-event analyses are regularly used to report dental outcomes, but, "surviving" inanimate objects differ conceptually from surviving humans. I hypothesized that this nuance would affect how research was described and indexed, and thus affect retrieval yields when sought in bibliographic databases.

Those searching the literature are seeking evidence for different reasons. These may include patients, clinicians, academicians, systematic reviewers, insurance actuaries or government departments. For example, a 19-year old man who lost his front tooth while playing a game of football may have it replaced by a dental implant or a three unit fixed dental prosthesis. The patient may be looking on the internet for guidance to help make the decision. His treating dentist may be seeking evidence to see whether the survival of one treatment is greater than another. An academician may be interested in undertaking a cohort study regarding the survival and outcomes of implants placed in young adults, and wish to review whether research regarding age-related survival data had been undertaken. A systematic reviewer may be exploring the survival of implants placed in the anterior maxilla when teeth replaced were lost due to trauma, carious activity or periodontal disease. An insurance company, offering coverage for amateur sporting trauma may wish to assess the complications that occur over time with prosthetic tooth replacement to determine premium levels to cover replacement only or replacement and ongoing maintenance. Finally, government health-care schemes covering university students may be reviewing the survival of alternative treatment options to decide which option would be provided at taxpayer's expense.

Every prosthetic replacement has a limited lifespan. Those placing fillings, crowns, dentures or implants need access to reliable survival data to recommend appropriate treatment options for their patients. This survival data provides information about time-to-failure that results in treatment termination, time-to-complications that results in maintenance requirements, and overall value for money over the lifespan of the prosthesis.

To make these decisions, clinicians must be able to find appropriate evidence, and once found, must be able to understand the results reported. The findings of the research presented in this thesis should improve their ability to do so.

Chapter 2. Identification of articles published in the dental literature to facilitate assessment of time-to-event dental data

Contents

2.0 SUMMARY

Objective: This research aimed to systematically identify articles published in the dental literature that did and did not use time-to-event methods to report outcomes, by completing a systematic handsearch of a pre-defined set of dental articles. The identified articles would form the basis for the subsequent programme of research to facilitate assessment of studies reporting time-to-event dental data.

Methods: The "subjects" for this research, articles which did and did not report dental outcomes with time-to-event methods, were identified by methods that maximized objectivity. The year 2008 was chosen and journals were included if they were in the top 50 as defined by the ISI impact factor for that year. All articles contained in this defined cohort of journals were then handsearched in a systematic manner.

Results: The handsearch of these 50 dental journals identified articles reporting the survival of dental prostheses in humans either with time-to-event statistics (which formed the included 'case' articles, n=95) or without time-to-event statistics (active 'control' articles, n=91), as well as all other articles that did not report studies of the survival of dental prostheses (passive 'control' articles, n=6796). In total, 6955 articles were checked and categorised. Screening was completed by a single reviewer twice, with the second search undertaken six months after the first (Kappa was 0.92). Eligibility was assessed by two independent reviewers (Kappa was 0.86). The included 'case' articles were the true positives, those definitely reporting time-to-event outcomes of dental prostheses in humans over time. The active 'controls' reported such outcomes, but without time-to-event statistics. These active controls were the most likely to be false positives in electronic searching, which is why they

were categorised separately from the other true negative articles, the passive controls.

Implications: Identification and categorization of these articles facilitates further research to provide information on what can be considered the “burden of disease” in this context, namely the “burden” faced by users of the dental literature because of poor reporting or inaccurate indexing of dental survival analyses.

2.1 BACKGROUND

Time-to-event analyses are regularly used to report dental outcomes, but "surviving" inanimate objects differ conceptually from surviving humans. The definition of survival as it relates to a living being is straightforward. However, the definition of survival as it relates to an inanimate object, is more difficult to contrive. It is likely that the concept of "survival" in dentistry varies from that of "survival" in other medical areas. Differences in interpretation of dental and medical vocabulary and its impact on literature searches has been previously described.[1] Failure to account for this difference is likely to affect the article yield and undermine the identification of relevant articles, resulting in waste in this field of research.

It was hypothesized that this nuance in survival vocabulary would affect how research was described and indexed, and thus effect retrieval yields for dental articles when sought in bibliographic databases.

This Doctor of Philosophy research seeks to answer two fundamental questions:

- How is time-to-event data in the dental literature indexed and reported?
- What might be done to improve this, so that studies with time-to-event dental data are not lost in the literature?

Different people look for articles indexed in the bibliographic databases for different reasons. They could be seeking background information to assist in new research, be completing an assignment for university, writing a lecture for colleagues, seeking information to support clinical decisions or be involved in an in-depth analysis of published data.

Treatments provided to dental patients have a finite lifespan. They experience complications, require maintenance, and eventually require full revision. Patients undergoing such treatments understandably wish to know how long it may be until such adverse events occur, prior to committing time and resources to treatment. Patients seek assistance from their clinicians to explore these risks, and clinicians in turn seek assistance from their clinical experience and published data to answer patient questions.

Finding data about dental outcomes is not necessarily easy. The articles are indexed in many databases, such as MEDLINE, Embase, CINAHL, PsycLit and the Cochrane Library. The databases contain the data, and are separate entities to the search platforms that retrieve the data. Common search platforms come from providers such as OVID, PubMed and SilverPlatter. Some databases, such as MEDLINE, can be searched via multiple search platforms, including OVID and PubMed. So, the databases are much like the World Wide Web, which can then be accessed using search platforms and engines such as Google or Yahoo. The data are there for the reader to find, but the seeker needs to know what they are looking for to conduct an effective search.[2]

Articles can be sought by a word search. In the bibliographic databases of MEDLINE and Embase, a word search searches for any word that was used by the authors, but in the title or abstract only, as well as searching other fields in the record, including the index terms, author names and correspondence address; but it cannot access the full text of the article. In theory, this sounds effective. In practice, if the author did not describe their research in full, readers will not necessarily find their article.

Alternatively, articles can be searched for by an indexing term. These terms are allocated to the articles by indexers who have read the entire article. This means that similar types of articles should be allocated similar indexing terms. It also means that indexers who come across articles that were not described completely in the abstract can combat this by allocating an appropriate indexing term after reading the full article. Therefore, the article is no longer "hidden", and can be found with an index term search.

Different databases use different indexing terms and perhaps the most well known of these are MeSH, medical subject headings. These terms are allocated by indexers at the National Library of Medicine to articles in the MEDLINE database.[3] These terms have also been adopted by other databases as a source of thesaurus terms, enabling index searches. For example, the Cochrane Library,[4] CINAHL[5] and PsycLit[6] use MeSH, while Embase uses an alternative thesaurus database known as Emtree, with this thesaurus also including all MeSH terms.[7]

Articles can also be identified by electronic full-text searches.[8] For example, many documents on the internet can be searched across the full text by Google, and all Cochrane Reviews in the Cochrane Library can be searched across their full text. These search strategies are becoming increasingly available, but are not yet possible for a broad range of journals.

Within prosthodontics, time-to-event analysis is often referred to as "survival", with the event for statistical purposes defined as a "failure" (such as fracture). Differences in "survival" between restorative-types can be compared, length of "survival" can be observed, and prognostic markers deemed relevant to “survival” can be assessed. The term may appear as survival, survival analysis, survival rate, survival data, cumulative survival, cumulative estimated survival or Kaplan-Meier survival.

Authors also use a plethora of other time-to-event analysis terms. These may include success, clinical performance, clinical outcome, longevity, lifespan, failure rate, incidence of aftercare, complication rate and follow-up. These other terms have multiple meanings in dentistry and could describe many aspects of clinical outcomes unrelated to time-to-event “survival”. Therefore, use of these terms as search words will not have high specificity, and is likely to identify many irrelevant articles.

Possible MeSH include survival, survival rate, survival analysis, Kaplan-Meier estimate, actuarial analysis and life tables.[9] The first two terms relate to the meaning or “subject” of survival, and the next four terms relate to a methodology. There is no MeSH for the generic term “time-to-event” analyses.

The dental application of “survival” and the medical application of “survival” differ. The first two MeSH exemplify this difference. In medicine, survival and survival rate relate intimately to “life or existence” and are not transferable to inanimate objects such as dental prostheses.

The four methodological MeSH are applicable across all health fields. ‘Actuarial analysis’ was adopted as a MeSH term in 1979; ‘Survival analysis’ and ‘Life tables’ were included in 1990; with the specific MeSH for ‘Kaplan-Meier estimate’ introduced in 2007.

To explore possible problems with article identification, a test search was conducted in 2010. This test search was first published in a dissertation submitted for partial fulfillment of the degree of Master of Science in Evidence Based Health-Care at the University of Oxford in 2011.[10] Twenty articles known to describe time-to-event analyses of dental prostheses published in English prosthodontic journals between 2005 and 2009 were included. All 20 articles had the word "survival" in the title or abstract, and were included in MEDLINE. Of these, six[11-16] (30%) were not indexed with any of the afore-mentioned MeSH. Kaplan-Meier was specifically mentioned in the text of all six articles, and was in the abstract of half of them. Furthermore, of the fifteen articles published from 2007, eleven[11-14, 17-23] (73%) did not index the new MeSH 'Kaplan-Meier estimate'. Of these, eight[11, 13, 14, 17-19, 21, 22] specifically mentioned the term in the abstract. The mis-match between MeSH and report content was concerning, and it was likely that the mis-match would be worse if the reporting standard was poor.

This test search was exploratory, but highlighted the role that human error can play, and the importance for diligence in any search efforts.

Clearly, errors in indexing of dental survival analyses have occurred in the past. These errors would undermine the identification of relevant articles for dental researchers and clinicians. A gold standard cohort of dental survival articles was required to explore this "burden of identification", which might be considered to be akin to a "burden of disease", which is associated with poor reporting or inaccurate indexing of dental survival analyses.

2.2 OBJECTIVE

This research aimed to identify articles published in the dental literature that used time-to-event methods to report outcomes, by completing a systematic handsearch of a pre-defined set of published dental articles. The identified articles would then be used in further research to facilitate assessment of studies reporting time-to-event dental data.

2.3 METHODS

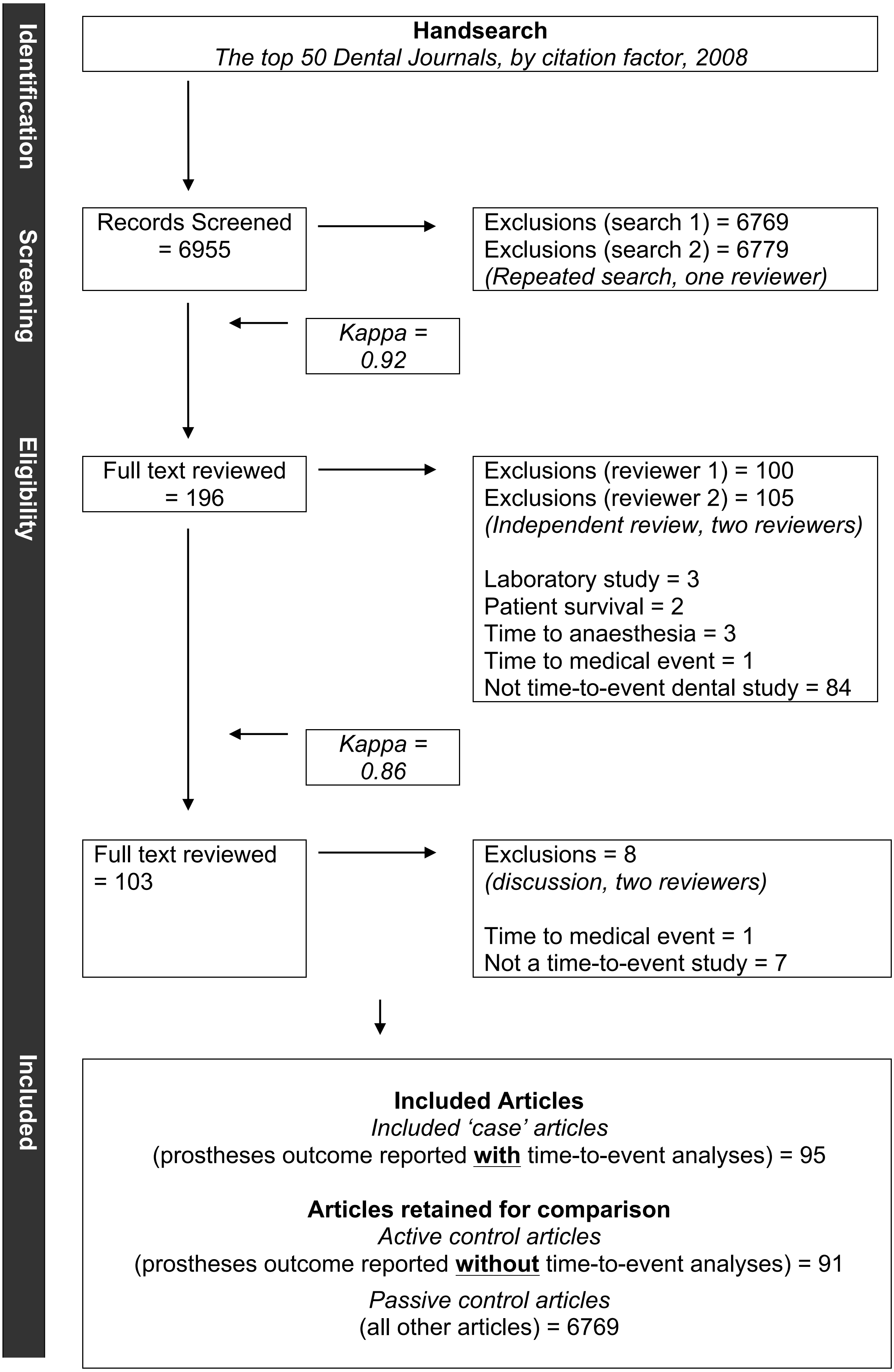
The systematic search was divided into four sections: The identification of articles, full-text screening, assessment for eligibility and selection for inclusion. The flow of the search process is outlined in Figure 2.1.

The 50 dental journals with the highest impact factors in 2008 were identified from the ISI Journal Citation Reports reported in the Web of Knowledge. In total, 6955 articles were published across those 50 journals in 2008. Articles that reported outcomes of dental treatments in humans over time and may have employed time-to-event analyses were then sought by full-text handsearching of each journal. No electronic search strategy was employed. All articles were published in English.

Article identification for full-text screening was accomplished by a single reviewer who completely reviewed the 50 journals a second time following a wash-out period of six months. Assessments of article eligibility and inclusion were undertaken by two independent reviewers. Disagreement was resolved by discussion. The measure of agreement (Kappa statistic) between the two searches, and the two reviewers was determined.

Inclusion criteria were prospective and retrospective studies that employed time-to-event statistics for reporting dental treatment outcomes over time in humans (included 'case' articles, true positives). Articles that reported such outcomes without using time-to-event statistics were retained for comparison ("active controls", the most likely false-positives). All other articles were retained as "passive controls".

Figure 2.1. Flow chart of systematic search



Time-to-event analyses were considered to be those using Kaplan-Meier, Life tables, actuarial analyses and survival functions. Additional articles may also have used time-to-event methods, but not reported their use so clearly. Therefore, articles using Cox regression, log rank and hazard ratios, and those reporting outcome as a rate were also retained for further screening to determine whether a time-to-event analysis had actually been completed.

In vitro and animal studies were excluded from the included 'case' articles. Studies where methods used time-to-event statistics, but outcomes were not specifically related to dental treatments (such as death, cancer, time to anesthesia) were also excluded. These ineligible time-to-event articles were retained in the passive controls.

As noted above, agreement between searches and reviewers in their identification and categorization of articles was assessed with the Cohen's Kappa statistic.[24] This statistic assesses the proportion of agreement that was observed to occur versus the proportion that would be expected due to chance alone. The distribution of articles across the 50 dental journals, and the themes of those articles are provided as percentages.

2.4 RESULTS

Of the 6955 articles published in these 50 journals, full-text screening identified 196 articles that potentially reported dental outcomes with time-to-event methods. Of those, 186 and 176 were noted respectively during search 1 and search 2 (Kappa 0.92) done by one reviewer but separated by six months. From the initial 196 articles, laboratory (n=3), patient morbidity (n=2), time-to-anesthesia (n=3) and time-to-medical event (n=2) articles were excluded. Upon further review, 103 unique articles were selected for possible inclusion as reports of time-to-event analyses of dental prosthesis by two independent reviewers (Kappa 0.86), and 95 were subsequently determined by discussion to meet the inclusion criteria to be included ‘case’ articles.

Articles reporting a prosthesis outcome over time but without using time-to-event statistics were retained as active controls (n=91). These active controls were considered to be the most likely false-positives for people searching for time-to-event analyses and were categorised separately from all other true negative articles, the passive controls (n=6769). These passive controls also contained the “ineligible” time-to-event articles, such time-to-anesthesia and patient morbidity as outlined above.

Therefore, out of the 196 articles screened for eligibility, 95 were included as ‘case’ articles, 91 were retained as active controls, and 10 were excluded from these two groups but retained in the passive controls.

References for the articles in the included ‘case’ (n=95) and active control group (n=91) are provided in Appendix 11.1 and 11.2.

The distribution of articles from the 50 journals is outlined in table 2.1.

The articles in the included ‘case’ group and active controls reported outcomes across a variety of dental treatments. The most common article theme within both the included ‘case’ and active controls related to implant outcomes (64%, 60%). In total, approximately 80% of the included ‘case’ articles (n=74) and 70% of the active controls (n=62) reported outcomes of either implant-related treatment or tooth-supported prostheses. The distribution of the themes of the articles is outlined in table 2.2. The themes of the articles in the passive control group were not reviewed.

Table 2.1. The distribution of article selected from the 50 journals

Impact Factor	Rank	Journals	Total	'Case' Articles	Active Control	Passive Control
1.412	32	Acta Odontologia Scandanavia	59	1	0	58
1.314	36	American Journal of Dentistry	74	3	1	70
1.327	33	American Journal of Orthodontics and Dentofacial Research	313	1	1	311
1.649	24	Archives or Oral Biology	166	0	0	166
1.22	41	Australian Dental Journal	72	1	0	71
1.089	44	British Dental Journal	412	1	2	409
1.327	33	British Journal of Oral and Maxillofacial Surgery	229	0	0	229
2.462	8	Caries Research	60	0	0	60
2.452	9	Clinical Implant Dentistry and Related Research	33	6	3	24
2.92	6	Clinical Oral Implants Research	163	12	19	132
2.233	12	Clinical Oral Investigations	62	1	1	60
0.969	49	Community Dental Health	49	0	0	49
2.418	10	Community Dentistry and Oral Epidemiology	63	0	0	63
2.882	7	Dental Materials	231	2	0	229
1.316	35	Dental Traumatology	173	2	2	169
1.229	39	Dentomaxillofacial Radiology	79	0	1	78
1.024	46	European Journal of Dental Education	55	0	0	55
1.956	19	European Journal of Oral Science	85	0	0	85
0.975	48	European Journal of Orthodontics	94	3	0	91
1.014	47	Gerodontology	38	0	0	38
1.505	28	Implant Dentistry	58	2	2	54
2.223	13	International Endodontic Journal	145	1	0	144
1.978	17	International Journal of Oral and Maxillofacial Implants	130	15	13	102
1.444	31	International Journal of Oral and Maxillofacial Surgery	206	1	3	202
1.141	43	International Journal of Paediatric Dentistry	65	1	1	63
1.702	22	International Journal of Periodontal and Restorative Dentistry	62	1	4	57
1.227	40	International Journal of Prosthodontics	91	11	4	76
1.638	25	Journal of Adhesive Dentistry	59	5	1	53
1.726	21	Journal of the American Dental Association	172	2	1	169
3.549	1	Journal of Clinical Periodontology	66	0	1	65
1.252	38	Journal of Craniomaxillofacial Surgery	151	0	0	151
2	16	Journal of Dentistry	206	0	0	206
1.087	45	Journal of Dental Education	161	2	2	157
3.458	2	Journal of Dental Research	336	2	5	329
2.953	5	Journal of Endodontics	452	2	11	439
1.58	27	Journal of Oral and Maxillofacial Surgery	99	0	0	99
2.144	15	Journal of Oral Pathology and Medicine	121	0	0	121
1.483	30	Journal of Oral Rehabilitation	38	0	0	38
1.263	37	Journal of Orofacial Pain	97	0	0	97
1.966	18	Journal of Periodontal Research	313	9	5	299
2.192	14	Journal of Periodontology	149	3	1	145
1.215	42	Journal of Prosthetic Dentistry	41	0	0	41
0.961	50	Journal of Public Health Dentistry	249	2	0	247
1.683	23	Operative Dentistry	104	1	1	102
1.922	20	Oral Diseases	117	0	0	117
2.336	11	Oral Microbiology and Immunology	80	0	0	80
3.123	3	Oral Oncology	171	0	1	170
1.499	29	Oral Surgery, Oral Medicine, Oral Radiology and Endodontics	440	2	5	433
1.607	26	Orthodontic and Craniofacial Research	30	0	0	30
3.027	4	Periodontology 2000	36	0	0	36
Total			**6955**	**95**	**91**	**6769**

Table 2.2. Article themes of included ‘case’ articles and active controls.

		‘Case’ articles (n=95) No.	%	Active controls (n=91) No.	%
1	Implant-related Implant fixtures, Temporary anchorage devices, Implant prostheses	61	64	55	60
2	Tooth-related prosthodontics Fixed dental prostheses, Crowns, Posts, Resin bonded bridges	13	14	7	8
3	Periodontal related Papilla presence, Periodontal indicies	0	4	2	2
4	Endodontic related Infection resolution, Tooth vitality, Pulp capping	4	4	7	8
5	Orthodontic related Bracket/retainer debonding	3	3	0	0
6	Tooth-related, other Fillings, Tooth survival (ankylosis, resorption, extraction), Transplantation, Caries	14	15	10	11
7	Other TMJ fracture healing, Orofacial grafts, Odontogenic infection resolution	0	0	10	11

2.5 Discussion

Exploration of the dental time-to-event articles has been completed in a systematic manner. The subjects of interest for this research were published articles in the dental literature.

It was not possible to search all dental journals ever published because of the enormity of the task. Therefore, I decided to identify a specific subset of articles in a systematic and objective manner. To do so, the following inclusion criteria were selected: articles published in 2008 in one of the top 50 dental journals (based on ISI impact factor in that year), which were identified via a systematic handsearch.

The year 2008 was chosen for a number of reasons. This programme of research began in 2011, when the year 2008 was the most recent year to be indexed in full in the electronic databases. Indexing takes time, and often a lag period is involved. To complete the assessment of this dataset, it was important that the indexing terms had been allocated, and the titles and abstracts were available to be reviewed. The year 2008 was also chosen because a new indexing term, ‘Kaplan-Meier estimate’ had been included in the indexing options in 2007 in MEDLINE. This allowed indexers to be more specific in the classification of survival analyses, and allowed the allocation of a term that did not include the possibly subjective concept of “survival”.

The ISI impact factor was chosen as an objective means for selecting a cohort of journals to study. This system has already classified journals as belonging to the dental subset, and within this subset has ranked journals based on a citation formula. Not all journals or industry publications related to dentistry are included in this subset, but the most commonly used academic journals would have been captured by this selection method. Research has shown that over 70% of dental research indexed in MEDLINE under the journal subset of Dentistry in the year 2009 were also classified by the Web of Science within the corresponding ISI category[25]. The next highest relationship between such categories was Ophthamology, with an agreement of 48%. The ISI impact factor was not considered to be an ideal method of identifying the highest quality or most highly cited journals, but was simply a widely understood marker that would allow the methods to be repeatable over time.

It was necessary to undertake the laborious handsearching of the journals, because a full sample of time-to-event dental articles could not be identified by any electronic search. The hypothesis of this programme of research related to inaccuracies in both the authors' descriptions and indexers' classification. Therefore, each of the 6955 articles were sourced and searched by hand.

To maximize the objectivity of the method, the handsearch was repeated by the same researcher a second time after a wash-out period of six months. The two searches identified 186 and 176 articles respectively for further full-text screening. All the 95 included 'case' articles were identified in each of the searches, but some of the active controls were missed by one of the two searches. The level of agreement between these identification searches was high, with a kappa of 0.92.

There is a risk that relevant records may be missed if a search is completed only once.[26] For this particular search, it was not possible to enlist another colleague to assist with a second independent full text search of the 6955 articles. Therefore, a repeated search protocol was used. Repeated searches by the same reviewer in a systematic protocol is not common, but has been reported.[27]

The repeated search protocol was supplemented by an independent review during screening, eligibility and inclusion assessments. At the level of screening, agreement between the independent reviewers was high, with a kappa of 0.86. It was interesting but not surprising that the kappa of the repeated searches was higher than the kappa of the independent searches. By definition, the repeated searches were completed by one person, and a high level of internal consistency would be expected.

The repeated search supplemented with independent review has minimized but not eliminated the errors in article identification. It is probable that some articles have been mis-classified, especially if such articles did not report the time-to-event outcomes clearly. Despite this inevitable error rate, the articles identified are suitable to facilitate the assessment of indexing and reporting of such dental literature.

Another way to identify articles included reducing the number of journals and extending the search over multiple years. This was not done because it was important that the articles were published after 2007, when the new Kaplan-Meier indexing term had come into use. Therefore, inclusion of journals from earlier years would have precluded their indexing with terms available today. Inclusion of journals in years later than 2008 for this initial sample was also hampered by the delay in indexing of articles in the bibliographic database.

Another alternative would have been to use a system other than the ISI impact factor to select the sample of journals, such as the 5-year impact factor, immediacy index or Eigenfactor score.[28] When the bibliometrics of Eigenfactor and impact factor have been compared, it has been shown these instruments rank journals in a significantly different order.[25] However, by including the top 50 on the basis of the 2008 impact factor, it is unlikely that a markedly different subset of journals would have been captured. For example, if the top 50 dental journals by Eigenfactor associated with the year 2008 had been included, six journals would not have been included (which had captured five included 'case' articles and four active controls). These journals (Dental Materials Journal, International Dental Journal, Journal of the Canadian Dental Association, Quintessence International and Pediatric Dentistry) would have been replaced by Australian Dental Journal, Community Dental Health, European Journal of Dental Education, Gerodontology, Implant Dentistry and the Journal of Dental Education

There are a number of limitations associated with the methods chosen to build the cohort of articles. It was difficult to find all articles in print across all 50 dental journals and it was laborious to check through the journals by hand. A repeated search method was required, rather than the conventional two independent searchers for the identification, as it was not possible to motivate another colleague to handsearch nearly 7000 articles. Use of a single year, 2008, will provide information about a snap-shot in time, and results should be interpreted with this in mind. However, it is likely that the style of reporting of these article types have not changed markedly in the surrounding decade and therefore results will be applicable to the recent literature.

Finally, choice of the impact factor for identification of journals may provide the greatest source of bias for this research. Although the impact factor is not a proxy for high quality reporting and editorial input, it would select journals that were towards the higher end of this spectrum.[29, 30] This may mean that articles in such journals are reported with higher quality, which may mean that the articles are indexed with greater consistency. Therefore, the results from this programme of research will also need to be interpreted in the light of this identification bias.

The journals assessed were all published in English. This was not a specific inclusion criterion, but no journal in a language other than English was included in the top 50 journals when classified by the 2008 ISI impact factor. Therefore, it is uncertain if the results can be generalized to articles published in languages other than English.

Also, as published articles were sought, to allow assessment of indexing terms, the results do not apply to un-published research or grey literature, such as that contained in conference proceedings, abstracts and manuscripts not yet accepted for publication.

In summary, the 6955 articles identified in the 2008 journal cohort are the “subjects” of this “case-control” research. The identification process was not free from bias, but the decisions made in the methods have been taken to maximize objectivity and repeatability, and reduce the impact that bias may have on the interpretation and generalizability of the programme of research.

2.6 IMPLICATIONS

Identification of these articles facilitates further research to provide information on what can be considered the “burden of disease”, namely the “burden” faced by users of the dental literature because of poor reporting or inaccurate indexing of dental survival analyses.

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CHAPTER 3. ASSESSMENT OF THE ALLOCATION OF MEDLINE MEDICAL SUBJECT HEADINGS (MESH) TO ARTICLES REPORTING TIME-TO-EVENT DENTAL DATA

CONTENTS

3.0 SUMMARY

Objective: This research aimed to assess the Medical Subject Headings (MeSH) indexing of articles that used time-to-event analyses to report outcomes of dental treatment in patients.

Methods: Articles identified by the systematic search to have reported dental outcomes with time-to-event statistics (included 'case' articles, n=95), without time-to-event statistics ('active controls', n=91), and all other articles in the 2008 cohort ('passive controls', n=6769) were included in this study. The MeSH allocated to the included 'case' and active control records were read. Those that related to (1) time-to-event statistical techniques, (2) time-to-event prosthesis outcomes, or (3) the conduct of research over time were identified and extracted manually from the included 'case' and active control articles. Relevant MeSH were extracted as they were identified, and were not determined prior to review of the records. When these terms had been identified, the 6769 passive controls were checked for their use. The accuracy of, and differences between, allocation of the terms between the included 'case', active and passive control groups were analysed with Chi-square and Fischer's exact statistics.

Results: Seventeen different outcome-, statistic- and time-related MeSH were identified. The most frequently allocated MeSH for the included 'case' articles and active controls were 'Dental restoration failure' (77%, 52%) and 'Treatment outcome' (54%, 48%). The use of at least one outcome MeSH was similar between the 'cases' and active controls (86%, 77%), but significantly greater than in the passive controls (10%, P<0.001). Significantly more included 'case' articles were allocated at least one statistical MeSH when compared to the active or passive controls (67%, 15%, 1%

P<0.001). Sixty-nine included ‘case’ articles specifically used Kaplan-Meier or life table analyses, but only 42% (n=29) were indexed as such. Significantly more included ‘case’ articles were allocated at least one time-related MeSH compared to the active controls (92%, 79%, P=0.02), and to the passive controls (22%, P<0.001).

Implications: The allocation of MeSH to time-to-event dental articles in MEDLINE was sometimes inaccurate and inconsistent. Statistical MeSH were omitted from 30% of the included ‘case’ articles and incorrectly allocated to 15% of active controls. Such errors adversely impact search accuracy.

3.1 BACKGROUND

Dental patients who require prostheses such as restorations, crowns and implants realize that such mechanical replacements have a limited lifespan. The anticipated lifespan, given the fiscal and opportunity costs required to receive the treatment, is of great interest to patients, clinicians and those allocating community funding. Assessment of time-to-fatigue is now commonplace in engineering, but entered mainstream scientific assessment after World War II,[1] when the reliability of military equipment was of interest. It has evolved to become the accepted reporting methodology for survival of cancer patients, and as such the statistic has become specifically associated with the survival of human beings who have experienced a life-threatening condition.

Assessments of time-to-event, regardless of whether the event is mechanical fatigue, prosthesis failure or patient death utilize a common statistical methodology: often referred to as survival analyses. This analysis is becoming more common in the dental literature, particularly for the reporting of outcomes of prostheses. However, as noted in Chapter 2, the concept of 'survival' for inanimate dental objects differs from that of 'survival' in other medical areas. The concept that an inanimate object, such as a 'crown', may survive is quite different from the concept that a person with a life-threatening condition may survive. It was hypothesized in this DPhil research project that this linguistic nomenclature will affect clinicians' ability to identify articles reporting the survival of prostheses in the dental literature.

To practice evidence based health-care, clinicians, reviewers and others making decisions must be able to locate relevant evidence. Clinicians generally wish to identify the high quality synthesized evidence, and may seek a systematic review. On the other hand, systematic reviewers wish to identify all evidence relating to a topic, to allow analysis and facilitate dissemination. Failing to identify some specific articles is unlikely to greatly hinder individual clinicians, but failing to identify those same articles for a systematic review might have important implications for the results and conclusions; including the introduction of bias and a loss of statistical power. Eventually, this will impact individual clinicians when they rely on the aforementioned systematic reviews to guide clinical practice.

Articles can be identified by hand, electronic full-text and database searches. Handsearching will identify relevant articles, but not in a timely manner.[2] Electronic full-text searches are becoming increasingly available. Research has shown that full-text searching is more likely to identify relevant articles when compared with searching abstracts only,[3] but challenges in modifying current algorithms or developing new data retrieval systems still remain.[4] Multiple bibliographic databases such as MEDLINE, Embase and the Cochrane Library index dental journals and facilitate electronic searching by word or subject heading. This latter search method remains the most common way to identify evidence.

A simple search of the indexed bibliographic databases generally accesses words contained in an article's title and abstract only.[3] Index terms, or subject headings are assigned to an article based on its full text, and are potentially a more powerful search tool than a simple word search string. The use of index terms underpins the indexing of databases such as MEDLINE (MeSH, Medical Subject Headings), Embase (Emtree) and some parts of the Cochrane Library (MeSH).

Early researchers using Medlars (a precursor to today's MEDLINE) encountered problems identifying relevant dental articles. They found MeSH were restrictive, and were tailored towards medicine[5]. The MeSH library has since increased, but, my hypothesis was that differences in interpretation of dental vocabulary would continue to impact search yields. Specifically, if the understanding of 'survival' differs between MeSH indexers and those searching, relevant studies will remain elusive, and undermine the provision of evidence based dental care.

Assessing the accuracy and consistency of MeSH assignment is challenging. The list of main heading MeSH increased from approximately 20 000 in 2000[6] to over 27 000 in 2014.[7] These main headings can be further qualified by 83 individual subheadings,[8, 9] and more than 200 000 supplementary concepts.[7] MeSH are manually allocated to articles, and therefore indexing variation is expected and disparity is not necessarily considered inaccurate. However, omission or misallocation of important terms clearly undermines search performance. Studies evaluating their use found lower consistency associated with subheadings, methodology categories (E: analytic, diagnostic, therapeutic techniques) and, those categories whose definitions were less stable (F: psychiatry; N: health care).[10-12] Further errors with the assignment of methodology MeSH, specifically those for controlled trials were highlighted in the early years of The Cochrane Collaboration.[13]

3.2 OBJECTIVE

This research aimed to assess the allocation of MeSH within MEDLINE to articles in the dental literature that employed time-to-event analyses to report outcomes of dental treatment in patients.

3.3 METHODS

As discussed in Chapter 2, the 50 dental journals with the highest impact factors in 2008 were handsearched for that year, identifying articles reporting dental treatment outcomes over time in human subjects with time-to-event statistics (included 'case' articles, n=95), without time-to-event statistics (active controls, n=91), and all other articles (passive controls, n=6769).

The MEDLINE bibliographic electronic record of all articles in the included 'case' and active control groups were read, and Medical Subject Headings (MeSH) allocated by indexers were reviewed. To be clear, an electronic MeSH search was not used to identify articles that had used a specified list of MeSH. Rather, the articles themselves were identified by the systematic handsearch described in Chapter 2, and then MeSH that had been allocated to the electronic record by indexers were collated.

Those MeSH that related to (1) time-to-event statistical techniques, (2) prosthesis outcomes, or the (3) conduct of research over time were identified and extracted manually by one reviewer from the included 'case' and active control articles. Relevant MeSH were extracted as they were identified, and added to a growing list. In total, 17 relevant MeSH were identified, and these had not been determined in advance. Two additional MeSH 'Acturial analysis' and 'Survival' may have been applicable to this set of articles, and their definitions have been included with the identified 17 terms (table 3.1). However, these terms had not been allocated to the articles.

The MeSH were classified into three groups: statistic, outcome and time-related (table 3.2).

Once the MeSH were identified, the 6769 passive controls were checked electronically for their use of these terms.

3.3.1 Statistical analysis

The allocation of MeSH was reported as a frequency and percentage per article. Differences in the allocation of MeSH between two groups, the included ‘case’ articles and active controls, were analyzed with Pearson’s chi-square and Fischer’s exact test (where expected cell counts were less than 5). Differences between all three groups (i.e. including the passive controls) were analyzed with Pearson’s chi-square statistic. Where expected cell counts were less than 5, data from the three groups was used to construct a two group, 2 by 2 contingency table, and Fischer’s exact test was employed. Significance was set at $P<0.05$.

Table 3.1. MeSH definitions from MEDLINE (OVID)

MeSH	Definition
Actuarial analysis *Year introduced: 1979*	The application of probability and statistical methods to calculate the risk of occurrence of any event, such as onset of illness, recurrent disease, hospitalization, disability, or death. It may include calculation of the anticipated money costs of such events and of the premiums necessary to provide for payment of such costs.
Dental prosthesis repair *Year introduced 1993*	The process of reuniting or replacing a broken or worn dental prosthesis or its part.
Dental restoration failure *Year introduced: 1995*	Inability or inadequacy of a dental restoration or prosthesis to perform as expected.
Fatal outcome *Year introduced 1994*	Death resulting from the presence of a disease in an individual, as shown by a single case report or a limited number of patients. This should be differentiated from DEATH, the physiological cessation of life and from MORTALITY, an epidemiological or statistical concept.
Follow up studies *Year introduced 1967*	Studies in which individuals or populations are followed to assess the outcome of exposures, procedures, or effects of a characteristic, e.g., occurrence of disease. A subgroup under Longitudinal studies.
Graft survival *Year introduced: 1999*	The survival of a graft in a host, the factors responsible for the survival and the changes occurring within the graft during growth in the host.
Kaplan-Meiers estimate *Year introduced: 2007* ***Kaplan-Meier estimate*** *Amended spelling: 2011*	A nonparametric method of compiling LIFE TABLES or survival tables. It combines calculated probabilities of survival and estimates to allow for observations occurring beyond a measurement threshold, which are assumed to occur randomly. Time intervals are defined as ending each time an event occurs and are therefore unequal. (From Last, A Dictionary of Epidemiology, 1995)
Life tables *Year introduced: 1990*	Summarizing techniques used to describe the pattern of mortality and survival in populations. These methods can be applied to the study not only of death, but also of any defined endpoint such as the onset of disease or the occurrence of disease complications.
Longitudinal studies *Year introduced 1979*	Studies in which variables relating to an individual or group of individuals are assessed over a period of time.
Proportional hazards model *Year introduced: 1989*	Statistical models used in survival analysis that assert that the effect of the study factors on the hazard rate in the study population is multiplicative and does not change over time.
Prospective studies *Year introduced 1967*	Observation of a population for a sufficient number of persons over a sufficient number of years to generate incidence or mortality rates subsequent to the selection of the study group. A subgroup under Longitudinal studies.
Prosthesis failure *Year introduced: 1999*	Malfunction of implantation shunts, valves, etc., and prosthesis loosening, migration, and breaking.
Retreatment *Year introduced 1997*	The therapy of the same disease in a patient, with the same agent or procedure repeated after initial treatment, or with an additional or alternate measure or follow-up. It does not include therapy which requires more than one administration of a therapeutic agent or regimen. Retreatment is often used with reference to a different modality when the original one was inadequate, harmful, or unsuccessful.
Retrospective studies *Year introduced 1967*	Studies used to test etiologic hypotheses in which inferences about an exposure to putative causal factors are derived from data relating to characteristics of persons under study or to events or experiences in their past. The essential feature is that some of the persons under study have the disease or outcome of interest and their characteristics are compared with those of unaffected persons.
Survival *Year introduced: not stated*	Continuance of life or existence especially under adverse conditions; includes methods and philosophy of survival.
Survival analysis *Year introduced: 1990*	A class of statistical procedures for estimating the survival function (function of time, starting with a population 100% well at a given time and providing the percentage of the population still well at later times). The survival analysis is then used for making inferences about the effects of treatments, prognostic factors, exposures, and other covariates on the function.
Survival rate *Year introduced: 1990*	The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the beginning of a time interval who survive to the end of the interval. It is often studied using life table methods.
Time factors *Year introduced: 1999*	Elements of limited time intervals, contributing to particular results or situations.
Treatment outcome *Year introduced: 1999*	Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series

Table 3.2. Classification of MeSH

Group	Description	
1	MeSH for a statistical time-to-event technique *(MeSH: Statistical)*	Kaplan-Meier estimate Life tables Proportional hazards model Survival analysis Survival rate
2	MeSH which indicated that an outcome was studied *(MeSH: Outcome)*	Dental prosthesis repair Dental restoration failure Fatal outcome Graft survival Prosthesis failure Retreatment Treatment outcome
3	MeSH which indicated that a study occurred over time *(MeSH: Time)*	Follow up studies Longitudinal studies Prospective studies Retrospective studies Time factors

3.4 RESULTS

3.4.1 Distribution of MeSH

A total of 530 different MeSH were allocated to the 95 included 'case' articles. Articles had been allocated between 11 and 32 terms, with a mean of 20. In total, 2031 MeSH were allocated to these 95 articles, with 345 (17%) of these MeSH collated for this research. The additional MeSH related to other aspects of the study design including the type of subjects, such as human, adult, adolescent, female, male; their age group, such as age factors, middle aged, aged 80 and over; and type of treatment studied such as tooth socket, osseointegration, reconstructive surgical procedures and surface properties.

There were 611 different MeSH allocated to the 91 active controls. Articles had been allocated between 7 and 31 each, with a mean of 20. In total, 1861 MeSH were allocated to these 91 articles, with 214 (12%) collated for this research.

The MeSH allocated to the 6769 passive controls were also reviewed, but as there were a large number, the overall distribution of MeSH amongst those articles were not sought.

3.4.2 Comparisons between groups (Table 3.3, Figure 3.1)

Within both the included 'case' articles and active controls, the most frequently allocated MeSH were 'Dental restoration failure' (77% and 52% of articles, respectively) and 'Treatment outcome' (54%, 48%). There was no significant difference between the allocation of Outcome MeSH between these groups (86%, 77%, Chi-square 2.75, P=0.10).

In relation to the MeSH identified by this study, 'Treatment outcome' was the second most frequently used MeSH (7% of articles) within the passive controls, whilst 'Dental restoration failure' was 6th (2.5% of articles). The allocation of Outcome MeSH between the three groups was different, with significantly fewer passive controls being allocated one of these terms. (86%, 77%, 10%, Chi-square 850, P<0.001).

Significantly more included 'case' articles were allocated at least one Statistical MeSH compared to the active controls (67% versus 15%, Chi-square 51.58, P<0.001). Specifically, the Statistical MeSH 'Kaplan-Meier estimate' and 'Life tables' were not allocated to any active controls, but were assigned to 21% and 16% of the included 'case' articles, respectively. Sixty-nine included 'case' articles specifically stated they used either Kaplan-Meier or life table analyses, but only 42% of those (n=29) were indexed as such.

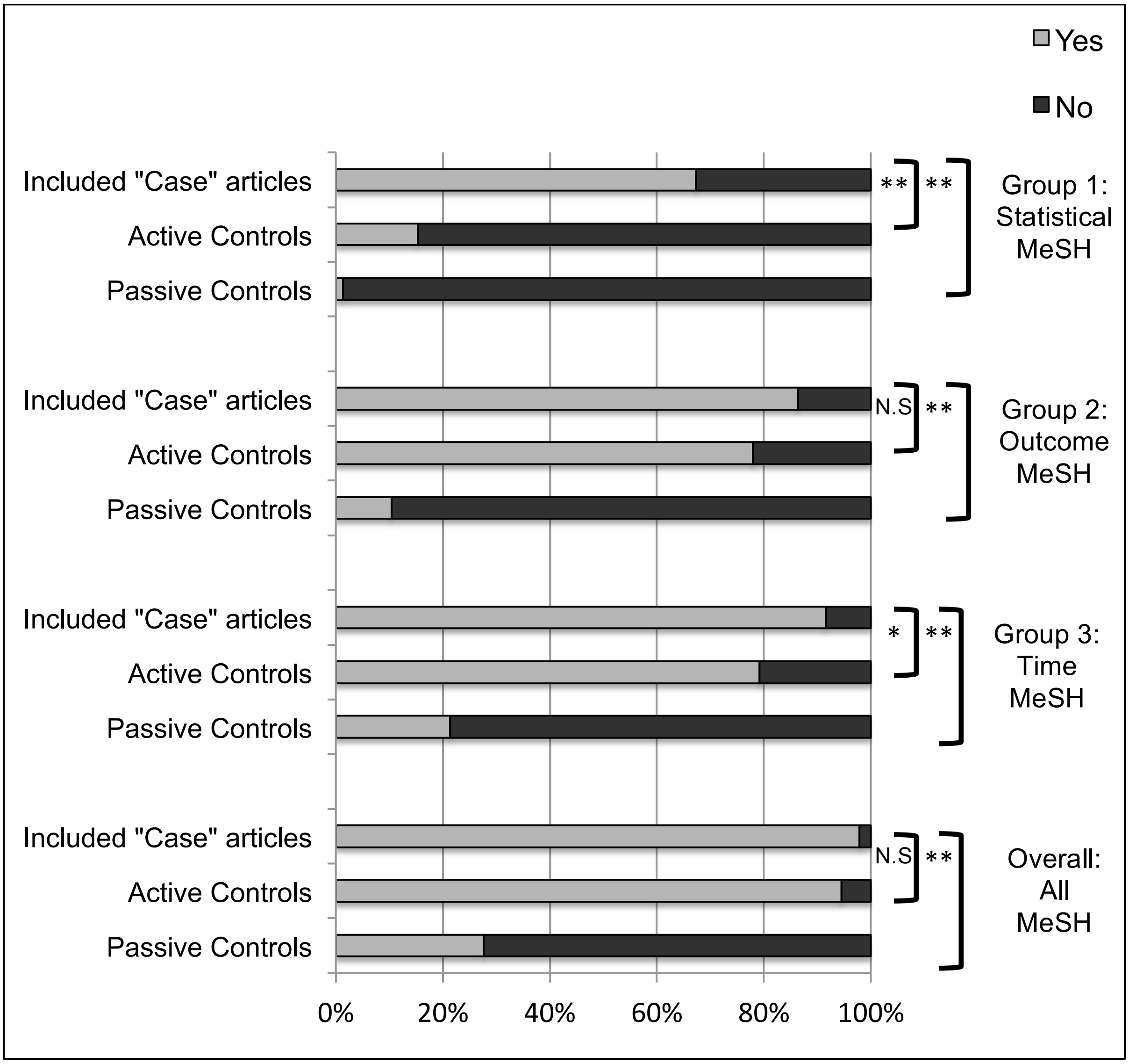
Within the passive controls, 101 Statistical MeSH were allocated to 89 of the 6769 articles. These included 42 patient survival, 5 non-patient or prosthesis time-to-events, 2 mortality analyses and 14 review articles. The other 26 articles reported percentage outcomes but did not employ time-to-event analyses.

Table 3.3. Distribution of MeSH across the included 'case', active control and passive control articles

Description	Included 'case' (n=95)	Active controls (n=91)	Passive controls (n=6769)
Group 1: Statistical			
Kaplan-Meier estimate	20	0	25
Life tables	15	0	1
Proportional hazards model	6	1	13
Survival analysis	30	12	42
Survival rate	1	1	20
Total frequency#	72	14	101
*Total articles**	*67.37%, n=64*	*15.39%, n=14*	*1.32%, n=89*
Included 'case' vs Active controls: Chi-square 51.58, P<0.001+			
*Comparison between all groups, Chi-square 1262, P<0.001^*			
Group 2: Outcome			
Dental prosthesis repair	2	0	12
Dental restoration failure	73	47	169
Fatal outcome	0	1	28
Graft survival	2	3	18
Prosthesis failure	3	1	6
Retreatment	4	0	46
Treatment outcome	51	44	479
Total frequency#	135	96	758
*Total articles**	*86.32%, n=82*	*76.92%, n=70*	*10.37%, n=702*
Included 'case' vs Active controls: Chi-square 2.75, P=0.10+			
Comparison between all groups, Chi-square 850, P<0.001			
Group 3: Time			
Follow up studies	49	29	446
Longitudinal studies	13	4	142
Prospective studies	23	25	209
Retrospective studies	37	23	282
Time factors	16	23	619
Total frequency#	138	104	1697
*Total articles**	*91.58%, n=87*	*79.12%, n=72*	*21.39%, n=1448*
Included 'case' vs Active controls: Chi-square 5.82, P=0.02+			
Comparison between all groups, Chi-square 414, P<0.001			
Total			
MeSH, as listed above	NA	NA	NA
Total frequency#	345	214	2556
*Total articles**	*97.89%, n=93*	*94.51%, n=86*	*27.66%, n=1872*
Included 'case' vs Active controls: Chi-square 1.48, P=0.23+			
Comparison between all groups, Chi-square 404, P<0.001			

 # Total frequency of term use. Some articles were allocated more than one term within each group.
** Total number of articles which were allocated at least one term within a given group.*
+ Pearson's Chi square test, 2 x 3 contingency table
^ Fischer's exact test, 2 x 2 contingency table

Figure 3.1. Distribution of MeSH across the included 'case', active control and passive control articles



When analyzing Statistical MeSH, cell counts were found to be less than five. Therefore, to explore MeSH allocation mathematically, data from the included ‘case’ articles and active controls were combined, allowing the Fisher exact test to be used. The allocation of Statistical MeSH between the groups were different, with significantly fewer articles from the passive controls being allocated one of these terms. (42%, 1%, Fischer’s exact test, Chi-square 850, P<0.001).

Significantly more included ‘case’ articles compared with active controls were allocated at least one Time-Related MeSH (92%, 79%, Chi-square 5.82, P=0.02). Although these terms indicate that research occurred over time, they do not specifically indicate that time-to-event analyses were used.

Of the total of 17 MeSH relating to time-to-event analyses identified during this research, those relating to time were the most frequently allocated for the passive controls. These were assigned to 22% (n=1448), with ‘time factors’ the most frequently allocated term (10%). Despite their increased use, they still remained infrequent in comparison with the included ‘case’ and active controls (92%, 79%, 22%, Chi-square 414, P<0.001).

Overall, at least one of the 17 MeSH relating to time-to-event analyses were assigned to 93 included ‘case’ articles (98%, frequency 345), 86 active controls (95%, frequency 214) and 1872 passive controls (28%, frequency 2556). There was no significant difference in the allocation of the 17 terms between the ‘cases’ and the active controls (Chi-square 1.48, P=0.23). Overall, significantly fewer passive controls were allocated one of these terms, in comparison with other groups (98%, 95%, 28%, Chi-square 404, P<0.001).

3.5 DISCUSSION

This research has identified a key challenge that impacts identification of published articles reporting 'survival' and 'time-to-event' outcomes of dental prostheses. It was observed that the allocation of MeSH in MEDLINE was inaccurate and inconsistent for the methodology of many of the articles.

These findings are based on an assessment of MeSH allocated to articles published in 2008 in the 50 dental journals with the highest impact factors for that year. None of these journals were published in languages other than English. The search for the different types of article was completed in a systematic manner by hand. For analysis, all 6955 articles published in the cohort were allocated to one of three groups: 95 included 'case' articles, 91 active controls and 6769 passive controls.

The articles in these journals are the "subjects" of this research, and inclusion related to the ISI impact factor has pre-selected articles and edited journals which could be considered at the "higher" end of the quality spectrum.[14, 15] The journals that were included in this research were in the top 50 for 2008, as defined by the ISI impact factor for that year. Impact factor for a journal, for a given year is calculated by dividing the number of citations of all articles from that journal over a two year period, by the number of items that could be cited.[16] This selection of journals on the basis of the high citation rate for their articles suggest that the sample of articles used for this research may be a biased subset of the dental literature in that they are, in general, likely to be easier to find and judged more important (and therefore more likely to be cited) than articles in other dental journals. With this in mind, although misallocation of MeSH may be related the indexer, errors might be compounded by poor reporting quality. As it is likely that articles included in this research are of higher than average quality, the error rate found in this research is therefore likely to underestimate the size of the problem of poor indexing.

The complexity of the English language confounds word standardization. Fields such as medicine and law have adopted words from Latin and Ancient Greek, 'dead' languages, in attempts to keep use of terms and their meanings stable and understandable across the professions.[17] For example, terms in medicine such as hypertension (excessive-pressure), macroglossus (large-tongue) and pericoronitis (surrounding-heart-inflammation) are understood across cultures and languages, with the definitions of the words actually incorporated into their very syllables. However, such stable words are not available for time-to-event outcomes and the associated statistics.

To help clarify definitions across the medical fields, a controlled vocabulary, the Medical Subject Heading system was introduced in 1960, and these terms are manually assigned to articles for inclusion in MEDLINE by indexers who read the full article.[18] These terms provide a standardized vocabulary for searchers to use, increasing their ability to identify and cross reference relevant articles. Their usefulness, however, is directly related to the accuracy of the indexing.

Errors in indexing have been identified in the past, with a particular high profile error being the misallocation of MeSH to controlled trials, which influenced an extensive programme of handsearching for such articles by The Cochrane Collaboration and their re-indexing in MEDLINE.[13] Also, differences in linguistic vocabulary have been shown to effect the identification of relevant articles in the dental field.[5]

For the study presented in this chapter, relevant MeSH were identified as the electronic records of individual ‘case’ and active control articles were reviewed. The list was a living list, and it grew as new terms were identified and considered to be relevant. Terms were classified into three groups: Statistical, Outcome and Time.

Errors in the allocation of these MeSH to the included ‘case’ articles occurred across all three MeSH groups. For searchers to identify articles by index term, they need to be able to predict which indexing terms have been allocated to which articles. Articles cannot be found if there is an error in indexing, or if there is a difference between the expectations of searchers and indexers.

The MeSH most frequently allocated to the included ‘case’ articles related to treatment outcomes: ‘Dental restoration failure’. Use of this term in particular was a surprising finding. It was the most common MeSH allocated to time-to-event articles, and also the most common MeSH describing outcomes. This indicates that there is a great mis-match between the terms indexers and MEDLINE feel are the most appropriate to allocate, and the terms which readers are expecting to be allocated.

Similarly, high proportions of both the included ‘case’ and active controls had been allocated at least one treatment outcome MeSH (86%, 77%), but these terms were much less common in the passive controls (10%). It is not surprising that these terms were common for both the included ‘case’ and active controls, because these indicated that the article investigated a treatment outcome and this is the reason they were selected for this study. However, as both article groups studied an outcome, such MeSH should have been allocated to each record in both groups. This equates to an error rate for those records of approximately 15% to 25%.

Of the 17 MeSH relating to time to event analyses, those relating to time were the most frequently allocated of these terms in all three article cohorts. More than 90% of the included 'case' articles were allocated at least one of those terms, with this high frequency reflecting the content of each article. Fewer time-related MeSH were allocated to the active controls, but the frequency of nearly 80% also remains high. Despite these high frequencies, it is concerning that all the included 'case' articles and active controls were not allocated at least one MeSH relating to research over time.

In comparison, significantly fewer of the passive controls were allocated a time-related MeSH, with an indexing frequency of 22%. These terms were used to index articles in the passive controls for a great variety of reasons, unrelated to time-to-event statistical methods. For example, "Time Factors" indexed a laboratory article reviewing the effects of resinous monomer on the cohesive strength of composite resin;[19] "Prospective Studies" indexed the sequelae of events occurring following perforations of the schneiderian membrane during sinus floor elevation;[20] "Longitudinal Studies" indexed the patterns of caries experienced by study participants;[21] "Retrospective Studies" indexed a study reviewing the medical claims history assessing relationships between use of bisphosphonates and osteonecrosis of the jaw;[22] and "Follow-Up Studies" indexed a study exploring the aetiology of denture stomatitis.[23]

Although the indexing frequency is low, inclusion of these terms in a search strategy would result in an additional 1448 false positive yield from this overall article cohort, increasing the burden of identification for searchers.

The misallocation of MeSH was greatest for statistical themes. Firstly, misallocations related to complete omission of relevant MeSH. In total, 67% of included 'case' articles were allocated at least one statistical related MeSH. Therefore, indexers incorrectly omitted vital statistical terms when assigning MeSH to 31 articles, a third of the included 'case' cohort.

Secondly, misallocations related to inaccurate use of updated terms. MeSH are updated yearly, with an additional survival function term, 'Kaplan-Meier estimate' entered in 2007. It is known that at least 42 of the 95 included 'case' articles used the specific Kaplan-Meier survival method, but less than half (16 articles) were assigned the term 'Kaplan-Meier estimate'. Previous survival function terms of 'Survival analysis', 'Survival rate' and 'Life tables' had been introduced in 1990. Of those 26 articles that were not allocated the updated term, 18 were allocated an alternative, but nearly one fifth (8 articles), were not allocated any survival MeSH at all.

Thirdly, misallocation related to the incorrect use of such MeSH for the indexing of articles that had not performed survival analyses. Amongst the active controls, 14% were incorrectly allocated the terms 'Survival analysis' or 'Survival rate'. These false positives represent a moderate percentage, which would lead to a relatively small inaccurate yield. I consider that this increase in yield would not be an excessive burden for researchers identifying them during an electronic search.

Within the passive controls, allocation of these MeSH were uncommon, being allocated to 89 articles (1.3%). These MeSH were correctly allocated to 42 patient survival (cancer) studies, 5 non-patient or prosthesis related time-to-event articles, 2 reporting hazard or mortality rates, and 14 review articles. They were incorrectly allocated to an additional 26 articles, which reported percentage outcomes across laboratory and clinical settings or discussed percentage outcomes in a letter or item of news. These articles did not employ time-to-event analyses, and such MeSH should not have been assigned.

It is known that at least an additional 20 time-to-event articles were present within the passive control group.[24-43] These articles reported cancer and patient-related survivals, and therefore were not eligible for inclusion in the 'case' articles for this research. These articles should have been allocated at least one of the survival MeSH, but this did not occur. Therefore, survival MeSH were also incorrectly omitted from the passive control articles.

Overall, significantly fewer passive controls were allocated at least one statistical MeSH, whilst they were equally frequent amongst the included 'case' and active controls.

Inclusion of all these terms in a search strategy would identify nearly 2000 false positives from the article cohort of 6955, but would correctly identify nearly 98% of articles reporting time-to-event analyses for prostheses outcome.

Error in allocation of MeSH amongst the articles has occurred, and contributes to an error rate in identification of relevant articles. It is estimated that the MEDLINE indexing load will increase substantially to over one million articles per year by 2015 - a 45% increase from 2007.[11] Therefore, errors may become even more prominent. Automatic indexing strategies including Inductive Logic Programming[10] and Latent Semantic Indexing systems[11] are being trialed, and may reduce error in indexing accuracy and consistency.

It was interesting to note that since initial collation of these data, the spelling of 'Kaplan-Meier estimate' has been amended in MEDLINE. This term was introduced in 2007, and by 2011 its spelling had changed from 'Kaplan-Meiers estimate' to 'Kaplan-Meier estimate', and the indexed records were updated. MEDLINE indexers map MeSH to articles by selecting the term from a pre-determined list, and therefore spelling errors should not occur. Hence, the change in spelling would have occurred centrally, and was not an aberrant finding or misspelled term.

Overall, indexing errors are clearly multifactorial. They may relate to the misunderstanding of reporting by indexers, poor reporting quality by authors, abbreviation in reporting due to editorial constraints or, simply, human error. It is not yet clear whether one particular factor may have a greater influence on such indexing errors than others. No indexing process would ever be perfect, but the research reported in this chapter shows that accuracy in the indexing of time-to-event, survival-related MeSH to dental articles varies.

3.6 IMPLICATIONS

The allocation of MeSH within MEDLINE to articles in the dental literature that used time-to-event analyses to report the outcome of dental treatment in patients was inaccurate and inconsistent. Specifically, statistically related MeSH were incorrectly omitted from 30% of the included ‘case’ articles and incorrectly allocated to 15% of the active controls. Such errors reduce the accuracy of search strategies and impact the identification of relevant dental outcome articles.

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CHAPTER 4. IDENTIFICATION OF THE WORDS AND PHRASES THAT AUTHORS HAVE USED TO DESCRIBE TIME-TO-EVENT DENTAL DATA

CONTENTS

4.0 SUMMARY

Objective: The objective of this part of my programme of research was to identify the words and phrases that authors used to describe time-to-event outcomes of dental treatments in patients.

Methods: The 95 included 'case' and 91 active control articles were read and this identified 43 English words that the authors had used in their title, aim and abstract, indicating that dental outcomes were studied over time. Once identified, these words were sought within the same sections in the 6796 passive controls. The 43 words were divided into six groups. Group 1 related to time-to-event statistics, groups 2 to 4 indicated that an outcome was studied over time, group 5 indicated that an outcome was studied, and group 6 related to time. Differences in use of words among the three types of article were analysed for groups 1 to 4 and between the 'cases' and active controls for groups 5 and 6, across all three locations (title, aim and abstract). Chi-square and Fischer's exact statistics were used.

Results: In the abstracts, included 'case' articles used group 1 (statistical technique) and group 2 (statistical terms) more frequently than the active and passive controls (group 1: 35%, 2%, 0.37%, P<0.001 and group 2: 31%, 1%, 0.06%, P<0.001). The included 'case' and active controls used group 3 (quasi-statistical terms) equally, but significantly more often than the passive controls (82%, 78%, 3.21%, P<0.001). In the aims, use of target words in groups 1, 2, 3, 4, 5 and 6 was similar for 'cases' and active controls (P values 0.10 to 0.59), but less frequent for groups 1, 2, 3 and 4 in the passive controls (P values <0.001). In the titles of the 'cases' and active controls, group 2 terms were not used, groups 1, 3, 4 and 5 were used with a similar

frequency (P values 0.15 to 0.96), and group 6 were used in significantly greater number of included ‘case’ articles (54%, 30%, P=0.001). When compared with the titles of passive controls, use of group 2 and 3 terms was significantly less frequent (P values <0.001). Across the abstracts, aims and titles of the passive controls, terms in groups 5 and 6 were not assessed.

Implications: All included ‘case’ articles used time-to-event analyses, but two-thirds did not include words to highlight this in the abstract. Also, use of specific survival-related words was not unique to the included survival articles, but use beyond these included ‘case’ articles was rare. Such use was not necessarily incorrect, and was nearly always associated with cancer survival. Additionally, there was great variation in the words used by authors to describe dental time-to-event outcomes. Such variation in reporting adversely impacts the ability of text “keyword” searches to identify relevant articles. This will make it difficult for those searching to identify the research they seek.

4.1 BACKGROUND

The ability to identify relevant articles in the dental literature is related to both the accuracy of database indexing and the words that the original authors used to describe their research. If articles cannot be found, they cannot be reviewed or used in decision making.

Systematic reviews use a combination of free text and index terms as part of their search methods to identify articles of interest in bibliographic databases.[1] Although other search techniques including handsearching,[2] assessment of reference lists[3], contact with experts and review of conference proceedings are also used, research from 2003 found that authors of systematic reviews of therapeutic interventions found most of the high quality articles by searching one of four bibliographic databases.[4]

Research by Hopewell and colleagues in 2007 analyzed how randomized trials may be identified with search algorithms, and found the retrieval rate was directly related to the complexity of the search string. [2] The research was completed as a Cochrane methodology review, and was based on 34 studies that compared article yields of different types of search strategies, finding that the Cochrane Highly Sensitive Search Strategy identified 80% of articles, while “simple” search strategies only identified 42%.

Identifying articles is central to improving our knowledge, answering clinical questions and designing new studies.

Survival analytical methods allow assessment of outcomes over time, and are applicable to a large variety of research topics in dentistry. Examples relating to dental care that have been investigated in the articles identified in Chapter 2 include the fracture of a crown, the loss of integration of an implant, the debonding of orthodontic brackets, the decay of a restorative margin, the healing of endodontic lesions or the time taken until anaesthesia is established.

Such outcomes can be reported qualitatively or quantitatively. When reported quantitatively, they are generally expressed as a ratio, describing the relationship between two categories. However, there are many types of ratios including proportions, rates or estimated cumulative proportions. These also differ by whether the numerator is included in the denominator, and whether they are measured over a period of time. For example, dental researchers may report the number of failures out of the total number of prostheses (a proportion, the risk), where the number of failures is included in the total number of prostheses. Secondly, they may report the number of failures versus the number of survivors (a ratio, the odds), where the number of failures is not included in the number of survivors. Thirdly, they may report the number of failures per prosthesis per year (a rate), where the number of failures is included in the number of prostheses for that given time. Fourthly, they may report the number of failures out of the number of prostheses over a combination of several time intervals (an estimated cumulative proportion), where the number of failures is included in the number of prostheses for each interval, but not the entire study period. This last method is a time-to-event analysis and is often termed a Kaplan-Meier, survival, actuarial or lifetime analysis.

Clearly, the difference between the ratios can be confusing, and the words used by authors to describe such results in the healthcare literature may also be inaccurate and inconsistent, compounding difficulties in the retrieval of articles.

Time-to-event analyses have three concepts in common. An event is monitored, over time, and a combined estimated cumulative proportion is calculated. For example, a group of people who have received an implant may be monitored over a period of years, and the occurrence and timing of an event such as implant failure is noted. The lifespan of the implant prior to failure, the lifespan of other implants within the group that are known not to have failed, and the lifespan of implants prior to becoming lost to follow up are analysed, and the estimated cumulative survival is calculated.

Time-to-event analyses can appear similar to a proportion, and care should be taken by researchers to ensure that they clearly report their statistical method, and care should be taken by readers to seek out these descriptors in the articles. Therefore, when writing the abstracts and manuscripts for those studies, authors should report the event, the time and the statistical method.

The abstracts play a critical role: they aid identification, help searchers decide whether the article may be relevant, and can also be the only source of information for those who do not or cannot find the complete article.

An additional CONSORT document providing guidance on reporting of randomized trials in abstracts for journals and conferences was published in 2008,[5] and these recommendations were incorporated into the updated CONSORT explanatory document in 2010.[6] Review of the literature had revealed abstracts often lacked transparency, were an unsuitable screening tool for readers to decide whether to proceed with reading or reviewing the article, and lacked details such that the abstract could not serve as an accurate record of the trial.

I am unaware of reporting guidelines for articles that present time-to-event outcomes, but many of these outcomes are reported within randomized trials and observational studies. Recommendations for title and abstract writing have been incorporated into guidelines for both types of study.[5-8] However, as both these research designs can incorporate a variety of statistical analyses, it is not surprising that the statistical guidance provided is of a non-specific nature, and care is required when using the recommendations across the field at large.

Although there do not appear to be any studies devoted to the quality of the titles and abstracts of time-to-event articles, some research has been undertaken regarding the full text of these articles, and this is outlined briefly below. Further details regarding the findings from these researchers[9-11] are presented in Chapter 5.

Needleman and colleagues[9] explored the outcome measures used to evaluate implants in a systematic review, finding approximately 60% of the 196 articles used time-to-event outcomes. They judged the reporting quality to be low, and this related to both the descriptions and execution of the technique. Problems with reporting quality of survival articles have also been identified in the medical literature, but much research has focused on the presentation of graphic aids rather than the description of research. Although identified and discussed as a problem that needed addressing by Pocock and colleagues in 2002,[10] a further survey by Vervolgyi in 2011[11] showed that the quality of reporting remained low.

While these specific findings do not shed light directly on the quality of abstracts, the problems with the quality of the articles themselves could be considered a surrogate marker for problems with the quality of the abstracts and titles as well.

In this research, I hypothesize that the words that authors use to describe their time-to-event analyses differ. Such differences complicate the use of text words to search databases, and may impact on the allocation of index terms (such as MeSH) by database indexers. This affects our ability to identify relevant articles electronically. My earlier research, as presented in Chapter 3, explored the allocation of MeSH to survival analyses in the dental literature.[12] Omission of survival-related statistical MeSH was found to affect 30% of a test group of articles that had used such analyses, and incorrect assignment was found for 15% of the control group of articles where such analyses had not been used. The research for that earlier chapter addressed the challenge faced by readers wishing to identify dental survival analyses, who need to know the indexing terms allocated to those articles by indexers. Furthermore, readers need to know the words that authors used to describe their research, thus enabling them to identify the articles by a textword search of the titles and abstracts in a database such as MEDLINE. This chapter moves my research into the domain for the second of these challenges.

4.2 OBJECTIVES

The research reported here aimed to identify the words that authors used to describe time-to-event outcomes of dental treatments in the titles and abstracts of their journal articles.

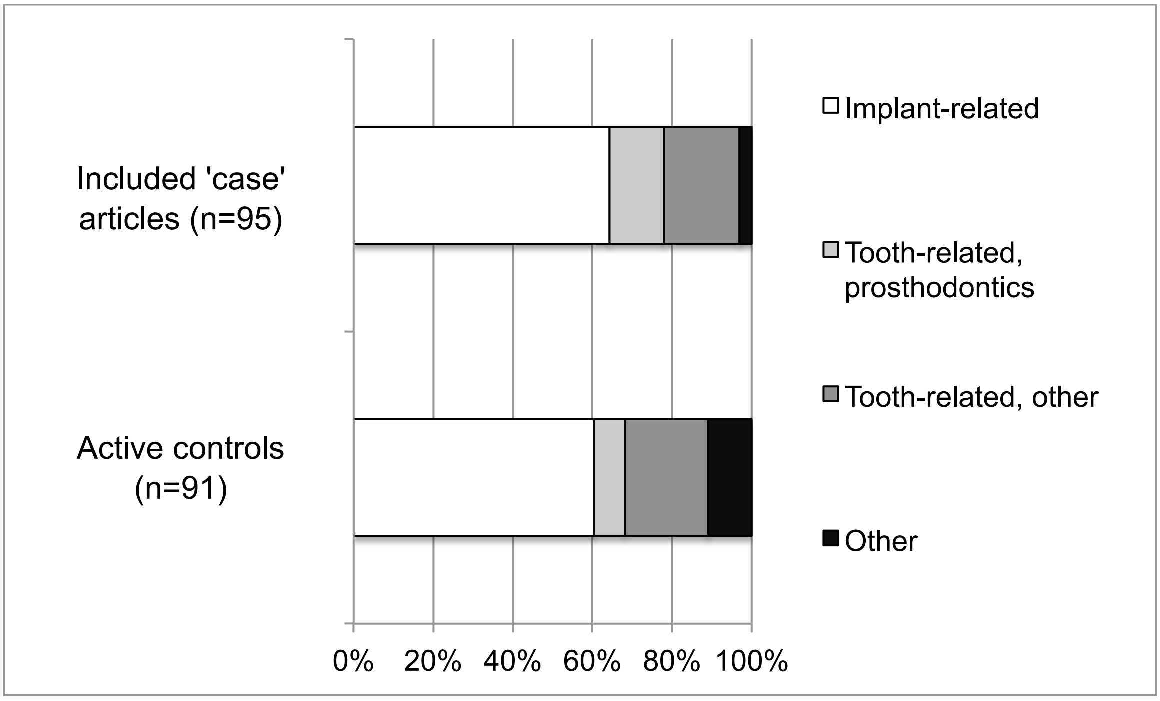
4.3 METHODS

4.3.1 Time-to-event dental articles

As reported in Chapter 2, the 50 dental journals with the highest impact factors for 2008 were handsearched for that year to identify articles that reported a time-to-event analysis. Prospective and retrospective studies that employed time-to-event statistics for reporting outcomes of dental treatment over time in humans subjects were identified for inclusion as 'case' articles (n=95). Those reporting such outcomes, but without using time-to-event statistics were retained as active controls (n=91) and all others were retained as passive controls (n=6769). The active controls and the passive controls are used in this research to allow controlled assessment of the included 'case' studies. The search was systematic, with a Kappa of 0.92 for one researcher screening records twice over a 6 month period to identify possible articles for inclusion, and 0.86 for two people who assessed the eligibility of those articles for inclusion.[12]

The research reported by articles in the included 'case' group and active controls ranged across a variety of dental treatments. The most common dental treatment studied in both the included 'case' and active controls related to implant outcomes (64%, 60%). In total, approximately 80% of the included 'case' articles (n=74) and 70% of the active controls (n=62) reported outcomes of either implant-related treatment or tooth-supported prostheses. The distribution of the themes of the articles is outlined in figure 4.1. The themes of the passive control group were not reviewed.

Figure 4.1. Type of research studied by the included 'case' articles (n=95) and active controls (n=91).



Implant-related articles included:

- Implant fixtures, Temporary anchorage devices, Implant prostheses

Tooth-related, prosthodontics articles included:

- Fixed dental prostheses, Crowns, Posts, Resin bonded bridges

Tooth-related, other articles included:

- Restorations, Tooth survival, Caries, Papilla presence, Periodontal indicies, Endodontics

Other articles included:

- Orthodontics, TMJ fracture healing, Orofacial grafts, Odontogenic infection resolution

4.3.2 Identification of target words

The 95 included articles (‘cases’) and the 91 active control articles were read to identify and extract English words used in the title, the aim of the abstract and abstract (excluding the aim) that the authors had used to indicate that their research studied a dental outcome over a period of time. These words were searched for and identified manually by one person. The list was compiled as the search continued, rather than being determined prior to reading the articles. Four included ‘case’ articles and one active control did not report an aim in the abstract. These aims were not sought from the body of the document, and therefore no words were tallied for the aims for these five articles.

A list of 43 words or similar phrases were identified, and classified into six groups (table 4.1) as outlined below.

Group 1: Statistical Technique. Use of words that described a specific statistical time-to-event technique

Group 2: Statistical term: outcome with time. Use of a statistical term which indicated that an outcome was studied over time

Group 3: Quasi-statistical: outcome with time. Use of a quasi-statistical term which indicated that an outcome was studied over time

Group 4: General term: outcome with time. Use of a general term which indicated that an outcome was studied over time

Group 5: General term: outcome. Use of a general term which indicated that an outcome was studied

Group 6: Time. Phrases or words which specifically stated the study duration

In summary, group 1 related to a specific statistical time-to-event technique, groups 2, 3, and 4 included words which indicated that an outcome was studied over time, group 5 included words which indicated that an outcome was studied, and group 6 indicated that the study occurred over a specific time period.

The frequency of use of the target words was recorded, along with the frequency of use of at least one word or phrase from each of the six groups. This distinction was made, because some articles used two or more terms from one of the six groups.

Once the target words were identified, the titles, aims and abstracts (excluding the aims) of the passive controls were searched electronically to see whether these words had also been used within the passive controls (n=6769). The total frequency of use of the target words for all six groups was initially recorded, and the number of articles that used at least one term then tallied for groups 1, 2, 3 and 4. The frequency of the words within groups 5 and 6 was found to be high: 12,842 and 3425 counts respectively, with words from each group used more than once in the same article. It was decided that these two word groups were non-specific descriptors, and the number of articles which used at least one group 5 or 6 term was not tallied across the 6769 passive control articles.

Table 4.1. Word groups identified from article summaries: title, aim, abstract (excluding aim)

Group	Description	Specific words
1	Group 1: Statistical Technique *Description of a statistical time-to-event technique*	Actuarial analysis Cox proportional hazards model Hazard ratio Kaplan-Meier Life table Lifetime analysis Survival analysis
2	Group 2: Statistical term: outcome with time *Use of a statistical term which indicated that an outcome was studied over time*	Cumulative estimated survival/success/failure Cumulative survival/success/failure rate
3	Group 3: Quasi-statistical: outcome with time *Use of a quasi-statistical term which indicated that an outcome was studied over time*	Censored/drop out Complication rate Dental rehabilitation/caries/healing rate Failure/fracture/loss rate Morbidity/mortality rate Rate, other^ Probability of survival/lifetime/failure Probability, other+ Retention rate/estimate Success rate/estimates Survival rate/estimates Time-to-event
4	Group 4: General term: outcome with time *Use of a general term which indicated that an outcome was studied over time*	Durability Life span Longevity Mortality Prognosis
5	Group 5: General term: outcome *Use of a general term which indicated that an outcome was studied*	Adverse events Assess/ assessment Behaviour Complications/problems Efficacy/ effectiveness End point Evaluation Experience Failure Incidence Investigation Loss/fracture Maintenance/aftercare Observations (clinical observations) Outcome Performance Prognosis Reliable Response Results Success Survival
6	Group 6: Time *Phrases or words which specifically stated the study duration*	For example: 10 year outcome, 5 year duration, 8 year follow-up, 2 year recall.

^ Rate, other included flow, polymerization, loading, secretion, gastric emptying, canine retraction, dissemination, distraction rate
+ Probability, other included probability of avoiding dental treatment

4.3.3 <u>Statistical analysis</u>

Differences in the use of the target words between the articles were analysed across the six target-word groups, and the three locations (title, aim, abstract (excluding aim)) for all three types of article. Analyses of target-word groups 5 and 6 were restricted to the comparison of the included 'case' articles and the active controls.

The Pearson's chi-square statistic was used to compare the frequencies. Where the expected cell counts were less than 5, the included 'case' articles and the active controls were combined to create a 2 by 2 contingency table, and if the count persisted below 5, the Fischer's exact test was employed. Statistical significance was set at $P<0.05$.

4.4 RESULTS

4.4.1 Abstract (excluding aim)

Statistical comparisons are reported in table 4.2. Results are outlined in figures 4.2, 4.3 and 4.4, and in table 4.3.

Comparison between the included 'case' articles, the active controls and the passive controls revealed that the term "life table" was specific for articles using time-to-event methods.

In comparison with the active controls, seven words and phrases were specific to the included 'case' articles. Five of these were in groups 1 to 4, and indicated that an outcome was studied over time (Kaplan-Meier, Life table, Probability of survival/lifetime/failure, Lifespan, Longevity). Two were in group 5 and indicated that an outcome was studied (Adverse event, Response). However, given the general nature of these group 5 words, their observed specificity to the included 'case' articles in this sample is likely to be due to chance.

The use of target words in the abstract differed between the included 'case' articles and the active controls in two of the six groups: Group 1 (statistical technique) and Group 2 (statistical term). Additionally, they differed across the included, active and passive controls in three of the four groups: Group 1 (statistical technique), Group 2 (statistical term), and Group 3 Quasi-statistical term.

A higher proportion of the included 'case' articles used at least one statistical technique term (group 1) than the active controls (35% versus 2%, Chi-square 32.21, P<0.001), and the proportion for the passive controls was significantly lower (0.37%, chi-square 713, P<0.001). All included 'case' articles used a time-to-event analysis, but 65% of these authors did not describe this in their abstract and it was only apparent from the reading of the full articles as part of the original project to identify this sample,[12] where the relevant information was usually found in the methods section.

The included 'case' articles used the group 2 term "Cumulative" more often than the active controls (31% versus 1%, Chi-square 29.75, P<0.001), and it was much less common in the passive controls (0.06%, chi-square 952, P<0.001). This term relates to the estimated cumulative proportion, and time-to-event analyses.

Similar proportions of the 'cases' and active controls used group 3 (quasi-statistical terms, indicating that an outcome was followed over time) terms (82% versus 78%, Chi-square 0.49, P=0.49). This shows that these terms are not useful in this sample for distinguishing articles reporting dental outcomes that do, and do not, include time-to-event analyses. These terms were significantly less frequent amongst the passive controls (3.21%, Chi-square 2139, P<0.001).

There were no significant differences in the use of group 4 words in the abstract (excluding aim) for the three sets of articles, or the use of group 5 or 6 target words between the included 'case' articles and the active controls.

Figure 4.2. Words used by authors in the included 'case' articles (n=95)

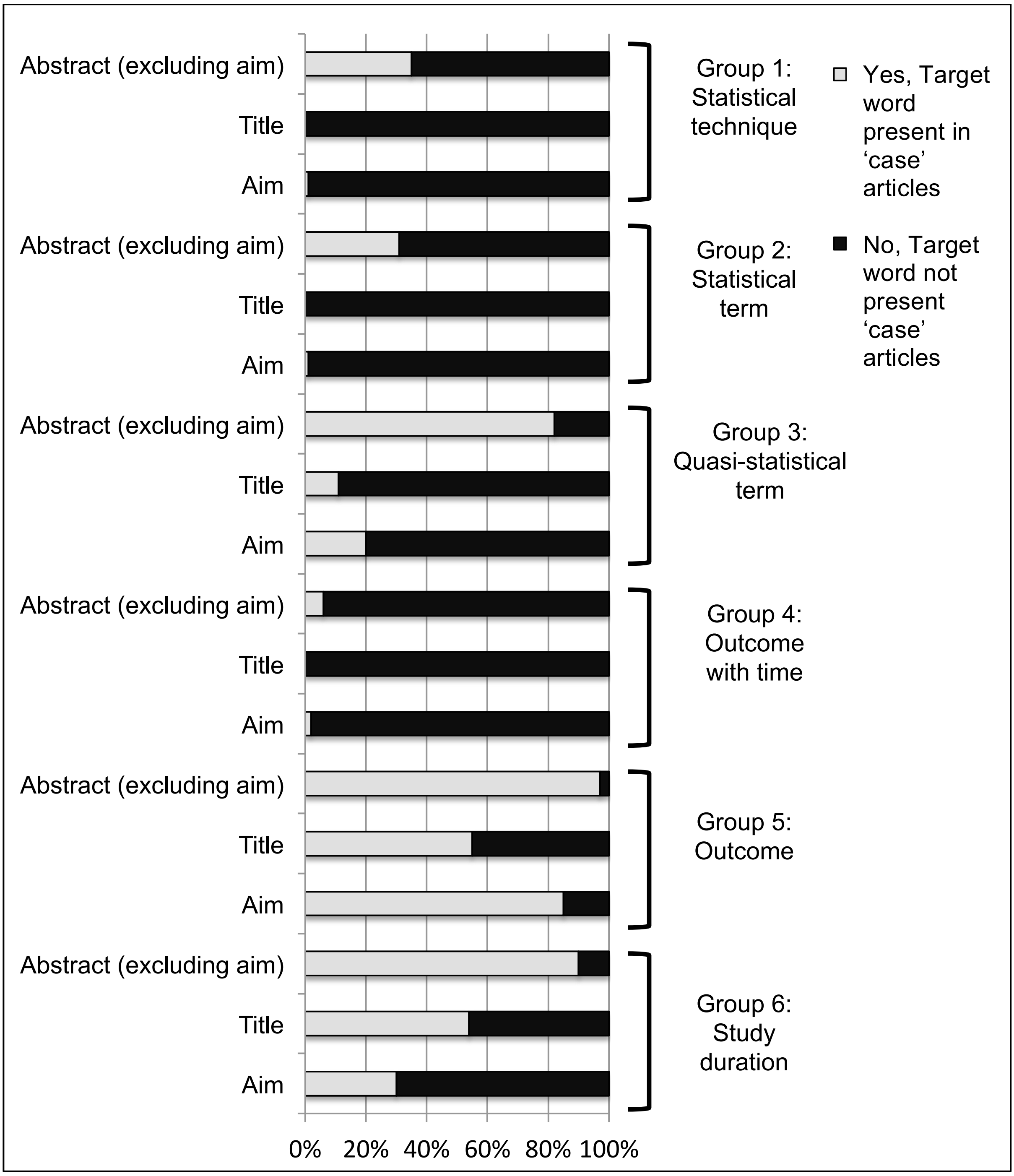


Figure 4.3. Words used by authors in the active controls (n=91)

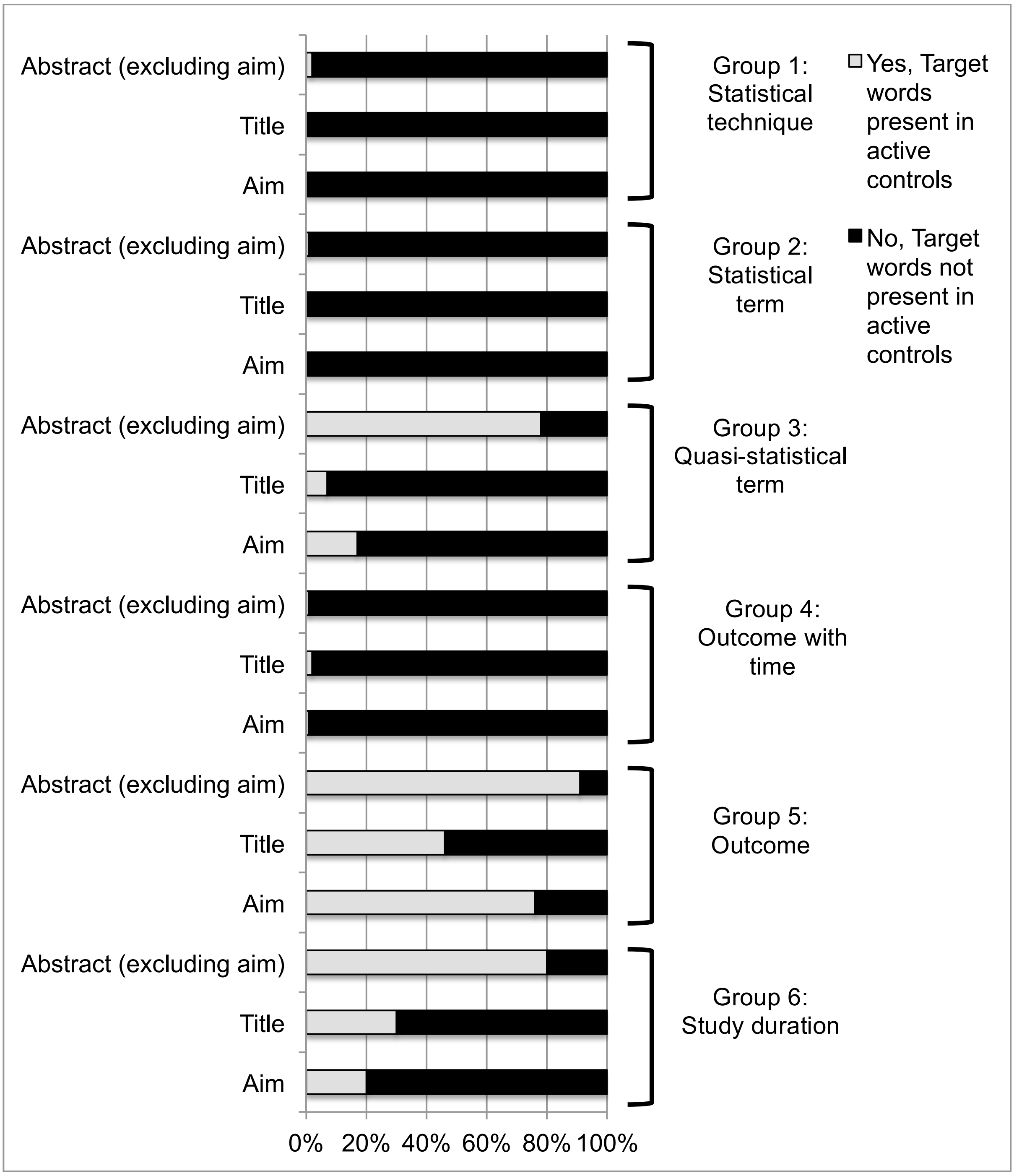


Figure 4.4. Words used by authors in the passive controls (n=6797)

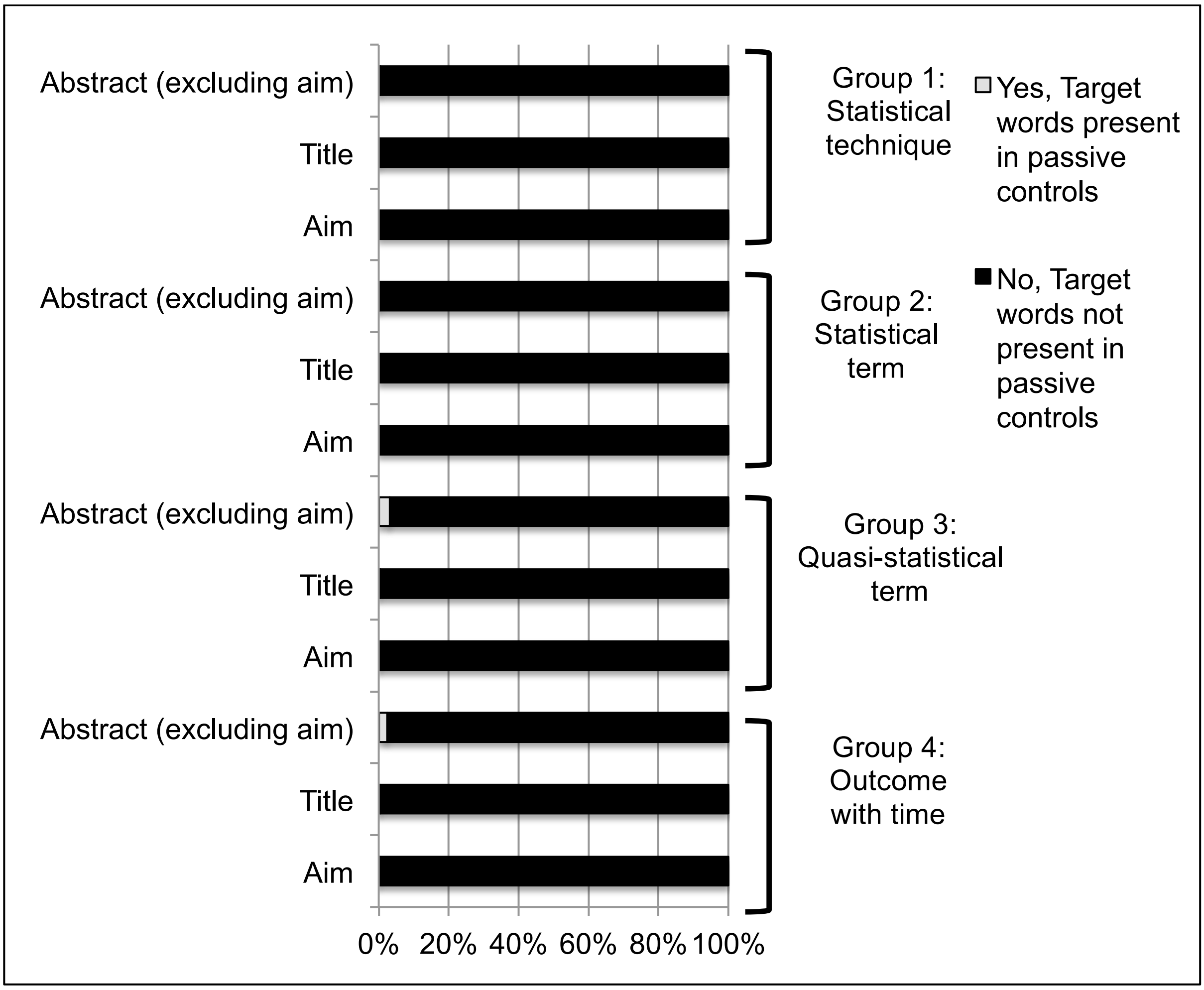


Table 4.2. Analysis of differences in use of target words between the included 'case', active control and passive control articles.

Outcome of Group Comparisons Across Each Location		
Abstract		
	1	Group 1 vs Group 2 Chi-square 32.21, P<0.001 (34.74%, 2.20%) Comparison: All groups, Chi-square 713, P<0.001^ (18.82%, 0.37%)
	2	Group 1 vs Group 2: Chi-square 29.75, P<0.001 (30.53%, 1.10%) Comparison: all groups, Chi-square 952, P<0.001^ (16.13%, 0.06%)
	3	Group 1 vs Group 2: Chi-square 0.49, P=0.49 (82.11%, 78.02%) Comparison: All groups, Chi-square 2139, P<0.001+ (80.11%, 3.21%)
	4	Group 1 vs Group 2: Chi-square 3.49, P=0.06 (6.32%, 1.10%) Comparison: All groups, Chi-square 0.967, P=0.34+ (3.76%, 2.46%)
	5	Group 1 vs Group 2: Chi-square 2.65, P=0.10 (96.84%, 91.21%) Comparison: All groups, NA
	6	Group 1 vs Group 2: Chi-square 3.11, P=0.08 (89.47%, 80.22%) Comparison: All groups, NA
Title		
	1	Group 1 vs Group 2: Chi-square 0.96, P=0.33 (1.05%, 0%) Comparison: All groups, Chi-square 17, P=0.053^ (0.54%, 0.01%)
	2	Group 1 vs Group 2, not assessed Comparison: All groups, NA
	3	Group 1 vs Group 2: Chi-square 0.91, P=0.34 (10.53%, 6.60%) Comparison: All groups, Chi-square 2139, P<0.001+ (8.60%, 0.37%)
	4	Group 1 vs Group 2: Chi-square 2.11, P=0.15 (0%, 2.20%) Comparison: All groups, Chi-square 1.8, P=0.193^ (1.10%, 0.41%)
	5	Group 1 vs Group 2: Chi-square 1.4, P=0.24 (54.74%, 46.15%) Comparison: All groups, NA
	6	Group 1 vs Group 2: Chi-square 11.0, P=0.001 (53.68%, 29.67%) Comparison: All groups, NA
Aim		
	1	Group 1 vs Group 2: Chi-square 0.96, P=0.33 (1.05%, 0%) Comparison: All groups, Chi-square 36.06, P=0.027^ (0.54%, 0%)
	2	Group 1 vs Group 2, Chi-square 0.96, P=0.33 (1.05%, 0% Comparison: All groups, Chi-square 36.06, P=0.027^ (0.54%, 0%)
	3	Group 1 vs Group 2: Chi-square 0.34, P=0.54 (20.00%, 16.48%) Comparison: All groups, Chi-square 594, P<0.001^ (19.36%, 0.49%)
	4	Group 1 vs Group 2: Chi-square 0.30, P=0.59 (2.11%, 1.10%) Comparison: All groups, Chi-square 12.43, P=0.014^ (1.62%, 0.24%)
	5	Group 1 vs Group 2: Chi-square 2.65, P=0.10 (85.26%, 75.82%) Comparison: All groups, NA
	6	Group 1 vs Group 2: Chi-square 2.35, P=0.13 (29.47%, 19.78%) Comparison: All groups, NA

 # Total frequency of term use. Some articles were allocated more than one term within each group.
** Total number of articles that were allocated at least one term within a given group.*
+ Pearson's Chi-square test, combined 2 x 2 contingency table
^ Fischer's exact test, 2 x 2 contingency table
NA, Not assessed

Table 4.3. Detailed information of words used by authors in the abstract (excluding aim)

Groups	Specific words	Included 'case' (n=95)	Active controls (n=91)	Passive controls (n=6769)
Group 1: Statistical Technique	Actuarial analysis	0	0	0
	Cox hazards model / hazard ratio	9	1	12
	Kaplan-Meier	20	0	17
	Life table	6	0	0
	Lifetime analysis	0	0	0
	Survival analysis	4	1	6
	Total frequency[#]	39	2	35
	*Total articles**	35%, n=33	2%, n=2	0.37%, n=25
Group 2: Statistical term	Cumulative estimated survival/success/failure/rate	29	1	4
	Total frequency[#]	29	1	4
	*Total articles**	31%, n=29	1%, n=1	0.06%, n=4
Group 3: Quasi-statistical	Censored/drop out	4	3	3
	Complication rate	3	5	18
	Dental rehabilitation/caries/healing rate	1	2	8
	Failure/fracture/loss rate	12	12	20
	Morbidity/mortality rate	2	4	17
	Rate, other	0	0	128
	Probability of survival/lifetime/failure	6	0	6
	Probability, other	0	0	1
	Retention rate/estimate	4	1	10
	Success rate/estimates	26	29	75
	Survival rate/estimates	63	36	81
	Time-to-event	0	1	11
	Total frequency[#]	121	93	378
	*Total articles**	82%, n=78	78%, n=71	3.21%, 215
Group 4: Outcome with time	Durability	0	0	23
	Life span	1	0	7
	Longevity	2	0	20
	Mortality	0	0	28
	Prognosis	3	1	96
	Total frequency[#]	6	1	174
	*Total articles**	6%, n=6	1%, n=1	2.46%, n=165
Group 5: Outcome	Adverse events	4	0	Not individually assessed
	Assess/ assessment	3	10	
	Behaviour	0	0	-
	Complications/problems	16	20	-
	Efficacy/ effectiveness	7	6	-
	End point	0	1	-
	Evaluation	39	41	-
	Experience	0	1	-
	Failure	43	32	-
	Incidence	0	2	-
	Loss/fracture	36	16	-
	Maintenance/aftercare	2	1	-
	Observations (clinical observations)	0	0	-
	Outcome	20	19	-
	Performance	8	7	-
	Response	1	0	-
	Results	13	6	-
	Success	18	29	-
	Survival	32	16	-
	Total frequency[#]	242	207	12 842
	*Total articles**	97%, n=92	91%, n=83	Not assessed
Group 6: Time	For example: 10 year outcome, 5 year duration, 8 year follow-up	NA	NA	NA
	Total frequency[#]			51%, n=3425
	*Total articles**	90%, n=85	80%, n=73	Not assessed

[#] *Total frequency of term use. Some articles were allocated more than one term within each group.*
* *Total number of articles that were allocated at least one term within a given group.*

4.4.2 Title

Statistical comparisons are reported in table 4.2. Results are outlined in figures 4.2, 4.3 and 4.4, and in table 4.4.

The target words regarding the statistical technique (group 1) and the reporting of outcome (groups 3-5) used in the title were similar between the included ‘case’ articles and the active controls. Significantly more included ‘case’ articles used group 6 words in their title, specifically stating the duration of the study, compared to the active controls (54% versus 30%, chi-square 11.0, P=0.001).

The words used in the titles regarding statistical techniques (group 1) and quasi-statistical terms (group 3) differed across the three sets of article. These terms were significantly less common in the passive controls, with 0.33% and 0.37% articles using them, respectively (P values <0.001 compared to the included ‘case’ articles and the active controls).

None of the articles used target words from the statistical term group (group 2) in the title.

Table 4.4. Detailed information of words used by authors in the title

Groups	Specific words	Included 'case' (n=95)	Active controls (n=91)	Passive controls (n=6769)
Group 1: Statistical Technique	Actuarial analysis	0	0	0
	Cox hazards model / hazard ratio	0	0	0
	Kaplan-Meier	0	0	0
	Life table	0	0	0
	Lifetime analysis	0	0	0
	Survival analysis	1	0	1
	Total frequency#	n=1	n=0	n=1
	*Total articles**	1%, n=1	2%, n=0	0.01%, n=1
Group 2: Statistical term	Cumulative estimated survival/success/failure/rate	0	0	0
	Total frequency#	n=0	n=0	n=0
	*Total articles**	0%, n=0	0%, n=0	0%, n=0
Group 3: Quasi-statistical	Censored/drop out	0	0	0
	Complication rate	1	1	2
	Dental rehabilitation/caries/healing rate	0	0	1
	Failure/fracture/loss rate	2	2	1
	Morbidity/mortality rate	0	0	1
	Rate, other	0	0	15
	Probability of survival/lifetime/failure	0	0	0
	Probability, other	0	0	1
	Retention rate/estimate	0	0	0
	Success rate/estimates	1	4	2
	Survival rate/estimates	7	2	1
	Time-to-event	0	0	1
	Total frequency#	n=11	n=6	n=25
	*Total articles**	11%, n=10	7%, n=6	0.37%, n=25
Group 4: Outcome with time	Durability	0	1	10
	Life span	0	1	0
	Longevity	0	0	3
	Mortality	0	0	7
	Prognosis	0	0	8
	Total frequency#	n=0	n=2	n=28
	*Total articles**	0%, n=0	2%, n=2	0.41%, n=28
Group 5: Outcome	Adverse events	0	0	2
	Assess/ assessment	0	0	145
	Behaviour	0	1	57
	Complications/problems	1	2	38
	Efficacy/ effectiveness	2	0	116
	End point	0	0	0
	Evaluation	14	12	296
	Experience	2	2	56
	Failure	2	3	29
	Incidence	0	3	34
	Loss/fracture	2	0	54
	Maintenance/aftercare	0	0	8
	Observations (clinical observations)	0	0	19
	Outcome	8	8	94
	Performance	5	2	31
	Response	0	0	81
	Results	9	8	59
	Success	2	1	30
	Survival	7	3	25
	Total frequency#	n=54	n=45	n=1198
	*Total articles**	55%, n=52	46%, n=42	Not assessed
Group 6: Time	For example: 10 year outcome, 5 year duration, 8 year follow-up	NA	NA	NA
	*Total articles**	54%, n=51	30%, n=27	Not assessed

 # Total frequency of term use. Some articles were allocated more than one term within each group.
** Total number of articles that were allocated at least one term within a given group.*

4.4.3 Aim in the abstract

Target words were sought in the aim in the abstract, and their presence was classified separately from other sections of the abstract. This additional step was undertaken to allow the wording of aims of the included ‘case’ articles to be examined. Statistical comparisons are reported in table 4.2. Results are outlined in figures 4.2, 4.3 and 4.4, and in table 4.5.

Five articles, four ‘cases’ and one active control did not report an aim. Those with no aims did not contribute data to the tallied items, the aims were not sought in the body of the article, and the articles were not excluded from the analysis. The number of passive controls not reporting an aim was not tallied.

The use of target words in the aims reported in the abstracts of the articles was similar for the included ‘cases’ and active controls. Use of a statistical term was rare (group 1 and 2, less than 1%), whilst use of a general term relating to outcome (group 5) was common (85% versus 76%, chi-square 2.65, P=0.10).

However, important differences were found when the included ‘case’ articles and active controls were compared with the passive controls. Words in groups 1, 2, 3 and 4 were used with significantly less frequency in the passive controls. None of the target words for the statistical technique or statistical terms appeared in the aim of the passive controls, but their use was also rare amongst the included ‘case’ and active controls. The frequencies for quasi-statistical terms were 20% and 17% versus 0.49% (Chi-square 594, P<0.001) and those for general outcome with time terms were 2% and 1% versus 0.24% (Chi-square 12.43, $P<0.001$) across the three groups.

Table 4.5. Detailed information of words used by authors in the aim.

Groups	Specific words	Included 'case' (n=95)	Active controls (n=91)	Passive controls (n=6769)
Group 1: Statistical Technique	Actuarial analysis	0	0	0
	Cox hazards model / hazard ratio	0	0	0
	Kaplan-Meier	0	0	0
	Life table	0	0	0
	Lifetime analysis	0	0	0
	Survival analysis	1	0	0
	Total frequency#	1	0	0
	*Total articles**	1%, n=1	0%, n=0	0%, n=0
Group 2: Statistical term	Cumulative estimated survival/success/failure/rate	1	0	0
	Total frequency#	1	0	0
	*Total articles**	1%, n=1	0%, n=0	0%, n=0
Group 3: Quasi-statistical	Censored/drop out	1	0	0
	Complication rate	1	1	1
	Dental rehabilitation/caries/healing rate	0	1	0
	Failure/fracture/loss rate	0	1	0
	Morbidity/mortality rate	0	0	3
	Rate, other	0	0	17
	Probability of survival/lifetime/failure	0	0	0
	Probability, other	0	0	1
	Retention rate/estimate	0	0	1
	Success rate/estimates	7	6	3
	Survival rate/estimates	13	9	6
	Time-to-event	0	1	1
	Total frequency#	22	19	33
	*Total articles**	20%, n=19	17%, n=15	0.49%, n=33
Group 4: Outcome with time	Durability	0	0	8
	Life span	0	0	0
	Longevity	2	1	2
	Mortality	0	0	1
	Prognosis	0	0	5
	Total frequency#	2	1	16
	*Total articles**	2%, n=2	1%, n=1	0.24%, n=16
Group 5: Outcome	Adverse events	0	0	Not assessed
	Assess/ assessment	3	4	-
	Behaviour	0	0	-
	Complications/problems	4	5	-
	Efficacy/ effectiveness	6	7	-
	End point	1	0	-
	Evaluation	41	34	-
	Experience	1	2	-
	Failure	8	5	-
	Incidence	0	1	-
	Loss/fracture	4	2	-
	Maintenance/aftercare	1	1	-
	Observations (clinical observations)	0	0	-
	Outcome	18	14	-
	Performance	13	9	-
	Response	2	0	-
	Results	4	2	-
	Success	7	10	-
	Survival	18	3	-
	Total frequency#	131	99	-
	*Total articles**	85%, n=81	76%, n=69	Not assessed
Group 6: Time	For example: 10 year outcome, 5 year duration, 8 year follow-up	NA	NA	Not assessed
	*Total articles**	30%, n=28	20%, n=18	Not assessed

 # Total frequency of term use. Some articles were allocated more than one term within each group.
** Total number of articles that were allocated at least one term within a given group.*

4.5 DISCUSSION

Readers wishing to search bibliographic databases for dental articles with survival outcomes need to know which MeSH have been allocated by indexers, which words authors have used to describe their research or, ideally, both. I used three groups of articles to focus on the second part of this challenge.

The entire article cohort of 6955 represent the population, of which the included 'case' articles are true positives. These included 'case' articles have used survival analytic methods to report outcomes of dental prostheses. Both the passive and active controls represent the population of articles which are true negatives, but the active controls are the article that are most likely to appear as false positives when searching. Therefore, identifying words that distinguish between the true positives (included 'case' articles), possible false positives (active controls) and true negatives (passive controls) will aid readers who wish to identify such studies.

There is a vast and increasing volume of health care literature. The U.S. National Library of Medicine estimates that there are approximately 13 000 active biomedical journals, with 5300 included in the MEDLINE database.[13] This database, and others such as Embase and the *Cochrane Library* are widely used to identify articles. These databases catalogue article details including author, journal, reference, title and summary (abstract). In addition, databases such as MEDLINE and Embase employ specialist indexers to read the articles, and assign standardized vocabulary (such as Medical Subject Headings – MeSH – in MEDLINE) to describe the content of the research.

For searchers to identify articles in the bibliographic databases, they must know details about the article, be able to predict the words used by authors within their summaries, or rely on the accuracy of the index terms. Research described in Chapter 3 identified errors in the allocation of MeSH to articles about survival following dental treatments.[12] Errors in the assignment of index terms, or an inability to predict the terms used by authors would adversely impact on the identification of relevant research, and result in waste in the literature.

Quality of reporting has been a focus of much research over the past two decades, with the release of reporting guidelines for systematic reviews (PRISMA),[14] randomized trials (CONSORT)[7] and observational studies (STROBE),[8] to name a few. A guideline for compiling guidelines has also been published.[15] Many such guidelines are available from the EQUATOR network (www.equator-network.org). Currently, there are no general guidelines for the reporting of time-to-event methods within articles in the medical literature at large, or the dental literature specifically. Therefore, it is not surprising that the structure, language and presentation of analyses in these studies vary.

Such variation was found to be present amongst the studies identified in this research and this thesis provides the first estimate of the scale or “burden”, of this problem for the dental literature. It was found that time-to-event research was described in ways that showed that an outcome was being observed, that this outcome was observed over time, and that the analysis of the outcome employed time-to-event, or survival statistics. In total, 43 different words or phrases were used.

Electronic database searching of target words depends on the ability of both the author to describe their research accurately, and the searcher to consider which descriptive words the author may have chosen. Hence, if the author describing and the searcher looking for evidence approach the research from different perspectives, identifying relevant articles becomes problematic.

The target words for this research were compiled as the articles in the included ‘case’ articles and the active controls were read. The words had not been determined prior to reading the articles, with the list growing as additional relevant words were identified. This is an article-based approach and systematic in methodology. The work was completed by hand, and given the impact of human error it is possible that some relevant target words were overlooked. If this was the case, however, it is unlikely that there would have been many such words and unlikely that the error would substantially alter the interpretation of the findings from this research. Also, if the number of articles in the included ‘case’ cohort was greater, additional words describing time dependent outcomes may have been used, and identified.

The words were categorized into one of six groups. Words in group 1 were particularly specific terms that could describe survival analyses, while words in groups 5 and 6 were the least specific. Groups 2, 3 and 4 contained words that ranged from more to less specific. For example: authors may choose “Kaplan-Meier”, whilst another may choose “Life table” as descriptors. Both terms were specific for survival analyses, and were therefore in group 1. Likewise, authors may choose “Evaluate” or “Investigate”, or related derivatives such as “Evaluated/Evaluation”, “Investigated/Investigation” as outcome descriptors (group 5). These words generally indicate that an outcome has been studied, but not necessarily over time.

It was therefore not surprising to find these words occurring with high frequency amongst the articles. Grouping the words has allowed the nuances of the choice of words between the articles to be explored.

Across the articles, the word or phrase specific to the included 'case' articles only was "Life table", which was present in six (6.3%) of the abstracts of the included 'case' articles and in none of the other titles or abstracts. This term can refer to a statistical technique (life table survival analyses) or to a graphic representation of tabular results.

When looking at differences between the included 'case' and active control articles, words reporting use of time-to-event statistics should not have been frequently present within the active control group. The terms Kaplan-Meier and Life table were unique to the included 'case' articles, but in two instances the active controls used the terms survival analysis and cumulative. One article reported a 100% "cumulative survival rate".[16] The article assessed changes in bone levels around implants, made no reference to gathering data for survival analyses, and the two reviewers assessing its classification concluded that the result was reported through extrapolation, rather than computation. Another article used survival analytic techniques to assess complications associated with peripherally inserted central catheters, a non-dental outcome.[17] This article could have been placed in the passive controls, but also reported outcomes of maxillofacial infections, and thus fitted the inclusion criteria for the active control group. Other uses of these words, not specifically relating to time dependent dental outcomes were rare, with occurrence of a group 1 (statistical technique) and group 2 words (statistical term) being significantly less common in the active controls.

Within the passive controls, the use of words from these two groups was also rare and significantly less common than in the included ‘case’ articles. Their use was associated correctly with 28 articles (0.42%, group 1, n=25, group 2, n=4) that did report time-to-event statistics for dental treatment but reported outcomes related to cancer (n=22), mortality (n=2), animal models (n=1), laboratory experiments (n=1) and length of hospitalisation (n=1), which made them ineligible as “cases” for this study.

Superficially, this finding appears positive; but the use of these terms by the included ‘case’ articles was also low, with only about one-third of these 95 articles using the terms in their title or abstract. Only 33 and 29 of the included ‘case’ articles, respectively, used a statistical technique term or a statistical term in the abstract but full reading of all 95 of these articles revealed that the authors had used a time-to-event technique, and the absence of at least one of these terms from two-thirds of the abstracts indicates how the quality of reporting would hinder the retrieval of these articles if searching was limited to titles and abstracts. This high specificity and low sensitivity for these words in articles is not helpful when searching for all relevant evidence.

Quasi-statistical target words, group 3, were present for all three types of article. Terms or phrases using words such as Censored, Drop out, Rate, Estimate, Probability or Time to an event are suggestive that a survival analysis was used, but they lack specificity for such techniques. Use of these terms was similar amongst the included ‘case’ and active control articles (approximately 80%), but they were significantly less common in the passive controls (less than 5%). These quasi-statistical terms therefore have a lower specificity for time-to-event articles when compared with terms in groups 1 and 2, but they have high specificity for outcome analyses. A search using these terms within the whole population of the 6955 articles, would yield approximately 80% of the true positive articles, approximately 300 false positives, and discard over 6000 (over 85% of the total 6955) true negatives.

The fourth word group indicated that an outcome was studied, and that this study occurred over time. The words identified included Durability, Life span, Longevity, Mortality and Prognosis. Two of these words (Life span and Longevity) were specific to the included ‘case’ articles, rather than the active controls. However, they were rare with total frequencies of use of 6% and 1% respectively, and it is likely that the specificity of these words might be due more to chance than a true association. These terms were also used by the passive controls, and occurred in about 3% of the titles and abstracts for those articles.

Two additional word groups were studied in detail for the included ‘case’ articles and the active controls, but not the passive controls. The fifth group related to the general use an outcome term (such as Performance, Response, Result), whilst the sixth group indicated a study was completed over a period of time (such as Duration, Follow up, 10-year outcome). Words in both groups were present in more than 80% of the included ‘case’ articles and active controls, and were found to be equally frequent. The total frequency of use within the passive controls was also tallied, with multiple articles using more than one term. The frequency was so high (group 5: 12,842, group 6: 3425) for this set of articles that further analyses would not contribute to our understanding and was not completed. Therefore, the comparative incidence of use of these terms between the three article sets was not analysed.

This research has found great variation in the words used by authors to describe time-to-event dental outcomes. Without care, use of such words for an electronic database text search for articles reporting survival analyses in the dental literature would produce results with both low sensitivity and specificity. This clearly undermines the identification of relevant articles and increases the workload of systematic reviewers as they check through the vast numbers of erroneous results.

Techniques for searching literature are expanding. More journals are providing full text articles online, and databases facilitating the search of the complete article are continuing to be developed. Sophisticated search methods are employed by well-known internet platforms for data on the world wide web, such as Google. In 2006, JSTOR teamed with Google, indexing the content of their database to allow direct Google searches, making it easier for researchers not associated with academic libraries to access articles.[18] MEDLINE is providing links to access full text articles through MEDLINE full text and MEDLINE complete, but the search engines do not yet search the full text of those articles. Google scholar and PubMedCentral allow searching of complete manuscripts, while BioText[19] and Yale Image Finder[20] provide platforms to search article figures and their legends. Over time, these tools will change how people search for evidence, and identifying relevant articles will rely less on how titles and abstracts are written, and more on how the articles are presented in their entirety.

4.6 IMPLICATIONS

There is great variation in how time-to-event outcomes of dental treatments are described in their abstracts in the scientific literature. The use of particular words when searching summaries in bibliographic databases will provide inconsistent results with both low sensitivity and specificity. This will make it difficult for those searching to identify relevant articles. Once identified, details of the methods and results in these time-to-event articles should be reported clearly and transparently to allow the findings to be assessed and translated into practice. To this end, the quality of reporting of these articles will be reviewed in Chapter 5.

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CHAPTER 5. QUALITY OF REPORTING OF METHODS, RESULTS AND GRAPHICS OF DENTAL ARTICLES CONTAINING TIME-TO-EVENT DATA

CONTENTS

5.0 SUMMARY

Objective: This research aimed to examine the quality of reporting (writing and graphics) of articles that used time-to-event analyses to report dental treatment outcomes.

Methods: The articles reporting treatment outcomes with (n=95) and without (n=91) time-to-event statistics identified by the systematic search described in Chapter 2 were reviewed further. Survival descriptive words used in the methods and results sections of the articles in each of the two groups were identified, tallied and the differences between the groups analysed (Peason's chi-square). The presence and reporting quality of life tables and survival curves and the use and reporting quality of time-to-event statistical methods in the time-to-event articles was assessed. Two investigators independently assessed subjective criteria (using the kappa statistic to analyse agreement), and one investigator completed all other assessments. Survival curves and life tables that included all graphic quality measures were considered to be of high quality. Those graphics that included all measures except for the standard error or confidence interval were considered to be of acceptable quality. Articles that reported all quality measures regarding the statistical tests in the methods of the article were considered to be of high quality. Those that reported the type of survival statistic and summary figure only were considered to be of acceptable quality.

Results: Words describing dental outcomes "over time" were much more common in the time-to-event compared with the control articles (77%, 3%, P<0.001). Non-specific use of "rate" was common across both groups. Life tables and survival curves were used by 39% and 48% of the time-to-event articles, with at least one of

these used by 82%. Construction quality was poor in general: 21% of life tables and 28% of survival curves achieved an acceptable standard. Time-to-event statistical reporting was poor for many articles: 3% achieved a high and 59% achieved an acceptable standard. The survival statistic, summary figure and standard error was reported in 76%, 95%, and 20% of time-to-event articles.

Implications: Individual statistical terms and graphic aids were common in and unique to time-to-event articles. Unfortunately, important details were regularly omitted from statistical descriptions and survival figures, making the overall quality of reporting poor. It is likely this will mean such articles will be incorrectly indexed in databases, missed by people seeking them, and unnecessarily difficult to understand and interpret if they are identified.

5.1 BACKGROUND

Interest in the quality of reporting of research has increased since the publication of one of the first reporting guidelines, CONSORT, in 1996.[1] The "scandal of poor medical research", was lamented by Altman in 1994,[2] and a series of statistical notes written by Bland and Altman began that year in the British Medical Journal, highlighting ways in which the quality of statistical reporting could be improved to make it easier for readers to understand these aspects of research articles.

Problems with reporting quality impacts on the usefulness of the underlying research. First, reporting quality affects the ability of database indexers to allocate appropriate subject heading (such as MeSH) to the article, which then impacts on searchers' ability to find the articles. Second, the quality of reporting affects the ability of readers to interpret results.

As discussed in the previous chapters, articles indexed in an electronic database, such as MEDLINE, can be sought by searching for various article details (title, author, journal), searching for specific words or phrases in the title and abstract, or by searching the index terms (such as MeSH in MEDLINE) assigned to those articles. In theory, basing the search on the index terms is a more powerful way to identify articles, as indexers read the entirety of the articles whilst allocating those terms. Therefore, identification of relevant articles in MEDLINE is related to accurate allocation of MeSH, and the same is true of other databases and their index terms. If the quality of reporting is poor, appropriate index terms may not be allocated, and the articles might be missed during electronic searching.

Poor, inconsistent and inaccurate reporting has been studied by various groups, with a summary of errors affecting clinical trials appearing in the introduction to the 2010 CONSORT update discussion paper.[3] Failure to explain methods of assignment of participants to comparative groups, define primary outcomes and calculate sample sizes occurred in 20% to 50% of trials indexed in MEDLINE (PubMed) during 2000 to 2006.

A discussion paper presented by Bland at a conference in France in 2010 provided an insight into the statistical quality of medical reporting over the past 40 years.[4] He found that reporting had improved over this time, with greater emphasis on the reporting of confidence intervals, P-values, improved sample sizes and summaries of statistical inference now occurring in the abstracts of journal articles. Bland postulated that these improvements related to many factors, including the promotion of evidence-based medicine, increased prevalence of systematic reviews, education of researchers and journals in employing proper statistical methods and reporting, use of statistical referees by journals, publication of reporting guidelines, and continued editorials on reporting quality.

Researchers are exploring ways to improve reporting further, with guidelines for several types of studies now available, including systematic reviews (PRISMA),[5] randomized trials (CONSORT)[3] and observational studies (STROBE).[6] A guideline for compiling guidelines has also been published[7]. Currently, there are no formal reporting guidelines for the completion and presentation of survival analyses. However, researchers have begun the task of reviewing the reporting quality of these articles and their findings[8-10] were outlined briefly in chapter 4, when exploring how titles and abstracts of time-to-event dental articles were written. I argued that problems in reporting of complete articles could indicate that the titles and abstracts of those articles were similarly affected. The findings from these researchers also provide insight into the quality and transparency of the complete articles, and additional details about their research,[8-10] and that of two other research groups[11, 12] have been provided below.

An assessment of survival analyses published in five oncology journals between October and December 1991 found multiple flaws in the reporting of the studies.[12] There were errors in reporting of length of follow up, defining end points and detailing log rank and multivariate analyses. Survival curves were presented in 95% of the papers, with nearly 20% not stating the type of time-to-event statistical method used. Details regarding censoring, confidence intervals and standard errors were omitted. Additionally, there was incorrect use of connecting lines and confusing choice of axis numbers. The authors suggested a set of recommendations for describing and presenting survival analyses and published these as an appendix to their paper. The recommendations cover collecting data, describing data, justifying methodology decision, writing results, drawing survival curves, portraying life tables and writing abstracts.

Research by Zakrzewska and Lopez in 2003 regarding the reporting quality of surgical treatment for trigeminal neuralgia published between 1966 and 2001 included some trials that used time-to-event methods.[11] They stated it was evident that the Kaplan-Meier methodology and curves construction were not uniform across those papers, and details regarding loss to follow up were lacking from some.

Additional problems with the quality of reporting of survival analyses in the medical literature were identified in other research. Pocock and colleagues[9] reviewed 35 medical research trials published in 1999 which used survival plots. Reporting practices that undermined the quality of presentation were summarized and recommendations on how to draw survival plots were provided. Such recommendations covered choice of time-intervals, presentation of data on axes and inclusion of statistical uncertainty. However, a survey by Vervolgyi and colleagues[10] in 2011 of 319 medical articles published from 2003 to 2005 using Kaplan-Meier plots found that less than half reported loss to follow up, and it appeared that the quality of survival plots remained low.

A systematic review by Needleman and colleagues in 2012 summarised how implant success and survival was reported.[8] Of the 196 articles identified, time-to-event statistics were used by approximately 60% of articles (life table analysis 40%, Kaplan-Meier 17%), the estimated cumulative survival appeared to be reported by approximately 55%, and life tables and survival plots were present in 40% and 7% of articles respectively. The review explored a broad range of reporting topics, including, but not specifically focusing on time-to-event statistics. The quality of reporting of the time-to-event outcomes appeared to be poor. The authors commented that problems with this methodology continued to pervade the medical literature and that it was unsurprising that the dental literature was similarly affected.

Clearly, problems with reporting quality are multifactorial and could relate to a variety of features in research reports, including appropriate use of time-to-event methods, accurate execution of the techniques, clarity of the written results, and presentation of graphics.

Research findings from chapter 3 have shown that the allocation of indexing terms to time-to-event dental analyses is inconsistent and inaccurate. Findings from chapter 4 have shown that the words chosen by authors to describe such research in their abstract were often non-specific and varied greatly between articles. Together, these two findings show how difficult it might be for interested readers to locate appropriate time-to-event dental articles by either an indexing term or text word search.

The present chapter continues to explore how authors reported the methods and results in the body of these papers, and provides insight into the challenges faced by readers even after they have found articles that used time-to-event analyses to report dental treatment outcomes.

5.1 OBJECTIVE

This research aimed to examine the quality of reporting (writing and graphics) of articles that used time-to-event analyses to present their findings on the outcomes of dental treatment in patients.

5.3 METHODS

5.3.1 Time-to-event dental articles

As reported in Chapter 2, journals from 2008 were handsearched, and articles were categorised into one of three groups. Those reporting dental treatment outcomes over time in human subjects with time-to-event statistics (n=95, included 'case' articles) and without time-to-event statistics (n=91, active controls) were reviewed further for the research presented in this chapter. The articles in the passive control group (n=6769) were not required.[13]

Within the two groups, the words used to describe time-to-event statistical techniques in the methods and results were identified and assessed.

Within the time-to-event articles only (n=95), the use and reporting quality of life tables, survival curves and statistical explanations in the methods and results of the papers were assessed.

5.3.2 Identification of words in the article

Words in the body of the article that reported that a time-to-event statistical technique had been used were identified and extracted manually by one investigator. The discovery technique that had been used when searching the abstracts of these articles was also adopted when reading the articles in their entirety. The words eventually identified for this research had not been determined prior to searching the articles, but were formed as a living list, which grew as the search continued. This discovery method reduced preconceived ideas of how survival methods may be reported, and minimized data collection bias.

A list of 15 words or similar phrases were identified, and further classified into three groups (table 5.1). All terms indicated that an outcome was studied over time, with group 1 describing a specific statistical technique, group 2 being a statistical term and group 3 being a quasi-statistical term.

The frequency of use of the target words was recorded. Some articles used multiple words from the same group, and thus the frequency of use of at least one of the words within each group was also recorded.

Table 5.1. Word groups identified from the methods section in the body of the included 'case' (n=95) and active control (n=91) articles.

Group	Description	
1	Group 1: Statistical Technique *Use of a statistical time-to-event technique*	Actuarial method Regression/ Proportional hazards Hazard ratio Kaplan-Meier Life table/ Life table analysis Lifetime analysis Log rank Survival analysis Survival curve/ Survival plot Survival function
2	Group 2: Statistical term: outcome with time *Use of a statistical term which indicated that an outcome was studied over time*	Cumulative estimated survival/ success/ failure Cumulative survival/ success/ failure rate
3	Group 3: Quasi-statistical: outcome with time *Use of a quasi-statistical term which indicated that an outcome was studied over time*	Failure/ Complication rate Survival probability/ Probability of event Survival/ Success/ Retention rate Time-to-event (or time to a specific outcome)

5.3.3 Use and quality of graphics in the body of the article to report results

Two different graphic presentations of time-to-event outcomes had been used in the results of articles: survival curves and life tables. A survival curve was considered to be a graph that showed a probability or percentage outcome (such as percent surviving) over time. A life table was considered to be a table that reported the number of prostheses in situ, and the number or percentage of those that experienced the outcome (such as number failed or percentage surviving) in different time intervals. Two independent investigators reviewed the articles to determine whether the authors had used graphics to present their results. Disagreement was resolved by discussion. The level of agreement between the investigators was assessed numerically, using the Kappa statistic.

The quality of the survival curves, life tables and the reporting of statistical tests were assessed with criteria that were determined by the authors. These criteria were based on recommendations made by and concerns raised by authors who had reviewed time-to-event reporting.[8-12]

The quality of the survival curves was assessed using the following criteria:

1. Meaningful time intervals
2. A stepped curve
3. Different lines to represent different groups assessed
4. Censored observations notated on the curve
5. Notation of the standard error or confidence interval.

The quality of the life table was assessed using the following criteria:

1. Meaningful time intervals

2. Notation of the number of patients/prostheses at risk, those lost to follow up and the number of events that occurred during each time interval
3. Notation of the survival of individual time intervals, and the survival of cumulative time intervals
4. Notation of the standard error or confidence interval

Assessing whether articles fulfilled criterion one, “use of meaningful time intervals” is subjective. Two independent investigators assessed whether the survival curves and life tables satisfied this criterion. The level of agreement between investigators was assessed numerically and disagreement was resolved by discussion. Non-meaningful time intervals included those

- That did not commence the x-axis at zero
- Reporting time in words rather than numbers (for example, “during implant loading”), such that the actual timing of a period was unclear
- Reporting uneven time periods, and those that omitted large sections of data
- Reporting unusual time periods that did not make sense in the context or the study, or were not intuitively translated into clinically relevant intervals (eg. 120 months instead of 10 years, 1095 days instead of 3 years).

The concept of “meaningful” would differ between assessors, and between studies. For example, it would be sensible to report the 1-year outcome of an implant intervention monthly if implants were reviewed regularly, such as 3, 6 and 9 monthly, over the 1 year period. Equally, it would be sensible to report outcomes yearly if participants returned for review on a yearly basis, where different participants were assessed during different months of that same year. A more subjective decision is whether reporting outcomes over an extended number of years (such as 9 to 10 years) in days (such as 3500 days[14]) remains meaningful. In theory, readers could convert 3500 days to 9.58 years and then use the information reported. However, reporting should be as transparent as possible, making it simple for readers to interpret the information clearly. Therefore, articles that reported extended observation periods in weeks or months, instead of months or years were also considered to have not fulfilled the criteria.

Articles where the time intervals were not considered to be “meaningful” are identified individually in the results presented below.

A single investigator assessed whether the graphics fulfilled the remaining criteria.

5.3.4 Use and quality of reporting of statistical tests

The reporting of the type of statistical tests used for time to event analysis was tallied and explored. These criteria included the reporting of the

1. Type of survival statistic used (eg. life table analysis, Kaplan-Meier analysis)
2. Method used to calculate the standard error or confidence interval (eg. Greenwood’s, Clopper and Pearson’s)
3. Method used to compare different groups (eg. log rank test)
4. Type of summary figure used (eg. cumulative survival rate, mean survival time)

5.3.5 Assessment of high and acceptable quality levels

Survival curves and life tables that included all graphic quality measures were considered to be of high quality. Those graphics that included all measures except for the standard error or confidence interval were considered to be of acceptable quality.

Articles that reported all quality measures regarding the statistical tests in the methods of the article were considered to be of high quality. Those that reported the type of survival statistic and summary figure only were considered to be of acceptable quality.

5.3.6 Statistical analysis

Differences in the use of relevant words in the methods in the included ‘case’ articles compared to the active controls were analysed across the three word categories. The Pearson’s chi-square statistic was used. Where the expected cell counts were less than 5, the Fisher’s exact test was employed. Statistical significance was set at $P<0.05$. One investigator assessed objective quality criteria, and two investigators assessed subjective quality criteria. Agreement between investigators was assessed with Kappa.

5.4 RESULTS

5.4.1 Relevant words in the article (Tables 5.2)

The use of words for statistical technique (64% in the included 'case' articles, 0% in the active controls, Chi-square 86.95, P<0.001), statistical terms (18%, 0%, chi-square 17.92, P<0.001) or quasi-statistical terms (40%, 2%, chi-square 37.14, P<0.001) was significantly higher in the included 'case' articles than the active controls. Use of at least one of those 15 relevant words was significantly more common in the included 'case' articles than the active controls (77%, 3%, chi-square 107.62, P<0.001).

All included 'case' articles used a time-to-event analysis, but 36% of these articles did not include a specific time-to-event statistical term in their methods section. Across the three word categories, 23% of articles failed to use any of those terms. This made it difficult to identify that the studies had completed time-to-event analyses, and made it difficult to determine whether studies fulfilled the overall inclusion criteria as included 'case' articles for this body of research. Criteria that determined how articles were identified were outlined in chapter 2, and included additional assessment of the statistics in the context of the methods, results and figures.

The use of a quasi-statistical term (such as survival "rate") anywhere in the body of the article was common. The term "rate" indicates that an event is occurring over time. However, with 83% of included 'case' articles and 77% of active controls using these words, these terms are clearly not specific to the reporting of time-to-event analyses.

Table 5.2. Words used by authors in the methods section

Description	Included 'case' (n=95)	Active controls (n=91)
Group 1: Statistical Technique		
Actuarial method	5	0
Cox regression/hazard model	17	0
Hazard ratio	4	0
Kaplan-Meier	42	0
Life table/ Life table analysis	17	0
Lifetime analysis	1	0
Log rank	11	0
Survival analysis	10	0
Survival curve/ Survival plot	5	0
Survival function	0	0
Total frequency#	112	0
*Total articles**	64%, n=61	0%, n=0
Chi-square 86.95, P<0.001		
Group 2: Statistical term (outcome with time)		
Cumulative estimated survival/success/failure/rate	17	0
Total frequency#	17	0
*Total articles**	18%, n=17	0%, n=0
Chi-square 17.92, P<0.001		
Group 3: Quasi-statistical (outcome with time)		
Failure/ Complication rate	6	0
Survival/ Event probability	6	0
Survival/ Success/ Retention rate	24	2
Time-to-event/ Specific outcome	3	0
Total frequency#	39	2
*Total articles**	40%, n=38	2%, n=2
Chi-square 37.14, P=P<0.001		

 # Total frequency of term use. Some articles were allocated more than one term within each group.
** Total number of articles that were allocated at least one term within a given group.*

5.4.2 Presence of time-to-event graphics

Life tables and survival curves were present in 39% (n=37) and 48% (n=46) of the included 'case' articles. At least one of these graphic aids was used by 82% (n=78) of included 'case' articles, while 5% (n=5) used both a life table and survival curve. No active controls completed time-to-event analyses and, therefore, none used either of these graphics.

Kappa agreement between investigators that articles contained life tables or survival curves was 0.79 and 0.92 respectively. Disagreement regarding life tables concerned ten articles with unusual table presentations. Following discussion, all ten were judged to not fulfill the life table criteria. Disagreement regarding survival curves concerned four articles. Three had ascending curves, and two lacked stepped curves. Following discussion, all four were judged to be survival curves and were included for further assessment.

5.4.3 Presence and quality of life tables (Figure 5.1, Table 5.3)

As noted above, 37 of the 95 included 'case' articles included at least one life table. The construction quality of multiple life tables within the same article was consistent across each article, and the data gathered has been combined for tables within those articles. In total, 75 life tables were present across the 37 articles, with a median of 1, and a range between 1 and 9. In life tables within these 37 articles, 100% (n=37) gave the number of prostheses that were at risk, 57% (n=21) reported the loss to follow up, 89% (n=33) reported the number of events, 43% (n=16) reported individual survival rates, 92% (n=34) reported the estimated cumulative survival and 8% (n=3) reported the standard error or confidence interval at each time interval.

Figure 5.1. Quality of reporting of life tables (number of articles = 37)

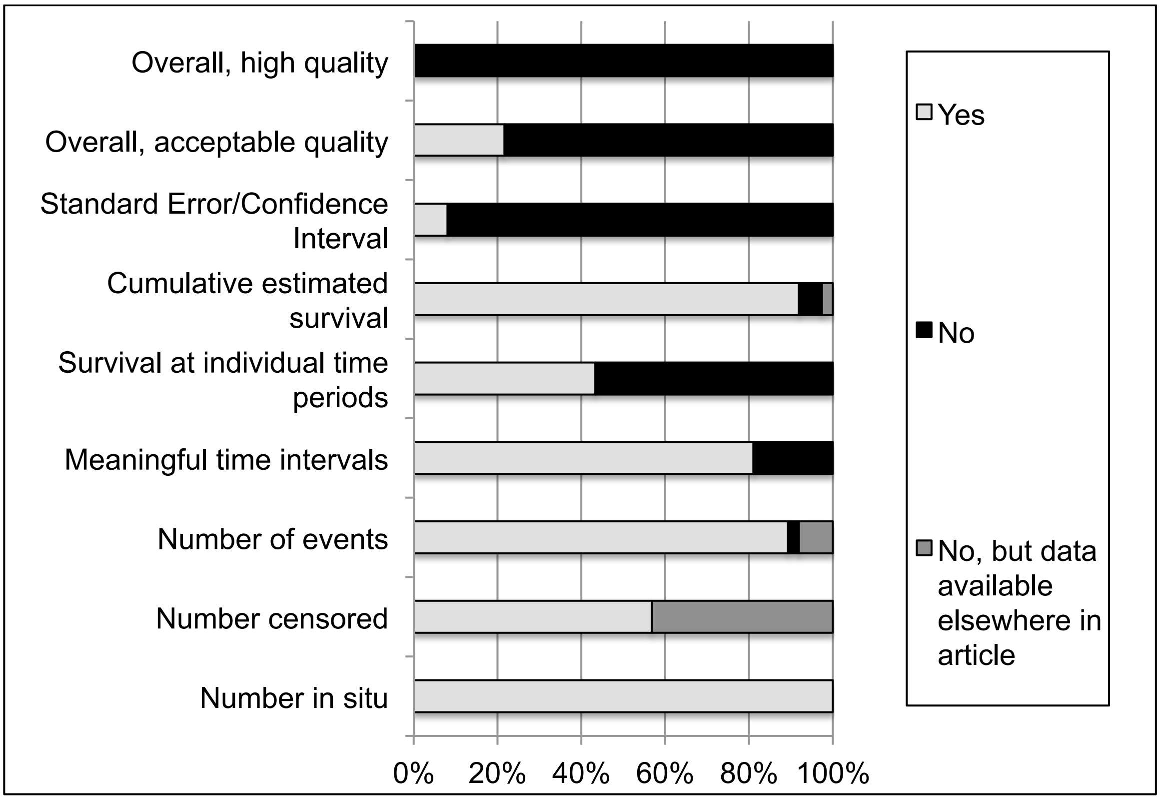


Table 5.3. Quality of reporting of life tables (number of articles = 37)

Did authors report the following?	Yes	No	No, but data available elsewhere in article	Percent of 37 articles (%)
Overall, high quality	0	37	0	0
Overall, acceptable quality	8	29	0	22
Standard error or confidence interval	3	34	0	8
Cumulative estimated survival	34	2	1	92
Survival at individual time periods	16	21	0	43
Meaningful time intervals	31	6	0	83
Number of events	33	1	3	89
Number censored	21	0	16	57
Number in situ	37	0	0	100

The data were reported across meaningful time intervals for 83% (n=31) of the 37 articles. The remaining articles omitted data (n=5, such as omission between 3 to 20 years,[15] 12 and 60 months,[16] 36 to 60 months,[17] 4 and 8 years,[18] and 5 to 9 years[19]), or only reported time intervals in words (n=1, such as "implant placement to implant loading").[20] Kappa for investigator agreement of this subjective measure was 0.72. Disagreement concerned three articles that omitted time intervals, and was resolved by discussion.

Across the 37 studies, no life table included all these quality measures, and thus none were classified as having "high" reporting quality. However, 21% (n=8) reached an "acceptable" reporting quality by including all measures except a standard error or confidence interval.

5.4.4 Presence and quality of survival curves (Figure 5.2, Table 5.4)

Of the 95 included 'case' articles, 46 included at least one survival curve. The construction quality of multiple survival curves within the same article was consistent across each article and the data gathered have been combined for curves within those articles. In total, 123 survival curves were present across the 46 articles, with a median of 2, and a range between 1 and 12. In survival curves within these 46 articles, 91% (n=42) used a stepped-curve, 43% (n=20) noted censored observations and 97% (n=36, out of 37 articles with comparative curves) used different graphic lines to represent different groups when applicable.

The data were reported across meaningful time intervals on the x-axis for 65% (n=30) of the 46 articles. Reporting problems included not commencing the graph at time zero (n=2),[21, 22] use of uneven time scales (n=2),[22, 23] and reporting in time periods which were not meaningful to readers and were not clearly required for study methods. Examples of these were 3500 days,[14] 250 days,[24] 600 weeks, [25] and 100 months[26] (n=4). Articles that reported outcomes greater than 3 years, and used axes scaled in months rather than years were considered not to be using time intervals that were meaningful to readers (n=9).

Of the remaining studies, 2 reported in weeks, 6 reported in months, and 22 in years. These were subjectively considered to have time scales that were meaningful both to the article and readers. However, some were unique enough to merit mention here. These included reporting in weeks up to 70 weeks;[27] reporting in 6 month intervals up to 36 months,[28] reporting in years based on participant age,[29] and in years based on post-eruptive age.[30] Kappa for investigator agreement of this subjective measure was 0.86. Disagreement concerned three articles utilizing unusual time periods, and was resolved by discussion.

None of the survival curves included the number of patients at different time intervals, or the standard error or confidence interval graphically. Of the 46 curves, 28% (n=13) included all other quality measures and were classified as having “acceptable” reporting quality.

Figure 5.2. Quality of reporting of survival curves (number of articles = 46)

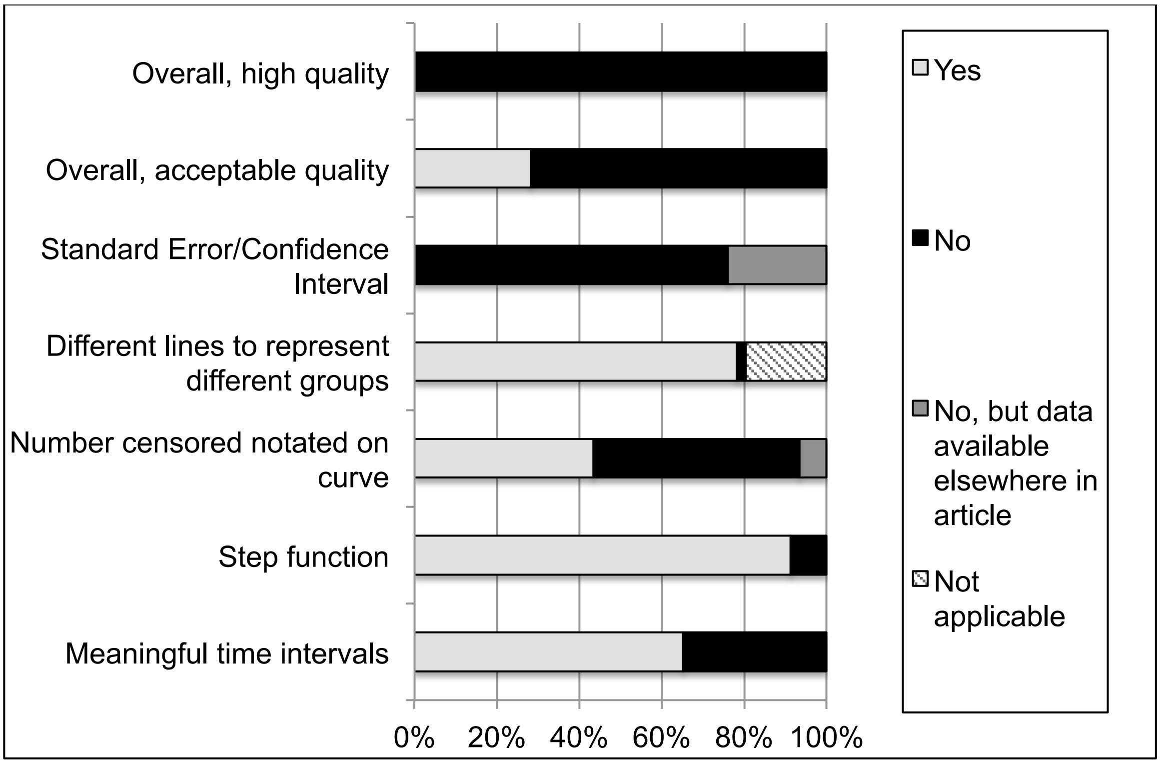


Table 5.4. Quality of reporting of survival curves (number of articles = 46)

Did authors report the following?	Yes	No	No, but data available elsewhere in article	NA	Percent of 46 articles (%)
Overall, high quality	0	46	0	0	0
Overall, acceptable quality	13	33	0	0	28
Standard error or confidence interval	0	35	11	0	0
Different lines to represent different groups	36	1	0	9*	97
Number censored notated on curve	20	23	3	0	44
Step function	42	4	0	0	91
Meaningful time intervals	30	16	0	0	65

Note: Nine articles did not compare different groups, and were excluded from the criteria of "different lines to represent different groups.

5.4.5 Use and quality of reporting of statistics (Figure 5.3, Table 5.5)

The type of survival statistic used was reported clearly by 76% (n=72) of the 95 articles, while 3% (n=3) reported conflicting information and 21% (n=20) did not report the type of statistic used. This information appeared in the methods section of 65% (n=62) of the articles, and in the results section or in the legend of tables for 5% (n=5) and 8% (n=8) of articles, respectively.

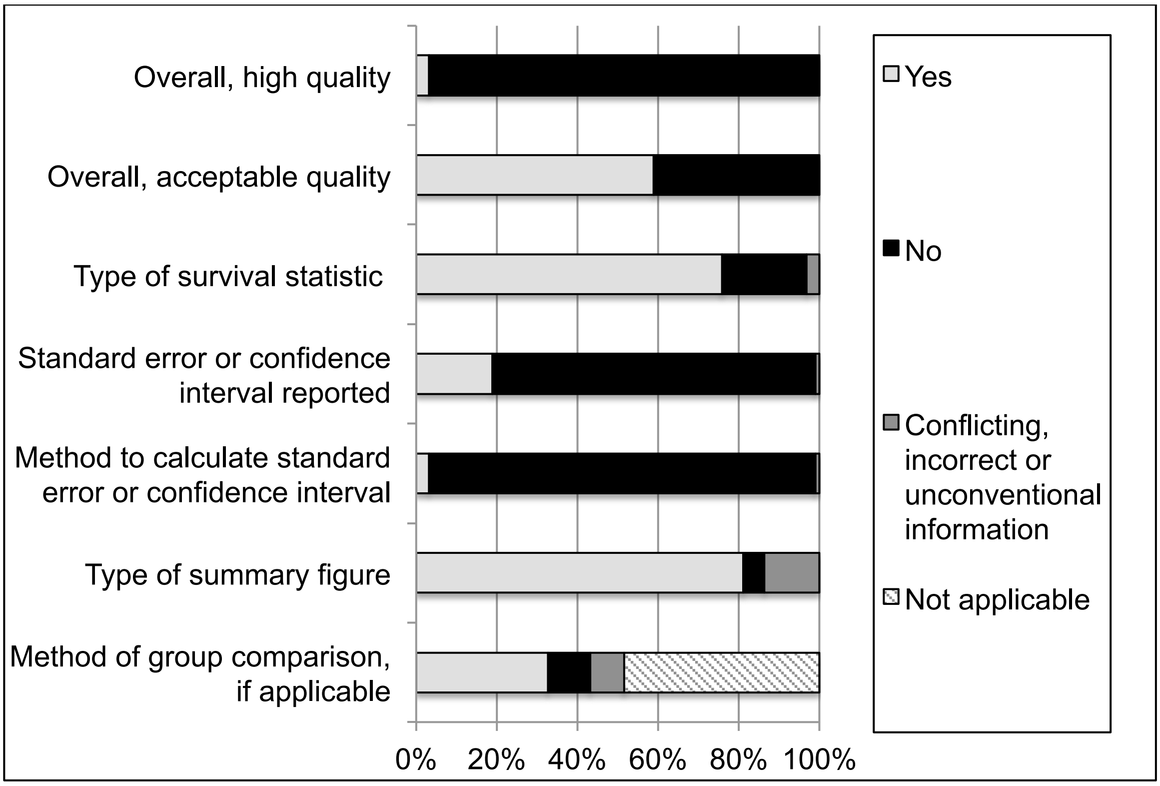
A standard error or 95% confidence interval was reported by 20% (n=19) of the 95 articles, with one of these articles incorrectly stating that the standard error was equivalent to the 95% confidence interval. The method of calculating these measures of variance was reported in only 3% (n=3) of the articles.

An analysis of the difference between the outcomes of groups was reported by 51% (n=49) of the 95 articles. The method to compare groups was reported by 85% (n=39) of these 49 articles. The most common method used was a log rank test (44%, n=17), but 16% (n=8) used a method which was incorrect for time-to-event data such as contingency tables, chi-square test, Fisher's exact test, binominal test for independent samples and T-tests.

The type of summary survival statistic used was reported by 95% (n=90) of the 95 articles. Of these 90, 14% (n=13) used a descriptor that was not specific for time-to-event analysis such as the survival probability, retention rate and percentage without complication. The estimated cumulative survival or cumulative survival rate was reported by 76% of the 90 articles (n=72), mean/median survival time was reported by 3% (n=3), annual failure rate by 3% (n=3), and 3% (n=3) used more than one of these figures.

Of the 95 articles, 3% (n=3) fulfilled all five categories of quality criteria when describing the survival analysis and were classified as having “high” reporting quality. A further 12% (n=11) did not define or report standard errors or confidence intervals, but fulfilled the other three categories. An additional 44% (n=42) reported the type of survival statistic and summary figure, fulfilling two of the five quality categories, and were classified as having “acceptable” reporting quality.

Figure 5.3. Quality of reporting of time-to-event statistics (number of articles = 95)



Note: Forty-six articles did not compare different groups, and were excluded from the criteria of “method of group comparison.”

Table 5.5. Reporting and quality of statistical methods

Criteria	Further Information	No.
Type of survival statistic	Life table analysis	26
	Kaplan-Meier	42
	Life table analysis AND Kaplan-Meier	1
	ADA guideline function (referenced)	2
	Modified Kaplan-Meier (referenced)	1
	Conflicting information (one method stated in the methods, and another elsewhere)	3
	Not reported	20
Type of standard error or confidence interval	95% Confidence interval of CSR, method not reported	11
	95% Confidence interval of CSR, Clopper and Pearson	1
	95% Confidence interval of CSR, marginal method for multivariate survival analysis	1
	95% Confidence interval of CSR, Jackknife method	1
	95% Confidence interval of mean/ median survival, method not reported	3
	Standard error, method not reported	1
	Incorrect use of standard error and 95% confidence interval	
	None reported	1
		76
How groups were compared	Not compared	46
	Log rank test / Cox Mantel	17
	Wilcoxon-Gehan	4
	Comparison of groups associated with Cox regression	8
	Contingency tables / Chi-square / Fisher’s exact test / Binomial test for independent samples / T test	8
	Compared 95% confidence intervals or standard errors, details of method not reported	2
	Multiple groups reported, compared statistically, method not reported	10
What summary figure was used	CSR	67
	CSR and mean survival time	2
	CSR and 95% confidence interval	2
	CSR and annual failure rate	1
	Mean survival time and 95% confidence interval	2
	Median survival time	1
	Annual failure rate	2
	Estimated survival / Percentage without complication / Probability of survival / Rate of survival / Rate of retention / Survival probability / Survival rate / Retention rate	13
	Not reported	5
Overall assessment of reporting quality	Included all measures of statistic reporting quality	3
	Included all measures of statistic reporting quality, but did not define how the standard error or confidence interval was calculated	11
	Reached a minimum quality standard by reporting the type of survival statistic and summary figure in the methods	42
	Did not reach the minimum reporting quality	39

5.5 DISCUSSION

This research found that the presence of high quality life tables, survival curves and statistical descriptions was uncommon in articles reporting time-to-event analyses in these top 50 dental journals, and that words used to describe the methods varied greatly between articles.

The presentation of results also varied greatly across the articles. Use of certain statistical technique descriptors and statistical terms in the body of the articles were unique to the 95 included ‘case’ articles when compared with the active controls, but were not used in all the included ‘case’ articles. As reported in Chapter 4, these words were also found to be significantly more common in the abstracts of those articles compared with the nearly 7000 control articles published in these journals in 2008.[31] It is not surprising that these words were unique to the included ‘case’ articles, as their presence triggered the eligibility of the articles for this research.

The absence of these terms from some included ‘case’ articles, however, was more of an issue of concern. Although the words used by authors did not clearly alert the reader that a time-to-event analysis had been completed, review of the statistics in the context of their other descriptions in the methods, results and figures allowed us to accept that the authors had indeed completed a time-to-event analysis. About one third of the articles did not adequately describe their time-to-event statistic in their methods, and 20% did not describe their statistic anywhere in their article. This made it difficult to determine whether articles did indeed conduct a time-to-event assessment, and it would make it difficult for indexers and readers to examine the research properly.

The authors of the included ‘case’ articles seemed to prefer using terms in a “quasi” statistical manner, rather than the definitive statistical words. It was common that the outcomes and statistics were described as “survival rates”, with this occurring in more than 80% of the included ‘case’ articles. This phrase indicates that an event is being monitored over time, and it is a specific type of ratio. Statistically, this term would relate to the reporting of the number of events (such as failures) per prosthesis per year. Unfortunately, it was used more generally, usually to indicate that “something was studied over time”, rather than to correctly and accurately describe a particular rate. Use of “quasi” statistical descriptors was equally commonly in the active controls as in the true ‘case’ articles. Again, they were used in a “quasi” manner, and not to accurately describe a specific statistic. Their presence makes it difficult to determine the type of analyses conducted by the authors, and whether a time-to-event analysis had indeed been done.

The quality of reporting was reviewed in most depth for the included ‘case’ articles, with particular attention to the use and quality of survival curves, life tables, and the statistics. This has not been studied previously for dental outcomes, and has rarely been reviewed for medical outcomes. The presence and quality of these three aspects of a time to event analysis directly impacts the reader’s ability to interpret the results, the indexer’s ability to classify the papers, and systematic reviewers’ ability to extract and reanalyse the data.

Over 80% of the 95 included ‘case’ articles used at least one graphic aid, either a life table or survival curve, to illustrate and report their time-to-event results. Approximately 5% used both, but one fifth used neither.

Despite relatively high use of these graphic aids, none of the life tables or survival curves included all aspects of the quality criteria. These criteria were extrapolated from those proposed by Altman and coworkers in 1995[12] which investigated the reporting of survival analyses in five clinical oncology journals in the latter half of 1991. Altman et al found that many articles omitted data and did not describe their methodology well. This led them to draft a set of recommended reporting criteria, which appear to be the only proposed criteria for reporting survival analyses.

Over half the included ‘case’ articles used life tables. The quality of these life tables was generally poor. No article had life tables that met all quality criteria, but approximately 20% reported all measures except for the standard error or related confidence interval. Reporting a measure of variance was rare, and only occurred in about 10% of the life tables. A life table analysis is a method of statistical analysis, and the table can also be used to graphically display results. Although the table is named after the “life table analysis” technique, it can also be used to display results from other time-to-event analyses such as Kaplan-Meier and actuarial methods. It provides readers with detailed information about the number of prostheses in situ, the number that have experienced “events” and those that have become lost to follow up or been censored for other reasons. From this information, the individual survival rates for each time period, the cumulative survival rates for consecutive periods and the reliability of those estimates (with a standard error or confidence interval) can be calculated. Readers and systematic reviewers can also extract information to allow comparison of similar time periods across different articles or studies, and to compare the reported treatment with other treatment modalities.

A good life table allows readers to track the event and censorship rate over the study period, and allows them to assess the reliability of the estimated cumulative survival. Unfortunately, approximately half of the life tables did not report censorship and nearly 10% did not report the number of events during each time interval. Without these three basic figures, the individual survivals, cumulative survivals or levels of variance cannot be assessed. Although authors provided some summary figures for their data, readers and systematic reviewers may be interested in reviewing different aspects of the data. Omission of these raw data from the articles prevents review of these calculations, and impedes further exploration and understanding of the results.

Nearly half the included ‘case’ articles used survival curves to aid their reporting. No survival curve reported the number of patients at risk at each time interval, and no survival curve included a graphic representation of the level of variance. The omission of the former is common, and its addition would actually prove challenging. The omission of the latter is also unfortunately common, but its inclusion is important for interpreting results, especially if multiple survival outcomes are being compared. Graphic representation of the standard error or confidence interval allows readers to assess the similarity of comparative results and also allows readers to review the change in the level of accuracy of the estimated cumulative survival over time. However, some readers forget that this summary figure, the estimated cumulative survival is simply that - an estimation. As patients or prostheses become censored, the amount of data decreases and the accuracy of the estimations also decreases. Inclusion of the level of variance highlights time periods when the data become unstable, and this is most obvious when the error bars become larger on the graph. Omission from the survival curve limits the ability of the reader to interpret the results.

Although data instability can be discussed in the text of the article, a graphic presentation is likely to have more impact.[32, 33]

Generally, the choice of the reporting time intervals, use of stepped curves and utilization of different lines for different groups was relatively well represented on the survival curves. The notation of censored observations, on the other hand, was not. Over half of the articles did not indicate censorship times. Where survival curves are presented in isolation to life tables, lack of censorship data again reduces the utility and external applicability of the data.

It was concerning that approximately one quarter of the included 'case' articles did not report basic details, such as the type of survival statistic that was used. Many health professionals do not understand health statistics in general,[34, 35] and how risks and probabilities[36] are interpreted specifically. Most commentary and research in this field has focused on medical doctors, but levels of statistical illiteracy would also extend to those practicing dentistry, and those relying on survival statistics[37, 38] to make everyday clinical decisions. Therefore, it is important that relevant statistical information is provided in articles, and that previous knowledge on the part of readers is not assumed. The survival analysis could use a variety of methods including Kaplan-Meier, life table or actuarial analysis. There are subtle differences between these, and the impact of different statistical assumptions on the estimated cumulative survival could be quite dramatic. When authors reported the type of survival statistic employed, only two-thirds did so in the methods section of their article, with details of that statistic being reported in the figure legends and results of 15% of articles.

Only 20% of the 95 included ‘case’ articles reported the variance (standard error or 95% confidence interval) of the summary figure, and, of these only 3 articles reported the statistical method used. The omission of confidence intervals and standard errors, and misunderstanding of what these figures mean had been reported as a common problem in the medical[39-41] and dental[42-44] literature. However, with the continued efforts of editorial teams and improved guidance to authors[45, 46] (such as the statistical notes by Bland and Altman in the British Medical Journal), these important figures are becoming more common in journal articles in general. For example, Bland recently reported a great improvement in use of confidence intervals in articles reporting individual participant data in the Lancet and British Medical Journal between assessments completed in 1972 and 2010.[4] In 1972, 1 out of 39 papers in the Lancet and 0 out of 32 papers in the British Medical Journal reported confidence intervals. This had improved to 15 out of 16 papers in the Lancet and 13 out of 15 papers in the British Medical Journal for a similar sample of papers in 2010.

The survival statistic provides an estimate for the rate of events in participants in the study over time. It is a single figure that informs readers about the outcome of the treatment for the patient group in the study. The confidence interval (CI) allows readers to review the precision of the point estimate, and is a guide to its external applicability to other, similar patient populations. For example, if the estimated cumulative survival was 85%, with a 95% CI ranging from 80% to 90%, then readers could be fairly confident that the survival would be at least 80% when they provided similar treatment to a similar patient population. However, if the estimated cumulative survival was 85%, and had a 95% CI ranging instead from 70% to 100%, then readers would be aware that the survival estimate was less certain, and could be as low as 70%, or indeed lower, if similar treatment was provided to a similar patient population.

Furthermore, if the statistics were used to compare the outcomes of different treatments, and it was found that the outcomes were not statistically significantly different between the treatments, readers could then review the confidence intervals of these samples. For example, if each sample had a narrow confidence interval, then readers could be more certain that there was no (or little) difference between these two groups than if the samples had wide confidence intervals. If there are wide confidence intervals for the samples, this might indicate that the sample size was too small to identify a difference that might be regarded as important for practice. Therefore, review of the confidence intervals, and levels of variance, should help with the correct interpretation and future use of the results of the study being reported.

Approximately half the included 'case' articles assessed differences in the outcome of two or more groups. Of these 49 articles, about 80% reported the method that they used, but over 15% used a method that was not statistically correct. Incorrect tests included the use of contingency tables, chi-square test, Fisher's exact test, binominal test for independent samples and T-tests. Most of these tests can be used to review differences in proportions, and initially seem to be well chosen but they cannot accommodate censored prostheses over time, and therefore their results are unreliable in the presence of censoring. Use of Log-rank, Cox-Mantel, Wilcoxon-Gehan or more detailed assessments with Cox regression would be more appropriate, and were used by about 60% of the 49 articles that included a comparison of groups.

The type of summary figure for the time-to-event outcome was reported by more than 95% of the included ‘case’ articles, but nearly 15% used a descriptor that was not specific for time-to-event outcomes. These descriptors could be considered “unconventional”. Over 80% used a mean/median survival time, annual failure rate or estimated cumulative survival, with the latter summary figure accounting for nearly three quarters of the figures. Unconventional descriptions included survival probability, retention rate and percentage without complication. Although these descriptors did not alert the reader that a time-to-event analysis had been completed, review of the statistics in the context of their other descriptions of the methods allowed us to accept that the authors had indeed completed a time-to-event analysis.

The quality of reporting of the statistics was generally low. Only 3% of articles met all criteria. A further 12% met all criteria, but did not define how the standard error or confidence interval was calculated. Additionally, almost half of the articles met only the minimum quality standard. To meet these minimum standards, articles were to report in the methods which survival statistic and which summary figure had been used.

Generally, the reporting quality of life tables and survival curves was low and the reporting quality of the statistics was also low. The words used by authors to describe their time-to-event statistics and results varied greatly, with 20% not reporting their statistical tests anywhere in their article, and 40% not reaching the acceptable reporting quality. Using quasi-statistical words rather than statistical terms was common in both the time-to-event articles and the active controls, and this is likely to cause confusion when reading these articles.

Results from Chapter 4 showed that the reporting quality of the abstracts of these time-to-event articles was poor, with more than two thirds not describing that time-to-event statistics was employed.[13] Instead, a great variety of words were used to describe that time-to-event outcomes had been studied. The inconsistency of descriptions and variety in language limits the ability of searchers to find such articles by conducting a textword search of bibliographic databases.

Furthermore, results from Chapter 3 found that the allocation of MeSH indexing terms these time-to-event dental articles in MEDLINE was inaccurate.[31] Statistically related MeSH were incorrectly omitted from 30% of the true time-to-event articles and incorrectly allocated to 15% of the active controls. Such errors compounds the challenge of identifying relevant articles in bibliographic databases, as the addition of MeSH to searches are unable to overcome all of the errors that arise with text-only searching.

MeSH searching has been considered more powerful than text-word searching,[47] or an integral tool to complement text word searching.[48] MeSH are allocated to articles after indexers have read the full text, theoretically bypassing abstracts of poor quality and enabling identification of articles that would have otherwise been missed by a search of the database. However, if the reporting quality of both the abstract and the article is poor, the correct allocation of MeSH is complicated, and the use of MeSH in a search strategy would not necessarily identify the articles.

5.6 IMPLICATIONS

The use of specific time-to-event statistical terms was common and distinctive to the included 'case' articles, but written descriptions were incomplete, confusing and were of poor quality. Use of at least one survival graphic aid was common, but pertinent details were regularly omitted from these and quality of construction was generally poor.

Overall quality of reporting of dental survival analyses was poor. It is likely that this will mean that relevant outcome articles are missed by people searching bibliographic databases and that they might struggle to make full use of those they do identify.

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CHAPTER 6. REVIEW OF THE "BURDEN OF THE PROBLEM" OF INDEXING AND REPORTING TIME-TO-EVENT DENTAL DATA

CONTENTS

6.0 BACKGROUND

If one thinks about challenges in the provision of effective care and the prioritization of research or action to meet these challenges, the “burden of disease” identified in this thesis, namely the “burden” of poor reporting or indexing of dental survival analyses, is considerable. To explore the magnitude of the problem, articles reporting dental survival outcomes were sought from 2008, identifying three groups of articles: those reporting dental outcomes in humans with (n=95, survival ‘case’ articles), and without (n=91, active controls) time-to-event statistics, and all other articles (n=6965, passive controls). In this chapter, I draw the evidence presented in the earlier chapters together, to show the foundation for the research reported in the chapters in the second part of this thesis.

As highlighted in earlier chapters, time-to-event articles have three concepts in common: an event is monitored, over time, and a survival statistic is calculated. The authors reporting such articles should describe three things: the event, such as failure; the time period, such as 10 years; and the statistic, such as an estimated cumulative survival. Then, when the article is indexed in a database, the indexers should choose indexing terms (such as MeSH) that capture those three entities: the event, that it was monitored over time, and the statistic.

Therefore, authors may state that they assess, evaluate or observe the performance, result or outcome; over a certain follow-up, duration or recall period; and report the probability of survival, loss rate, failure estimates, lifetime analyses, estimated success or cumulative survival.

Also, indexers may indicate the dental restoration failure, fatal outcome, retreatment or treatment outcome of longitudinal, follow up, prospective studies with time factors using life tables, survival analysis or Kaplan-Meier estimate.

If potential users of the research, or systematic reviewers, are to identify articles they must be able to “predict” the words that authors have used to describe their research (and conduct a free text search accordingly), or know which indexing terms were used by indexers (and conduct a MeSH search). Flaws in the quality of reporting by authors, flaws in the quality of indexing by indexers or flaws in the ability of the potential user to predict which words and terms have been used will mean that the articles are not found.

The initial test-search of 20 known survival articles, published in my 2011 MSc dissertation, found there was a substantial mismatch between the reporting content and the allocated indexing terms. Following these test findings, further research was undertaken, as presented in the preceding chapters of this thesis.

Time-to-event analyses are regularly used to report dental outcomes, but there is clearly a conceptual difference between “surviving” inanimate objects and surviving humans. I hypothesized that this nuance would affect how research was described and indexed, and thus affect retrieval yields from bibliographic databases: resulting in a level of waste in the literature.

In the preceding chapters, I explored how time-to-event data in the dental literature was indexed and reported.

To do so, a “gold standard” set of articles was identified and its composition reported (Chapter 2). The MeSH allocated to (Chapter 3), the words used by authors in the titles and abstracts to describe (Chapter 4), and the quality of reporting of the methods and results within the articles were assessed (Chapter 5).

Across the 95 dental survival articles that were published in the target journals in 2008 and included in MEDLINE, 17 relevant indexing terms were identified. The most frequently allocated MeSH within both the survival articles and active controls was “Dental restoration failure”. Its high frequency allocation was a surprising finding during the analysis. It was allocated to 77% and 52% of survival articles and active controls respectively, and 3% of the passive controls.

This MeSH, “Dental restoration failure” can be considered to be an outcome MeSH. Overall, the use of outcome MeSH was similar between the survival articles and the active controls (P=0.10), but they were significantly less common in the passive controls (86%, 77%, 10%, P<0.001).

Considering the statistical MeSH, significantly more were allocated to the survival articles compared with the active and passive control groups (67%, 15%, 1% P<0.001). However, although this seems positive for the quality of the indexing, out of the 95 survival articles, 69 used Kaplan-Meier or life table analyses, but only 29 were indexed with those terms. This accuracy of less than 50% is concerning. When all the survival statistical MeSH were considered together, none were allocated to one third of the survival articles, and some were incorrectly allocated to 15% of non-survival articles.

This shows that allocation of MeSH was inaccurate and inconsistent, making it difficult to identify such articles by a search of the MeSH index terms in MEDLINE. Hence, the “burden” of poor indexing of dental survival articles is substantial.

This raises the question: did the authors report their abstracts and titles with sufficiently high quality to counterbalance the burden of inaccuracies in MeSH? Chapter 4 showed that there were problems here, too.

Across the 95 survival articles, authors used 43 different words and phrases to describe their research in the titles and abstracts. The most frequently used of these words or phrases in the time-to-event articles was “survival rate”. This was a non-specific statistical term, a quasi-statistical phrase. It could report the proportion of events over time, or simply the proportion of events out of the total cohort. It was used in nearly 70% of the titles and abstracts of the dental survival articles, and it was also used by a relatively large proportion of the active controls, 40%; but by very few of the passive control articles (1.2%).

Use of time-related words was common in both survival articles (90%) and the active controls (80%). Their use was so common in the passive controls, with the words occurring more than 3400 times across the titles and abstracts, that the number of individual articles that used at least one of these words was not sought and not tallied as a frequency.

The number of general outcome-related words was also common across all articles. These words were found to be the most frequently used word-group (97% of survival articles, 91% of active controls and greater than 12,000 counts across the passive controls). In relation to the passive controls, these outcome words were so common that the number of individual articles that used at least one of these words was not sought, and the count was not converted into a frequency.

Unfortunately, relevant statistical words and phrases appeared in a minority of the abstracts and titles of the dental survival articles, being used in only 35% of articles' titles and abstracts. This was concerning, because these are the terms that will help readers find the time-to-event survival articles, and readers might focus on the titles and abstracts either in their electronic searching or when starting to read an article. If the authors do not make it sufficiently clear to readers that they have completed a survival analysis, it will be difficult to identify them. These articles risk remaining hidden in the literature, contributing to research waste.[1-3]

When seeking articles, potential readers would wish to use words in their search that will identify the relevant articles, and avoid articles that are irrelevant (or "false positives"). To this end, my findings might be considered to be encouraging. The active and passive controls used significantly fewer statistical words, with frequencies of 2% and 0.37% respectively, compared with 35% ($P<0.001$) for the survival articles.

In comparison, looking back at the outcome-related words, use was extremely common and similar across the survival articles and active controls (97% versus 91%, $P=0.10$). Of note, these words included two particularly common words: survival and success. Clearly, using the word "survival" in a search to identify a dental "survival" article would identify a fair number of irrelevant articles.

Overall, I have shown a great variation in the words used by authors to describe survival analyses in the titles and abstracts of such articles. This makes it difficult to identify such articles by a free text search. Combined with the challenges of MeSH searching, those seeking these articles would clearly struggle to identify many of them.

Going beyond the title and abstract and into the body of the articles, chapter 5 explored how the results were reported in the body of the time-to-event survival articles, and whether this reporting was of acceptable quality. Criteria for quality were assessed across three elements of the articles: the text of the article, life tables and survival curves. In summary, the criteria related to the reporting of the survival statistic, summary figure and confidence intervals, how groups were compared, the choice and graphic representation of the time interval, the clear reporting of numbers of patients experiencing events or censorship, and use of stepped curves.

The quality of reporting was considered high if all criteria were fulfilled, and adequate if all criteria with the exception of reporting confidence intervals were fulfilled.

The quality of reporting of the time-to-event statistical methods in the survival papers was poor for a large proportion of the articles, with 59% achieving acceptable quality and 3% achieving high quality. Life tables and survival curves were used in 39% and 48% of the time-to-event articles, respectively. Overall, use of at least one of these survival graphics was common, and at least one of them was present in 82% of those articles. Unfortunately, pertinent details were regularly omitted. Overall, construction quality was poor: 21% of life tables and 28% of survival curves achieved an acceptable standard and none achieved a high quality standard.

It is likely that the generally poor quality of the reporting in the time-to-event survival articles will make it more difficult for indexers to index them accurately, for searchers to then find them, and for users to understand the research completely if it was identified.

6.1 THE BURDEN OF THE PROBLEM

In the preceding chapters, I have shown how MeSH indexing of time-to-event dental data was inconsistent and inaccurate, how author descriptions of research in their abstracts and titles varied greatly, and that the use of graphic aids and the quality of survival-related reporting in the body of those articles was poor.

Errors in indexing and poor reporting quality mean that dental survival articles would not be readily identified when sought in MEDLINE by a MeSH or free text search, and that even if potentially relevant articles are found, it might be difficult to make best use of them because of the poor reporting quality in the full article.

To reduce the impact of this "burden", the following chapters focus on the second half of my research, to answer the question: What might be done to improve this reporting and indexing problem, so that studies with time-to-event dental data are not lost in the literature? This is approached from two points of view: looking towards the past, and looking towards the future.

Chapter 7 looks to the past. It reports the development of electronic search strategies to improve the identification of dental survival analyses that have been published. This addresses the problem of failing to identify relevant, existing articles, but not the problem of the quality of the articles. The search strategies aim to identify articles that have already been written and indexed in the databases.

Chapter 8 looks to the future. It describes the development of preliminary guidance to improve the reporting quality and indexing consistency of dental survival analyses that will be published in the future. Following validation (post-doc research), use of these guidelines by researchers should help to improve the quality of their reporting, and use of these guidelines by manuscript reviewers should improve critical feedback that can be given to authors. Improved quality of reporting may increase the likelihood that articles will be indexed accurately by bibliographic indexers, which should make them easier to identify and of greater use to readers when identified.

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CHAPTER 7. DEVELOPMENT AND VALIDATION OF ELECTRONIC SEARCH STRATEGIES TO IDENTIFY TIME-TO-EVENT DENTAL DATA

CONTENTS

7.0 SUMMARY

Objective: Articles reporting time-to-event and survival outcomes of dental prostheses in patients over time are challenging to identify in the literature. Research shows words used to describe dental survival analyses vary, and allocation of Medline (OVID) indexing terms is inconsistent. This undermines accurate article identification. This research aimed to develop and validate an objective search strategy that identifies survival analyses reporting of dental outcomes indexed in the bibliographic database MEDLINE (Ovid).

Methods: Systematic searches of the top 50 dental journals identified a gold standard collection of time-to-event articles published in 2008 (n=95, handsearched from 6955 articles) and 2012 (n=148, handsearched from 6514 articles) for search construction and independent validation. Descriptive words and indexing terms were identified objectively, and used to construct electronic search strategies. Performances of sensitivity, precision and number needed to read (NNR) were calculated.

Results: Performance of sensitive (92% sensitivity, 14% precision, 7.11 NNR), precise (93% precision, 10% sensitivity, NNR 1.07) and optimized filters (83% sensitivity, 24% precision, 4.13 NNR) were validated in the 2012 cohort. The construction and validation cohorts contained different journal titles and publication years, enhancing the generalizability of the results.

Implications: The research has successfully constructed validated search protocols with conservative sensitivities up to 92%, precisions up to 93% and NNR to identify

relevant records lower than two articles. This research has highlighted the impact that variation in reporting and indexing has on article identification, and should improve researchers ability to identify time-to-event dental articles. Future research is needed to verify the validity of the search protocols in alternative databases, and other fields of time-to-event reporting.

7.1 BACKGROUND

Bibliographic databases provide access to a digital collection of published literature such as articles, editorials and commentaries.

Databases commonly associated with medical fields include MEDLINE, Embase, CINAHL, PsycINFO and the Cochrane Library. Each contains different electronic records that can be searched with various platforms. When conducting a search, it is important to understand both the database and the search platform.

The database indexes information about the record in a uniform way. In MEDLINE, the National Library of Medicine (NLM) and their indexers organise records under a series of aliases that are derived directly from the article (Author, AU; Abstract, AB; Title, TI), that relate to the article (Journal subset, SB; Textword, TW), or that are created based on an understanding of the article (Subject heading, SH). A full list of fields and aliases for MEDLINE is available from the NLM.[1]

Searchers wishing to retrieve records from MEDLINE (Ovid) can complete a simple, field, or advanced search. A simple word search seeks records that include this "word" in the title and abstract. A field search seeks records indexed in special fields, including the field for MeSH. An advanced search involves programming terms that combine information (such as OR, AND), that seek words written in specific sequences (such as ADJ, FREQ) and look for truncation and wildcards (such as $, #, *).

Identification of articles is challenging when it is not clear which textwords are most relevant, and which data has been allocated to fields.

The burden of these problems in the subject of dental survival analyses has been analysed, and reported in the preceding chapters of this thesis. This showed that articles reporting time-to-event outcomes such as survivals and failures of dental prostheses in patients over time are challenging to identify in the literature. Assessment of a gold standard of time-to-event dental survival articles published in 2008 revealed that authors chose a confusing variety of words when describing their research in titles and abstracts.[2] Assessment also revealed that MEDLINE indexers allocated MeSH indexing terms inconsistently, with the most relevant terms of Survival analyses, Life tables and Kaplan-Meier estimate were omitted from 30% of time-to-event articles. I hypothesized that the survival of “inanimate objects” such as dental prostheses differed conceptually from the survival of “humans”, and that this may adversely impact accurate indexing.[3] The quality of reporting of the survival analyses within articles was also reviewed. Construction quality of survival figures was poor, with 0% of high quality and 25% of acceptable quality. Time-to-event statistical reporting was also poor, with 3% of high quality and 59% of an acceptable standard.[4]

Clearly, the reasons for inconsistent descriptives, reduced reporting quality and inaccurate MeSH indexing are multifactorial. The end result, however, is that retrieval of dental survival analyses from the bibliographic databases is challenging.

Errors in indexing, and problems with identifying articles is not a unique problem. A well known example relates to inaccurate indexing of randomized controlled trials

(RCTs). The problem was quantified by Dickersin and colleagues in 1994,[5] resulting in the development of the Cochrane highly sensitive search strategy (CHSSS) from a subjectively derived set of search terms. It aimed to retrieve RCTs from MEDLINE. This search strategy has been employed to aid systematic searches, and has also been used to identify and re-index RCTs in MEDLINE with the correct indexing terms.

Search terms can be derived subjectively[5, 6] or objectively.[7-9] The performance of the strategy is then assessed within the original dataset[7] or a validation cohort that had not been used to derive the search strategy, either split from the original dataset[6, 9] or new "gold-standard" records.[8, 10]

Haynes and colleagues[6] might be considered the pioneers of search methodology. They derived search terms subjectively from a survey of librarians and clinicians in the USA and Canada in 1994. The ability of such terms to detect studies of etiology, prognosis, diagnosis or therapy was assessed by reviewing the yield of articles from a handsearched gold standard. These search strategies have been integrated into the MEDLINE (PubMed) clinical queries interface.

Boynton and colleagues[7] identified 288 systematic reviews published in six journals between the years 1992 and 1995, and completed a word frequency analysis of the titles, abstracts and subject keywords to determine an objective list of possible search terms. They found that the objectively-derived filters appeared to out-perform previous subjectively-derived search strategies, but these performance assessments were evaluated in the same set of articles used to derive the search.

In the early 2000s, researchers further emphasized the importance of objective term determination and appropriate validation techniques,[9] with previous search strategies at times being revalidated on new and more recent data sets.[10]

7.2 OBJECTIVE

This research aimed to develop and validate an objective search strategy to identify survival analyses reporting dental outcomes that had been indexed in the bibliographic database MEDLINE (Ovid).

7.3 METHODS

Two gold standard article sets were identified. One was used to determine search terms objectively, and the other to validate search strategy performance.

7.3.1 Gold standard evaluation and validation articles

A handsearch of the 50 dental journals with the highest impact factor for 2008 identified articles reporting dental treatments in humans with time-to-event statistics (n=95) out of a total of 6955 articles. The search was systematic (Figure 7.1). Additional details regarding the search have been published previously[3], and outlined in chapter 2.

An independent validation cohort was derived from a different publication year. A handsearch of the 50 dental journals with the highest impact factor for 2012 identified articles reporting dental treatments in humans with time-to-event statistics (n=148) out of a total of 6514 articles. The search was systematic. (Figure 7.2)

The screening for the 2008 handsearch was repeated by a single investigator a second time after six months. The Kappa was 0.92. All articles identified as eligible (n=95) had been captured by both systematic handsearches, and, so, the laborious double screening of the 2012 articles was not done, because it would not be likely to identify additional articles of interest. Assessment of eligibility for inclusion was completed by two independent investigators for 2008 (Kappa = 0.86) and 2012 (Kappa = 0.83). Disagreement was resolved by discussion.

Figure 7.1. Flow chart of systematic search, from the top 50 dental journals in 2008

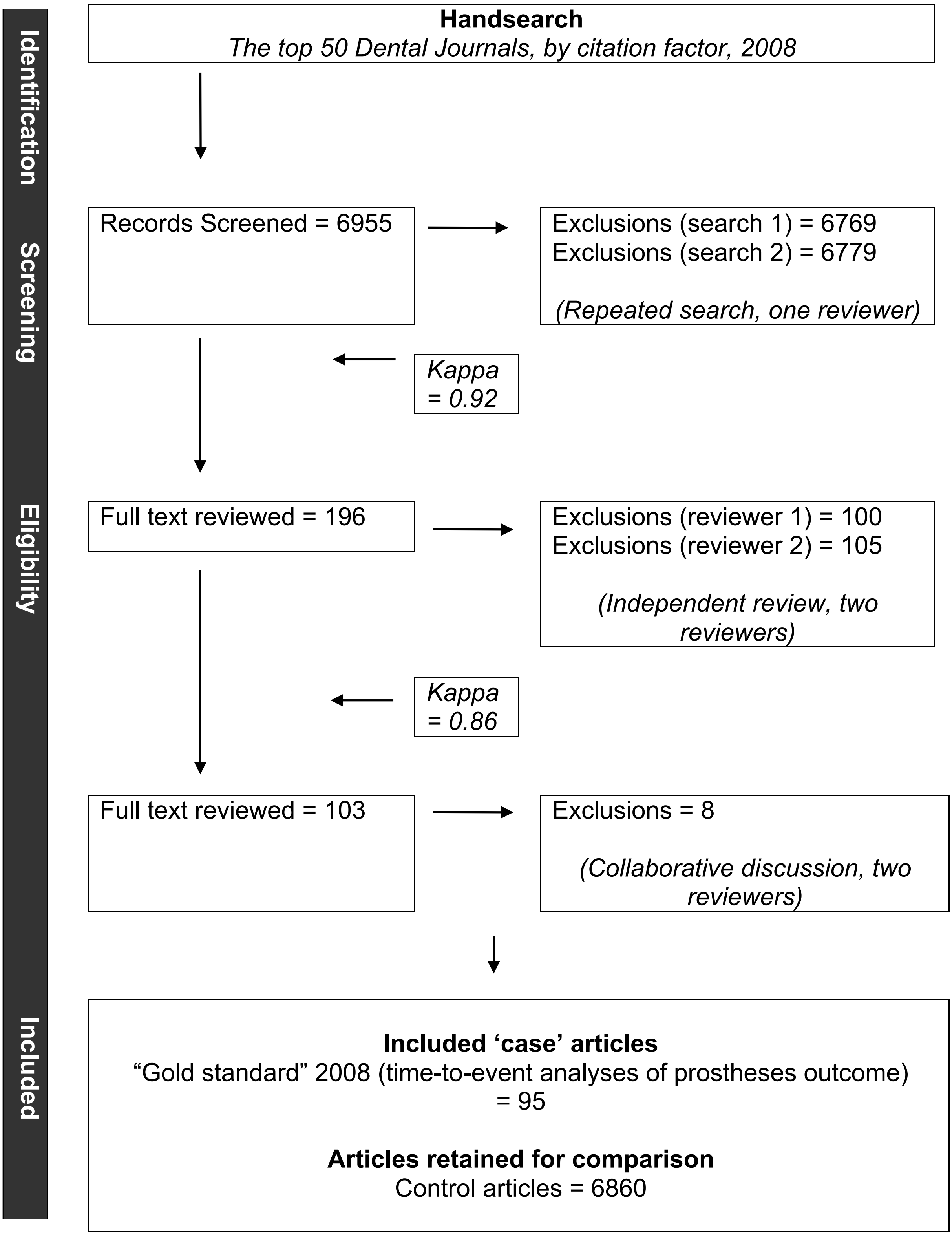
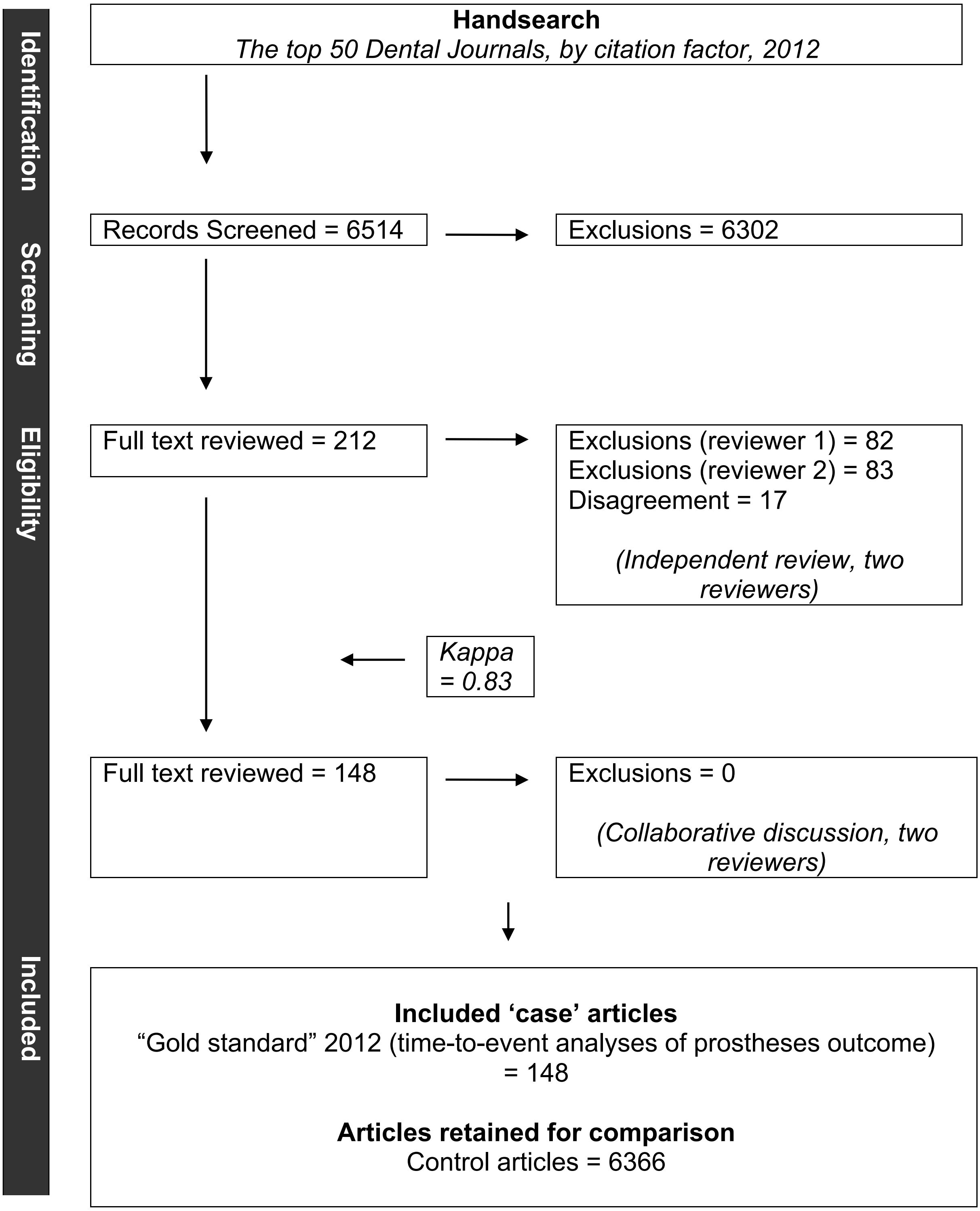


Figure 7.2. Flow chart of systematic search, from the top 50 dental journals in 2012



Inclusion criteria were prospective and retrospective studies that employed time-to-event statistics for reporting dental treatment outcomes over time in humans ("gold standard"). Time-to-event analyses were considered to be those using Kaplan-Meier, life tables, actuarial analyses, survival functions and reporting estimated cumulative survivals and cumulative survival rates. Studies that were in vitro, animal or reported outcomes unrelated to dental treatments (such as death, cancer, time to anesthesia) were excluded.

Across the two data searches, 60 different journals were included. Of those 60, 40 appeared in both searches, and 10 journals were unique to each data set (Table 7.1). The ISI impact factor was chosen as a way to identify journals in an objective and repeatable manner. The decision to validate the search strategy in journals in a different year, as well as in articles from different journals sets was made to improve the generalizability and external validity of the results.

7.3.2 Identifying search terms

The 2008 articles were analysed. MeSH indexing terms from the electronic database relating to time-to-event statistics, prosthesis outcomes, or the conduct of research over time were reviewed manually, and this identified 17 relevant MeSH.

The titles and abstracts of the 2008 article set were read and this identified 43 words or similar phrases that the authors had used to indicate that their research studied a dental outcome over a period of time with time-to-event statistics.

Table 7.1. Details regarding the 2008 and 2012 top 50 dental journals, and the distribution of "gold standard" articles

Journals	Rank		Impact factor		Gold standard records	
	2008	2012	2008	2012	2008	2012
ACTA ODONTOL SCAND	32	38	1.412	1.358	1	0
AM J DENT	36	-	1.314	-	3	NA
AM J ORTHOD DENTOFAC	33	34	1.327	1.458	1	0
ANGLE ORTHOD	-	45	-	1.184	NA	0
ARCH ORAL BIOL	24	31	1.649	1.549	0	0
AUST DENT J	41	37	1.22	1.371	1	1
BRIT DENT J	44	-	1.089	-	1	NA
BMC ORAL HEALTH	-	39	-	1.339	NA	0
BRIT J ORAL MAX SURG	33	10	1.327	2.717	0	3
CARIES RES	8	14	2.462	2.514	0	1
CLEFT PALATE-CRAN J	-	42	-	1.238	NA	0
CLIN IMPLANT DENT R	9	3	2.452	3.821	6	25
CLIN ORAL IMPLAN RES	6	6	2.92	3.433	12	12
CLIN ORAL INVEST	12	19	2.233	2.2	1	9
COMMUNITY DENT HLTH	49	-	0.969	-	0	NA
COMMUNITY DENT ORAL	10	26	2.418	1.797	0	1
CRANIO	-	48	-	1.111	NA	0
DENT MATER	7	4	2.882	3.773	2	0
DENT TRAUMATOL	35	-	1.316	-	2	NA
DENTOMAXILLOFAC RAD	39	46	1.229	1.148	0	0
EUR J ORAL IMPLANTOL	-	13	-	2.571	NA	3
EUR J DENT EDUC	46	-	1.024	-	0	NA
EUR J ORAL SCI	19	35	1.956	1.42	0	1
EUR J ORTHODONT	48	50	0.975	1.078	3	0
GERODONTOLOGY	47	24	1.014	1.828	0	2
IMPLANT DENT	28	36	1.505	1.404	2	6
INT ENDOD J	13	21	2.223	2.051	1	0
INT J ORAL MAX IMPL	17	23	1.978	1.908	15	16
INT J ORAL MAX SURG	31	32	1.444	1.521	1	1
INT J ORAL SCI	-	9	-	2.719	NA	0
INT J PAEDIATR DENT	43	-	1.141	-	1	NA
INT J PERIODONT REST	22	49	1.702	1.081	1	3
INT J PROSTHODONT	40	28	1.227	1.625	11	15
J ADHES DENT	25	-	1.638	-	5	NA
J AM DENT ASSOC	21	25	1.726	1.822	2	3
J CLIN PERIODONTOL	1	5	3.549	3.688	0	6
J CRANIO MAXILL SURG	38	29	1.252	1.61	0	2
J DENT	16	7	2	3.2	0	7
J DENT EDUC	45	-	1.087	-	2	NA
J DENT RES	2	2	3.458	3.826	2	7
J ENDODONT	5	8	2.953	2.929	2	2
J ORAL IMPLANTOL	-	47	-	1.148	NA	1
J ORAL MAXIL SURG	27	40	1.58	1.333	0	4
J ORAL PATHOL MED	15	20	2.144	2.055	0	1
J ORAL REHABIL	30	18	1.483	2.344	0	4
J OROFAC PAIN	37	16	1.263	2.387	0	0
J PERIODONTAL RES	18	22	1.966	1.99	9	0
J PERIODONTOL	14	15	2.192	2.398	3	5
J PROSTHET DENT	42	27	1.215	1.724	0	2
J PUBLIC HEALTH DENT	50	43	0.961	1.209	2	0
MOL ORAL MICROBIOL	-	12	-	2.648	NA	0
ODONTOLOGY	-	30	-	1.576	NA	0
OPER DENT	23	41	1.683	1.312	1	1
OR SURG OR MED OR PA*	-	33	-	1.495	NA	3
ORAL DIS	20	17	1.922	2.377	0	0
ORAL MICROBIOL IMMUN	11	-	2.336	-	0	NA
ORAL ONCOL	3	11	3.123	2.695	0	1
ORAL SURG ORAL MED O*	29	-	1.499	-	2	NA
ORTHOD CRANIOFAC RES	26	44	1.607	1.186	0	0
PERIODONTOL 2000	4	1	3.027	4.012	0	0

** Journals were renamed in 2011*

The list of indexing terms and words were compiled as each search continued, rather than being determined prior to reading the articles. This reduced preconceived bias of how survival analyses may be described.

In total, 89 individual search terms were identified.

7.3.3 Evaluating the search filter

Articles from the 2008 gold standard (n=95), and all articles from the 50 journals (n=6955) were identified in MEDLINE (Ovid) and placed into saved data sets. As the research progressed, additional articles were indexed online, resulting in an increase in the record numbers from 6955 to 7117. This is a consequence of continued indexing undertaken by MEDLINE, and means that articles might appear in MEDLINE several years after publication.

The 7117 articles were filtered by the individual search terms. The article yield was tallied and cross-referenced with the 2008 known-positives (the gold standard), allowing sensitivity, specificity, precision and NNR to be calculated (Figure 7.3). Search terms were used in two fields, textword (.tw) and subject heading (.sh). The textword alias limits the search to the content of the abstract and title. Use of terms to individually search the titles (.ti) or abstracts (.ab) was tested, but did not improve the search performance.

Figure 7.3. Search filter performance parameters

		Systematic handsearch 2008 (n=6955) and 2012 (6514)	
		Relevant "Gold standard"	**Not Relevant**
Search filter	**Retrieved**	a	b
	Not retrieved	c (n – a)	d (n – b)
	Total	n=95 (2008 cohort) n=148 (2012 cohort)	n=6860 (2008 cohort) n=6366 (2012 cohort)

Sensitivity

The proportion or percentage of relevant records identified by the search filter, in relation to the total number of relevant records

$$\frac{a}{a + c} = \frac{\text{Number of relevant records retrieved}}{\text{Total number of relevant records}}$$

Specificity

The proportion or percentage of non-relevant records omitted by the search filter, in relation to the total number of non-relevant records

$$\frac{d}{b + d} = \frac{\text{Number of non-relevant records omitted}}{\text{Total number of non-relevant records}}$$

Precision

The proportion or percentage of relevant records identified by the search filter, in relation to the total number of records identified

$$\frac{a}{a + b} = \frac{\text{Number of relevant records retrieved}}{\text{Total number of records retrieved}}$$

Number needed to read (NNR)

The number of records that need to be read before one relevant record is identified

$$\frac{a + b}{a} = \frac{1}{\text{Precision}} = \frac{\text{Total number of records retrieved}}{\text{Number of relevant records retrieved}}$$

Sensitivity x Precision

A summary figure to assess the balance between sensitivity and precision

$$\frac{a}{a + c} \times \frac{a}{a + b} = \text{Sensitivity} \times \text{Precision}$$

Combinations of the 89 search terms were tested by hand, the yield recorded and combinations then modified by trial-and-error. Search strategies maximizing sensitivity, maximizing precision and optimizing results were retained for validation.

There is no agreement in the literature defining "acceptable" levels of sensitivity and precision for a maximizing sensitivity search, maximizing precision search or an optimized search. Different groups have used different definitions, with the ability of the searches to perform to such levels dependent on the type of literature sought. For this research, I developed the search strategies to the following specifications:

- A maximizing sensitivity search was considered to have sensitivity greater than 95%
- A maximizing precision search was considered to have precision greater than 75%, therefore the number of articles NNR before finding a relevant article being no more than 1.3
- An optimized search was considered to have sensitivity above 75% and precision above 25%

7.3.4 <u>Validating the search filter</u>

Articles from the 2012 gold standard (n=148), and all other articles from the 50 journals (n=6514) were identified in MEDLINE (Ovid) and placed into saved data sets. As the research progressed, the numbers of articles in the saved sets fluctuated resulting in an increase from 6514 to 7123. Inclusion of these additional records will result in an underreporting of the performance parameters.

Research efforts were hampered by delay in indexing of some journal issues. Within the 2012 cohort, four journals containing 8 time-to-event articles and 81 other articles had not been indexed by March 2014. These were excluded but do not undermine the validation process.

The 2012 article cohort was filtered by the sensitive and precise search strategies. The article yield was tallied and cross referenced with the 2012 gold standard allowing the sensitivity, specificity, precision and NNR to be calculated.

7.4.5 Exclusion

To review the effect that records for journal content other than full articles may have on the performance parameters, I excluded editorials, letters and comments from the 2012 validation cohort, and recalculated the performance parameters.

7.5.6 Statistical analysis

Sensitivity, specificity, precision and NNR were calculated for the performance of the search strategies within both the 2008 and 2012 cohorts. In addition, the sensitivity multiplied by the precision was calculated as a summary figure to assess the balance between these parameters. Differences and average differences in performance between the 2008 and 2012 were calculated, and expressed as a percentage ± standard deviation.

7.4 RESULTS

Performance of individual and combined search terms in filtering the 7117 articles to identify the 2008 gold standard are outlined in tables 7.2 through 7.6.

7.4.1 Sensitive search strategy

Two highly sensitive terms (humans.sh, 100%; and result*.tw 92%) were eliminated from the search filter strings. The specificity and precision of the terms were 15% and 1.5%; and 42% and 2% respectively. They were considered to be non-helpful terms. In total, 23 individual search terms had sensitivities between 20% and 85%.

Ten individual search terms with the highest sensitivities were combined sequentially, and the performance of the search filters tested. Following initial assessment, the search strings were modified, all terms in the top 23 utilized, and the performances tested on the 2008 article cohort. Search strings with sensitivities above 95% were retained for validation. The performance parameters of five well-performing search strategies are presented in table 7.3.

The performance of each search strategy had decreased in sensitivity between the construction and validation phase. On average, this decrease was 9%±2%. The precision of all the search strings increased, on average by 2%±0.3%.

Search strategy A has been retained as the sensitive search filter to identify time-to-event dental analyses. It was validated with a sensitivity of 92%, precision of 14% and number NNR of 7.11 (8 articles).

7.4.2 Precise search strategy

Ten individual search terms with the highest precision were combined sequentially, and the performance of the new filters calculated. The precisions of three terms were between 75% and 95%, while seven terms were 100%. Five of those seven terms were unique, and two overlapped as truncations. All five unique terms with 100% precision were included in the precise search strategies. Following initial assessment, the other search terms were adjusted and additional terms with a precision greater than 30% were added.

Six search strategies were found with a precision greater than 75%, and these strategies had sensitivities varying from 14% to 58%.

The search filters were cross-referenced with the validation data, giving performance parameters (Table 7.4). The performance parameters of each of the search strategies decreased between the construction and validation performance by an average of 12±3% for sensitivity and 12±7% for precision.

Search strategies A (precision 93%, sensitivity 10%, NNR 1.07) and B (precision 81%, sensitivity 32%, NNR 1.37) have performed well during validation. Five of the six strategies have a NNR of below 1.5. Search strategy A has been identified as the precise search filter for time-to-event dental analyses.

Table 7.2. The performance of individual search terms in filtering the construction cohort (n=6955) to identify the 2008 gold standard

	No. Retrieved from 2008		Search Performance Parameters				
	Gold standard (n=95)	Cohort (n=7117)	Sen. (%)	Spec. (%)	Prec. (%)	Sen. x Prec. (%)	NNR
Adverse event*.tw	0	15	0.00	99.79	0.00	0.00	0.00
Aftercare.tw	0	2	0.00	99.97	0.00	0.00	0.00
Assess*.tw	22	1266	23.16	82.28	1.74	40.24	57.55
Assessment*.tw	2	394	2.11	94.42	0.51	1.07	197.00
Behaviour*.tw or Behavior*.tw	2	240	2.11	96.61	0.83	1.75	120.00
Caries rate*.tw	1	7	1.05	99.91	14.29	15.04	7.00
Censor*.tw	0	2	0.00	99.97	0.00	0.00	0.00
Clinical observation*.tw	1	13	1.05	99.83	7.69	8.10	13.00
Clinical perform*.tw	8	37	8.42	99.59	21.62	182.08	4.63
Clinical outcome*.tw	13	101	13.68	98.75	12.87	176.13	7.77
Complication rate*.tw	3	21	3.16	99.74	14.29	45.11	7.00
Complication*.tw	18	320	18.95	95.70	5.63	106.58	17.78
Cox proportional hazard*.tw	6	8	6.32	99.97	75.00	473.68	1.33
Cumulative estimated fail*.tw	0	0	0.00	100.00	0.00	0.00	0.00
Cumulative estimated success.tw	0	0	0.00	100.00	0.00	0.00	0.00
Cumulative estimated surviv*.tw	0	0	0.00	100.00	0.00	0.00	0.00
Cumulative fail* rate.tw	1	1	1.05	100.00	100.00	105.26	1.00
Cumulative fail*.tw	1	1	1.05	100.00	100.00	105.26	1.00
Cumulative Success rate.tw	4	4	4.21	100.00	100.00	421.05	1.00
Cumulative Success.tw	4	4	4.21	100.00	100.00	421.05	1.00
Cumulative surviv* rate.tw	16	17	16.84	99.99	94.12	1585.14	1.06
Cumulative surviv*.tw	22	25	23.16	99.96	88.00	2037.89	1.14
Dent* rehab* rate*.tw	0	0	0.00	100.00	0.00	0.00	0.00
Dental prosthesis repair.sh	2	14	2.11	99.83	14.29	30.08	7.00
Dental restoration failure.sh	73	289	76.84	96.92	25.26	1940.99	3.96
Drop out*.tw	1	4	1.05	99.96	25.00	26.32	4.00
Durability.tw	0	23	0.00	99.67	0.00	0.00	0.00
Effective*.tw	10	528	10.53	92.62	1.89	19.94	52.80
Efficacy*.tw	5	218	5.26	96.97	2.29	12.07	43.60
End point*.tw or Endpoint*.tw	0	14	0.00	99.80	0.00	0.00	0.00
Evaluat*.tw	68	2107	71.58	70.96	3.23	231.01	30.99
Experience.tw	6	226	6.32	96.87	2.65	16.77	37.67
Fail*.tw	56	467	58.95	94.15	11.99	706.86	8.34
Failure rate*.tw	13	37	13.68	99.66	35.14	480.80	2.85
Fatal outcome.sh	0	29	0.00	99.59	0.00	0.00	0.00
Follow up.tw	44	453	46.32	94.18	9.71	449.87	10.29
Follow up studies.sh	49	525	51.58	93.22	9.33	481.40	10.71
Fractur*.tw	16	409	16.84	94.40	3.91	65.89	25.56
Fracture rate*.tw	1	3	1.05	99.97	33.33	35.09	3.00
Graft survival.sh	2	23	2.11	99.70	8.70	18.31	11.50
Hazard ratio*.tw	2	5	2.11	99.96	40.00	84.21	2.50
Healing rate*.tw	1	2	1.05	99.99	50.00	52.63	2.00
Humans.sh	95	6072	100.00	14.88	1.56	156.46	63.92
Incidence.tw	4	199	4.21	97.22	2.01	8.46	49.75
Investigat*.tw	18	1214	18.95	82.97	1.48	28.09	67.44
Kaplan-Meier*.tw	20	36	21.05	99.77	55.56	1169.59	1.80
Kaplan-Meier estimate.sh	20	45	21.05	99.64	44.44	935.67	2.25
Life span.tw or lifespan.tw	0	7	0.00	99.90	0.00	0.00	0.00
Life table*.tw	6	6	6.32	100.00	100.00	631.58	1.00
Life tables.sh	15	16	15.79	99.99	93.75	1480.26	1.07
Lifetime analys*.tw	0	0	0.00	100.00	0.00	0.00	0.00
Long term.tw	28	324	29.47	95.78	8.64	254.71	11.57

Long term follow up.tw	3	31	3.16	99.60	9.68	30.56	10.33
Longevity.tw	1	22	1.05	99.70	4.55	4.78	22.00
Longitudinal studies.sh	13	160	13.68	97.91	8.13	111.18	12.31
Loss rate*.tw	4	6	4.21	99.97	66.67	280.70	1.50
Loss.tw	38	468	40.00	93.88	8.12	324.79	12.32
Maintenance.tw	6	83	6.32	98.90	7.23	45.66	13.83
Morbidity rate*.tw	0	1	0.00	99.99	0.00	0.00	0.00
Mortality rate*.tw	0	7	0.00	99.90	0.00	0.00	0.00
Mortality.tw	0	31	0.00	99.56	0.00	0.00	0.00
Observation*.tw	21	235	22.11	96.95	8.94	197.54	11.19
Outcome*.tw	36	588	37.89	92.14	6.12	232.01	16.33
Performance.tw	15	181	15.79	97.64	8.29	130.85	12.07
Probability of fail*.tw	1	4	1.05	99.96	25.00	26.32	4.00
Probability of Life*.tw	0	1	0.00	99.99	0.00	0.00	0.00
Probability of surviv*.tw	1	1	1.05	100.00	100.00	105.26	1.00
Problem*.tw	8	339	8.42	95.29	2.36	19.87	42.38
Prognosis.tw	4	105	4.21	98.56	3.81	16.04	26.25
Prognosis.tw	4	105	4.21	98.56	0.00	0.00	0.00
Proportional hazards models.sh	6	20	6.32	99.80	30.00	189.47	3.33
Prospective studies.sh	23	257	24.21	96.67	8.95	216.67	11.17
Prosthesis failure.sh	3	10	3.16	99.90	30.00	94.74	3.33
Rate*.tw	81	742	85.26	90.59	10.92	930.77	9.16
Reliable.tw	9	120	9.47	98.42	7.50	71.05	13.33
Response.tw	4	384	4.21	94.59	1.04	4.39	96.00
Result*.tw	87	4119	91.58	42.58	2.11	193.43	47.34
Retention estimate*.tw	0	0	0.00	100.00	0.00	0.00	0.00
Retention rate*.tw	4	11	4.21	99.90	36.36	153.11	2.75
Retreatment.sh	4	50	4.21	99.34	8.00	33.68	12.50
Retrospective studies.sh	37	342	38.95	95.66	10.82	421.36	9.24
Success estimate*.tw	0	0	0.00	100.00	0.00	0.00	0.00
Success rate*.tw	26	105	27.37	98.87	24.76	677.69	4.04
Success.tw	29	227	30.53	97.18	12.78	389.98	7.83
Surviv* estimate*.tw	2	2	2.11	100.00	100.00	210.53	1.00
Surviv* rate*.tw	59	149	62.11	98.72	39.60	2459.20	2.53
Surviv*.tw	76	306	80.00	96.72	24.84	1986.93	4.03
Survival analys*.tw	6	17	6.32	99.84	35.29	222.91	2.83
Survival analysis.sh	30	84	31.58	99.23	35.71	1127.82	2.80
Survival rate.sh	1	22	1.05	99.70	4.55	4.78	22.00
Time factors.sh	16	662	16.84	90.80	2.42	40.71	41.38
Time to event.tw	0	1	0.00	99.99	0.00	0.00	0.00
Treatment outcome.sh	51	574	53.68	92.55	8.89	476.99	11.25
Year* follow up.tw or Yr* follow up	13	105	13.68	98.69	12.38	169.42	8.08

Table 7.3. Sensitive search strategy: Search strategy A has been retained as the sensitive search filter to identify time-to-event dental analyses

			No. Retrieved		Search Performance		
			Gold Standard	Total Cohort	Sen. (%)	Prec. (%)	NNR
A	Dental restoration failure.sh or Surviv* rate*.tw or Cumulative surviv*.tw or Kaplan-Meier estimate.sh or success rate*.tw or year* follow up.tw or yr follow up.tw or long term.tw or clinic* performan*.tw or Kaplan-Meier.tw	**2008 cohort (n=7117)**	94	780	98.95	12.05	8.30
		2012 cohort (n=7123)	128	910	92.09	14.07	7.11
B	Dental restoration failure.sh or Surviv* rate*.tw or Cumulative surviv*.tw or Kaplan-Meier*.tw or Kaplan-Meier estimate.sh or success rate*.tw or rate*.tw	**2008 cohort (n=7117)**	92	943	96.84	9.76	10.25
		2012 cohort (n=7123)	123	1064	88.49	11.56	8.65
C	Dental restoration failure.sh or Surviv* rate*.tw or Survival analysis.sh or Success rate*.tw or Cumulative surviv*.tw or Kaplan-Meier*.tw or Kaplan-Meier estimate.sh	**2008 cohort (n=7117)**	91	480	95.79	18.96	5.27
		2012 cohort (n=7123)	121	584	87.05	20.72	4.83
D	Dental restoration failure.sh or Surviv* rate*.tw or Cumulative surviv*.tw or Kaplan-Meier*.tw or Kaplan-Meier estimate.sh or success rate*.tw	**2008 cohort (n=7117)**	91	456	95.79	19.96	5.01
		2012 cohort (n=7123)	118	553	84.89	21.34	4.69
E	Dental restoration failure.sh or Surviv* rate*.tw or Cumulative surviv*.tw or Kaplan-Meier*.tw or Kaplan-Meier estimate.sh or success rate*.tw or Surviv* rate*.tw	**2008 cohort (n=7117)**	91	456	95.79	19.96	5.01
		2012 cohort (n=7123)	118	553	84.89	21.34	4.69

Table 7.4. Precise search strategy: Search strategy A has been retained as the precise search filter to identify time-to-event dental analyses

			No. Retrieved		Search Performance		
			Gold Standard	Total Cohort	Sen. (%)	Prec. (%)	NNR
A	Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw or Life tables.sh	**2008 cohort (n=7117)**	25	26	26.32	96.15	1.04
		2012 cohort (n=7123)	14	15	10.00	93.33	1.07
B	Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw or Life tables.sh or Cumulative surviv*.tw	**2008 cohort (n=7117)**	41	45	43.16	91.11	1.10
		2012 cohort (n=7123)	44	54	31.43	81.48	1.23
C	Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw	**2008 cohort (n=7117)**	14	14	14.74	100.00	1.00
		2012 cohort (n=7123)	8	10	5.71	80.00	1.25
D	Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw or Life tables.sh or Cumulative surviv*.tw or Loss rate*.tw	**2008 cohort (n=7117)**	44	50	46.32	88.00	1.14
		2012 cohort (n=7123)	45	57	32.14	78.95	1.27
E	Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw or Life tables.sh or Cumulative surviv*.tw or Cox proportional hazard*.tw	**2008 cohort (n=7117)**	44	50	46.32	88.00	1.14
		2012 cohort (n=7123)	52	75	37.14	69.33	1.44
F	Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw or Life tables.sh or Cumulative surviv*.tw or Kaplan-Meier*.tw	**2008 cohort (n=7117)**	55	73	57.89	75.34	1.33
		2012 cohort (n=7123)	65	101	46.43	64.36	1.55

Table 7.5. Optimized search strategy: Search strategy A has been retained as the optimized search filter to identify time-to-event dental analyses

			No. Retrieved		Search Performance		
			Gold Standard	Total Cohort	Sen. (%)	Prec. (%)	NNR
A	Surviv* rate*.tw or Dental restoration failure.sh or Kaplan-Meier estimate.sh or life tables.sh or Cumulative surviv*.tw	**2008 cohort (n=7117)**	89	385	93.68	23.12	4.33
		2012 cohort (n=7123)	116	479	82.86	24.22	4.13
B	Surviv* rate*.tw or Dental restoration failure.sh or Cumulative surviv*.tw or Kaplan-Meier estimate.sh or success rate* or year* follow up.tw or yr follow up.tw or Kaplan-Meier.tw or Cumulative fail*.tw or Cumulative Success.tw or Life table*.tw or Probability of surviv*.tw or Surviv* estimate*.tw	**2008 cohort (n=7117)**	91	526	95.79	17.30	5.78
		2012 cohort (n=7123)	122	632	87.14	19.30	5.18
C	Surviv*.tw or Dental restoration failure.sh or Life tables.sh	**2008 cohort (n=7117)**	90	490	94.74	18.37	5.44
		2012 cohort (n=7123)	114	662	81.43	17.22	5.81
D	Surviv*.tw or Dental restoration failure.sh or Life tables.sh or long term.tw	**2008 cohort (n=7117)**	92	739	96.84	12.45	8.03
		2012 cohort (n=7123)	118	924	84.29	12.77	7.83

7.4.3 Optimised search strategy

The product of sensitivity x precision was calculated. Fifteen search terms with the highest product were combined sequentially. Use of terms beyond these fifteen did not aid search performance. The performances of the filters were calculated, and the search terms modified to test alternative arrangements, to seek improved performance parameters.

No search filter with a sensitivity above 75% had a precision greater than 25%. Three search filters had precisions of 23%, two between 20-23% and a further nine between 15-20%. Search filters with sensitivities above 75% and precisions above 15% were retained for validation. The performance parameters are outlined for four well-performing filters in Table 7.5.

Search strategy A had a sensitivity of 94% and precision of 23% during construction, and achieved a sensitivity of 83% and precision of 24% upon validation. The sensitivities of each of the search strategies decreased by an average of 11%±2%, while the precisions increased for three of the strategies with an average change of -0.5%±1%. The NNR to find a study of interest has remained below 5, at a level of 4.13. Search strategy A has been identified as the optimized search filter to identify time-to-event dental analyses.

7.4.4 Exclusion of editorials, letters and comments

When records marked to be editorials, letters or comments were excluded from the validation set, this resulted in a revised total of 6772 records. Review of all performance parameters for each of the three search strategies resulted in improvements of less than 0.1%

7.5 DISCUSSION

This research has developed three search filters for three different audiences. The sensitive filter for in-depth researchers, the precise filter for quick, everyday identification of evidence and the optimized filter for those wishing to balance the performance parameters.

The search strategies have been derived and validated objectively, enhancing external validity. However, there are some caveats.

The derivation and validation cohorts were from different, but recent, publication years. The searches performed well over this time, and are likely to perform well across the recent publication decade. However, reporting and indexing terms may have changed as survival reporting became more commonplace. Therefore, a limitation of the study is that the performance of the search strategies in identifying some historical articles remains unknown.

The choice of journals related to their ISI impact factor. This may have led to a sample of articles with higher reporting quality than the dental literature generally, facilitating keyword search accuracy. Impact factor was chosen as a standardizing feature, and not from a belief that this index was an industry standard. It has been used by other researchers,[6, 7, 10] but other indices such as the 5-year impact factor, immediacy index, Eigenfactor score could have been used instead.

In total, 60 journals were included across both journal cohorts, with 10 titles unique to each cohort. The search strategies performed well across both cohorts, with it therefore unlikely that performance was influenced by individual journals. This result improves the confidence in the generalizability of the strategies.

Keyword and MeSH search terms were identified objectively, with the lists growing as new terms were identified. Therefore relevant terms were not likely to be missed and the terms sought were not confined by preconceived ideas. Other researchers have employed subjective, or different objective search term identification methods.

Subjective methods have a higher risk that relevant terms are missed, and that some selected terms are erroneously considered specific for the topic. For example, research completed by White and colleagues[9] in 2001 found that the term "systematic" was not widely used in systematic reviews. However, subjective methods[5, 6] have been used effectively in the past, and created strategies that remain relevant to today's database users.

Objective methods have employed word analysis programmes, such as Idealist,[8] ListIndex[7] and Textalyser.[11] However, these programmes can identify non-specific words. For example, an analysis of the 23,423 words in all the abstracts of the 2008 gold standard using Textalyser[11] identified that the top 10 words used were implant, implants, survival, bone, patients, results, fdps (fixed dental prostheses), teeth, two and rate. Use of these words in a search string would result in 98% sensitivity, 2% precision, and 5700 false positives from the 7100 validation records.

Initial search strings were constructed objectively. Individual terms with the highest sensitivity, precision, or sensitivity-precision product (optimized) were identified. Search strings were compiled sequentially, as terms with the next highest performance were incorporated, much like a pyramid. Their performances were calculated, and then modified with an educated trial-and-error strategy. Other researchers have used computer programmes to test term combinations, allowing a highly objective exploration of the data. It is possible that the final subjective modifications may have missed other similar, or better search strategies. However, the trial-and-error system used was extensive, and I believe that most, if not all, maximizing combinations were identified.

Following construction, the search strategy was validated objectively. I completed a second systematic search of the 2012 dental literature, and identified 148 articles that reported time-to-event dental outcomes. The search strategy performances relate to Medline (OVID) records of 50 journal titles, limited to 2012 during the first week of March 2014. At that time, 7123 records were present. The records represent a contained dataset, eliminating inconsistency in calculations. The dataset, however, included over 500 unintended records, and therefore performance calculations and accuracy forecasts are conservative.

The validation records were identified systematically. Use of an independent cohort has allowed the performance of the search strategies to be validated. Calls for proper use of validation cohorts began in the early 2000s,[9, 10, 12] as search strategy methodology was maturing. Authors[9, 12, 13] have discussed the nature of the self-fulfilling prophecy, arguing that the performance of the terms will inevitably be greater in the construction dataset compared with other record cohorts.

The validation approach that I used found that sensitivity decreased across all three strategies, and that precision decreased in the precise strategy but improved in both the sensitive and optimal filters. The parameter that changed the most was sensitivity of the precise strategy, decreasing from 26% to 10%. However, as this strategy maintained a precision of 93% (3% lower than in the construction cohort), and was intended to maximize precision and not sensitivity, this reduction was not considered problematic.

Search terms included in the three strategies varied, and included a total of 13 textwords and three indexing terms. The search terms in the precise and sensitive strategies were unique, but overlapped with the optimized terms. The precise strategy included six textwords, as well as one indexing term “Life tables”, that had an individual precision of 94%, but sensitivity of 15%. It was the only indexing term to be present in the top 10 precise terms. The next indexing term was Kaplan-Meier’s estimate at number 14, but it had a precision of only 44%, and a sensitivity of 21%. However in considering this term it is important to remember that Kaplan-Meier’s estimate was a new indexing term in 2008, and indexers may have been employing the term Survival Analysis instead. Unfortunately, its precision was even lower, 35%, in the 2012 cohort. It was apparent that accurate allocation of indexing statistic terms to these articles was poor. When compared with the 2008 cohort, the performance of these terms within the 2012 cohort showed no marked improvements, with individual sensitivities of 4%, 19% and 30%, and individual precisions of 100%, 65% and 35%.

The sensitive search strategy included eight textwords and three indexing terms, of which Dental Restorative Failure had the highest individual sensitivity of 77%. This appears encouraging, until the precision of 25% is noted. The most common indexing term should have related to the survival statistic. Four different terms could be applied. If indexing allocation was accurate, a combined search of all four indexing terms should return a sensitivity of 100%. This was not the case. The performance in the 2012 validation articles of a combined search including “life tables.sh or Kaplan-Meier estimate.sh or survival analysis.sh or survival rate.sh” returned a 54% sensitivity and 32% precision. Clearly, inaccurate allocation continues to plague this literature.

The term Kaplan-Meier estimate was included in both the optimized and sensitive search. It was not present in the precise strategy. This is of note, as this term was only added to MEDLINE in 2007 and the database does not routinely back-index historical articles with new terms. Therefore, use of this term will not aid the retrieval of articles published earlier than 2006.

The performance parameter, NNR was adapted from the number needed to treat by Bachmann and colleagues in 2002.[8] I have used it in this research to help translate the search results into everyday language. For those seeking a sensitive search strategy, one out of every eight articles identified will be reporting dental time-to-event outcomes. This NNR sounds low, but in practical terms if the search identified 5000 articles, approximately 4300 would be false positives. The precise strategy maximized the NNR to 1.07, with one out of every two articles being relevant, while this was optimized to 4.13, one out of every five, for the balanced strategy. Again, in practical terms, the precise strategy would incorrectly identify about 300, and the optimized strategy would incorrectly identify 3800 articles out of a 5000 strong cohort.

The search filters may be applicable across the medical literature at large. The only specific dental term involved in the filters is the indexing term Dental Restorative

Failure. Time-to-event analyses are regularly used to report dental outcomes, but, there is a conceptual difference between “surviving” inanimate objects and surviving humans. My hypothesis that this nuance would affect how research was described and indexed, and thus affect retrieval yields when sought in bibliographic databases drove this research and it is unclear whether this may be problematic for other sections of the medical literature. Nonetheless, validation of these search filters within a gold standard cohort from the medical literature would be of value.

Although the search filters performed well in the validation cohort, continued review of their applicability over time is warranted. Quality of reporting has become a major topic of research, with high profile groups such as the Cochrane Collaboration and EQUATOR promoting improvements. It is hoped that the quality of reporting of time-to-event analyses will also improve, in the same way that randomized trial and systematic review reporting has improved following the release of reporting guidelines.[14] Improvements in accurate and consistent indexing may also occur, as indexers themselves become more knowledgeable about time-to-event reporting. As changes in the style of reporting occur, the performance of the search filters will alter, and validation on future datasets will be required.

7.6 IMPLICATIONS

The research has successfully derived and used objective search terms to construct validated searches that identified time-to-event dental articles with sensitivities up to 92%, precisions up to 93% and NNR to identify relevant records lower than two articles. The search protocols are generalizable across time and dental journals for MEDLINE (Ovid). Future research is needed to verify the validity of the search protocols in alternative databases, and other fields of time-to-event reporting.

This programme of research has highlighted the impact that variation in reporting and indexing has on article identification, and the proposed search strategies should improve the ability of researchers to identify time-to-event dental articles.

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CHAPTER 8. RECOMMENDATIONS FOR REPORTING TIME-TO-EVENT DENTAL SURVIVAL ANALYSES

CONTENTS

8.0 Summary

Objective: This research aimed to develop and present guidance on writing time-to-event survival analyses. Feedback from a selected group of experts in the dental field was sought to aid this objective.

Experts and Feedback: The proposed checklist, tables and figures, explanatory document and background information were sent to 78 experts in 19 countries by email. Over 60% of those invited to participate had published time-to-event related articles. Over 85% of experts were from the field of prosthodontics. Fifty-five acknowledged receipt, 46 completed feedback, 9 initial responders did not continue, and 23 of the invitees did not respond. Feedback received was across 14 domains (such as title, abstract, checklist, and example figures) and 9 themes (such as endorsement of the importance of the guidance, editorial recommendations and suggestions for additions). Out of the 130 comments received, almost all were used to revise the draft guidance. Opinions on the modified document, which is presented here, have not been sought as part of this DPhil research; since the next step (as post-doctoral research) will be to seek endorsement and validation of the guidelines.

Guidance: The guidance includes an explanatory document and abbreviated checklist; lists of MeSH and words that may be used to describe the research; as well as examples of life tables, survival curves and abstracts.

Implications: Experts in the dental field have endorsed the importance of improving the quality of reporting of studies that present time-to-event survival outcomes, and indicated that the draft guidance document was pertinent, timely, and well written.

Endorsement of the guidance by key journals in the prosthodontic and periodontal fields will expose authors and manuscript reviewers to the recommendations, and this should help to improve the reporting quality of these articles over time. The interest of the participants in improving reporting quality of time-to-event survival analyses indicates that this dental community would support post-doctoral research validating the guidelines.

8.1 BACKGROUND

My research has shown that the quality of reporting of time-to-event outcomes, survival outcomes, in the dental literature is poor[1-3], and that this directly impacts on the ability of potential users of this literature to find the published articles and make use of the data that they do find.

Historical sources indicate time-to-event sciences commenced in Rome in the 3rd century[4], were used further by Edmund Halley in the 16th century, and had an entry into main-stream sciences in the modified survival analyses forms of actuarial estimators in 1912[5] and Kaplan-Meier estimators in 1958[6]. Increased use of this suite of statistical techniques was also driven during World War II, when the reliability of military equipment and exploration of mortality data[7] was of high interest.

As highlighted in Chapter 1, time-to-event analyses are regularly used to report dental outcomes. Research reported in previous chapters has emphasized the three factors that are common to such outcomes: an event is monitored, over time, and an estimated cumulative proportion is calculated for these events.

Events are transitions from one state to another. They can relate to a broad range of medical and non-medical topics such as time-to disease, time-to recurrence, time-to death, time-to recovery, time-to equipment failure, time-to earthquakes, time-to stock market crash.

Prior to commencing this DPhil project, previous research had been published which highlighted concerns about the reporting quality of survival analyses. These findings have been discussed in Chapters 4 and 5 but, to set the scene for the guidance proposed in this final research Chapter, a summary of these previous findings has been included again below.

Over 20 years ago, Altman and colleagues[8] raised concerns regarding the reporting quality of cancer-related time-to-event outcomes in the medical literature from 1991. Continuing concerns were identified almost 10 years later, in 2002[9] during an assessment of a larger sample of literature; and again in 2011[10]. A systematic review in 2012[11] of outcome measures used to evaluate dental implants highlighted that reporting quality continued to be problematic, and certainly extended beyond traditional medical fields. Each research team recommended changes to reporting approaches, but the research from this DPhil in relation to dental time-to-event outcomes[1-3] has again highlighted that the message, at least in dentistry, is not reaching the target audience.

Authors have commented on the ethical implications of poor reporting quality, stating "it is a moral duty of researchers to publish as clearly as possible"[12] and "inadequate reporting borders on unethical practice when biased results receive false credibility"[13] This is of concern across health care, and researchers have published guidelines aimed at improving reporting transparency and quality of specific study designs such as systematic reviews (PRISMA),[14] randomized trials (CONSORT)[15] and observational studies (STROBE);[16] and general guidelines, such as Standards of Quality Improvement Reporting Excellence (SQUIRE).[17] Additionally, specific resources collated by the database of EQUATOR[18] are available. A guideline for compiling guidelines has also been published.[19]

Generally, guidelines relate to reporting study designs, but at least two of these also provided recommendations on statistical reporting. The 2009 update of the QUOROM systematic review guidelines, PRISMA, incorporates both study methodology (systematic reviews) and statistical technique (meta-analyses),[14] and STARD included reporting information for diagnostic test accuracy.[20] However, guidance for specific statistical reporting remains sparse for controlled trials and cohort studies.

A new guideline, SAMPL[21] was released in 2013, providing guidance for authors on the reporting of common statistical techniques. The authors commented that despite a review of biomedical statistical reporting highlighting problems from as far back as 1966,[22] problems with reporting quality remained “widespread”, “potentially serious” and “largely unsuspected by most readers”.

The document I describe in this chapter suggests guidance for authors, manuscript reviewers and journal editors for reporting of time-to-event dental survival analyses. It is complementary with current recommendations provided by STROBE and CONSORT, and covers:

1. Choice of keywords
2. Description of time-to-event details in the title and abstract
3. Description of the time-to-event details in the methods and results of the study
4. Representation of survival curves and life tables in the results
5. Discussion of time-to-event study characteristics that may affect result interpretation and generalizability, and may contribute to study limitations

The first full draft of the guidance was sent to a purposive sample[23] of authors, journal editors and stakeholders who have an interest in dental survival analyses and evidence based dentistry. They are not considered to be representative of dentistry or time-to-event methodologies as a whole, but were identified as having expertise in this area and the potential to contribute to improvements in the guidance.

8.2 OBJECTIVES

The objective of this research was to develop and present guidance on writing reports of studies that include time-to-event survival analyses. Feedback from a selected group of experts in the dental field was sought to aid this objective.

8.3 CONTACTING AND RECEIVING FEEDBACK FROM EXPERTS

The proposed checklist, tables and figures and explanatory document were emailed to 78 experts. I also sent a one page summary of the findings of my research so far, to provide them with background information. The emails were addressed personally, and included a personalized introduction explaining why the individual was being approached to participate. Following this introduction, all emails contained the following correspondence:

"The recommendations are meant for use by authors when writing articles, as well as reviewers when assessing manuscripts. I plan to review feedback and critique to help improve the guidelines. Would you be willing to look through the proposed recommendations? In particular, I am keen to seek your opinion on the proposed checklist, and the example generic life tables and survival curves. I would be very grateful for any feedback, positive or critical."

A follow up request was sent to non-responders two months after the initial correspondence, and an additional request was sent the following month. No one was contacted by the telephone or voice-over-internet.

Each of the experts that I contacted had published journal papers, and was a reviewer for at least one journal. Out of the 78 experts, 48 were contacted because they had published either time-to-event articles or systematic reviews that included time-to-event articles, 10 because they were editors of dental journals, 10 to increase responses from a larger international body, 7 because they were academic staff for specialist dental training programmes, and 3 because it was known they had a specific interest in evidence based dentistry.

Of the 78 experts, 55 were current or retired directors, chairs or deans of university programmes, of which 10 were also current or retired journal editors. Nineteen were involved in teaching at universities and 3 were in full time private practice. Ten were periodontists, 66 were prosthodontists, 3 were statisticians or methodologists, 1 was an endodontist and 1 was an orthodontist; and 3 had double dental specialty qualifications. They resided in 19 different countries.

A total of 55 invitees acknowledged receipt of the information and stated that they wished to be involved. Many stated that they were quite busy, and intended to respond within a few weeks. I received 46 complete responses, with 9 of the initial responders not continuing. Figures 8.1 to 8.5 provide information on the country of residence, specialty of the expert, reason for inclusion and academic/practice background of the responders, initial responders and non-responders.

Responses were received by email. I did not provide a structured feedback form, in order to allow responders to explore the documents without constraints. All 46 were in paragraph form, and 8 included an edited, marked-up document. All feedback received was usable, and I reviewed and summarized it into domains and themes.

Figure 8.1. Country of residence of experts contacted

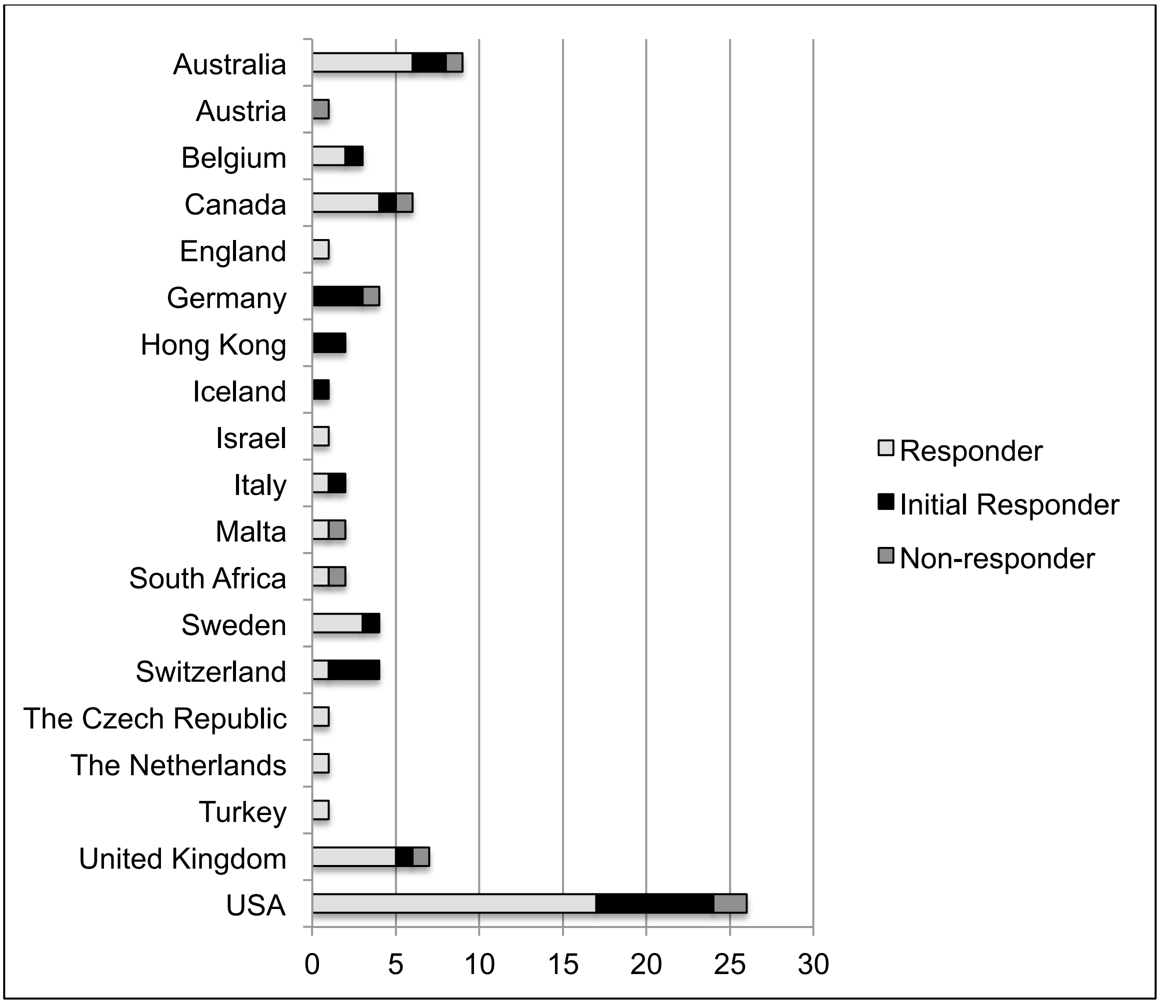


Figure 8.2. Specialty field of experts contacted

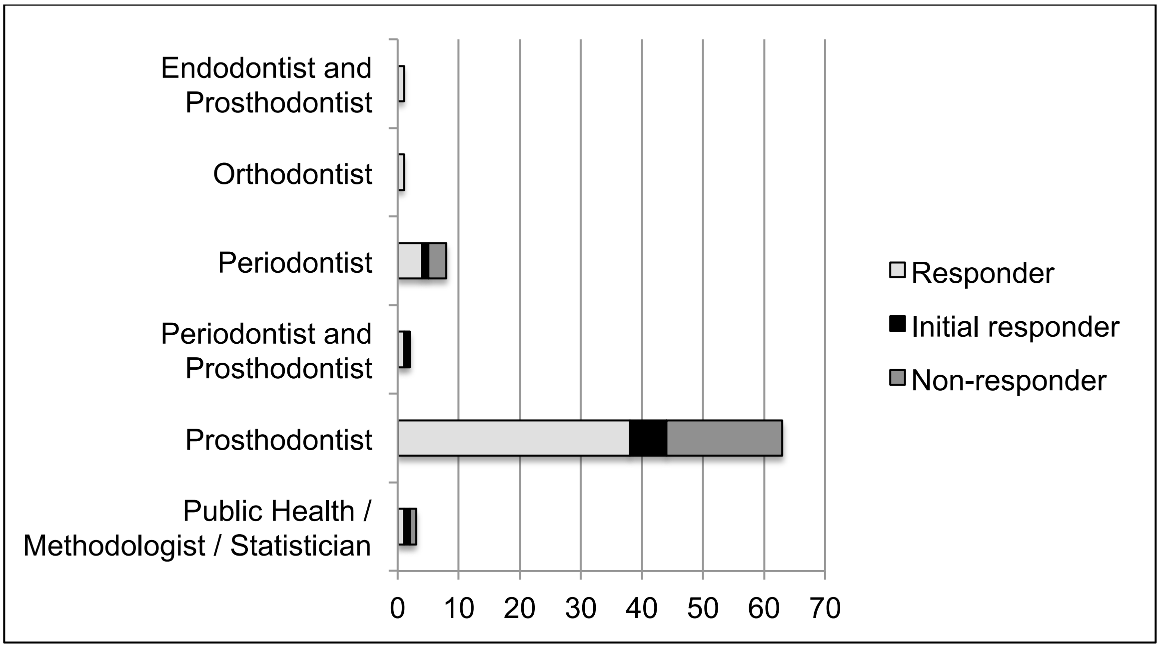


Figure 8.3. Reason experts were invited to participate

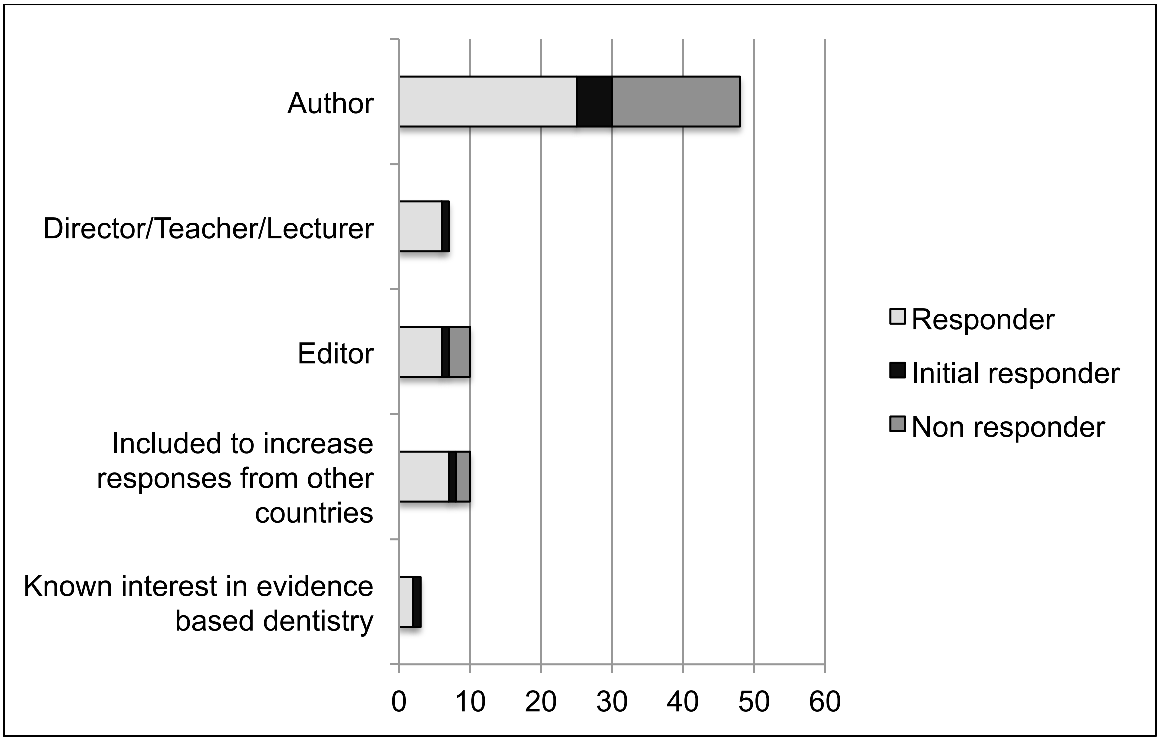


Figure 8.4. The academic/practice background of experts contacted

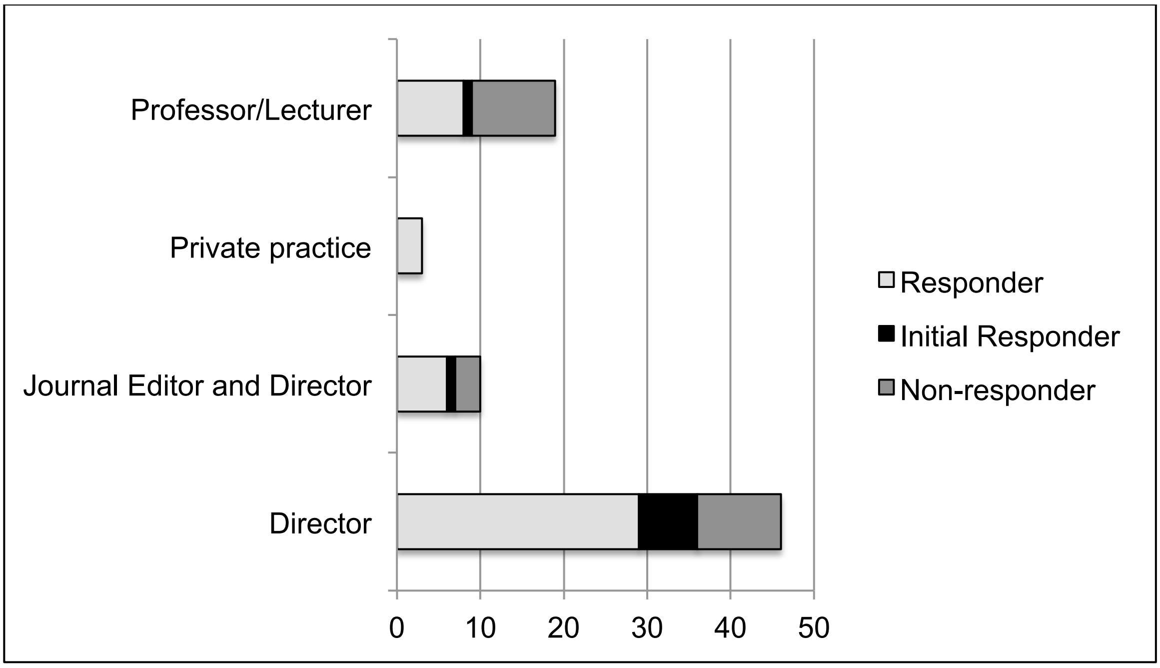
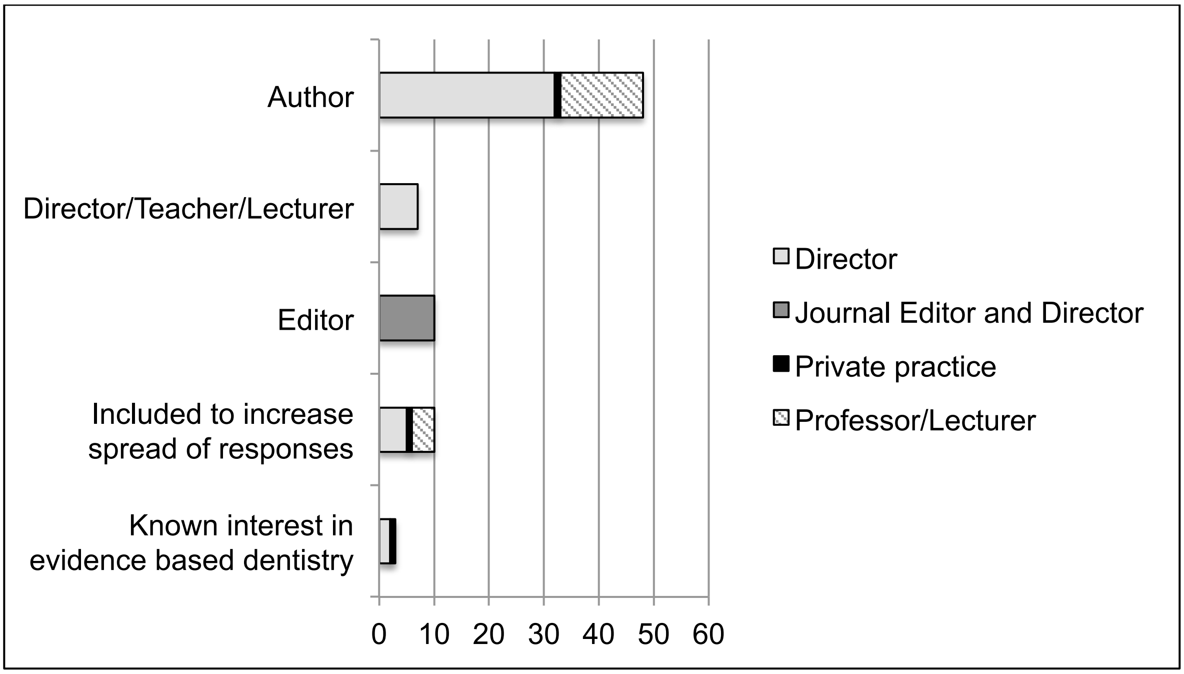


Figure 8.5. Cross reference of reasons why experts were invited to participate, and their academic/practice background



Feedback was naturally structured around the topic headings and explanatory tables within the documents. The areas covered in these domains included (Figure 8.6):

1. Title and Abstract = 5
2. Aims = 2
3. Methods = 6
4. Definition of outcomes = 7
5. Discussion and conclusion = 2
6. Example life tables = 9
7. Example survival curves = 10
8. Proposed checklist = 8
9. MeSH table = 14
10. Word list table = 9
11. Statistical analysis = 3
12. Editorial recommendations = 15
13. Suggestions for additions = 28
14. Additional comments = 12

I also identified 9 themes within the comments (Figure 8.7).

1. Endorsement of merit or importance of the proposed guidance n = 20
2. Endorsement of quality of writing and helpfulness of examples provided n=18
3. Endorsement of comments n=10
4. Editorial recommendations n=15
5. Request for clarification n= 11
6. Highlight possible problems n=13
7. Suggestions for addition n=28
8. Suggestions for abbreviation n=8
9. Comments exemplifying how reporting problems have impacted respondents = 7

The feedback included 130 comments from the 46 responders across 9 themes. No respondent provided feedback across all 9 themes. The maximum covered by any single responder was 5 of the themes, with a median of 2 and a range of 1 to 5. The proportion of feedback across the 14 domains and 9 themes is depicted in Figures 8.6 and 8.7. A summary of feedback provided across the 9 themes, and changes made to the guidance document in response is outlined in Appendix 11.3.

Out of the 130 comments received, approximately 90% were used to revise the draft guidance. Opinion on the modified document was not sought at this stage, because efforts to have it endorsed and validated will be part of a post-doctoral research project. In the following sections, I present the version of the guidance that I prepared following the feedback. This is followed by a discussion of the feedback that had been received and how this had been used in the revised guidance.

Figure 8.6. The proportion of feedback across the 14 domains

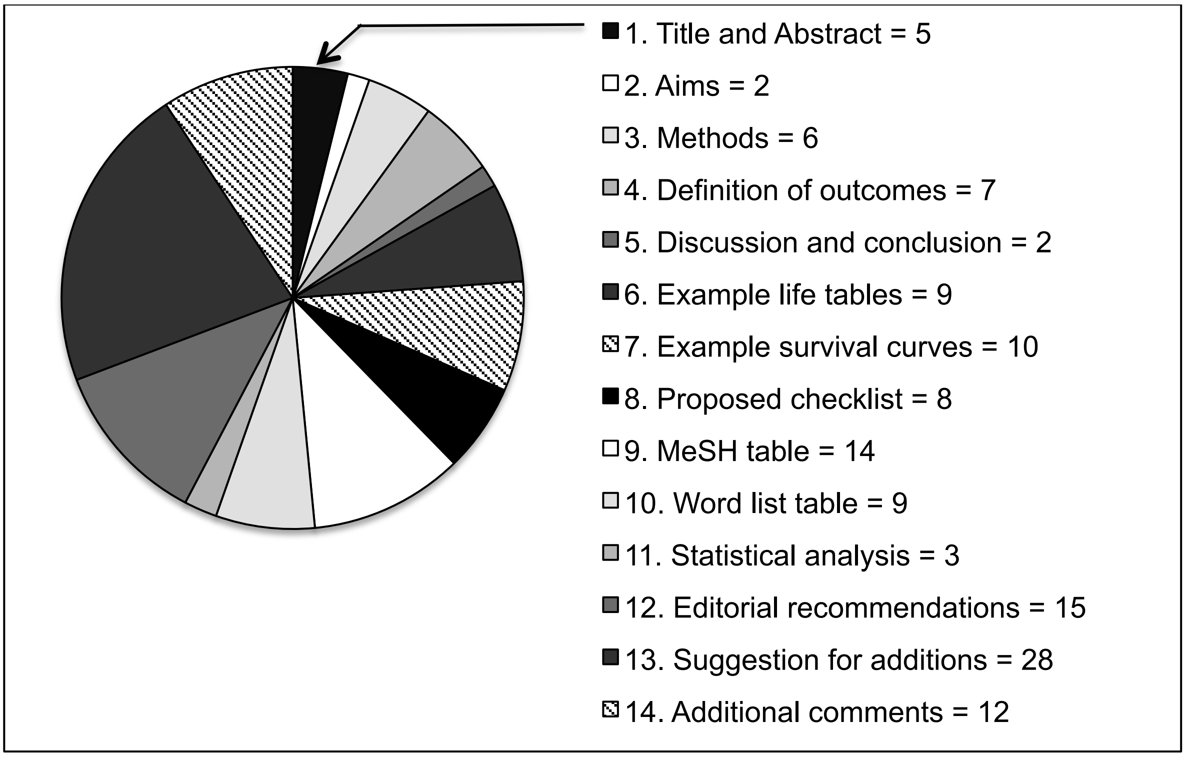
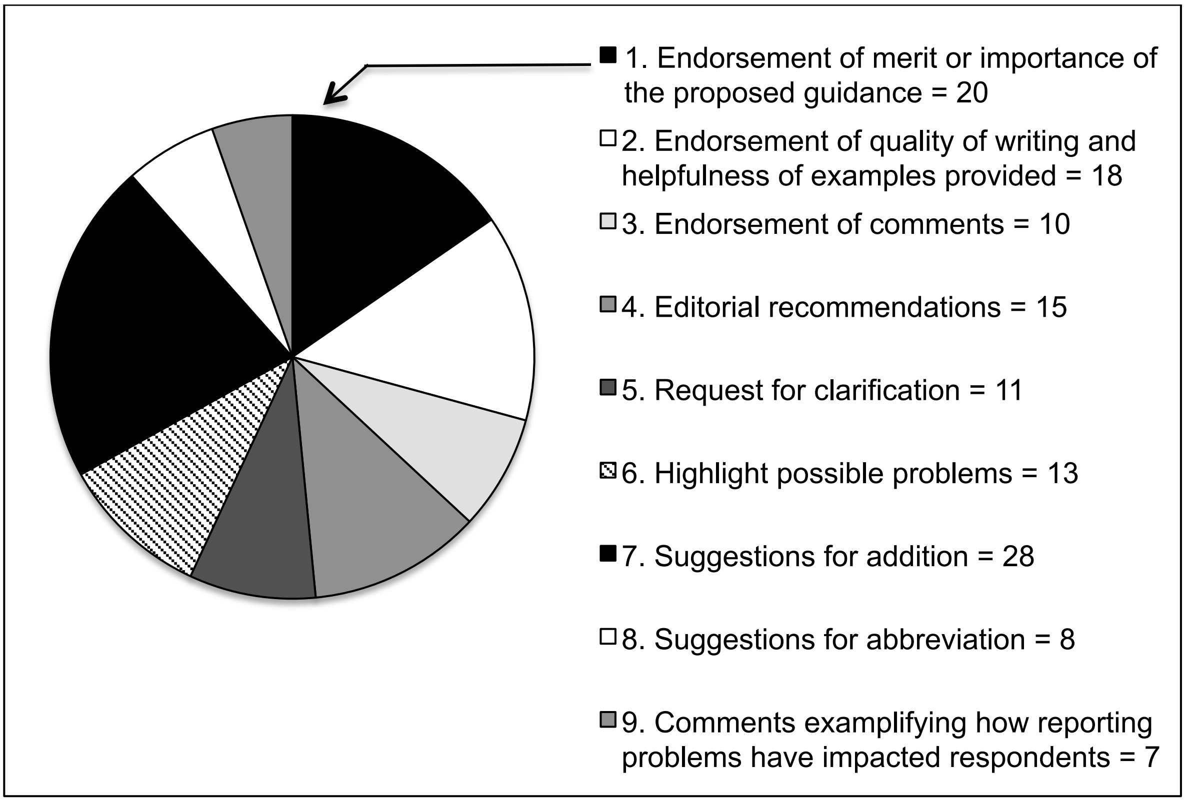


Figure 8.7. The proportion of feedback across the 9 themes



8.4 EXPLANATION OF GUIDANCE (TABLES 8.1 AND 8.2)

8.4.1 General

This guidance on time-to-event statistical reporting is designed for use in conjunction with reporting guidelines for the relevant study designs, such as STROBE for observational cohort studies and CONSORT for randomised trials. For example, specific guidance for well written introductions; differences between hypotheses, objectives and aims; and methods of participant recruitment and inclusion criteria will not be covered in this guideline.

Keywords, generally five to six in number,[24] are provided by authors upon submission of manuscripts, and may or may not appear in print on the final article. Review of approximately 15,000 full length articles in PubMed Central showed that approximately two-thirds of keywords chosen by those authors overlapped with Medical Subject Headings (MeSH).[24] Electronic algorithms assisting indexers suggest terms based on author abstracts and keywords,[25] and indexers would also manually review the keywords when allocating indexing terms. It has been shown that allocation of MeSH by MEDLINE indexers to dental articles that report survival statistics is inconsistent, which undermines the ability of researchers and others to find these indexed articles[1]. Review of survival analyses published in the 50 dental journals with the highest impact factor in 2008 identified 17 different MeSH indexing terms that had been allocated to such articles, as well as an additional indexing term that may have been relevant but had not been used.

Table 8.1. Checklist for recommendations for reporting time-to-event (TTE) data in the dental literature

Section	Checklist item	Page
Overall		
Additional resources	Use guidelines such as STROBE[16] for cohort studies and CONSORT[15] for controlled trials	
Keyword choice *Table 8.4*	Consider choosing one statistic-related MeSH, and consider use of outcome- and time-related MeSH if space permits	
Title & Abstract		
Title	Identify that the study reports a time-dependent outcome	
Structured abstract *Figure 8.8*	Aim: State the outcome and the time span Methods: Define groups, outcome/s and study duration. State the TTE statistic and measure of variance (such as a confidence interval) Results: Report TTE outcomes, loss to follow up, and variance Conclusions: Justified by results, circle back to the aims	
General *Table 8.5 & 8.6*	Use many words which describe the TTE statistic, outcome and study duration	
Introduction		
Aim	State the time-dependent outcome/s studied, and the time period	
Methods		
Censoring	Describe how censoring was minimized and managed	
Outcome	1. Define outcomes, events monitored and when events terminated 2. Classify outcomes as primary or secondary, true or surrogate 3. Report the unit of analysis (e.g. participant level)	
Time	State the study duration, review periods and whether investigators could be notified of events occurring outside the usual reviews	
Statistics	Describe the: 1. Survival statistic (e.g. life table analysis, Kaplan-Meier analysis) 2. Method used to calculate the standard error or confidence interval (e.g. Greenwood's, Clopper and Pearson's) 3. Method used to compare groups (e.g. Log rank test) 4. Summary statistic (e.g. Estimated cumulative survival) 5. Reasons for and methods used to adjust for clustering	
Results		
Written results	Report the 1. Summary statistic and its variance for each time period 2. Outcomes of group comparisons, stating the P-value 3. Occurrence, timing and reasons for events and censoring	
Survival curve *Figure 8.9 & 8.10* *Table 8.7*	Construct a survival curve for each outcome which includes: 1. The outcome / event / group 2. Meaningful time intervals 3. A stepped curve, with different lines representing each group 4. Censored observations (if practical without cluttering the data) 5. Standard error or confidence interval	
Life / survival table *Table 8.7 & 8.8*	Construct a life table for each outcome which includes: 1. The outcome / event / group 2. Meaningful time intervals 3. Numbers of participants at risk, lost to follow up and experiencing events during each time interval 4. Individual and cumulative survival calculations for each interval 5. Standard error or confidence interval	
Additional results	Retain unpublished data for a reasonable period to allow for further analyses and to answer queries from other researchers	
Discussion		
Censoring	Discuss impacts of censoring on the validity and applicability of results	
Outcome definition	Discuss the impact of outcomes / event definitions on the results	
Conclusions		
	Report conclusions that are justified by the results	

Table 8.2. Extended checklist for recommendations for reporting time-to-event data in the dental literature

Section	Checklist item	Page
Overall		
Additional resources	Use guidelines such as STROBE[16] for cohort studies and CONSORT[15] for controlled trials.	
Keyword choice *Table 8.3* *Table 8.4*	Improve the likelihood of consistent and accurate MeSH indexing by choosing appropriate keywords, guided by MeSH. Choose at least one MeSH to indicate that a time-to-event statistic was used. Additionally, consider allocating keywords relating to the outcome/s and study timeline if space permits.	
Title and Abstract		
Title	Identify that the study reports a time dependent outcome, if this is a primary purpose of the study.	
Structured abstract *Figure 8.8*	Aim: State the outcome and the time span. Methods: Define groups, outcome/outcomes and time involved. State the time-to-event statistic and measure of variance. Results: Report time-to-event outcomes, loss to follow up, and variance. Use appropriate nomenclature. Conclusions: Justified by results, circle back to the aims of the study.	
Word count	Maximise the length of the abstract.	
General *Table 8.5* *Table 8.6*	Use words that state a time-to-event outcome was measured. Exercising logical caution, use multiple synonyms to indicate that: 1. An outcome was studied, 2. Over time, and 3. A time-to-event statistic was used to analyse results.	
Introduction		
Aim	State the time-dependent outcome/s studied, and the time period.	
Methods		
Censoring	Describe how censoring was minimized and managed.	
Outcome	Define outcomes, events monitored and when events terminated. Classify outcomes as primary or secondary, true or surrogate. Report the unit of analysis and adjust for clustering where appropriate.	
Time	State the study duration, review periods and whether investigators could be notified of events occurring outside the usual reviews.	
Statistics	Describe the: 1. Survival statistic (e.g. life table analysis, Kaplan-Meier analysis), 2. Method used to calculate the standard error or confidence interval (e.g. Greenwood's, Clopper and Pearson's), 3. Method used to compare groups (e.g. Log rank test), 4. Summary statistic (e.g. Estimated cumulative survival, mean survival time), and 5. Reasons for and methods used to adjust for clustering.	
Results		
Written results	Report the: 1. Summary statistic and its variance for each time period, 2. Outcomes of group comparisons, stating the P-value, and 3. Occurrence, timing and reasons for events and censoring.	
Survival curve *Figure 8.9* *Figure 8.10* *Table 8.7*	Construct a survival curve for each outcome which includes: 1. The outcome / event / group, 2. Meaningful time intervals, 3. A stepped curve, 4. Different lines to representing each group, 5. Censored observations (if practical without cluttering the data), and 6. Standard error or confidence interval (notation of the standard error takes precedence over notation of censored observations).	

Life / survival table *Table 8.7* *Table 8.8*	Construct a life table for each outcome which includes: 1. The outcome / event / group, 2. Meaningful time intervals, 3. Numbers of participants at risk, lost to follow up and experiencing events during each time interval, 4. Survival calculations for each interval, and cumulative survival calculations for successive intervals, and 5. Standard error or confidence interval.	
Additional results	Include an abbreviated life table below each survival curve if space is limited. If all life tables or survival curves cannot be included in print, provide for electronic publication if possible. Retain all data for a reasonable period to allow for further analyses and to answer queries from other researchers.	
Discussion		
Censoring	Discuss the impact of censoring on the internal validity and external applicability of the results.	
Outcome definition	Discuss the impact of outcome and event definitions on the results, and compare with other research in the field.	
Conclusions		
	Report conclusions that are justified by the results, and circle back to the aims of the study.	

However, approximately one third of these articles did not have any statistic-related MeSH assigned to it, even though all of them used survival analyses to report the results. Outcome-related terms were allocated to approximately 85% of the articles, and time-related terms were allocated to approximately 90% of articles. The two most commonly allocated terms were dental restoration failure (77%) and treatment outcome (54%), rather than a term such as “survival analysis”.

Guidance: If keyword spaces are available, authors should consider listing MeSH from the statistic-, outcome- and time-related MeSH categories as a keyword for their article, prioritising use of those from the statistic category. The list of relevant MeSH, and their definitions, is provided in tables 8.3 and 8.4.

Table 8.3. Statistic-, outcome- and time-related MeSH and their definitions from MEDLINE

MeSH	Definition
Actuarial analysis *Year introduced: 1979*	The application of probability and statistical methods to calculate the risk of occurrence of any event, such as onset of illness, recurrent disease, hospitalization, disability, or death. It may include calculation of the anticipated money costs of such events and of the premiums necessary to provide for payment of such costs.
Dental prosthesis repair *Year introduced 1993*	The process of reuniting or replacing a broken or worn dental prosthesis or its part.
Dental restoration failure *Year introduced: 1995*	Inability or inadequacy of a dental restoration or prosthesis to perform as expected.
Fatal outcome *Year introduced 1994*	Death resulting from the presence of a disease in an individual, as shown by a single case report or a limited number of patients. This should be differentiated from DEATH, the physiological cessation of life and from MORTALITY, an epidemiological or statistical concept.
Follow up studies *Year introduced 1967*	Studies in which individuals or populations are followed to assess the outcome of exposures, procedures, or effects of a characteristic, e.g., occurrence of disease. A subgroup under Longitudinal studies.
Graft survival *Year introduced: 1999*	The survival of a graft in a host, the factors responsible for the survival and the changes occurring within the graft during growth in the host.
Kaplan-Meier estimate *Year introduced: 2007*	A nonparametric method of compiling LIFE TABLES or survival tables. It combines calculated probabilities of survival and estimates to allow for observations occurring beyond a measurement threshold, which are assumed to occur randomly. Time intervals are defined as ending each time an event occurs and are therefore unequal. (From Last, A Dictionary of Epidemiology, 1995)
Life tables *Year introduced: 1990*	Summarizing techniques used to describe the pattern of mortality and survival in populations. These methods can be applied to the study not only of death, but also of any defined endpoint such as the onset of disease or the occurrence of disease complications.
Longitudinal studies *Year introduced 1979*	Studies in which variables relating to an individual or group of individuals are assessed over a period of time.
Proportional hazards model *Year introduced: 1989*	Statistical models used in survival analysis that assert that the effect of the study factors on the hazard rate in the study population is multiplicative and does not change over time.
Prospective studies *Year introduced 1967*	Observation of a population for a sufficient number of persons over a sufficient number of years to generate incidence or mortality rates subsequent to the selection of the study group. A subgroup under Longitudinal studies.
Prosthesis failure *Year introduced: 1999*	Malfunction of implantation shunts, valves, etc., and prosthesis loosening, migration, and breaking.
Retreatment *Year introduced 1997*	The therapy of the same disease in a patient, with the same agent or procedure repeated after initial treatment, or with an additional or alternate measure or follow-up. It does not include therapy which requires more than one administration of a therapeutic agent or regimen. Retreatment is often used with reference to a different modality when the original one was inadequate, harmful, or unsuccessful.
Retrospective studies *Year introduced 1967*	Studies used to test etiologic hypotheses in which inferences about an exposure to putative causal factors are derived from data relating to characteristics of persons under study or to events or experiences in their past. The essential feature is that some of the persons under study have the disease or outcome of interest and their characteristics are compared with those of unaffected persons.
Survival *Year introduced: not stated*	Continuance of life or existence especially under adverse conditions; includes methods and philosophy of survival.
Survival analysis *Year introduced: 1990*	A class of statistical procedures for estimating the survival function (function of time, starting with a population 100% well at a given time and providing the percentage of the population still well at later times). The survival analysis is then used for making inferences about the effects of treatments, prognostic factors, exposures, and other covariates on the function.
Survival rate *Year introduced: 1990*	The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the beginning of a time interval who survive to the end of the interval. It is often studied using life table methods.
Time factors *Year introduced: 1999*	Elements of limited time intervals, contributing to particular results or situations.
Treatment outcome *Year introduced: 1999*	Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series

Table 8.4. Classification of MeSH[1]

Group	Description	MeSH
1	MeSH for a statistical time-to-event technique *(MeSH: Statistical)*	Kaplan-Meier estimate Life tables Proportional hazards model Survival analysis Survival rate
2	MeSH which indicated that an outcome was studied *(MeSH: Outcome)*	Dental prosthesis repair Dental restoration failure Fatal outcome Graft survival Prosthesis failure Retreatment Treatment outcome
3	MeSH which indicated that a study occurred over time *(MeSH: Time)*	Follow up studies Longitudinal studies Prospective studies Retrospective studies Time factors

8.4.2 Title and abstract

Guidance: The words chosen in the title and abstract should reflect that an outcome was monitored, over time, and analysed with a time-to-event method.

Once indexed in a bibliographic database, articles can be identified by an index term search (MeSH search) or keyword search of the title and abstract.

Guidance: Authors should choose words that describe survival analyses, and may wish to use multiple synonyms to encompass the variety of words that end-users may employ. However, they should be cautious when doing so because by using a variety of words to maximise the likelihood that relevant research is identified, it may unintentionally make readers think that the different words indicate a subtle difference in meanings.

A list of descriptive words and related phrases regarding the statistic-, outcome- and time-aspects of time-to-event studies are provided in tables 8.5 and 8.6. Words that are specific to each topic are outlined in table 8.5, and words that could be used as additional descriptors are outlined in table 8.6. This list was derived from the titles and abstracts of dental survival articles published in 2008 in the 50 dental journals with the highest impact factors[2].

Use of relevant statistical words by researchers will make it clearer that time-to-event outcomes have been studied. It is recommended that at least one specific statistical term be used (such as Kaplan-Meier), with other statistical terms (such as cumulative or survival rate) used as supplemental descriptors. When choosing outcome words, it is recommended that those indicating an outcome is measured over time (such as life span or longevity) be used primarily, and more general outcome words such as (behavior, investigation, performance) are used as supplemental descriptors. All abstracts should include specific phrases or words that state the study duration.

Guidance: Authors should maximize the length of the article title and abstract, while remaining on topic and within the word limit of the publishing journal, and journals should consider allowing authors to submit an additional lengthened abstract for use on the electronic bibliographic record. The more words available for searching, the higher the likelihood that articles will be found. However, authors should take care that the words chosen are appropriate, otherwise articles will be erroneously identified, increasing the workload of researchers and others as they sift through irrelevant records.

Table 8.5. Words and phrases that are specific to statistic-, outcome- and time-aspects of dental survival analyses.[2]

Group	Description	Specific words
Statistic	*Terms relating to time-to-event statistics*	"Cumulative", such as Estimated cumulative survival Estimated cumulative success Estimated cumulative failure Cumulative survival rate Cumulative success rate Cumulative failure rate Terms relating time-to-event statistics, such as Actuarial analysis Cox regression Cox proportional hazards model Greenwood's formula Hazard ratio Kaplan-Meier Lifetime analysis Life table Log rank test Survival analysis Survival curve Time-to-event analysis "Time to event", such as Time to event Time to failure Time to complication
Outcome	*General words indicating that an outcome was studied over time*	Durability Life span Longevity Mortality Prognosis
Time	*Phrases or words which state the study duration, or indicate that time was involved*	Terms involving specific years, such as 10 year outcome 5 year duration 8 year follow-up 2 year recall Up to 15 years Over 20 years

Table 8.6. Additional descriptors that relate to statistic- and outcome- aspects of dental survival analyses.[2]

Group	Information
Statistic	*Description:* Quasi-statistical terms which indicated that an outcome was studied over time *Specific Words:* Indicating censoring, such as Censored Drop out Loss to follow up Non-attending "Estimate", such as Retention estimate Success estimate Survival estimate "Probability of", such as Probability of avoiding dental treatment Probability of failure Probability of lifetime Probability of survival "Rate", such as Caries rate Complication rate Dental rehabilitation rate Distraction rate Dissemination rate Failure rate Flow rate Fracture Healing rate Loading rate Loss rate Morbidity rate Mortality rate Polymerisation rate Retention rate Secretion rate Success rate Survival rate
Outcome	*Description:* General words which indicated that an outcome was studied *Specific Words:* Adverse events Assess / Assessment Behaviour Complications / Problems Efficacy / Effectiveness End point Evaluate / Evaluation Experience / Clinical experience Failure Incidence Investigation Loss / Fracture Maintenance / Aftercare Observations / Clinical observations Outcome / Clinical outcome Performance / Clinical performance Prognosis Reliable Response Results Success Survival
Time	*Description:* Terms relating to time *Specific Words:* Duration Follow-up Recall period

Guidance: The abstract should be structured, ensuring that appropriate descriptions of the time-to-event analyses are used, patient groups defined, outcome measures explained, statistical methods stated, key findings outlined, censoring reported and that conclusions are supported by the results.

Examples of hypothetical abstracts have been provided in figure 8.8 to help explain how these concepts can be put into practice.

Figure 8.8. Hypothetical example abstract

Descriptive legend
1. *Statistic-related words are highlighted in yellow, with more specific terms underlined* 2. *Outcome-related words are highlighted in green, with more specific terms underlined* 3. *Time-related words are highlighted in blue, with more specific terms underlined* 4. *A summary of specific words are outlined in table 8.5* 5. *A summary of supplemental descriptors are outlined in table 8.6*
Abstract written with high use of time-to-event related vocabulary
Title: *The up to 10 year clinical performance and survival analysis of 250 vital single tooth crowns.* ***Aim:*** *To assess and compare the estimated cumulative survival (ECS) of 250 crowns on vital anterior and posterior teeth that have been in-situ for up to 10 years.* ***Methods:*** *A cohort of 250 patients who each received only one crown (anterior, n=125, posterior, n=125) from a single private prosthodontist between 2000 and 2010 were sequentially included in this follow-up study. Exclusion criteria were non-vital teeth and xerostomic patients. Crowns were high noble metal ceramic and were fabricated by one laboratory technician. Patient demographics were reported as percent with standard deviation. Clinical outcome was expressed as the Kaplan-Meier estimated cumulative survival with standard error (Greenwood's formula). Differences in survival between anterior and posterior crowns were analysed with the log rank test, with P<0.05.* ***Results:*** *At the 10 year recall, 220 patients attended and 30 had dropped out and were censored. The 5 year and 10 year ECS for all crowns was evaluated to be 98±1% and 95±4% respectively. Anterior crowns had a significantly lower 10*

year survival probability when compared with posterior crowns (92±3%, 97±1% respectively, P=0.012). Ten anterior crowns experienced terminal complications, and these were associated with aesthetics (n=3), porcelain chipping (n=1), extrinsic trauma (n= 4) and root fracture (n=2). Failed posterior crowns (n=2) were associated with root fracture (n=2).

Conclusion: *Single tooth crowns offer a predictable long-term restoration for vital teeth with a low failure rate and high longevity. Over 10 years, crowns on posterior teeth performed better when compared with those on anterior teeth.*

Key words: *Kaplan-Meier estimate, Dental restoration failure, Prospective studies, Single tooth crown, Metal ceramic*

Abstract written with lower use of time-to-event related vocabulary

Title: *An up to 10 year prospective study of 250 vital single tooth crowns*

Aim: *To assess the survival of 250 single tooth crowns over 10 years.*

Methods: *A cohort of 250 patients who each received only one crown (anterior, n=125, posterior, n=125) from a single private prosthodontist between 2000 and 2010 were sequentially included in this study. Exclusion criteria were non-vital teeth and xerostomic patients. Crowns were high noble metal ceramic and were fabricated by the one laboratory technician. Patient demographics and crown survival rates were reported.*

Results: *The survival rates at 5 years and 10 years for all crowns was 98±1% and 95±4% respectively. Anterior crowns had a significantly lower 10 year survival when compared with posterior crowns (92±3%, 97±1% respectively, P=0.012). Failed anterior crowns (n=10) were associated with aesthetics (n=3), porcelain chipping (n=1), extrinsic trauma (n= 4) and root fracture (n=2); and failed posterior crowns (n=2) were associated with root fracture (n=2).*

Conclusion: *Single tooth crowns offer a predictable long-term restoration for vital teeth with a low failure rate. Over 10 years, crowns on posterior teeth performed better when compared with those on anterior teeth.*

Key words: *Survival Rate, Outcome, Prospective studies, Single tooth crown, Metal ceramic*

8.4.3 Introduction

Guidance: The aim of the study and its relationship to the time-to-event outcome should be clearly stated.

8.4.4 Methods

Methods should be described in sufficient detail to allow the study to be replicated.

Time-to-event analyses deal with censored data. Censoring is needed in time-to-event analyses because studies often recruit participants over time, and during the study period participants can become lost to follow up. This means that participants are not all present at the beginning of the study (because they have not all been recruited), and participants are not all present at the end of the study (because they have become lost to follow up). This results in censored data.

Guidance: Researchers should describe what was considered to be censored data, how it was minimized, and how such data were managed when it did occur.

As a practical example, researchers may expand on information about censoring in relation to non-attenders. They may classify non-attenders as those known to have ceased participation, moved location, become medically unable to attend, passed away, or those who failed to return for reasons unknown. Numbers of non-attenders may be minimized by various techniques including assessing participants in an alternative location (such as a nursing home), offering out-of-hours appointments, enlisting the help of a participant's new practitioner to provide information, offering monetary incentives to attend, contacting the participant through their referring practitioner. Some studies go to extreme lengths to locate non-attenders, with one in the orthopedic literature[26] enlisting the help of a private investigator. If non-attendance occurs, researchers should state whether participants were censored at the last known observation, immediately after the review period where they did not attend (as commonly occurs for Kaplan-Meier analyses) or half-way through the intervening observation period (as commonly occurs for life table analyses).

Researchers may choose a variety of different endpoints as outcomes. They could be primary or secondary outcomes, and could be true or surrogate markers. Particular confusion exists in the dental literature about the definitions of the subjective outcomes of success, survival and failure. If such outcomes are used, researchers should ensure that these are well defined.

The unit of analysis should be reported, and outcomes adjusted for clustering where appropriate. For example, outcomes could be reported per implant, or per patient. If multiple implants are present in the same patient, clustering occurs.

Guidance: Researchers should define the outcomes studied, events monitored and when events were considered terminal. Outcomes should be classified as primary or secondary, true or surrogate.

Guidance: The unit of analysis should be reported, and outcomes adjusted for clustering where appropriate.

The outcomes of time-to-event data are monitored over time.

Guidance: Researchers should define the overall study time period, the review periods and whether investigators could be notified that an event occurred outside the usual review periods.

Guidance: Researchers should define and justify how the study period was determined, how the review periods were chosen, and whether participants could notify the researchers or attend the clinic for assistance, if an event occurred outside the usual review period. The description of the time-to-event statistics should include

1. *Type of survival statistic used (eg. life table analysis, Kaplan-Meier analysis)*
2. *Method used to calculate the standard error or confidence interval (eg. Greenwood's, Clopper & Pearson's)*
3. *Method used to compare groups (eg. Log rank test)*
4. *Type of summary figure used (eg. Estimated cumulative survival, mean survival time)*
5. *Reasons for and methods used to adjust for clustering*

Further details regarding the calculation of time-to-event outcomes and measures of variance have been published previously for dental researchers.[27]

8.4.5 Results

8.4.5.1 Written results

Guidance: The summary survival statistic, bounded by a confidence interval or standard error, should be reported for each time point of interest in the written section of the results. Such time points are determined by the specific research question.

Guidance: When different groups are compared, individual results, the test chosen, the P-value calculated and the relevant confidence interval should be reported.

Survival statistics provide results that are an estimate of the true outcome because data are censored as the study proceeds forward in time, and such censoring results in loss of precision. All estimated data should be accompanied by a measure of variance, and this can be calculated when a single group is followed over time, as well as when multiple groups are compared and followed over time.

This reporting allows readers to understand the data in full. This reporting also allows the data to be included in future meta-analyses, for which not only the point estimate, but also some measure of variance, is needed. Meta-analyses may use the estimated cumulative survival for the summary data, and this cannot be used without some measure of variance.

Other meta-analyses may use an event rate method, and this cannot be used without knowing the mean time in-situ. For this reason, researchers may consider also reporting the mean time in-situ for the dental prostheses. If reported, researchers should be aware that this summary figure is inappropriate for skewed data sets, where continuous enrollment results in a large cohort of younger prostheses when compared with their older counterparts; or if there is a large amount of censoring because of loss to follow-up.

Guidance: When an event occurs, a summary of the number of those experiencing the event and the timing of the event should be reported. When censoring occurs, a summary of the number of those censored, the timing of censoring and the reasons for censoring should be reported. If this information is included in the text for the results, it would be complimentary to more detailed information included in the life tables and survival curves.

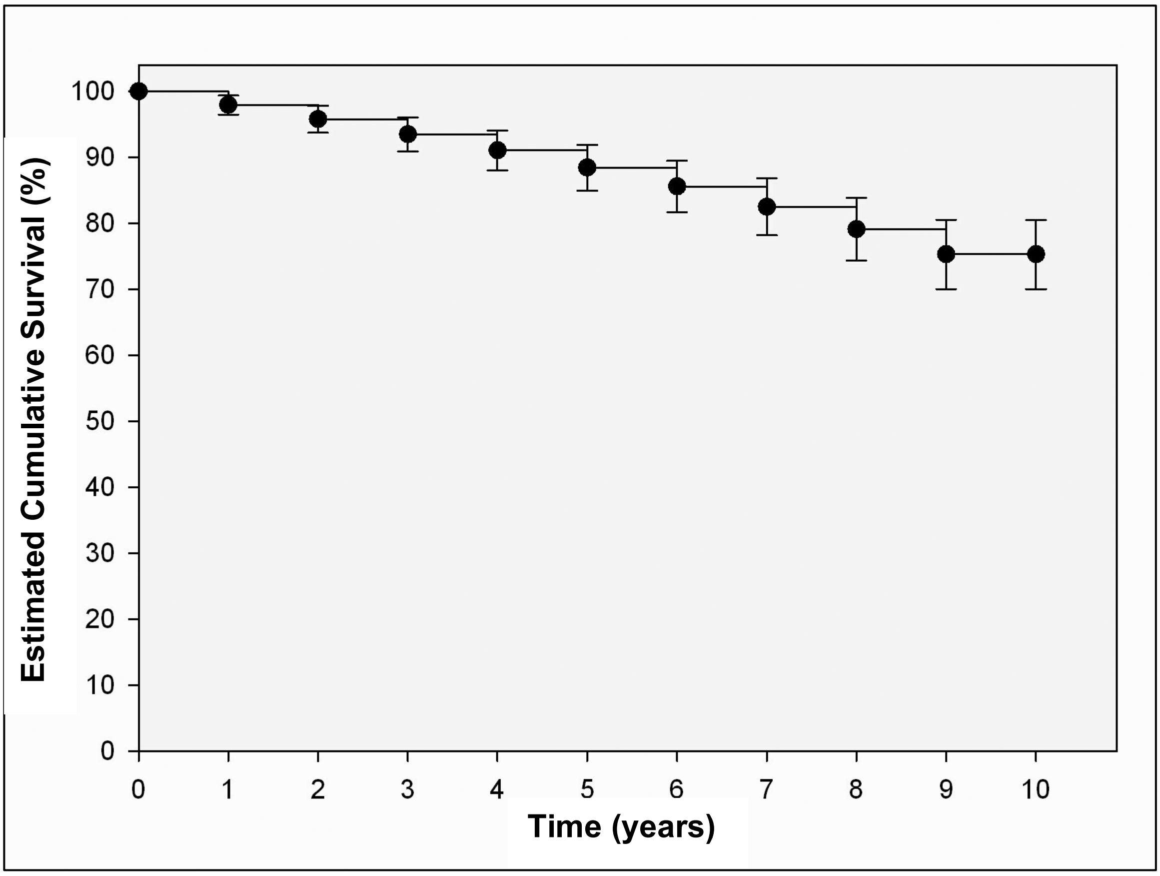
8.4.5.2 Survival curves

A survival curve is a graph that shows an estimated probability or percentage outcome (such as percent surviving) over time. The y-axis can be truncated if considered to be appropriate by the authors. An example survival curve is shown in figure 8.9. It is not appropriate to truncate the x-axis, as this prevents notation of the standard error or censored data over time.

Guidance: The legend for the survival curve should clearly state the event being monitored, the groups involved and the time period. The legend should also state the summary value, such as the estimated cumulative survival, for a major time point *of interest. If multiple groups have been compared, it should state the associated P-value.*

Guidance: Individual groups should be clearly labeled and identified by different graphic lines. The time intervals should be joined by a stepped curve, not diagonal lines. The standard error or confidence interval should be included graphically on the curve, with techniques such as error bars or shaded regions. Where practical, censored observations should be notated on the curve.

Figure 8.9. Example survival curve with hypothetical prostheses data: The estimated cumulative survival of prostheses at 10 years was 70.93% ± 5.78%[27]



This guidance would be implemented after assessing its practicality for any given dataset. It can be difficult to include both the censored observations and the measure of variance, and authors may decide to omit one of these measures from the survival curve, because the multiple lines can compete with each other, making interpretation difficult. It can also be difficult to include error bars for all time points, for all groups assessed, as marked overlap may occur between the lines making it hard for readers to see which error bar relates to which curve. Therefore, a practical approach to this guidance is required.

A graphical representation of the measure of variance may be more important than a graphical representation of the censored observations, because the error bars alert readers to the degree of variability within the results, and this may not be so apparent when the numbers are reported in writing. Also, when multiple groups are compared, error bars on the graph allow readers to quickly see whether the "groups overlap", supporting the interpretation of the statistical P-value. Censored observations can be included in the columns of the life tables, as discussed in the life table section 8.4.5.3. If researchers know the exact timing of censoring, then graphic inclusion on the survival curve is of value. Conversely, if researchers do not know the exact timing of censoring, and only know that patients did not attend a follow-up at a given time interval, then inclusion of the data in the life table instead may be a suitable compromise. However, researchers should judge each dataset on its individual merits.

Guidance: The choice of the time intervals for the x-axis should be meaningful for the study question. The x-axis should commence at time zero. Authors should ensure *that they can justify the decisions made about the time intervals and time period to use in light of the research being undertaken.*

Time periods should clearly state the number of days, weeks or months rather than simply naming a period such as "implant loading", for example. The x-axis should not omit large sections of data, such as "skipping" from 3 to 20 years.[28]

Where practical, authors should refrain from reporting unusual time periods that are not easily translated to clinical relevancy, such as 3500 days[29], 600 weeks[30] or 100 months.[31] Again, practical interpretation of this guidance is required. Some research questions review subjects on a weekly or four weekly basis, rather than a monthly basis or six monthly basis. In these instances, it would be more accurate to report the exact time periods, rather than converting the data to a natural time line. However, authors are cautioned to provide the simplest timeline possible, assisting transparent and easily understood reporting. Table 8.7 explores examples of the subjective concept of meaningful time intervals further.

8.4.5.3 Life tables

At a minimum, life tables report the number of prostheses in situ, and the number or percentage of those that experienced the event (such as number failed or percentage surviving) at different time intervals for the event being reported, and the patient group involved. Individual life tables will be required for different groups and different events.

Table 8.7. Examples of use of meaningful time intervals

Time interval	Examples of when the time period may be meaningful	Examples of when the time period may not be meaningful
Years	Reporting of outcomes over a long period of time, where the recall period occurs over a year. For example, those with implant single crowns may return for a review on a yearly basis, where different participants would be assessed during different months. This is common in long-term cohort studies. Reporting of outcomes that are greater than 3 years. From a practical point of view, the longer the study, the harder it becomes harder for readers to equate months to years. For example, 36 months is equivalent to 3 years, but not every reader quickly equates 84 months with 7 years. Unless there is a specific reason, this guidance recommends avoiding monthly intervals for longer-term studies.	A short-term follow-up, such as 12, 18 or 24 months.
Months	Reporting of outcomes where patients are followed up monthly. It is uncommon for such regular follow-ups to occur for medium- and long-term studies, such as those over 3 years. Reporting of outcomes where patients are followed up biannually. It is uncommon for biannual follow-ups to continue for medium- and long-term studies, such as those over 3 years.	A long-term follow-up, such as 5, 10 or 15 years. A long-term follow-up, such as 100 months.[31] A follow-up study with 4 weekly intervals.
Weeks	Reporting of outcomes where the follow up period is based on the number of weeks, such as participants attending 4 weekly recalls. It is not logical to convert 4 weekly data to monthly data	A long-term follow-up, such as 600 weeks.[30]
Days	Reporting of outcomes where assessments are made daily. This is common in laboratory studies.	A long-term follow-up, such as 3500 days.[29]

Guidance: As well as including the number of prostheses in situ, and the number or percentage of those that experienced the event at different time intervals, authors should also include:

1. *For each time interval, the number of patients or prostheses at risk, those lost to follow up and those experiencing an event,*
2. *The survival for individual time intervals, the cumulative survival as it progresses through each successive time interval and the associated measure of variance.*

Inclusion of this information allows readers to follow the outcomes of each group, assess the impact of censoring, and determine their confidence in the point estimates reported. As with survival curves, the choice of the time intervals should be meaningful and should be able to be both justified by the researchers and easily translated into clinical relevancy by the readers. An example of a life table is provided in table 8.8.

Table 8.8. Example life table of hypothetical prostheses data: The estimated cumulative survival of prostheses at 10 years was 70.93% ± 5.78%[27]

Time (yrs)	No.	Censored	Failed	Probability of survival	Estimated Cumulative Survival (%)	Standard Error (%)
0-1	100	5	2	0.9795	97.95	1.44
1-2	93	5	2	0.9779	95.78	2.06
2-3	86	5	2	0.9760	93.49	2.57
3-4	79	5	2	0.9739	91.05	3.03
4-5	72	5	2	0.9712	88.43	3.47
5-6	65	5	2	0.9680	85.60	3.89
6-7	58	5	2	0.9640	82.51	4.32
7-8	51	5	2	0.9588	79.11	4.76
8-9	44	5	2	0.9518	75.30	5.24
9-10	37	5	2	0.9420	70.93	5.78

8.4.5.4 Additional results

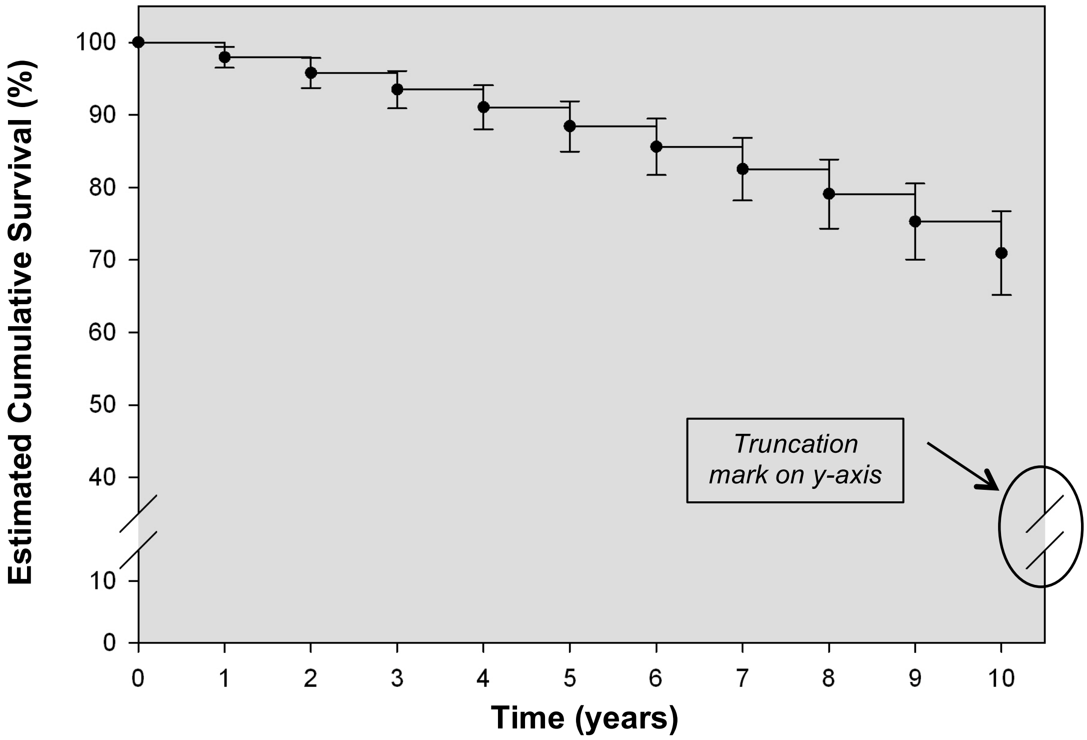
Many studies analyse multiple groups and multiple events. This can mean that a large number of survival estimates are made, with each accompanied by a survival curve and a life table. Survival curves and life tables each provide different but complementary information. For example, specific changes in participant numbers is well delineated in life tables, but the magnitude in changes in estimated cumulative survivals and variances is better explored graphically. Inclusion of both figures for all outcomes is ideal, but publication print space will limit the number of tables and figures that can be included.

Guidance: If authors are unable to include all tables and figures, those associated with the most important outcomes should be chosen for the printed article. Authors may also be able to provide journals with a combined survival curve and truncated life table.

An example of a combined survival curve and truncated life table is provided in figure 8.10.

Guidance: Authors should retain copies of all life tables and survival curves for their entire manuscript, regardless of whether they are accepted for inclusion in the article. Journals may allow this information to be included in an electronic publication or as an online appendix. Furthermore, readers, researchers or reviewers may seek this additional information from authors, and therefore collation at the time of publication will make it easier to retrieve the data for future use.

Figure 8.10. Example combined survival curve and truncated life table with hypothetical prostheses data: The estimated cumulative survival of prostheses at 10 years was 70.93% ± 5.78%[27]



Number at risk at the beginning of each 1 year interval Number censored or failed within each 1 year interval												
		0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Data	N	100	100	93	86	79	72	65	58	51	44	37
	C	0	5	5	5	5	5	5	5	5	5	5
	D	0	2	2	2	2	2	2	2	2	2	2

N = Number, C = Censored, D = Failed
Interval length = 1 year

8.4.6 Discussion

The discussion should highlight limitations of the study design, and their implications. Differences between clinical and statistical significance should be noted.

Guidance: The discussion should specifically highlight the impact that censored data may have had on the internal validity of the study, and the external applicability of the results. It should highlight the impact that the event definition (such as success, survival, failure) may have on the occurrence and the identification of the event, and whether the definitions chosen by the authors differed markedly from the literature norm.

Guidance: If multiple significant tests are completed, authors should discuss the risk that the results found are due to mass-significant, and which steps were taken to limit this impact.

8.4.7 Conclusions

Guidance: Conclusions stated should be justified by the results, and reflect the aims of the study.

8.5 DISCUSSION

This guidance document has been proposed to aid researchers reporting time-to-event survival outcomes, and it has been tailored for use in dentistry.

Stakeholders were contacted, and the guidance was sent to a purposive sample[23] of authors (n=48), journal editors (n=10) and educators (n=20). These experts were known to have an interest in dental survival analyses specifically (n=61) or evidence based dentistry in general (n=17).

The majority (85%) of stakeholders were from the field of prosthodontics. These dental specialists were included because over three quarters of survival articles that had been identified in this programme of research (Chapter 2) related to implant (64%) or tooth supported (14%) prostheses. Periodontists were also included, as these specialists are similarly involved in reporting implant related outcomes. However, this purposive sample has a larger number of prosthodontists compared with periodontists. This in part reflected my background, where as a prosthodontist, my reading exposed me to a greater number of authors in prosthodontics compared with periodontics. It also reflected the themes of survival articles, which were predominantly related to prosthodontics. Two periodontists who I contacted helped me improve the scope of comments from periodontists, and contacted colleagues on my behalf. Unfortunately, this did not yield additional responders. Four additional expert groups were also included. These were endodontics, orthodontics, and statistics/methodology, but these were in low numbers.

The type of feedback received from prosthodontists and periodontists did not markedly differ. There is no reason to expect those with knowledge of time-to-event outcomes would respond with different thematic content because their background was in prosthodontics rather than periodontics. However, subtle differences may have been present, and not detectable across this small sample.

A shortcoming in the stakeholders contacted was that they did not include many statisticians, methodologists and public health experts. Feedback was received from two such people. Unlike the probable similarities between prosthodontic and periodontic responders, it is likely that feedback from this methodology group would differ from that of others stakeholders. Additional involvement from this group may have resulted in more comment on statistical technique reporting than was received. My research for this guidance will continue as a post-doctoral project, and I will seek greater inclusion of these types of experts for the future consensus document.

Approximately 60% of experts contacted and 55% of those responding were authors that had published time-to-event related articles. All experts were reviewers for dental journals, and the majority (70% contacted, 76% responding) also had positions in education as a dean, chair or course director. In addition, seven of the responders were current or previous editors of journals. These journals included the International Journal of Prosthodontics (IJP, Dr. George Zarb, Dr. Gunnar Carlsson), The International Journal of Oral and Maxillofacial Implants (IJOMI, Dr. Steven Eckert), the Journal of Prosthetic Dentistry (JPD, Dr. Carol Lefebvre), The International Journal of Periodontics and Restorative Dentistry (IJPRD, Dr. David Cochrane), Community Dentistry and Oral Epidemiology (CDOE, Dr. John Spencer) and Gerodontology (GERO, Dr. Michael MacEntee). The three experts from private practice were included specifically because of their known interest in time-to-event outcomes and evidence based dentistry. An additional 10 experts were approached who had interests in evidence-based dentistry and were educators at universities. They were included to increase the international breadth of responses. These were from Australia, Canada, Hong Kong, Israel, Italy, South Africa and Turkey. Overall, these academic and scholastic stakeholders were in a position to provide comment on the guidance from the perspective of studies they had completed, graduate research they had guided, manuscripts they had reviewed and/or articles they had edited. Their input into the guidance document has improved its breadth and depth.

Nearly 40% of comments received related to positive endorsements. The comments endorsed the importance of the proposed guidance, endorsed the way in which the proposed guidance was presented or endorsed specific comments within the document. Responses from editors of the International Journal of Prosthodontics, the International Journal of Oral and Maxillofacial Implants and Gerodontology expressed a particular interest in the guidance, and wished to make the document available to their reviewers and potential authors.

Additionally, 4% of comments referenced specific problems that the respondents had encountered or observed that related to the reporting of time-to-event outcomes. These comments are discussed in detail below.

The remaining comments, approximately 60%, suggested changes to the document. Of those suggestions made, nearly 90% were adopted in the revision of the document. A summary of changes made, or areas that were not modified are outlined in Appendix 11.3. Major changes included completion of the explanatory document, truncation of the checklist to one page, modification of the word list to delineate between specific and supplementary terms, more detailed discussion regarding definition of outcomes, and addition of example abstracts. These changes have simplified the document, improved explanations, and I hope that this will translate into a greater likelihood that the guidance will be helpful to end users.

The amended guidance has not been sent to the experts for a second round of comments. The document has changed from its original form, and some respondents may not endorse all changes that have now been made. Therefore, the document, in its current form, cannot be considered a validated guideline. However, this step in my research did not aim to produce a validated document. The validation process is lengthy, and also costly. A guideline on writing guidelines by Moher and colleagues was published in 2010 to assist health researchers.[19] It is recommended that the need for guidelines is recognized and participants are identified to help with drafting the document through a combined Delphi process, and face-to-face meeting of a nominal expert group derived from the Delphi participants.[32, 33] Participants provide suggestions for inclusion and comment, the initial document or checklist is modified, and participants again provide comment with the aim of reaching agreement on items to discuss at a face-to-face meeting. A smaller number of people take part in the meeting (previous guidelines have included a median of 22 participants[19]) with the aim of achieving a specified level of agreement by consensus voting. A guidance checklist, explanatory document and publication pathway is often then developed. Participants are sought because they bring knowledge and expertise to the area, and are often from different international locations. The number of pre-meeting and post-meeting steps involved, and the actual travel and accommodation costs results in a high fiscal and time burden, which is beyond the scope of this preliminary guideline.

Furthermore, it is not clear that all of the steps in this "ideal model" for developing guidelines, are necessary in all circumstances. For example, a range of authors, including Warren-Howard in 2015,[34] have outlined advantages and disadvantages of Delphi exercises, consensus conferences and nominal expert groups when seeking formal consensus. Additionally, Echemandia and colleagues[35] reviewed a range of methods that had been used to develop guidelines on management of sports-related concussion, outlining positive and negative attributes of each approach. A recent guideline, SAMPL, was completed by Lang and Altman in 2013 without undertaking the full process outlined above.[21] This has been accepted by the European Association of Science Editors and it is published on the EQUATOR network.[36] It is likely that this has occurred because the authors are considered to be experts in the field, and their opinion has been accepted as sage advice.

As well as commenting on the document, the feedback highlighted areas where conflict existed between writing and publishing articles. The spectrum of writing titles and abstracts to capture the attention of an audience, and writing them to convey important scientific information was raised. There has been some interesting research on this, such as a review of 658 titles in two psychological journals published between 1985 and 1994, which ranked the titles for degree of amusement and pleasantness and found that those with highly amusing titles received fewer citations.[37] The time-to-event guidance prioritises scientific merit over sensationalism, but also recommends using a broad number of similar words to report the findings. In content lists, authors initially wish to attract readers, and use of catchy phrases may be helpful, but when considering bibliographic databases which contain millions of records, authors need to be confident that their articles will be found if readers are to be able to decide whether to read further. Therefore, a spectrum also exists in maximizing the length of abstracts and titles to contain as much information as needed to convey all the important evidence, while keeping the abstracts within journal and bibliographic database word limits and maintaining their purpose of summarizing the research. The more words used in the title and abstract, the higher the chance that the article would be found by a word search. A review in 2010 of 9031 articles across 22 journals concluded that articles with longer titles appeared to be associated with higher citation rates.[38] The final conflict raised related to use of multiple synonyms. The more synonyms used, the higher the chance that those searching would find the article, but if synonyms chosen do not reflect the purpose and content of the article, more articles that were not useful to searchers would be found. Clearly, a balance is required between attracting attention with abstracts, and writing them to be both specific and informative. Examples of hypothetical abstracts have been provided in figure 8.8 to help explain how these concepts can be put into practice.

Where it is acceptable to journals, the guidance recommends use of structured abstracts. Research undertaken by the National Library of Medicine (NLM) showed that between 1992 and 2005, the number of structured abstracts for articles indexed in MEDLINE had increased from 2.5% to 20.3%, and that this trend appeared to be continuing. The authors concluded that in addition to changes made to the abstract display in 2010 to improve utility, NLM would alter metadata allowing searching of individual sections of the abstract (such as the results, or objective) by end-users, and suggestion of MeSH for indexing use weighted towards the objective and results section of abstracts rather than the areas such as the "background".[39] Given these research objectives of the NLM, it is important that authors maximize the quality of their abstracts to allow these continued changes to aid accurate identification of their research. Problems in the writing of abstracts in journals and for conference proceedings have been highlighted in relation to controlled trials.[40, 41] A CONSORT document providing guidance on reporting of abstracts for conferences and journals was in published 2008,[42] and those recommendations were incorporated into the updated 2010 CONSORT guideline.[15] In their review of the literature, authors of the CONSORT guidelines reported that abstracts often lacked transparency, were unsuitable screening tools for readers to decide whether to proceed with reading or reviewing the article, and lacked details that meant the abstracts could not serve as accurate records of the research trial.

With full text electronic searching becoming increasing available, through engines such as Google Scholar, a poorly written title and abstract may become less of an obstacle to identifying studies. However, research in the early 1990s comparing article yields of full text file searches compared with MEDLINE searches found that the full-text searches lacked precision.[43] The records that had been missed in full-text searching, but identified with a MEDLINE search, were associated with errors in expression of or accounting for natural language. In addition to full-text searching, at least one search engine allows searching of figure captions, with the output field displaying title, abstract, figures and legends.[44] Researcher opinion regarding the BioText literature search engine was reviewed in 2010, finding that three quarters of the 20 participants would continue to use the search engine in the future.[45] In a 2013 commentary on how searching for studies for systematic reviews has altered, and may continue to alter, use of full-text databases was highlighted as one of many areas where technology was continuing to change.[46] In addition, many journals publish the complete articles online, and this means that their entire content can be searched electronically. Also, some publishing houses, including BioMed Central, ScienceDirect and Wiley-Blackwell facilitate searching of their full text articles across their entire suite of publications. The expanding access that researchers have to full articles again highlights the importance of clear and transparent reporting throughout an entire publication.

The guidance also suggests that authors' consider using MeSH relating to one or all three aspects of time-to-event articles as keywords, and prioritised choosing those from the statistical term list. Authors are limited to using a small number of keywords, often five to six.[24] The initial guidance had suggested devoting one keyword to each of the three MeSH topics, but concern was raised in the feedback that authors may be reluctant to devote this number, and the guidance was therefore modified. The keywords help inform indexers. Indexing terms chosen by indexers should be used to indicate "who" was studied (humans, animals, adults), "what" was studies (type of treatment, type of material, type of outcome), "when" it was studied (prospective or retrospective), "where" it was studied (in vitro, in vivo) and "how" it was studied (such as cohort, controlled trial, cross sectional, time-to-event). Indexers can allocate as many or as few terms as they wish, and provision of keywords by authors will guide this process.

One respondent also commented that the authors did not always have control over the keywords chosen. In their experience, half the journals allowed authors to select those words, while the other journals chose the keywords for the authors. Therefore, it would be important that both authors and journal editorial boards were aware of recommendations regarding keyword selection.

The draft guidance document did not include specific advice on defining outcomes, considering whether they were primary or secondary or whether they were true or surrogate. Seven comments were received that recommended this advice be added. The feedback highlighted that outcome definitions were a specific problem in the dental literature, in particular in relation to what was defined as a successful, surviving and failed prostheses. This concern has also been raised in systematic reviews, specifically in dentistry,[47, 48] where poorly worded definitions have undermined both qualitative and quantitative analytic techniques. The importance of defining outcome measures has been highlighted in other guidelines.[15, 16, 49] This guidance document was designed to be complementary to those guidelines, providing supplementary information about the specifics of reporting time dependent outcomes, regardless of the study design. However, because this feedback was received from a number of respondents, it was decided to add this additional information to this guidance.

The feedback received on the draft guidance mirrors concerns collectively raised by the COMET initiative – Core Outcome Measures in Effectiveness Trials.[50] In a commentary by Clarke in 2007, problems in comparing and methods that limit use of different outcome measures was explored.[51] A systematic review in 2014[52] highlighted research fields where core outcome measures were being developed, such as rheumatology[53] and ulcerative colitis,[54] and reported that the research team was undertaking work to inform future guidelines for developing and reporting core outcome measures.

Feedback was also received in other areas that overlapped with guideline documents. For example, feedback suggested providing guidance to authors on what to write in the study background, how to describe participant inclusion, and what to include in the methods to allow study replication. This information is relevant for all study designs, and not for time-to-event studies in particular. Therefore, it was decided to refer readers to the complementary guidelines, rather than include this advice in this specific guideline.

Two respondents provided an interesting insight into the use of life tables and survival curves. One stated "Upon reflection, I think that I have only used life tables a handful of times in my own research - but I always want them in the works of others." Another stated, "One concern I always have is that we present information in the form of survival curves because they create a visual appreciation of what is happening. Tables are a little less visual but if I ever need to look at someone else's data it's much better if I can see the tables showing the numbers that are being reported rather than trying to extrapolate these from a curve." Life tables are informative, and when constructed well they provide information that enables interested readers to recalculate results from the raw data. This is useful for systematic reviewers, manuscript reviewers and readers who may wish to reassess the reported percentages. Survival curves, on the other hand, provide very little information about the numbers of participants at each time point, but delineate relationships between groups effectively at a glance, and probably more effectively than life tables. This guidance has suggested using a combined life table and survival curve. The combined figure takes less space than would be required for the individual figures separately, helping to overcome journal space limitations. The guidance also suggests that life tables or survival curves that could not be published should be retained by the author, or provided to an electronic depository, so that interested readers can see the figures should they wish. To this end, another respondent commented, "To a great extent we don't want to have every article include every curve and every life table but the authors should probably be incurred to somehow save this data and make it shareable with other authors/researchers."

Three respondents discussed the impact that poor reporting quality has had on their ability to complete systematic reviews. Clearly, higher quality reporting of primary research, where endpoints are clearly defined and data are clearly reported would improve the quality of systematic reviews. These studies are reliant on retrospective data, the quality of reporting of the primary authors, and the ability to obtain additional information when required.

Guidance on reporting time-to-event analyses will have its greatest impact if authors of relevant research use it. This may occur through authors finding the guidance published, being exposed to the guidance during education, or being directed to the document by journals and reviewers. The last two routes of exposure would probably be more common than the first. Exposure through these methods would translate theory into practice, and through sustained efforts, this uptake could increase over time. However, a Cochrane Review on whether journal endorsement of one of the most well known and widely endorsed guidelines, CONSORT, had an impact on the completeness of reporting of controlled trials found that much work remains to be done. The authors found that endorsement was beneficial and not a hindrance, but that completeness of reporting remained suboptimal.[55] Research assessing the impact that journal endorsement of seven reporting guidelines (other than CONSORT) had on the completeness of reporting of health research, was inconclusive, finding there was insufficient evidence to assess whether a relationship was present.[56, 57]

Inviting experts to comment on this guidance document allowed the draft document to be disseminated across known interest groups. As stated above, three journal editors wish to use the document, and two other respondents said that they wished to introduce the document to their specialists in-training. Assessment of the 2008 and 2012 articles, reported in chapters 2 and 7, showed that the five journals publishing the highest number of time-to-event articles were the IJOMI (13%), Clinical Implant Dentistry and Related Research (CIDRR, 13%), IJP (10%), Clinical Oral Implants Research (COIR, 10%), and Clinical Oral Investigations (COI, 4%). Two editors from these journals, the IJP and IJOMI expressed an interest in endorsing the guidance for use by potential authors and journal reviewers. Uptake and endorsement by the editorial boards of the other three journals would also translate into higher exposure, and a higher chance that the guidance would be able to help primary authors, and thereby those who read their articles.

Authors will also be targeted by publishing the guidance in an appropriate journal, and approaching the EQUATOR Network[18] to ascertain whether the document would be considered suitable for inclusion on their website. Consideration will be given to publishing this guidance in a preliminary form, allowing additional feedback to be gathered prior to undertaking formal validation. Further details of future post-doctoral research towards this end are provided in the concluding chapter of this thesis.

Once published, the guidance should be freely accessible online, by organizing open access either through journals which offer this for all articles, or by special request of a specific journal. Authors of interest are those publishing time-to-event articles in the dental literature. Review of the 2008 articles indicated those authors were publishing predominantly in the prosthodontic field, and that this field included tooth-supported and implant-supported prostheses. For this reason, there is an overlap with the periodontal literature. Publication in an informatics or methodologist journal could be advocated, but the guidance may have more impact if it was published simultaneously in a prosthodontic and implant journal. This may be possible if the journals were under the financial banner of the same publishing company, and therefore the target journals of interest are the International Journal of Prosthodontics and the International Journal of Oral and Maxillofacial Implants, both from Quintessence publications.

8.6 IMPLICATIONS

A convenience sample of experts in the dental field have endorsed the importance of improving the quality of reporting of studies reporting time-to-event survival outcomes, and general comments indicated that the majority found the draft guidance document pertinent, timely, and well written. The guidance document has been reviewed and modified and presented in this chapter. Endorsement of the guidance by key journals in the prosthodontic and periodontal fields will expose authors and manuscript reviewers to the recommendations, and over time this may help to improve the reporting quality of these articles. Participants were interested in improving reporting quality of time-to-event survival analyses, indicating that this dental community would support post-doctoral research validating the guidelines. Therefore, it would be worthwhile to pursue a project to validate the guidelines.

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CHAPTER 9. CONCLUSIONS FOR INDEXING, REPORTING AND IDENTIFICATION OF TIME-TO-EVENT SURVIVAL ANALYSES IN THE DENTAL LITERATURE

CONTENTS

9.0 SUMMARY OF RESEARCH FINDINGS

The findings of this programme of research are the result of assessing approximately 14,000 dental articles published in the years 2008 and 2012, and feedback from 46 professionals from 15 countries who had knowledge of time-to-event dental articles. The results relate to articles published in dental journals in the recent decade (chapters 2-5), and may also extend to those published prior to this time. Using the search strategy (chapter 7) will help identify articles that had already been published by overcoming some of the reporting shortcomings; and implementing the reporting guidance (chapter 8) will improve the reporting quality such that articles become easier to find and simpler to understand once identified. This will reduce waste that arises from a failure to identify and use time-to-event dental research.

Articles were identified to facilitate this volume of research, providing information on what has been considered the “burden of disease”. In this context, this refers to the “burden” of poor reporting or inaccurate indexing of dental survival analyses. The articles were sought from 50 dental journals published in 2008 that had the highest impact factor for that year. In total, nearly 7,000 articles were reviewed and those reporting survival of dental prostheses in humans with time-to-event statistics (n=95) and without time-to-event statistics (n=91), as well as all other articles that did not report studies of the survival of dental prostheses (n=6796) were classified as included ‘case’ articles, active controls and passive controls respectively. Thereafter, details contained within these 7000 articles were used to inform how the research was reported and indexed.

Time-to-event research concerns time-dependent outcomes and should include information about the outcome, time and time-related statistic.

People indexing articles use a standardised vocabulary, such as the Medical Subject Heading terms (MeSH) to classify details about the research. The words chosen indicate who and what was studied, and where and how it was studied. This means that MeSH indicating participants in the research, the outcomes studied, the timeline involved, the study technique used and how it was analysed are attached to the bibliographic electronic record, and allow searchers to identify articles in a standard manner.

With this in mind, chapter 3 reviewed whether MeSH regarding “what” (outcome), “when” (timeline), and “how” (time-to-event statistic) had been allocated to the time-to-event ‘case’ articles, and then whether these terms had also been used for any of the other 7,000 articles[1]. It was found that the allocation of MeSH to time-to-event dental articles in MEDLINE was inaccurate and inconsistent. Regarding one of the three groups of indexing terms studied, an important finding was that statistical MeSH were omitted from 30% of the included ‘case’ articles and incorrectly allocated to 15% of active controls. Such errors will adversely impact search accuracy. Despite this shortcoming, the indexing terms allocated to this cohort were now known. This information was retained and used to develop the search strategy to help overcome this indexing burden.

Chapter 4 reviewed what words had been used by authors in the titles and abstracts of their time-to-event ‘case’ articles, and then whether these words were used in any of the other approximately 7,000 articles.[2] Words describing the "what" (outcome), "when" (timeline), and "how" (time-to-event statistic) were sought.

It was found that there was great variation in the words used by authors to describe dental time-to-event outcomes. Such variation in reporting adversely impacts the ability of text "word" searches to identify relevant articles. This makes it difficult for those searching to identify the research they seek. Specifically, two-thirds of the included 'case' articles did not use words in the title or abstract highlighting "how" (time-to-event statistic) the research was conducted; and that other articles in the cohort at times also used these words. This use by the control articles was not necessarily incorrect, and was nearly always associated with cancer survival. Despite these reporting problems, the words used by authors were now known. These were tallied and retained to assist development of the search strategy to help overcome this reporting burden.

Chapter 5 reviewed how the time-to-event methods and results were reported in the body of the articles.[3] It is important that all scientific articles are reported clearly and with transparency, allowing those seeking information to make full use of the research findings. It was found that the time-to-event articles regularly used life tables or survival curves to delineate findings, and also described the results with survival statistical terms. Assessment of the reporting quality, however, found that important details were regularly omitted from both statistical descriptions and survival figures, making the overall quality of reporting poor. It was likely this would make it unnecessarily difficult for such articles to be indexed correctly in databases, found by people seeking them, and understood if they were identified. The problems of reporting quality were assessed, and the information used to inform a draft guidance document that aimed to improve the way dental survival research was written.

Chapter 6 summarised the information that had been gathered by the research presented in the preceding chapters. I concluded that there is a significant reporting burden affecting time-to-event dental survival analyses, which would adversely impact on accurate article identification, and that many of the articles that are found would be difficult to understand. Therefore, the level of research waste could be high. The research findings reported in the first part of this thesis have been published,[1-3] and I have also disseminated them in lectures at international dental conferences.

Undertaking the assessment meant that the way the time-to-event articles, and their nearly 7,000 counterparts in the same journals, had been reported was now known. This provided valuable data. Although the high reporting burden was a negative finding, the information gathered could be used in a positive way, allowing a search strategy to be developed to help find articles that had been published but might be "lost" in the literature, and allowing a guidance document to be developed to assist future authors to report their research clearly, and improve its usefulness when found.

Chapter 7 focused on the first part of this task. Data from the 2008 cohort were used to develop the search protocol, and its search performance was then tested in an independent validation dataset. This was derived from an additional handsearch of articles published in 2012 in the 50 dental journals with the highest impact factor for that year. The 6514 articles identified were classified as reporting dental treatments in humans with time-to-event statistics (n=148) and all other articles (n=6366).

Validated search protocols with conservative sensitivities up to 92%, precisions up to 93% and NNR to identify relevant records lower than two articles were constructed. Their use will improve the ability of researchers to identify time-to-event dental articles. This research has been accepted for publication[4].

Chapter 8 focused on the second part of the task of reducing the reporting burden impact. The information gathered from the earlier phases of this programme of research was used to draft guidance for the reporting of time-to-event dental outcomes, and feedback on this was sought from a group of experts known to have knowledge about time-to-event reporting in dentistry. From the 78 experts contacted, 46 from 15 countries provided feedback. In summary, those participating endorsed the importance of improving reporting quality of time-to-event survival studies, and indicated that the draft guidance document was pertinent, timely, and well written. The guidance document was amended based on the feedback. A range of participants wished to commend the document to authors submitting manuscripts, reviewers of those manuscripts, and dentists in specialty training programmes.

Participants were interested in improving reporting quality of time-to-event survival analyses, indicating that this community would support post-doctoral work to validate the guideline, and its dissemination. Communication will also continue with key journals in the prosthodontic and periodontal fields, aiming to expose authors and manuscript reviewers to the recommendations, and help with translation into practice.

This programme of research has sought to explore how dental articles that contain time-to-event data are reported, and to use these findings to inform recommendations improving researchers' ability to identify and then use these studies. This research has sought to reduce identity-waste and utilization-waste in the field of time-to-event dental survival analyses.

9.1 COMPARISON WITH EXISTING LITERATURE

Identifying articles reporting time-to-event outcomes is different to identifying articles reporting outcomes of cohorts, or outcomes of controlled trials. Cohort and controlled trials are recognized study designs, while time-to-event outcomes are not specific to one study method, and could be employed across a range of categories. Therefore, language to describe, indexing terms to categorise and searchers' understanding of these types of articles is probably less well established than that of the classic study designs. This problem is not unique to time-to-event outcomes. For example, research reporting the off-label use of pharmaceutical drugs is difficult to identify, and search protocols have been designed to help improve identification.[5]

Regarding reporting quality, existing research has found that reporting of statistics in studies has improved over the past 40 years,[6] following concerted efforts of a range of people to highlight problems and reporting solution. Studies reporting results with specific study designs, such as cohort studies and controlled trials have received guidance to improve quality of reporting,[7, 8] and assessments have found some improvements, but that these improvements do not apply across the literature as a whole.[9, 10]

Poor reporting quality results in avoidable research waste. An article series in the Lancet in early 2014[11-16] was devoted to exploring the problems underpinning research waste, options available to improve the situation, and recommendations to consider for the future. In 2009, Chalmers and Glasziou estimated from their review of studies that approximately 85% of research was affected, and equated this to financial waste running into billions of dollars.[17] In addition to fiscal disadvantages, Macleod and colleagues[16] reported that many initially promising research results did not seem to be impacting health care, citing as an example that over 95% of articles regarding cancer prognostic markers identified by a research group in 2005 had reported at least one significant prognostic variable, but that the findings had not impacted either future research or clinical practice.

Reporting quality of studies regarding time-to-event outcomes across a range of medical topics have been assessed,[18-22] with researchers finding that the quality of statistical results and figures could be improved.

My programme of research has added to this existing identity and quality knowledge base. I found that reporting quality of time-to-event dental articles was low,[2, 3] and concluded that this adversely impacted efforts to identify relevant studies. To help manage these problems, I developed search strategies[4] to improve the ability of searchers to identify articles that had been published, and suggested guidance to improve the reporting quality of future time-to-event articles.

9.2 IMPLICATIONS OF RESEARCH FINDINGS FOR PRACTICE

The findings from my research have two main implications: better identification and better use.

The way articles have been written in the past makes them difficult to find, and to use them once found. As stated above, the outcomes of my research led to a search tool to help identify articles, and a guidance document to help those writing new articles to present their findings with greater transparency.

Identification problems affect those seeking evidence. Searchers might be seeking primary research, or synthesized research that relies on the finding of that primary research.

It is probable that primary research articles that have enrolled a large number of patients or have reported results of significant clinical merit have been published with a higher degree of reporting quality than their counterparts. The authors involved in these studies may have included methodology and statistical consultants during writing, and worked with experienced reviewers during manuscript review. Given this scenario, such articles may be written with “words”, and then indexed with terms that aid ready identification, and once found the results may be easily interpreted by end users.

In a hypothetical alternative scenario, articles that have enrolled fewer participants, and reported results with less conclusive significance, may not have been supported by methodologists or statisticians during writing, and may not have benefited from experienced feedback during the review process. Such articles may still contain results that are important to practice, but they would be more difficult to find when sought, and more difficult to interpret once found. This lack of identification will have a particularly important effect on systematic reviews, because it may lead to bias and reduced power in the meta-analyses.

When a large volume of evidence is available, there is an argument for systematic reviews to seek only the highest quality and largest studies, rather than including all studies reporting outcomes on a specific topic. This may be possible in some medical fields, such as investigation of outcomes of drug therapies in common conditions. However, in dentistry, many studies enroll small numbers of participants, rarely follow controlled trial designs, and are often retrospective in nature. Therefore, every effort to identify all data remains extremely important to ensure findings are as balanced as possible.

Therefore, primary clinicians and policy makers who require results from systematic reviews to guide decisions will be particularly affected by poor reporting quality of time-to-event dental survival analyses, if those systematic reviews are unreliable. In addition, if such studies are identified, it will be unnecessarily difficult to understand the results for primary use, or to extract data for systematic reviews.

This may manifest itself in various ways. Primary clinicians may not find suitable data to guide treatment decisions, such as whether to replace a missing tooth with a single implant crown or a three unit fixed dental prosthesis. Decision makers may not find suitable data to guide funding decisions, such as whether community elders derive sufficient value with acceptable maintenance burdens from conversion of a complete mandibular denture to an implant retained overdenture to justify funding at taxpayer's expense. Additionally, dental researchers may believe that there are gaps in a particular knowledge base, and undertake research that had already been completed, but was not able to be found in the literature.

For example, a systematic review by Nkenke and Stelzle in 2009[23] regarding outcomes of implants placed in the posterior maxilla, with and without sinus augmentation appeared to miss at least two potentially relevant articles. The articles were not included in their paper's final assessment, and were not listed in their exclusion bibliography; but were identified by my handsearch as part of the 2008 article cohort (Chapter 2). Nkenke and Stelzle had searched MEDLINE and Embase for 1 January 1966 to 31 December 2008, and completed a supplemental handsearch of a range of dental journals.

The first of the two missing articles was published in April 2008 by Schlegel and colleagues[24] in the International Journal of Oral & Maxillofacial Implants. The article was added to the PreMEDLINE database on 14th June 2008, and the indexing for MEDLINE was completed on 12th August 2008. Therefore, when Nkenke and Stelzle undertook their search, the complete electronic record was available, and the article was printed in one of the journals that they handsearched. The article was allocated 21 MeSH, and these included two outcome MeSH (Dental restoration failure, Treatment outcome), one time MeSH (Retrospective studies) and no statistical MeSH. In the title and abstract, the authors used no survival words, a number of general outcome words, and also indicated that the research was conducted over time. To summarize the abstract, the research "*used no specific statistical techniques, to compare and evaluate outcomes such as implant loss and implant* *stability in a retrospective, follow up study over a mean functional observation period of 1.6 years.*" This article reported implant survivals using Kaplan-Meier statistics, and this was noted in the methods and results, but not in the abstract.

The second article was published in October 2008 by Bornstein and colleagues in Clinical Oral Implants Research.[25] The article was added to the PreMEDLINE database on 10th October 2008, but it was not indexed in MEDLINE until 7th February 2009. Although the electronic record of the article was not available on MEDLINE when Nkenke and Stelzle completed the electronic search, it had been printed in one of the journals that they handsearched. Across their title and abstract, the authors used a variety of time and outcome related words, as well as a general statistical term, "survival rate". Based on the specific words the authors used, their abstract can be summaries to be: "*Clinical and radiographic findings of the stability and performance, reporting success rates with no known statistical techniques over a follow up period during a prospective study also reporting lost to follow ups and drops outs when recalled at 12 and 60 months.*" In addition, a life table and survival statistical details were provided in the body of the article, but not noted in the abstract. Out of interest, thirty-six indexing terms were allocated to this article, including two outcome MeSH (Dental restoration failure, Treatment outcome) two time MeSH (Retrospective studies, Follow-up studies) and no statistical MeSH.

The indexing of these two articles was limited at best, and arguably incorrect, and the writing of the abstract was incomplete. They do not appear to have been identified by Nkenke and Stelzle, by electronic or handsearch, and it is possible that the omission was related to poor reporting quality.

An additional example relates to the reporting of outcomes of porcelain veneers, which is an area of my own clinical research. My paper reporting survival outcomes over a 16-year period[26] were allocated two outcome MeSH (Dental restoration failure, Treatment outcome), one time MeSH (Follow up studies) and no statistical MeSH. The title and abstract included words relating to outcomes (outcomes, failed, complications), time (prospective, up to 16 years, long term) and statistics (Kaplan-Meier, survival estimation, cumulative survival and failure rate). The body of the article included both a life table and survival curve, and the survival statistics were detailed in the methods and results. This article was not quoted during two comprehensive international lectures on porcelain veneers (Academy of Prosthodontics 2009, Australian Dental Association 2009), with neither lecturer acknowledging that the article was found during their literature search. Additionally, the article was not quoted in three research articles[27-29] and one review[30] concerning porcelain veneers. This may have been because it was difficult to find when sought. The abstract included a range of descriptive words that would have aided identification, and therefore difficulty identifying the article was probably mostly related to the limited indexing. As this was my own research, I resolved the identity problem by including this “lost” article in a subsequent systematic review, and ensured that it was referenced.

However, not all authors seek whether their research has been identified, and not all authors can resolve the problem by highlighting the missing paper in a systematic review. Use of my proposed search tool will help identify many of these lost articles, and use of the proposed guidance document will improve reporting quality such that when articles are found the data can be useful for end-users. Additionally, including descriptive words in article titles and abstracts will help identify the time-to-event articles with the search tool.

Clearly, the ramifications of non-identity and poor utility could affect everyday clinical treatment, and impact health care policy decisions at a societal level. Both problems affect individuals in different ways. Implementing the recommendations that arise from the findings of my research will provide two positive solutions that will reduce this research waste.

9.3 IMPLICATIONS OF FINDINGS FOR FUTURE RESEARCH

My proposed post doctoral research has two aims: validation and dissemination.

The search strategy has been validated, an undertaking that drew on the approximate 7,000 articles used to develop it and an additional 7,000 articles as the independent, validation sample. However, there is scope for further research. For example, the search strategy could be modified and validated for other fields of health, such as cardiology assessments of time-to-recurrence of atrial fibrillation following ablation surgery, or traditional survival assessments in cancer management.

The guidance document has not yet been validated. Validation would involve support from the research community, providing comment on the proposed guidance, and meeting to explore issues face-to-face. This can be organized over time, but will involve significant planning and financial resources. It might be possible to organize the face-to-face meeting as an addition to an international conference. Participants invited would be chosen to represent different international locations and stakeholder groups. These would include prosthodontists, periodontists, statisticians and other methodologists, and could include people from the original expert group.

To decrease the fiscal burden, it would be better if the conference chosen already attracted many of those who would be considered for participation. An appropriate venue could be the biennial International College of Prosthodontics meeting (ICP), with key periodontists, statisticians and methodologists also invited. The next opportunity for this endeavor would be in 2017.

Recommendations in the time-to-event guidance have been based on findings from my programme of research, and on feedback from experts. As such, it is well informed. One recent guideline, SAMPL[31], has been endorsed by the guideline website EQUATOR, without formal validation. I therefore raise the question, is the time and cost of undertaking a formal validation process justified; or is it worthwhile considering a truncated validation process to facilitate a more timely dissemination of the guidance to the community? Formal validation is valuable if contentious issues may arise, but this did not seem to be a significant problem when the expert feedback was assessed. In discussing the guideline, perhaps the most contentious issues have related to the subjective assessment of “meaningful time intervals”, and whether it was appropriate to allocate three MeSH to descriptions of the time-to-event method.

In my opinion, it is worth considering early publication of the guidance, prior to formal validation, and use that publication to both disseminate information and gather feedback from the wider community about the usefulness of the suggestions.

Researchers cannot avail themselves of these new research tools if they do not know that they exist. Dissemination of the search strategies and the guidance document will be sought through an academic advertising campaign. This will involve publication of the research tools, of articles discussing use of the tools, and commentaries explaining why the tools are required. It will also involve lecturing and abstract submission at local and international conferences, dissemination to educators involved in dental specialist training, contact with editors of key journals to engage interest in endorsement on journal websites and discussions with colleagues at a less formal level. Much of this work has begun, and will continue with upcoming invited keynote lectures at the International College of Prosthodontics (September 2015) and International Academy of Dental Materials (October 2015). Publications and previous lectures arising from this thesis are detailed in appendix 11.4.

9.4 CONCLUSIONS

This programme of research has shown how dental articles that contain time-to-event data have been reported, and developed research tools to improve the ability of researchers to identify and then use these studies. Implementing the new research tools developed during this research will reduce waste that has affected time-to-event dental survival analyses, through the failure to identify the material and failure to use it.

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SECTION 10. ALPHABETICAL REFERENCE LISTING

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SECTION 11. APPENDICES

CONTENTS

11.1 APPENDIX 1. REFERENCES FOR INCLUDED 'CASE' ARTICLES, N=95

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11.3 APPENDIX 3. FEEDBACK FROM EXPERTS REGARDING THE PROPOSED GUIDANCE DOCUMENT

11.3.1 Summary of feedback provided across the 9 themes, and changes made to the guidance document in response

THEME	#	RESPONSE TO FEEDBACK
1. Endorsement of merit or importance of the proposed guidance		
Number of respondents providing a range of general comments	20	No action required
Total	20	
2. Endorsement of writing quality and helpfulness of examples		
Number of respondents providing a range of general editorial comments	18	No action required
Total	18	
3. Endorsement of comments		
General endorsement	5	No action required
Electronic storage of unpublished figures	1	No action required
Endorse importance of good selection of keywords	1	No action required
Truncation of y-axis	1	No action required
Prioritise plotting measure of variance over censoring notation	1	Prioritising measure of variance has been re-emphasized in the checklist
Endorse current engagement of stakeholders to seek feedback on guidance	1	No action required
Total	10	
4. Editorial recommendations		
General	12	Reviewed and modified
Table 8: it would be more realistic (and perhaps easier to understand) if the numbers for censored differed from period to period	1	It was decided not to vary censoring and failed for life tables and curves. However, it could be argued either way.
Comment regarding maximising the length of abstract in the checklist: Unhelpful without an explanation, and probably unnecessary	1	Explanation is present in the explanatory document; comment was removed from the checklist during final editing.
Can the example figures have a few dramatic drops in the outcomes?	1	It was decided not to vary censoring and failed for life tables and curves. However, it could be argued either way.
Total	15	
5. Request for clarification		
Improve definition for "meaningful time intervals"	2	Further in-text and tabulated explanation added
Aims are general, objectives specific. Many would consider an hypothesis to be an objective. Rephrase?	1	General advice, not added to explanatory document
Ensure discussion and conclusions are seen as different entities	1	Separated discussion from conclusion in the explanatory document and the checklist
Could it be correct insert one keyword for each MeSH and the remaining are "free"	1	Emendation: "Authors should consider listing at least one MeSH indexing term from the

	to identify the topic of the research?		statistic-, outcome- and time-related MeSH categories as a keyword for their article, prioritising use of those from the statistic category.”
	Are the MeSH term of the Group 1 are in order of importance or of use?	1	MeSH in group 1 are not listed in the order of importance, but are in alphabetical order. This has been clarified.
	Table 3 suggests that survival curves should notate censored data on the curve, but figure 1 survival curve does not seem to have these notated.	1	Prioritising measure of variance has been reemphasized in the checklist
	Why is x-axis from time zero? Can it also be truncated?	1	Emendation: "It is not appropriate to truncate the x-axis, as this prevents notation of the standard error or censored data over time."
	Explain "censored" more clearly	1	Emendation: "Censorship is a common problem in time-to-event analyses because studies often recruit participants over time, and during the study period participants can become lost to follow up. This means that participants are not all present at the beginning of the study (because they have not all been recruited), and participants are not all present at the end of the study (because they have become lost to follow up). This results in censored data."
	Point to the area on the y-axis that indicates truncation	1	Truncation mark on figure 2 has been highlighted
	Explain why survival curves and life tables provide complimentary information	1	Emendation: "For example, specific changes in participant numbers is well delineated in life tables, but a sense the magnitude in changes in estimated cumulative survivals and variances is better explored graphically."
	Total	11	

6. Highlight possible problems			
	Achieving international consensus will be "quite a task"	1	Highlighted in discussion
	Consider challenges associated with “translation” into practice	6	Highlighted in discussion
	Consider where it would be most appropriate to publish the guidance, taking into consideration target audience and dissemination of information	2	Highlighted in discussion
	Highlight competing problems: writing good abstracts and titles which "capture attention", but also provide "scientific information"	1	Highlighted in discussion
	In relation to choice of words in the abstract: There is a potential conflict between use of focused terms and a broader approach to maximize inclusion in a biographical database.	1	Highlighted in explanatory document and discussion
	You suggest three “obligatory” keywords. Usually only five keywords are allowed, so authors may hesitate to use three for these categories.	1	Highlighted in discussion. Emendation: “Authors should consider listing at least one MeSH indexing term from the statistic-, outcome- and time-related MeSH categories as a keyword for their article, prioritising use of those from the statistic category.”
	The importance of choosing a good title, but "not to let the cat out of the bag"	1	Highlighted in discussion

	Total	13	

	7. Suggestions for additions		
	Provide link to webpage for CONSORT and STROBE guidelines	1	Weblink added
	Checklist – add sentence about background, and sentence about conclusions to the abstract section of the checklist	1	Not changed, as this is covered in other guidelines. Emendation to emphasize this in the explanatory document: "This guidance on time-to-event statistical reporting is intended to be used in conjunction with reporting guidelines for the relevant study designs, such as STROBE for observational cohort studies and CONSORT for randomised trials. Therefore, specific guidance on topics such as inclusion of background information, participant recruitment and inclusion criteria will not be covered."
	Describe patient groups well, and timeline for inclusion	1	Not changed, as this is covered in other guidelines. Emendation: "For example, specific guidance for well written introductions; differences between hypotheses, objectives and aims; and methods of participant recruitment and inclusion criteria will not be covered."
	Recommend that methods are written a-priori. For example, if participant inclusion is sequential it would be incorrect to state the number of participants in the final cohort at the beginning of the methods, as this was not yet known.	1	Not changed, as this is covered in other guidelines. Emendations as above: "For example, specific guidance for well written introductions; differences between hypotheses, objectives and aims; and methods of participant recruitment and inclusion criteria will not be covered."
	Provide guidance to describe methods to allow study replication	1	Not changed in the checklist, as this is covered by other guidelines. It has been added in the explanatory document.
	Consider risk mass-significance	2	Emendation: "If multiple significant tests are completed, authors should discuss the risk that the results found are due to mass-significant, and which steps were taken to limit this impact."
	Delineate the difference between primary and secondary outcomes	2	Emendation, explanatory document: "Researchers may choose a variety of different endpoints as outcomes. They could be primary or secondary outcomes, and could be true or surrogate markers. Particular confusion exists in the dental literature about the definitions of the subjective outcomes of success, survival and failure. If such outcomes are used, researchers should ensure that these are well defined." Emendation, checklist: "Outcomes should be classified as primary or secondary, true or surrogate."
	Delineate the difference between true versus surrogate markers	2	As above
	Define outcomes studied, including success and terminal events to allow comparison across studies	3	As above
	Might it also be relevant to explore other weaknesses in the study, the measures taken to try to circumvent them and their implications?	1	Emendation: "The discussion should highlight limitations of the study design, and their implications."

	Addition / completion of an explanatory document	2	Explanatory document has been finished.
	Provide good / bad examples of use of words in the abstract	5	Example abstracts added, using words and MeSH terms outlined in the document.
	Provide an example of a well written and structured paper	1	Example not added to this document. It was considered to be beyond the scope of this current explanatory guidance.
	Unit of analysis	1	Emendation, explanatory document: "The unit of analysis should be reported, and outcomes adjusted for clustering where appropriate. For example, outcomes could be reported per implant, or per patient. If multiple implants are present in the same patient, clustering occurs. " Emendation, checklist: "Report the unit of analysis and adjust for clustering where appropriate."
	Provide guidance to structure a spread sheet to help with life tables	1	Spread sheet for statistical analysis is beyond the scope of this guidance
	Censoring: Report a practical example in addition after the guidance	1	Emendation: "As a practical example, researchers may classify non-attenders as those known to have ceased participation, moved location, become medically unable to attend, passed away, or those who failed to return for reasons unknown. Numbers of non-attenders may be minimized by various techniques including assessing participants in an alternative location (such as a nursing home), offering out-of-hours appointments, enlisting the help of a participant's new practitioner to provide information, offering monetary incentives to attend, contacting the participant through their referring practitioner. Some studies go to extreme lengths to locate non-attenders, with one in the orthopedic literature enlisting the help of a private investigator. If non-attendance occurs, researchers should state whether participants were censored at the last known observation, immediately after the review period where they did not attend (as commonly occurs for Kaplan-Meier analyses) or half-way through the intervening observation period (as commonly occurs for life table analyses)."
	Discuss clinical versus statistical significance	1	Emendation: "Differences between clinical and statistical significance should be highlighted."
	Add to MeSH terms: Incidence and Prevalence	1	Incidence and Prevalence are not related to time-to-event methodologies
	Total	28	

8. Suggestions for abbreviation			
	Abbreviate the checklist to 1 page	4	A shortened checklist has been provided
	Simplify the MeSH table	2	MeSH was not simplified. It was endorsed by a range of other respondents, and changes were not considered to be necessary.
	Simplify word list. This is a long list, and you might comment on terms which may be preferred.	2	Although the word list had been endorsed in its original format, the suggestion for change was undertaken and the word list table has been separated into two tables. Emendation: "A list of potential descriptive words and related phrases regarding the statistic-, outcome- and time-aspects of time-to-event

			studies are provided in tables 6 and 7. Words that are specific to each topic are outlined in table 6, and words that could be used as additional descriptors are outlined in table 7."
	Total	8	

9. Comments exemplifying how reporting problems have impacted respondents			
	Paraphrased: Experience with ORONet has highlighted the importance of understanding MeSH and choosing appropriate endpoints. The current document will be pertinent and helpful.	1	Highlighted in discussion
	Upon reflection, I think that I have only used life tables a handful of times in my own research, but I always want them in the works of others.	1	Highlighted in discussion
	Observation: MeSH seems to be chosen "half by authors, and half by the journal editors"	1	Highlighted in discussion
	Observation: One concern I always have is that we present information in the form of survival curves because they create a visual appreciation of what is happening. Tables are a little less visual but if I ever need to look at someone else's data it's much better if I can see the tables showing the numbers that are being reported rather than trying to extrapolate these from a curve.	1	Highlighted in discussion
	Observation: quality of reporting is affecting systematic review inclusions	2	Highlighted in discussion
	In the domain of implant research, which I have concentrated on for the last number of years, there are considerable transgressions. The PEARL (Practitioners Engaged in Applied Research Learning) network has made strides in using multi-centred clinical research more relevant to the average practitioner in a typical setting. The number lost to follow-up when not included degrades the data. A perfect example is not including in the N-size implants that were lost before restoration. Here a Kaplan-Meier analysis would clarify this error.	1	Highlighted in discussion
	Total	7	

11.4 APPENDIX 4. PUBLICATIONS DIRECTLY RELATED TO THE THESIS

11.4.1 References for publications directly related to the DPhil thesis

11.4.1.1 Layton DM, Clarke M. Accuracy of Medical Subject Headings indexing of survival analyses in the dental literature. Int J Prosthodont 2014; 27:236-244.

Related to Chapters 2 and 3

11.4.1.2 Layton DM, Clarke M. Quality of reporting of dental survival analyses. J Oral Rehabil 2014;41:928-940.

Related to Chapter 4

11.4.1.3 Layton DM, Clarke M. Will your article be found? Authors choose a confusing variety of words to describe dental survival analyses. Clin Oral Implants Res 2015:26:115-122.

Related to Chapter 5

11.4.1.4 Layton DM, Clarke M. Search strategy to identify dental survival analysis articles indexed in MEDLINE. Int J Prosthodont 2015:In Press.

Related to Chapter 7

11.4.1.5 Layton DM. How to find dental survival articles: Using the new search strategies. Int J Prosthodont 2015:In Press.

Related to Chapter 7

11.4.1.6 Layton DM. Clarke M. Lost in translation: review of identification bias, translation bias and research waste in dentistry. Dent Mater 2015: In Press

Related to the volume of work

11.4.1.7 Layton DM, Clarke M. Research waste: How are dental survival articles indexed and reported? Int J Oral and Maxillofac Implants 2015:In Press

Related to Chapter 6

11.4.2 References for publications related to time-to-event statistics in dentistry

11.4.2.1 Layton DM. Statistical Certainty: Understanding Kaplan-Meier Survival Statistics. Int J Prosthodont 2012:25:652-653.

11.4.2.2 Layton DM. Understanding Kaplan-Meier and survival statistics. Int J Prosthodont 2013;26:218-226.

11.4.2.3 Layton DM. Survey of the use of Statistical Methods in the International Journal of Prosthodontics. Int J Prosthodont 2015;28:315-322.

11.4.2.4 Layton DM. Understanding sources of bias within systematic search strategies. Int J Prosthodont 2015: In Press.