Leids Universitair Medisch Centrum

Research Waste in Total Knee Arthroplasty Studies: An Observational Study on Registered Trials

Start project 1st January 2021, expected date of completion 31st December 2024

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INTRODUCTION

- Total Knee Arthroplasty
  - widely performed orthopedic procedure
  - growing rapidly due to the increasing prevalence of knee arthritis
- Clinical studies vital up-to-date and evidence-based patient treatment.
- Trial discontinuation and selective reporting impact
  - Evidence-based clinical practice
  - Introduces research waste
- Various guidelines, recommendations, and studies focused on
  - Improving successful completion
  - Improving successful publication

AIM

Assessment of:

- Successful finalization (within 5 years),
- Timely publication (within 7 years),
- Consistent publication of preregistered primary outcomes,
- Associated factors

Total Knee Arthroplasty studies registered between 2000-2015 over time.

METHODS

- Search ClinicalTrials.Gov for Total Knee Arthroplasty studies registered between 2000-2015
  - Extraction required and optional elements.
- Search Embase, Cochrane Library, Web of Science, PubMed, and Google Scholar for published literature on the included studies
  - Extraction published primary outcome.
- Kaplan-Meier curves: the time to publication
- Cox regression analyses: associations between variables and on-time-publication

RESULTS

We included 1,014 registered studies on Total Knee Arthroplasty (816 interventional; 198 observational). We found 634 unique references linked to included studies.

Percentage successfully finished interventional trials

2000-2001: 9.1%

2014-2015: 61.2%

Percentage successfully finished observational studies

2002-2003: 20.0%

2014-2015: 49.1%

Percentage successfully published interventional trials

2002-2003: 22.2%

2014-2015: 52.3%

Percentage successfully published observational studies

2004-2005: 12.5%

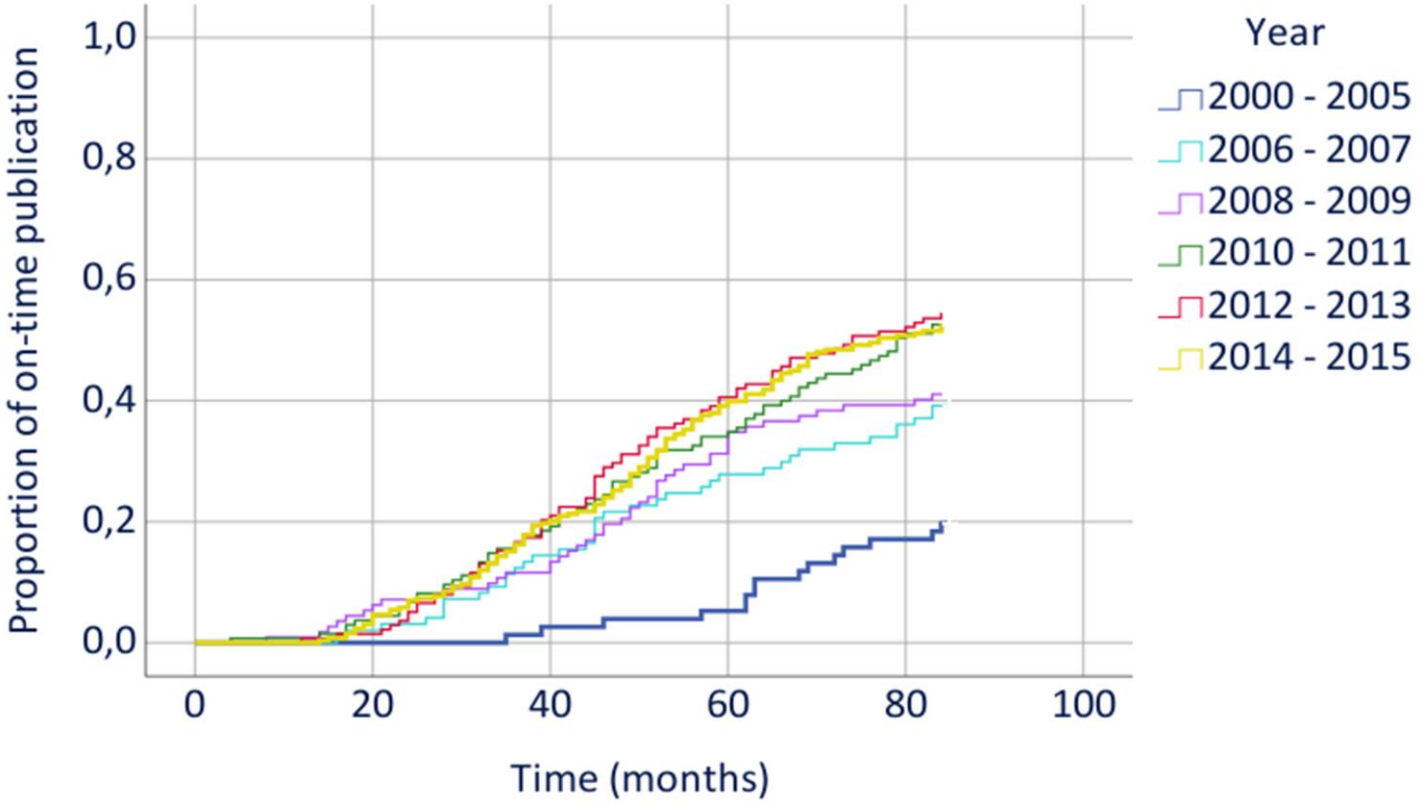
2014-2015: 43.4%

Industry-funded interventional trials were associated with a smaller chance of on-time publication (HR 0.73[95% CI 0.53 to 1.02]).

The association of a single-group assignment with on-time-publication reversed after adding this to the multivariable analysis, implicating assignment and allocation interfere.

Timely publication of the preregistered primary outcome

Interventional trails



* Kaplan Meier curves for the timely publication (within 7-years) of interventional trials and observational studies. The preregistered primary outcome is the primary outcome registered in the protocol on ClinicalTrials.gov.

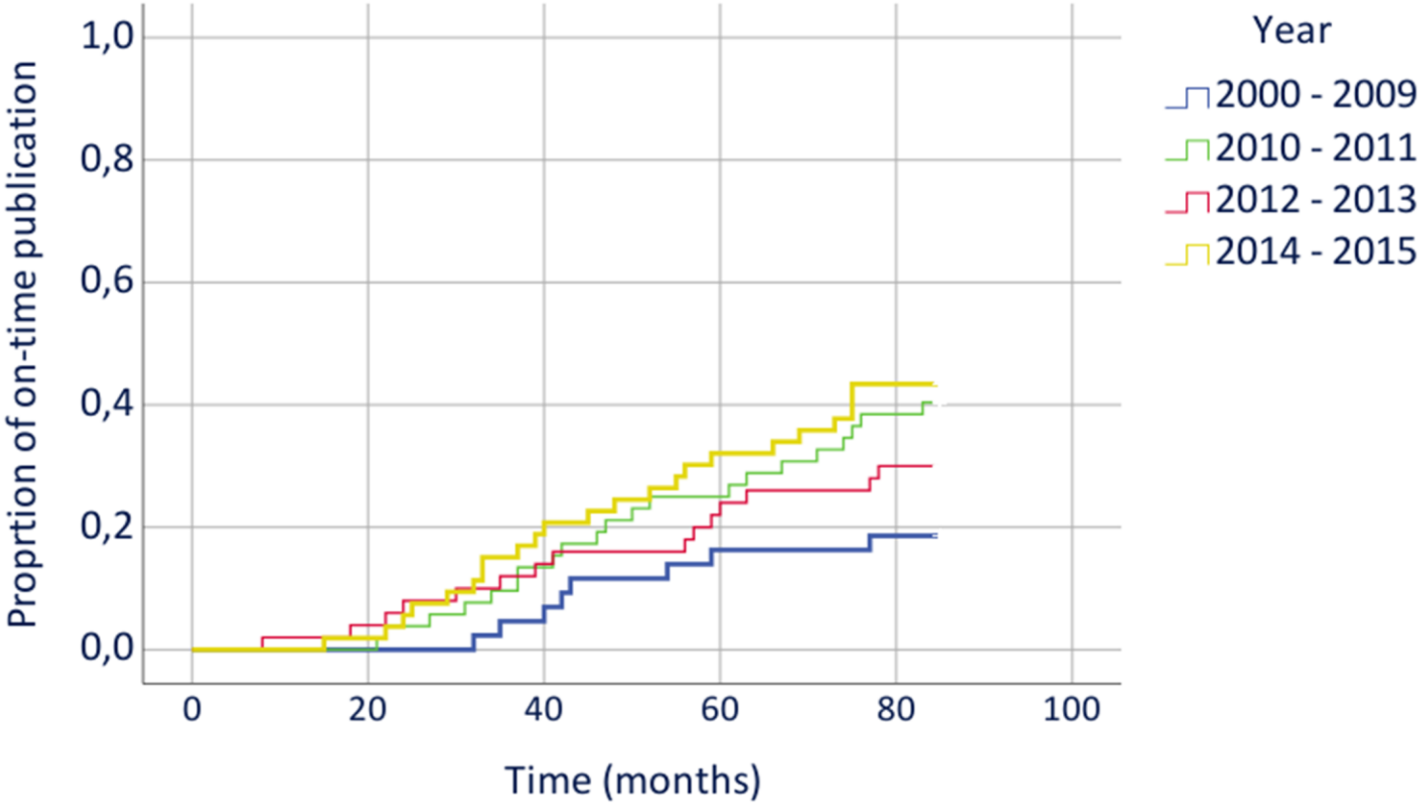
CONCLUSION

Our study showed that discontinuation and nonpublication were frequent, as were challenges in the timely and consistent publication of preregistered primary outcomes. While there was an improvement over time, the frequency remained substantial.

This emphasizes the need for better adherence to reporting guidelines and comprehensive information in registries, protocols, and results reports.

Timely publication of the preregistered primary outcome

Observational studies



* Kaplan Meier curves for the timely publication (within 7-years) of interventional trials and observational studies. The preregistered primary outcome is the primary outcome registered in the protocol on ClinicalTrials.gov.

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WILL YOUR STUDY BE COMPLETED ON TIME?

"Completion and Publication Rates of Total Knee Arthroplasty Studies Over Time: An Observational Study on Registered Trials"

INTRODUCTION

Total Knee Arthroplasty is a widely performed orthopedic procedure that is growing rapidly due to the increasing prevalence of knee arthritis. Clinical studies are vital in establishing the most up-to-date and evidence-based patient treatment. Trial discontinuation and selective reporting may significantly impact evidence-based clinical practice and introduces research waste. Various guidelines, recommendations, and studies focused on improving successful completion and publication of newly initiated trials in the last decade.

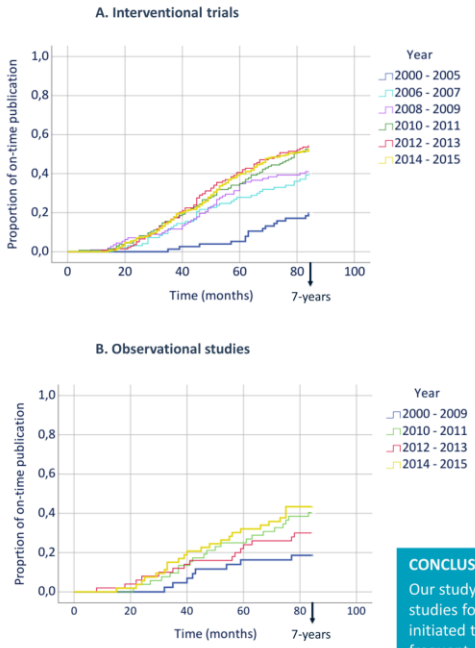
AIM

We aim to assess the successful finalization (within 5 years), timely publication (within 7 years), consistent publication of preregistered primary outcomes, and the associated factors of total knee arthroplasty studies registered between 2000-2015 over time.

METHODS

We searched ClinicalTrials.Gov for Total Knee Arthroplasty studies registered between 2000-2015 and extracted required and optional elements. We searched Embase, Cochrane Library, Web of Science, PubMed, and Google Scholar to identify published literature on the included studies and extracted the published primary outcome. We used Kaplan-Meier curves to visualize the time to publication of the preregistered primary outcome, and Cox regression analyses to explore associations between the variables and on-time-publication of preregistered primary outcomes.

Figure 1A + B: Timely publication of the preregistered primary outcome*



* Kaplan Meier curves for the timely publication (within 7-years) of interventional trials and observational studies. The preregistered primary outcome is the primary outcome registered in the protocol on ClinicalTrials.gov.

RESULTS

We included 1,014 registered studies on Total Knee Arthroplasty (816 interventional; 198 observational). We found 634 unique references linked to included studies.

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Industry-funded interventional trials were slightly associated with a smaller chance of on-time publication (HR 0.73[95% CI 0.53 to 1.02]). The association of a single-group assignment with on-time-publication reversed after adding this to the multivariable analysis, implicating assignment and allocation interfered.

CONCLUSIONS

Our study showed that despite various guidelines, recommendations, and studies focused on improving successful completion and publication of newly initiated trials in the last decade, discontinuation and nonpublication were frequent, as were challenges in the timely and consistent publication of preregistered primary outcomes. While there was an improvement over time, the frequency remained substantial.

This emphasizes the need for better adherence to reporting guidelines and comprehensive information in registries, protocols, and results reports.

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QUESTIONS – comments reviewers

My main comment is the Cox regression analysis. This study is more ecologic, pulling factors the authors could identify from studies themselves rather than knowing for each individual study what may or may not have led to success. Further, as there was a cut-point created by the authors (5 and 7 years) how many studies might still just be ongoing, taking longer than their cut-point? The interpretation of more or less likely to be published on time (yes/no) appears off as the Cox regression is looking at time-to-event. Also, is "on time" based on the author's own definition or each trials own definition?

QUESTIONS – comments reviewers

Is there a reason for the breakdown by 2-year intervals? With such narrow intervals, there's little information to be learned across many of the intervals until maybe 2008/2010 and later.

QUESTIONS – comments reviewers

A situation which may often arise is that a study that is still enrolling patients decides to publish preliminary data based on an interim analysis. In that case, the study may appear as still actively enrolling or NOT completed but still have a publication related to the study. How did you go around that situation? This situation may result in confounding, since the study definitely published the results but it is not completed yet. For those cases, I would advocate for dropping that study from the completion analysis as there is already a publication that derived from the study.

QUESTIONS – comments reviewers

Another question: The paper was rejected multiple times: JAMA, CORR, EFFORT Open and JBJS. Do you have advise on where to publish the article: which audience is most interested in the results or can learn something from this?

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