CLARISCIENCE

ARTICLE OUTLINE

Any manuscript should be designed appropriately before writing. Its logical strutcture can be described through an outline. This makes writing easier and ensures completeness and consistency.

Foreword

This outline simulates that of a comparative retrospective study concerning the use of two devices, named System 1 and System 2, which were used to treat a condition of interest. Usually, such condition calls for preliminary, early treatment. After this is done, it can be definitively treated according to Procedure 1 or Procedure 2 (the two approaches being utterly different). Some evidence seems to suggest that Procedure 2 might be better. Procedure 2 can be carried out using devices belonging to different "classes", the difference among classes being the main constructive and operating principles of the devices.

Both devices that were investigated, System 1 and System 2, belong to one of these "classes". The authors, working at a single Medical Center, compared them concerning their safety and effectiveness when they were used to treat the condition of interest, as no one had ever done it before. To get preliminary results, they assessed retrospectively their clinical records.

They drew up a clinical investigation protocol (XX_CIP) and a statistical analysis plan (XX_SAP). They sought for, and achieved, an EC approval. After assessing their clinical records as detailed in their CIP and carrying out statistical analyses as detailed in their SAP, they produced a full clinical investigation report (XX_CIR). They provided the medical writing team with the three documents (XX_CIP, XX_SAP, XX_CIR) and briefed the team concerning the clinical context and meaning of their findings. They also provided the team with the literature they retrieved for drawing up the CIP and the SAP.

The team, after being briefed, studied the documents provided by the authors and drafted the following outline which was the basis for further discussion and refinement. The final outline was then used to draw a first full draft of the manuscript.

The outline that follows refers to no actual study and should be adapted according to the study design involved (e.g., a prospective one, etc.). It must be construed as a simple example of how a manuscript outline could be organized to facilitate discussion between authors/writers, as well as writing a full manuscript draft.

All exemplificative text is written in dark gray and identified by this icon:

> 

Article sections

The article to be written will follow the classic structure of a clinical manuscript i.e., it will be divided into the following sections:

- Title
- Authors
- Affiliations
- Abstract
- Keywords
- Introduction
- Materials and Methods
- Results
- Discussion
- Conclusions
- Tables
- Figures
- References
- Acknowledgments

The present document lists, for each section, the main messages that will be included in that section in the form of a bullet points list. The list will be cross-referenced with relevant documents.

In the whole, this document aims to provide the logical backbone of the article. Specific objectives are:

1. The logical flow of the article must be linear, straight and simple
2. The logical flow must be consistent
3. Crucial statements must be clearly supported by sound evidence (published literature or study data)
4. The final message must be clinically sound and consistent

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ARTICLE OUTLINE

[INSERT TEMPTATIVE MANUSCRIPT TITLE HERE]

Article structure

Title

The following title is being proposed:

Management of the clinical condition of interest using two different "Class" Systems. A comparative retrospective study.

Authors and affiliations

The following persons will be listed as the Authors of the paper, in the following order:

1st Author; 2nd Author; ...

[1] Department 1, Institution 1
[2] Department 2, Institution 2
...

Note: when submitting the manuscript, usually the following information are required for each Author, and should be collected in advance:

1. *Full name*
2. *Full affiliation(s): Institution, department, address.*
3. *Titles (e.g., MD, others)*
4. *E-mail address*

The corresponding Author will be [Name of corresponding Author].

Abstract and keywords

The abstract will summarize the content of the manuscript. Keywords might be:

"Keyword1"; "Keyword2"; "Keyword3"; "Keyword4"; "Keyword5".

Introduction

The introduction section will develop through the following points:

This first part of the introduction will introduce the clinical context of the study. First, a clinical description of the condition of interest will be provided, by describing:

1. *Possibly, its epidemiology (see for example Author1, Year1 and references they cite, Author2, Year2 and references they cite).*
2. *Its etiology:* — *Cause no.1 or Cause no.2 (Author3, Year3; Author4, Year4).*
3. *Its clinical presentation:* — *Clinical signs at presentation including those requiring immediate attention (Author5, Year5)*
4. *The need for early treatment 1:* — *This condition requires early treatment 1 (Author6, Year6; Author7, Year7)*
5. *The need for early treatment 2:* — *This condition requires early treatment 2 (Author8, Year8)*

A section will follow stating that while a consensus exists on initial treatment, a debate is still open on what the most effective definitive treatment strategy is:

1. *Definitive treatment may be carried out either according to Procedure 1 (Sub-procedures 1.1 or 1.2) or to Procedure 2 (Author9, Year9)*
2. *At present, which is to be preferred is still subject of debate (Author10, Year10; Author11, Year11) but Procedure 2 might be more advisable (Author12, Year12; Author13, Year13).*

We propose to skip citing the history of treatment of this clinical condition and the fact that first evidence indicated the Procedure 1 was superior to Procedure 2, to keep the introduction as linear as possible [to be discussed with Authors].

Then, possible advantages or Procedure 2, compared to possible disadvantages of Procedure 1 will be discussed. The following advantages of Procedure 2 will be briefly cited (Author14, Year14; Author15, Year15)

1. *Advantages concerning invasiveness*
2. *Advantages concerning managing diversity at presentation*
3. *Advantages during treatment*
4. *Advantages concerning complications*
5. *Advantages concerning early patient's recovery*
6. *Advantages concerning effectiveness in fav oring healing.*

The two Systems allowing to apply Procedure 2 will be described. It will be underlined as they belong to a certain advanced "Class" and so they may present additional advantages compared to the traditional ones:

1. *Their common constructive and operating principles will be presented, reminding the reader they were developed by modifying the first historical system used for this purpose. Such modifications will be briefly summarized [possibly, some of the pioneering works by Author16, Year16 and Author17, Year17 will be cited here]*
2. *Systems belonging to this Class may provide Advantage 1 compared to historical, traditional systems they were developed from*
3. *They allow to get, thanks to their constructive and operating principles, also Advantage 2*
4. *They facilitate intra-treatment and post-treatment patient management thanks to an additional feature they both share*
5. *They allow for fine-tuned post-treatment additional management, thanks to one more additional feature the share.*

Other advantages, if any to be listed, will be derived by some reviews on the subject (for example, the review by Author18, Year18, may provide useful hints even if dealing with the medical condition in pediatric patients (not to be cited for this very same reason).

Different systems belonging to this Class are available on the market. System 1 and System 2 are among these. They are both indicated to treat the clinical condition of interest.

[Note, possibly, differences between the two systems will be reported here as highlighted by Author19, Year19]

1. *System 1 has been shown to provide early benefit to the patients (Author20, Year20) and to allow definitive treatment of the condition of interest (Author 21, Year21), the healing time and the complication rate being known with a certain degree of accuracy.*
2. *Yet no published data are available on the healing time and complication rates of patients affected by the clinical condition of interest when they are treated using System 2 and, further,*
3. *no studies have compared System 1 and System 2 when used for managing the clinical condition of interest in the adult population.*

For this, this study aims to compare System 2 and System 1 concerning their safety and effectiveness in treating the condition of interest through a retrospective analysis of clinical records of in-patients treated at Medical Facility [Name] from [Study Begin Time] to [Study End Time].

Materials and methods

The materials and methods section will develop through the following points:

For example:

First, criteria for record inclusion and exclusion will be provided:

1. *Clinical records were selected among those of patients admitted to the [Name] department at Medical Facility [Name] presenting the clinical condition of interest and treated between [Study Begin Time] and [Study End Time].*
2. *Records were included for further analysis if concerning patients who:*
   - *Had at least [Minimum allowed age] years when treated;*
   - *had the clinical condition of interest, presenting with the following clinical signs (Sign1, Sign2);*
   - *after early treatment, were definitively treated either by using System 1 or System 2;*
   - *had a regular indication for treatment with systems belonging to this Class;*
   - *completed the treatment by [Study End Time].*
3. *Records were excluded if patients:*
   - *Had a medical condition that is a contraindication according to System 1/2 manufacturers instruction leaflet, (these will be detailed in the manuscript);*
   - *were having a concomitant treatment with a device not permitted.*
4. *A statement will be then added concerning the fact that an Ethical Committee approval was sought for, even if the study was retrospective in nature, and the no. / date of approval.*

Second, a list of data extracted from the clinical records will be provided:

- *age at treatment,*
- *sex,*
- *comorbidities (Comorbidity 1, Comorbidity 2, Comorbidity 3...),*
- *type of clinical condition according to Standard Classification 1 and Standard Classification 2*
- *date of preliminary treatment*
- *date of definitive treatment*
- *system being used (either System 1 or System 2)*
- *details on the use of the systems,*
- *treatment duration, that is the duration of application of either System 1 or System 2*
- *healing time*
- *concomitant treatments*
- *number of intra-treatment instrumental images acquired*
- *number and time of post-treatment diagnostic images acquired*

- *complications (classified as minor or major according to Table [Number] of the XXX_ SAP)*
- *analgesic prescription*
- *pre-treatment and post treatment healing / function outcome scores (Standard Score 1, Standard Score 2)*

Third, statistical data analysis will be described

1. *Details of the sample / effect size calculation will be provided as described in Paragraph [Number] of the XXX_ SAP*
2. *The use of different tests to investigate differences between the characteristics at baseline of the two groups and treatments will be described, as reported in Table Number] and [Number] of the XXX_ SAP*
3. *The two main outcomes and the corresponding endpoints will be declared*
   - *Primary outcome: comparing the two systems as far as the time to healing is concerned*
   - *Secondary outcome: comparing the two systems as far as the following variables are concerned:*
     - *Complications*
     - *Time needed to use the system/ operative time*
     - *Number of intra-treatment and post-treatment instrumental images acquired*
     - *Function and healing scores*

The methods to investigate the effect of the different systems on the variables of interest i.e., the matched-analysis using GLM-Mixed (GLMM) models will be stated and described. Specifically, the difference between the two groups for the different variables of interest will be assessed using the following statistical tests:

- *Time to healing:* *Wilcoxon Test for independent samples*
- *Complications:* *Chi square*
- *Operative time:* *Wilcoxon Test for independent samples*
- *Number of images acquired:* *Wilcoxon Test for independent samples*
- *Function and healing scores:* *Chi square*

Results will be stated to be provided as medians, percentages, or mean +/- standard deviation and that test results were regarded as significant if p <0.05. It will be stated that data analysis was performed with the R System version 3.3.2 with RMS libraries.

Results

The results section will develop through the following points:

First, a description of the whole set and the two groups of patients will be provided, listing:

1. *Baseline characteristics, such as Number, Age, Sex (data will be extracted from table [Number] of the XX_CIR*
2. *Treatment characteristics, extracting data from table [Number] of the XX_CIR*

Second, results concerning the primary and secondary outcome will be presented, according to table X of the XX ANALYSIS REPORT

Third, results of the analysis carried out thanks to the General Linear Model will be described and specifically,

1. *Main results (concerning the primary outcome)*
   - *That System 2 performs better than System 1, with a difference – as far as healing time is concerned – of -YY.YY days, and a CI of -ZZ.ZZ to -XX.XX days. Accordingly, System 2 showed a smaller healing time of at least XX.XX days.*
2. *Other results (related to the secondary outcome)*
   - *That intra-treatment Action 1 has a significant (negative) effect on the healing time;*
   - *That concomitant Treatment 1 has a significant (negative) effect on the presence and number of major complications;*
   - *That the type of System (1 or 2) has no effect on the occurrence and number of major complications;*
   - *That the type of System (1 or 2) has no effect on the number of images acquired either during or after treatment.*

Discussion

The discussion section will develop through the following points:

First, a summary of open questions concerning the management of the condition of interest will be presented (no more than 5-7 lines)

Second, the main results of the study will be discussed.

1. *discussion will first focus on the main result, i.e., a significantly smaller healing time using System 2 compared to System 1. This part will take most of the discussion.*

   - *This result will be discussed at the light of the differences in construction of the two systems. It will be hypothesized that, since System 2 has a certain constructive and distinctive characteristic [Name], it might feature the property [Description], that is expected to be beneficial in treating the condition of interest.*
   - *It will be pointed out how this hypothesis should be verified through additional, properly designed studies (for example, bench studies).*
   - *If possible, study results will be then discussed at the light of previously published literature, both concerning System 1 (see, for example, Author22, Year22; Author 23, Year23; Author 24, Year24; Author25, Year25) and System 2 (Author 26, Year26; Author27, Year27) and, more generally, the use of Procedure 2 using Systems belonging to the same Class of System 1 and 2 to treat the clinical condition of interest.*

Third, the remaining results of the study will be discussed.

- *The fact that intra-treatment Action 1 has a significant (negative) effect on the healing time will be discussed at the light of the fact that that specific intra-treatment action is known to have a detrimental effect on the healing process [possibly, the discussion will reference here one of the initial works of Author28 on the subject, see Author28, Year28]*
- *The fact that concomitant Treatment 1 has a significant (negative) effect on the presence and number of major complications will be discussed at the light that applying concomitant treatment 1 is known to increase treatment time significantly (Author29, Year29), which – in turn - is known to increase the complication rate significantly (Author30, Year30)*
- *The fact that no difference were observed between System 1 and System 2 concerning occurrence and number of major complications and the number of images acquired either during or after treatment will be discussed at the light that while the two systems differs only for the constructive feature that is supposed to explain why System 2 performed better than System 1, but that this feature is clearly not expected to affect these two endpoints.*

Fourth, limitations of the study will be highlighted, i.e., that

1. *The study is retrospective in nature and that the number of subjects is limited.*
2. *That results concern a single medical center*

Fifth, suggestions to overcome these limitations will be provided, and specifically that

1. *Further studies, prospective and randomized in nature, are needed to confirm the study findings*

Conclusions

The conclusions might be as follows.

System 2 might be more effective than System 1 when used to treat patients affected by the clinical condition of interest as far as the healing time is concerned, while showing a similar safety profile. Such difference might be due to diversities in the systems' construction principles, and namely in their constructive characteristic [Name]. When such characteristic is of the kind as in System 2, the system might feature the property [Description], that is expected to be beneficial in treating the condition of interest. The hypothesis that characteristic [Name] provides the system with the property [Description] should be investigated by proper bench tests. Prospective controlled clinical investigations are needed to confirm the finding of the present study concerning the two systems under assessment.

References

Author1, Year1, Title1, Journal1, Volume1, Page X-XX
(...)
Author30, Year30, Title30, Journal30, Volume30, Page X-XX