RSA-tested TKA implants on average have lower mean 10-year revision rates than non-RSA-tested designs

Hasan, S.; Marang-van de Mheen, P.J.; Kaptein, B.L.; Nelissen, R.G.H.H.; Pijls, B.G.

Clin Orthop Relat Res (2020) 478:1232-1241
DOI 10.1097/CORR.0000000000001209

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

8th International Congress of Arthroplasty Registries (Guest Editor Ola Rolfson MD, PhD)

RSA-tested TKA Implants on Average Have Lower Mean 10-year Revision Rates Than Non-RSA-tested Designs

Shaho Hasan MD, Perla J. Marang-van de Mheen PhD, Bart L. Kaptein PhD, Rob G. H. H. Nelissen MD, PhD, Bart G. Pijls MD, PhD

Received: 12 September 2019 / Accepted: 19 February 2020 / Published online: 9 March 2020

Abstract

Background The number of revisions after TKA is expected to rise because of aging populations in many countries and because patients are undergoing TKA at younger ages. Aseptic loosening is a major reason for late revision, which can be predicted by radiostereometric analysis (RSA) of small groups of patients at 2 years of follow-up. RSA is therefore an ideal tool to assess new TKA designs before they are introduced to the market, although not every TKA design has been studied with RSA. If RSA-tested TKA designs have lower 10-year revision rates in national registries than non-RSA-tested TKA designs, RSA testing of all new designs could be advocated.

Questions/purposes In this study, we asked: Is there a difference in the all-cause revision rate between non-RSA-tested and RSA-tested TKA designs registered in national knee arthroplasty registries at 5 and 10 years of follow-up?

Methods Knee arthroplasty registries were identified through the European Federation of National Associations of Orthopaedics and Traumatology webpage and through a manual internet search. Inclusion criteria were a minimum follow-up duration of 10 years and available revision or survival data per TKA design. Twenty-six registries were identified; seven were included comprising 339 TKA designs, of which 236 designs were classified as RSA-tested and 103 as non-RSA-tested. Six registries were excluded because no report was published. One registry was excluded because no fixation method was mentioned (79 TKA designs). Another registry was excluded because there was no 10-year data available (22 non-RSA-tested designs; 10 RSA-tested designs). Eleven registries were excluded because they did not provide revision rates per design and had not reached 10 years follow-up. The revision rates with their standard errors were extracted per design. We used the data from a recent meta-analysis to identify whether a TKA design was previously tested with RSA. This meta-analysis found 53 RSA studies comprising 70 different TKA designs. The prosthesis model, fixation method and insert type were extracted from these RSA-studies. The design characteristics of the TKA reported in the knee arthroplasty registries were also extracted, and if possible, matched to the TKA designs reported in the RSA-studies. At 5 years of follow-up, 191 TKA designs were identified as non-RSA-tested and 92 were identified as RSA-tested. At 10 years of follow-up, 154 TKA designs

Each author certifies that neither he or she, nor any member of his or her immediate family, has funding or commercial associations (consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.
Clinical Orthopaedics and Related Research® neither advocates nor endorses the use of any treatment, drug, or device. Readers are encouraged to always seek additional information, including FDA approval status, of any drug or device before clinical use.
Each author certifies that his or her institution waived approval for the reporting of this investigation and that all investigations were conducted in conformity with ethical principles of research.

S. Hasan, B. L. Kaptein, R. G. H. H. Nelissen, B. G. Pijls, Department of Orthopaedics, Leiden University Medical Center, Leiden, the Netherlands

P. J. Marang-van de Mheen, Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, the Netherlands

S. Hasan (✉), Leiden University Medical Center, Albinusdreef 2, 2333ZA Leiden, the Netherlands, Email: S.Hasan@lumc.nl

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research*® editors and board members are on file with the publication and can be viewed on request.

Wolters Kluwer

and 74 TKA designs were classified as non-RSA-tested and RSA-tested, respectively. A random-effects model using the Metafor Package in R statistics was used to estimate the pooled revision rate at 5 and 10 years of follow-up for both groups. The difference in revision rates between groups at 5 and 10 years of follow-up was estimated by including RSA as a factor in the random-effects model.

Results Mean all-cause revision rates at 5 years for non-RSA-tested and RSA-tested implants were 3.6% (95% CI 3.4 to 3.8) and 2.9% (95% CI 2.7 to 3.0), with a mean difference of 0.6% favoring RSA-tested implants (95% CI 0.4 to 0.8; $p < 0.001$). Mean all-cause revision rates at 10 years for non-RSA-tested and RSA-tested implants were 5.5% (95% CI 5.2 to 5.9) and 4.4% (95% CI 4.1 to 4.7), with a mean difference of 0.9% favoring RSA-tested implants (95% CI 0.4 to 1.3; $p < 0.001$).

Conclusions Although there are exceptions, across registries, TKA designs that have been tested in an RSA setting have a slightly lower (about 1%) mean all-cause revision rate at 5-year and 10-year follow-up than those tested in a non-RSA setting. Acknowledging the inherent limitations of this observational study, a risk difference of 1% could potentially translate into an approximate 20% decrease in revision burden up to 10 years, which may have a profound impact on patient morbidity and health-related costs.

Level of Evidence Level III, therapeutic study.

Introduction

The number of revisions after TKA is expected to rise because of aging populations in many countries and because of increased usage of this procedure in younger patients [17, 32]. Unfortunately, the introduction of newer TKA designs has not always resulted in fewer revisions [1, 28]. A major reason for long-term revision of a TKA implant is aseptic loosening, which can be predicted using the 2-year postoperative prosthesis migration profile, measured using radiostereometric analysis (RSA) [34, 36]. RSA was first described in 1974 [38], has been improved for use with digital radiographs [16, 42], and has been used with various TKA designs [5, 18, 22, 41]. Given the high precision of RSA, RSA studies generally need only approximately 50 patients per group to detect a difference in prosthesis migration between TKA designs [25], making RSA an ideal tool to evaluate new TKA designs in early clinical trials. The importance of RSA studies before widespread market introduction of new designs has been noted in numerous reports that correlate early (1 to 2 years) migration patterns of knee implants with 10-year survival of these implants [25, 33, 34, 36]. Phased introduction of new TKA designs, including those evaluated in early clinical RSA trials, has been proposed to improve patient safety [15, 19, 20, 25, 37].

However, not every TKA design has been studied with RSA before market introduction. In the Australian Orthopaedic Association National Joint Replacement Registry for instance, nearly 194 different TKA design combinations have been registered, with reported 10-year survival rates ranging from 86.5% to 98.1% [2], and most designs were not evaluated in an RSA study. RSA could be used to warn clinicians about implants that are more likely to have an increased risk of aseptic loosening, thus safeguarding against the widespread use of such implants. Such a warning might result in withdrawal of designs from the market, thereby leaving only the better-performing implants and preventing many early revisions [25]. Following this mechanism, TKA designs tested with RSA may be expected to have a lower revision rate during long-term follow-up than non-RSA-tested TKA designs. In an earlier report with shorter follow-up, Nelissen et al. [25] found that RSA-tested TKA designs had a lower revision rate in three national knee arthroplasty registries with up to 5 years of follow-up.

Here, we used six national registries and one regional registry to answer the question: Is there a difference in the all-cause revision rate between non-RSA-tested and RSA-tested TKA designs registered in national knee arthroplasty registries at 5 and 10 years of follow-up?

Materials and Methods

Study Search

Through the Network Orthopaedic Registries of Europe—European Federation of National Associations of Orthopaedics and Traumatology webpage (EFORT) [26], we identified national and regional knee arthroplasty registries. We then conducted a manual web search to identify any knee arthroplasty registry not listed on the EFORT webpage. Published reports were extracted from these registries. Inclusion criteria were a minimum follow-up duration of 10 years and available revision or survival data for each TKA design. Knee arthroplasty registries were excluded if no information regarding the fixation method was provided. However, if a study or report stated that more than 90% of the TKA designs were cemented, we included the entire registry, and we assumed that all TKA designs were cemented (but we tested them in a sensitivity analysis, see below). We did not use a language restriction.

The search yielded 26 annual reports of knee arthroplasty registries, of which six national registries (from Australia [2], Finland [10], New Zealand [40], Norway [29], Sweden [39], and the United Kingdom [24]) and one regional registry (Emilia-Romagna, Italy [35]) were included (Fig. 1). TKA designs of one registry were

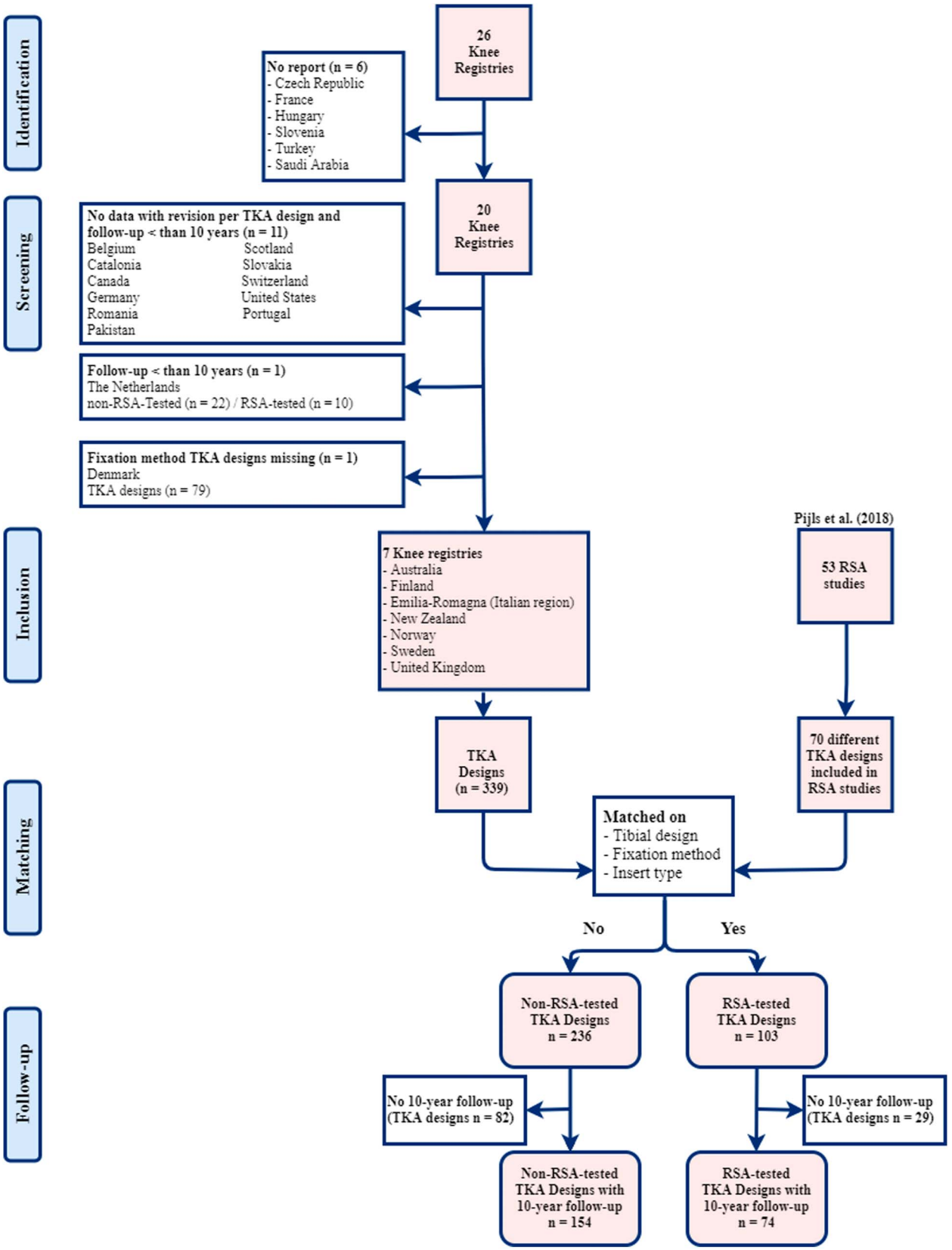

Fig. 1 This flowchart shows the registries and number of designs that were included in this study.

Table 1. Characteristics of included registries

	Australia	Finland	Emilia-Romagna (Italy)	New Zealand	Norway	Sweden	United Kingdom
TKAs (n)	547,407	194,787	39,782	93,497	29,834	109,393	975,739
Follow-up (years)	16	25	16	17	23	41	13
TKA designs (n)	143	35	39	34	19	13	56
Publication year	2017	2018	2017	2017	2018	2017	2017
Completeness (%)	98%	96%	98%	> 95%[a]	97%	97%	96%
Age (mean, years)	68.5	65-74	70.6	68	68.5	69	70
Sex (female, %)	56%	68%	71%	52%	63%	47%	57%
The three most-used TKA designs							
1	Triathlon[b]	Triathlon[b]	Attune[d]	Triathlon[b]	NexGen[c]	NexGen[c]	
2	NexGen Flex CR[c]	NexGen[c]	NexGen[c]	Attune[d]	LCS Complete[d]	PFC[d]	
3	NexGen Flex LPS[c]	PFC Sigma[d]	Legion[e]	Genesis II[e]	PFC Sigma[d]	Triathlon[b]	
Revision due to loosening of all TKA in registry (%)	26%	9%		19%		26%	26%

[a]In 95% of public hospitals.
[b]Stryker Inc, Mahwah, NJ, USA
[c]Zimmer Inc, Warsaw, IN, USA
[d]DePuy Synthes, Warsaw, IN, USA
[e]Smith & Nephew, Memphis, TN, USA

excluded due to unknown fixation method. TKA designs from another registry were excluded as only 7-year data was available. All other excluded registries did not have 10-year follow-up and also did not report revision rates per TKA design (Fig. 1). From the seven registries, 339 TKA designs were extracted. The maximum follow-up duration ranged between 13 and 41 years, and all registries had a completeness of ≥ 95% for primary TKA. The definition of completeness was not clarified in all registries but was defined as the percentage of patients receiving a primary TKA included in the registry in most registries. The mean age at the time of surgery ranged from 68 years to 71 years (Table 1). The Finnish registry did not report a mean age but divided patients into four age groups (younger than 55 years, 55 to 64 years, 65 to 74 years and 75 years and older), with most patients (39%) in the 65 to 74 years age group. The proportion of female patients in the registries ranged from 47% in the Sweden registry to 71% in the Emilia-Romagna, Italy registry (Table 1).

Data Extraction and Synthesis

Two authors (SH, BGP) independently assessed the eligibility of the reports. If eligible, data on the prosthesis model, fixation method, and insert type were extracted from the report [34]. The fixation method was classified as uncemented or cemented. Hybrid fixated TKAs were assumed to have a cemented tibial plateau and were therefore classified as cemented. The insert was classified as cruciate-retaining or posterior-stabilized, fixed-bearing or mobile-bearing, and a metal-backed modular tibia or an all-polyethylene tibia. In addition, the all-cause revision percentages, revision rates, and survival percentages with standard errors for each individual design were extracted from every registry report. If only the 95% CIs were available, the standard error was calculated by subtracting the lower limit from the upper limit of the interval, before dividing by 3.92 [14]. Ideally, revision due to aseptic loosening would be extracted because RSA is primarily used for early detection of loosening. However, the reason for revision was not reported for the designs individually, and therefore, all-cause revision was used as outcome. Any discrepancies in the data extracted by the two authors (SH, BGP) were resolved by discussion. Primary TKAs were included. Unicompartmental knee arthroplasties (including patellofemoral prostheses), hinged knee arthroplasty, and tumor reconstruction prostheses were excluded. The number of designs ranged between 13 and 143 per annual report.

To identify whether a TKA design was previously tested with RSA, we used the data from a recent meta-analysis [33]. In short, this meta-analysis searched PubMed, EMBASE, Web of Science, and the Cochrane Library for studies using RSA and primary TKA before July 2016.

Data on all designs were extracted from the 53 included studies, which included 70 different RSA-tested TKA designs (Fig. 1). Design characteristics of the TKA reported in the knee arthroplasty registries were extracted and, if possible, matched to the TKA designs reported in the RSA-studies. Every TKA design reported in the included knee arthroplasty registries was classified as non-RSA-tested or RSA-tested, resulting in two groups in every registry. For a design to be classified as RSA-tested, the design in the registry had to be identical to the design reported in a RSA study. If the insert was not specified in the registry, but the design and fixation matched the TKA design, the design was classified as RSA-tested (Fig. 1).

Seven registries with 339 TKA designs were included, of which 236 were classified as non-RSA-tested and 103 as RSA-tested. Fixation was uncemented for 54 designs and cemented for 285 designs. Cruciate-retaining inserts were used in 110 designs; in 72 designs, the inserts were posterior-stabilizing or not explicitly mentioned. Mobile bearings were used in 49 designs. The Norwegian registry only reported 3-year and 10-year revision rates, and could therefore not be included at 5 years. At 5 years, 191 TKA designs were identified as non-RSA-tested (see Fig. 1, Supplemental Digital Content 1, http://links.lww.com/CORR/A323). In addition, 92 TKA designs were identified as RSA-tested (see Fig. 2, Supplemental Digital Content 2, http://links.lww.com/CORR/A324). At 10 years, 154 TKA designs were classified as non-RSA-tested (see Fig. 3, Supplemental Digital Content 3, http://links.lww.com/CORR/A325) and 74 designs were identified as RSA-tested (see Fig. 4, Supplemental Digital Content 4, http://links.lww.com/CORR/A326). Between baseline and 10 years, 82 non-RSA-tested and 29 RSA-tested designs could not be included as these had not reached 10 years of follow-up.

Data Analysis

First, a random-effects model was used to calculate the pooled all-cause revision percentages and their standard errors at 5 and 10 years of follow-up for the non-RSA-tested and RSA-tested TKA designs, including a DerSimonian-Lard estimator to take into account the heterogeneity between the designs [7]. RSA-tested (yes or no) was included as a factor to test for a difference between groups at 5 and 10 years of follow-up. Moreover, pooled all-cause revision percentages and their standard errors were calculated separately for each registry for non-RSA-tested and RSA-tested TKA designs.

In all random-effects models, a DerSimonian-Lard [7] estimator was used to estimate heterogeneity. In a sensitivity analysis, the more conservative empirical Bayes estimator was used to test whether the heterogeneity estimator would affect the results [23]. The I^2 was used to estimate the extent of heterogeneity. Heterogeneity is the variation between the designs in both groups, which is considered low, moderate or high if I^2 is 25%, 50% or 75%, respectively [11, 12]. Outcomes are given in percentages with 95% CIs. The Metafor Package in R Statistics (version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses [43].

Post-hoc Sensitivity Analyses

We performed three post-hoc sensitivity analyses to test the impact of various assumptions on the primary outcome. The first analysis excluded data from registries for which the fixation method was missing (Sweden and Emilia-Romagna, Italy), and data from the registry that did not report the insert of the design (New Zealand). The second analysis included the four RSA studies from the meta-analysis that were excluded from the primary analysis because of not reporting migration data or other reasons. This resulted in reclassification of six non-RSA-tested TKA designs as RSA-tested. The third analysis included data from the Danish and Dutch knee arthroplasty registries that fulfilled all but one of the inclusion criteria [6, 8]. The Danish TKA designs lacked information on fixation and were assumed to be cemented in this sensitivity analysis, and the Dutch registry published 10 years follow-up data in November 2019 (after initial manuscript submission) and could only be included recently.

Results

Revision Rates of Non-RSA-tested and RSA-tested TKA Designs at 5 Years of Follow-up

All-cause revision at 5 years was slightly less for the RSA-tested designs than for the non-RSA-tested designs (Fig. 2). Mean all-cause revision rates at 5 years for non-RSA-tested and RSA-tested implants were 3.6% (95% CI 3.4 to 3.8) and 2.9% (95% CI 2.7 to 3.0), with a mean difference of 0.6% (95% CI 0.4 to 0.8; $p < 0.001$) favoring RSA-tested implants. Using the more conservative Empirical Bayes estimator, the mean difference was 0.7% (95% CI 0.3 to 1.0; $p < 0.001$) in favor of RSA-tested implants.

The revision rates of the RSA-tested TKA designs in the registries ranged between 2.3% and 3.9%, whereas revision rates of the non-RSA-tested TKA designs ranged from 2.5% to 4.7%. In all registries, the point estimate of RSA-tested TKA designs was lower than that of non-RSA-tested designs, but the absolute difference between groups was smallest in the United Kingdom (0.2% at 5 years of follow-up). The highest revision rate of RSA-tested implants was reported in

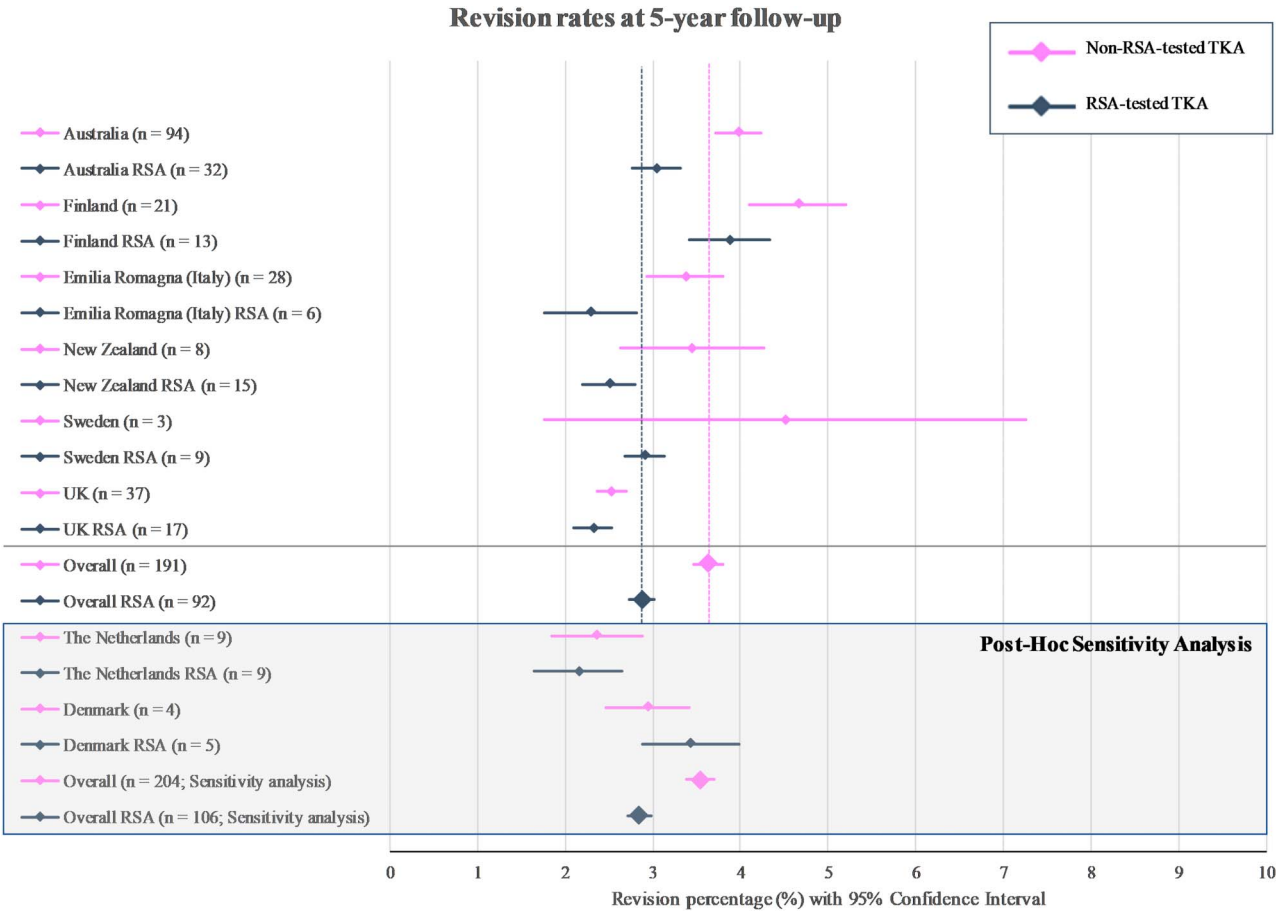

Fig. 2 This forest plot shows revision rates of the non-RSA-tested and RSA-tested TKA designs with 95% CIs at 5 years of follow-up per registry and the pooled revision rate per group with 95% CI. In addition, the sensitivity analysis including designs from the Dutch and Danish knee arthroplasty registry.

Finland (3.9% at 5 years of follow-up). New Zealand and Sweden used more RSA-tested TKA designs than non-RSA-tested TKA designs, in contrast with other countries. Australia had the greatest number of TKA designs registered (n = 126). Within the RSA-tested and non-RSA-tested groups, we found high variation between the TKA designs, expressed by the high heterogeneity (I^2 96% in the non-RSA-tested group and 98% in the RSA-tested group). Including fixation or insert in the model did not reduce the heterogeneity, suggesting that there is large variation in revision rates between designs. In addition, it is important to note that although we found a slightly lower mean all-cause revision rate for RSA-tested TKA, some non-RSA-tested TKA performed well and some RSA-tested TKA performed poorly.

Revision Rates of Non-RSA-tested and RSA-tested TKA Designs at 10 Years of Follow-up

Similarly, all-cause revision at 10 years was slightly less common among RSA-tested designs than it was in non-RSA-tested designs (Fig. 3). Mean all-cause revision rates at 10 years for non-RSA-tested and RSA-tested implants were 5.5% (95% CI 5.2 to 5.9) and 4.4% (95% CI 4.1 to 4.7), with a mean difference of 0.9% (95% CI 0.4 to 1.3; $p < 0.001$) favoring RSA-tested implants. Using the more conservative Empirical Bayes estimator, the mean difference was 0.9% (95% CI 0.2 to 1.6; $p = 0.01$) favoring RSA-tested implants. The revision rates in the registries ranged between 3.9% and 8.0% for non-RSA-tested and between 3.6% and 6.4% for RSA-tested TKA designs with large heterogeneity in both groups (I^2 97%).

Post-hoc Sensitivity Analyses

First, excluding the data from registries with assumed fixation method or inserts (Sweden, New Zealand and Emilia-Romagna, Italy) resulted in a slightly smaller mean difference in all-cause revision rate between groups of 0.5% (95% CI 0.2 to 0.8; $p < 0.001$) at 5 years and 0.7% (95% CI 0.2 to 1.2; $p = 0.003$) at 10 years. Second, reclassifying the

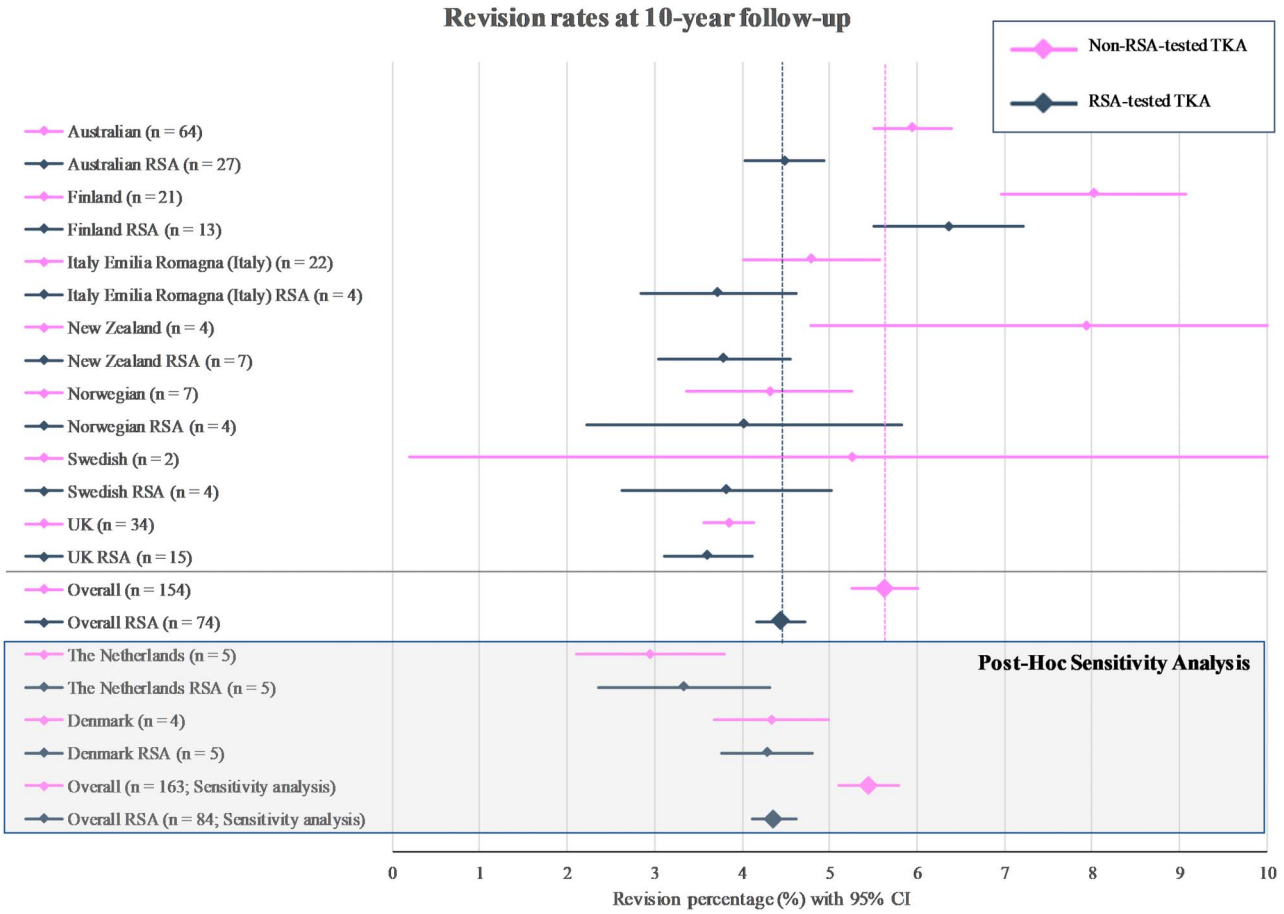

Fig. 3 This forest plot shows revision rates of the non-RSA-tested and RSA-tested TKA designs with 95% CIs at 10 years of follow-up per registry and the pooled revision rate per group with 95% CI. In addition, the sensitivity analysis including designs from the Dutch and Danish knee arthroplasty registry.

TKA-designs from the excluded studies did not effect the mean revision rates in both groups or the difference between groups (data not shown). Third, including both the Danish and Dutch registries, the mean difference of all-cause revision rate between RSA-tested and non-RSA-tested designs was 0.6% (95% CI 0.4 to 0.8; $p < 0.001$) in favor of RSA-tested designs at 5-year follow-up (Fig. 2). At 10-year follow-up, the mean difference in all-cause revision was 0.9% (CI 95% 0.4 to 1.3; $p < 0.001$) favoring RSA-tested implants (Fig. 3).

Discussion

Regulations regarding the introduction of new orthopaedic devices should have a healthy balance between innovation and patient safety [37]. To improve patient safety, new medical device regulations were established in Europe; they require clinical evidence before new implants are introduced to the European Union market [21]. RSA may be an important part of such clinical testing, and its use as an early-warning system for implants likely to fail as a result of aseptic loosening has often been proposed [9, 13, 19, 25, 37]. However, it is unknown whether RSA-tested TKA designs are associated with a lower revision rate during long-term follow-up in registries, though this may seem likely if problematic RSA tested designs are withdrawn from the market. By pooling data from several national registries and a regional registry, we found that implants that had undergone RSA testing had a slightly (about 1%) lower all-cause revision rate at 5 and 10 years compared with implants that had not undergone RSA testing.

We should consider the following limitations. First, our study was an observational study and cannot imply causation between RSA and a lower TKA revision rate, but rather it showed an association between these two factors. Second, the classification of TKA designs as RSA-tested or non-RSA-tested came from another meta-analysis [33]. However, a post-hoc sensitivity analysis showed similar results after reanalyzing the data from the meta-analysis and reclassifying the six TKA-designs that were excluded in the meta-analysis from non-RSA-tested to RSA-tested.

Third, we should consider the possibility that differential loss to follow-up may have influenced the results, although here the loss to follow-up was comparable between both groups. Fourth, revision rates as reported from the registries were used as the outcome measure, which is relatively crude. Such rates are influenced not only by the performance of a particular TKA design, but also by patients' complaints (for example, pain) and the surgical decision-making process, which is affected by factors such as patients' comorbidities, cultural differences between patients (such as pain acceptance), and waiting lists [30]. Nevertheless, many implants were included in the study, and we assume that both groups were similarly affected by these factors influencing revision. Fifth, mechanical loosening of the tibia is not the only reason for revision. Other common reasons are instability and infection [8], which are not assessed by RSA. A phased introduction should therefore include clinical trials to assess these contributing factors for revision. In addition, the absolute difference was small at both 5 and 10 years (less than 1%), raising the question of the relevance of this effect. However, this effect should be interpreted in light of the total revision rate, which is also low (about 5% at 10 years), meaning an absolute difference of 0.5% to 1% results in a decrease of approximately 10% to 20% for all-cause revision at 5 and 10 years. Considering the enormous number of TKA procedures performed globally, a 1% decrease in TKA revision could have a tremendous impact on the burden for patients needing a TKA revision and result in considerable reduction of health-related costs. Another limitation that should be noted is that there was high heterogeneity in all analyses, which could not be explained by the fixation method or the different inserts (data not shown). Heterogeneity is thus likely attributed to the many different designs included in the study with varying performance between the different designs. It should thus be emphasized that not all non-RSA-tested TKA designs performed poorly and not all RSA-tested TKA designs performed well. Finally, we had to assume the fixation method for two registries and the insert type for one registry, which might have results in misclassification of some TKA designs although our sensitivity analysis showed this was not likely to change the results or conclusions.

We found that RSA-tested TKA designs had a slightly (about 1%) lower mean all-cause revision rate at 5 and 10 years than non-RSA-tested designs. These results are in line with a previously published study comparing non-RSA-tested and RSA-tested TKA designs in three knee arthroplasty registries up to 5-year follow-up [25]. Our findings might be explained by the fact that RSA could provide an early warning about inferior TKA designs that fail because of aseptic tibial loosening. This early warning function could theoretically lower revision rates if poorly performing implants were withdrawn from the market or no longer used, and well-studied and excellent-performing TKA designs continue to be used. Given our observational study, we were unable to test this hypothesis in the present study or determine whether this is the case. Possible alternative explanations could be that RSA testing is a proxy for a rigorous clinical testing program by the manufacturer, or that more prudent surgeons are more likely to use RSA tested implants.

Before introduction of the new European medical device regulations, a phased introduction of new implants was proposed by several authors and the Idea, Development, Exploration, Assessment, Long-term Study—Devices (IDEAL) consortium to guide the introduction of novel devices [9, 13, 19, 25, 27, 37]. The best clinical introduction of a new TKA implant, in our opinion, would be to clinically evaluate implant fixation (that is, micromotion) and the surgical procedure. Thus, RSA studies and larger prospective studies could be nested in national or regional registries. Beyond Compliance [3], an initiative originating from the United Kingdom that supports the safe introduction of implants by bringing clinicians, implant manufacturers, and an independent expert panel together to assess outcomes of joint replacements [37], could be performed parallel to RSA studies. RSA studies or implant migration studies (Einzel-Bild-Röntgen-Analyse, CT-RSA [31]) could play an important role in such a phased, stepwise introduction of new implants. Because of the accuracy of the RSA technique, there is no need to expose large groups of patients to new implant designs that could potentially be inferior to the current state-of-the-art designs. In addition to exposing fewer patients, shorter follow-up is needed because migration results of implants after 2 years are often able to show differences in migration, in contrast to the long-term follow-up needed for classic observational studies, with survival of the implant as endpoint [19, 25].

Reducing the TKA revision rate is particularly of interest because this procedure is estimated to increase by approximately 600% between 2005 and 2030, resulting in 268,200 revisions in 2030 in the United States alone [17]. Considering that the mean cost of revision TKA in the United States is USD 49,360 [4], using only selected, well-performing TKA designs might save billions of dollars annually.

Conclusions

The number of different TKA designs is enormous, with new designs being introduced almost annually [2], and surgeons should remain skeptical about novel designs without proper evidence [28]. Several well-studied and excellent-performing TKA designs are currently available, and new designs should prove that they outperform these legacy products before replacing them. RSA testing is one method of testing new prosthesis introductions. Although

there are exceptions, we found that TKA designs tested in an RSA setting were associated with a slightly lower (about 1%) mean all-cause revision rate at 5-year and 10-year follow-up than those tested in a non-RSA setting. The relevance of this small effect should be interpreted in the context of this being a relative decrease of approximately 20% for all-cause revision at 5 and 10 years while also considering the enormous number of TKA procedures performed globally. Future studies should address the possible explanations for the association found between RSA-testing and a lower mean all-cause revision.

Acknowledgments None.

References

1. Anand R, Graves SE, de Steiger RN, Davidson DC, Ryan P, Miller LN, Cashman K. What is the benefit of introducing new hip and knee prostheses? *J Bone Joint Surg Am*. 2011;93:51-54.
2. Australian Orthopaedic Association. National Joint Replacement Registry: Hip, Knee & Shoulder Arthroplasty Annual Report 2017. Available from: https://aoanjrr.sahmri.com/documents/10180/397736/Hip%2C%20Knee%20%26%20Shoulder%20Arthroplasty. Accessed July 20, 2018.
3. Beyond Compliance Advisory Group. Beyond Compliance. Available from: www.beyondcompliance.org.uk/. Accessed August 23, 2019.
4. Bozic KJ, Kurtz SM, Lau E, Ong K, Chiu V, Vail TP, Rubash HE, Berry DJ. The epidemiology of revision total knee arthroplasty in the United States. *Clin Orthop Relat Res*. 2010;468:45-51.
5. Carlsson A, Bjorkman A, Besjakov J, Onsten I. Cemented tibial component fixation performs better than cementless fixation: a randomized radiostereometric study comparing porous-coated, hydroxyapatite-coated and cemented tibial components over 5 years. *Acta Orthop*. 2005;76:362-369.
6. Danish Knee Arthroplasty Register. Annual report 2019. Available from: https://www.sundhed.dk/content/cms/99/4699_dkr-aarsrapport-2019_til-offentliggoerelse.pdf. Accessed December 9, 2019.
7. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-188.
8. Dutch Arthroplasty Register (LROI). Online LROI annual report 2019 - PDF. Available from: http://www.lroi-rapportage.nl/media/pdf/PDF%20Online%20LROI%20annual%20report%202019.pdf. Accessed December 9, 2019.
9. Faro LM, Huiskes R. Quality assurance of joint replacement. Legal regulation and medical judgement. *Acta Orthop Scand Suppl*. 1992;250:1-33.
10. Finnish Arthroplasty Register. Total hip and knee arthroplasty report 2017. Available from: https://www2.thl.fi/endo/report/#data/knee_topmodels. Accessed July 14, 2018.
11. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21:1539-58.
12. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557-60.
13. Hirst A, Philippou Y, Blazeby J, Campbell B, Campbell M, Feinberg J, Rovers M, Blencowe N, Pennell C, Quinn T, Rogers W, Cook J, Kolias AG, Agha R, Dahm P, Sedrakyan A, McCulloch P. No surgical innovation without evaluation: evolution and further development of the IDEAL framework and recommendations. *Ann Surg*. 2019;269:211-220.
14. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5:13.
15. Huiskes R. Failed innovation in total hip replacement. Diagnosis and proposals for a cure. *Acta Orthop Scand*. 1993;64:699-716.
16. Kaptein BL, Valstar ER, Stoel BC, Rozing PM, Reiber JH. A new model-based RSA method validated using CAD models and models from reversed engineering. *J Biomech*. 2003;36:873-82.
17. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am*. 2007;89:780-5.
18. Laende EK, Richardson CG, Dunbar MJ. A randomized controlled trial of tibial component migration with kinematic alignment using patient-specific instrumentation versus mechanical alignment using computer-assisted surgery in total knee arthroplasty. *Bone Joint J*. 2019;101:929-940.
19. Malchau H. Introducing new technology: a stepwise algorithm. *Spine (Phila Pa 1976)*. 2000;25:285.
20. Malchau H, Garellick G, Berry D, Harris WH, Robertson O, Karrlholm J, Lewallen D, Bragdon CR, Lidgren L, Herberts P. Arthroplasty implant registries over the past five decades: Development, current, and future impact. *J Orthop Res*. 2018;36:2319-2330.
21. Melvin T, Torre M. New medical device regulations: the regulator's view. *EFORT Open Rev*. 2019;4:351-356.
22. Molt M, Toksvig-Larsen S. 2-year follow-up report on micromotion of a short tibia stem. A prospective, randomized RSA study of 59 patients. *Acta Orthop*. 2015;86:594-8.
23. Morris CN. Parametric emprical Bayes inference: theory and applications. *J Am Stat Assoc*. 1983;78:381:47-55.
24. National Joint Registry for England Wales Northern Ireland and the Isle of Man. 14th Annual Report 2017. Available from: https://reports.njrcentre.org.uk/Portals/0/PDFdownloads/NJR%2014th%20Annual%20Report%202017.pdf. Accessed July 20, 2018.
25. Nelissen RG, Pijls BG, Karrholm J, Malchau H, Nieuwenhuijse MJ, Valstar ER. RSA and registries: the quest for phased introduction of new implants. *J Bone Joint Surg Am*. 2011;93:62-65.
26. Network of Orthopaedic Registries of Europe. NORE research & publications. Available from: https://www.efort.org/about-us/nore/research/. Accessed July 14, 2018.
27. Nieuwenhuijse MJ, Nelissen RG. [The introduction of new medical devices] [In Dutch]. *Ned Tijdschr Geneeskd*. 2015;159:A8652.
28. Nieuwenhuijse MJ, Nelissen RG, Schoones JW, Sedrakyan A. Appraisal of evidence base for introduction of new implants in hip and knee replacement: a systematic review of five widely used device technologies. *BMJ*. 2014;349:g5133.
29. Norwegian Arthroplasty Register. Norwegian National Advisory Unit on Arthroplasty and Hip Fractures: 2018 Annual Report. Available from: http://nrlweb.ihelse.net/eng/Rapporter/Report2018_english.pdf. Accessed July 17, 2018.
30. OECD. Healthcare at a Glance 2017: OECD Indicators. Available from: https://www.oecd-ilibrary.org/docserver/health_glance-2017-en.pdf?expires=1576672859&id=id&accname=oid048188&checksum=4CFC37490313AEE20A3B7DCAE71C4DC4. Accessed August 23, 2019.
31. Otten V, Maguire GQ, Jr., Noz ME, Zeleznik MP, Nilsson KG, Olivecrona H. Are CT scans a satisfactory substitute for the follow-up of RSA migration studies of uncemented cups? a comparison of RSA double examinations and CT datasets of 46 total hip arthroplasties. *Biomed Res Int*. 2017;2017:3681458.
32. Patel A, Pavlou G, Mujica-Mota RE, Toms AD. The epidemiology of revision total knee and hip arthroplasty in England and

Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset. *Bone Joint J*. 2015;97:1076-1081.
33. Pijls BG, Plevier JWM, Nelissen R. RSA migration of total knee replacements. *Acta Orthop*. 2018:1-9.
34. Pijls BG, Valstar ER, Nouta KA, Plevier JW, Fiocco M, Middeldorp S, Nelissen RG. Early migration of tibial components is associated with late revision: a systematic review and meta-analysis of 21,000 knee arthroplasties. *Acta Orthop*. 2012; 83:614-624.
35. Regional Register of Orthopaedic Prosthetic Implantology. Hip, knee and shoulder arthroplasty in Emilia-Romagna Region (Italy) 2000-2016. Available from: https://ripo.cineca.it/authzssl/pdf/report_eng_2016.pdf. Accessed July 17, 2018.
36. Ryd L, Albrektsson BE, Carlsson L, Dansgard F, Herberts P, Lindstrand A, Regner L, Toksvig-Larsen S. Roentgen stereophotogrammetric analysis as a predictor of mechanical loosening of knee prostheses. *J Bone Joint Surg Br*. 1995;77: 377-83.
37. Sedrakyan A, Campbell B, Merino JG, Kuntz R, Hirst A, McCulloch P. IDEAL-D: a rational framework for evaluating and regulating the use of medical devices. *BMJ*. 2016;353:i2372.
38. Selvik G. Roentgen stereophotogrammetry. A method for the study of the kinematics of the skeletal system. *Acta Orthop Scand Suppl*. 1989;232:1-51.
39. Swedish Knee Arthroplasty Register. Annual Report 2017. Available from: http://www.myknee.se/pdf/SVK_2017_Eng_1.0.pdf. Accessed July 14, 2018.
40. The New Zealand Joint Registry. *Eighteen year report January 1999 to December 2016*. Available from: https://nzoa.org.nz/system/files/DH7827_NZJR_2017_Report_v4_26Oct17.pdf. Accessed July 10, 2018.
41. Tjornild M, Soballe K, Hansen PM, Holm C, Stilling M. Mobile- vs. fixed-bearing total knee replacement. *Acta Orthop*. 2015;86:208-14.
42. Valstar ER, Vrooman HA, Toksvig-Larsen S, Ryd L, Nelissen RG. Digital automated RSA compared to manually operated RSA. *J Biomech*. 2000;33:1593-9.
43. Viechtbauer W. Conducting meta-analyses in R with metafor package. *J Stat Softw*. 2010;36:1-48.