Younger age increases the risk of early prosthesis failure following primary total knee replacement for osteoarthritis
A follow-up study of 32,019 total knee replacements in the Finnish Arthroplasty Register

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Background and purpose  Total knee replacements (TKRs) are being increasingly performed in patients aged ≤ 65 years who often have high physical demands. We investigated the relation between age of the patient and prosthesis survival following primary TKR using nationwide data collected from the Finnish Arthroplasty Register.

Materials  From Jan 1, 1997 through Dec 31, 2003, 32,019 TKRs for primary or secondary osteoarthritis were reported to the Finnish Arthroplasty Register. The TKRs were followed until the end of 2004. During the follow-up, 909 TKRs were revised, 205 (23%) due to infection and 704 for other reasons.

Results  Crude overall implant survival improved with increasing age between the ages of 40 and 80. The 5-year survival rates were 92% and 95% in patients aged ≤ 55 and 56–65 years, respectively, compared to 97% in patients who were > 65 years of age (p < 0.001). The difference was mainly attributable to reasons other than infections. Sex, diagnosis, type of TKR (condylar, constrained, or hinge), use of patellar component, and fixation method were also associated with higher revision rates. However, the differences in prosthesis survival between the age groups ≤ 55, 56–65, and > 65 years remained after adjustment for these factors (p < 0.001).

Interpretation  Young age impairs the prognosis of TKR and is associated with increased revision rates for non-infectious reasons. Diagnosis, sex, type of TKR, use of patellar component, and fixation method partly explain the differences, but the effects of physical activity, patient demands, and obesity on implant survival in younger patients warrant further research.

Young patients suffering from rheumatoid arthritis have been treated with TKR with good long-term results (Lybäck et al. 2000). There have been more cautious indications in younger patients suffering from osteoarthritis because of doubts about compromised prosthesis survival (Rand et al. 2003, Himanen et al. 2005).

In some pioneering studies, the clinical results (Diduch et al. 1997) and the survival of TKR (Diduch et al. 1997, Duffy et al. 1998, Lonner et al. 2000, Tai and Cross 2006) have been good in younger osteoarthritis patients. However, these studies involved low numbers of patients and they were carried out in high-level, specialized centers, which may introduce provider-related bias. In unselected register-based series, young age in general has been associated with a relatively high rate of prosthesis failure (Robertsson et al. 2001, Harrysson et al. 2004, Himanen et al. 2005, Gioe et al. 2007).

Here we present a systematic analysis of the effect of the age of TKR patients on the short-term survival of the prosthesis, using nationwide data from the Finnish Arthroplasty Register. As prosthesis designs and surgical techniques have evolved rapidly with increase in operation volumes since the 1980s, the study was based on operations performed since 1997. Our hypothesis was that young age is associated with impaired prosthesis survival.

Materials and methods  From Jan 1, 1997 to Dec 31, 2003, 33,223 primary knee replacements performed for primary or secondary osteoarthritis in Finland were recorded in the Finnish Arthroplasty Register. Unicondylar knee replacements (n = 1,204) were excluded, leaving 32,019 TKRs for analysis. Information to the Finnish Arthroplasty Register was recorded prospectively using a specific report form (Puolakka et al. 2001). Reporting of joint replacement operations is obligatory in Finland, and the Finnish Arthroplasty Register covers approximately 96% of primary knee replacements performed in Finland (Jämsen et al. 2009).
The TKRs were followed until Dec 31, 2004 unless death or revision knee replacement occurred before. The mean follow-up time was 3.9 (1–8) years.

**Age groups**

Knees were grouped at 5-year intervals based on patient age, starting from 40 years to 80 years, to estimate survival trends using Kaplan-Meier regression analysis. For other analyses, knees were divided into 3 categories by patient age: ≤55 years (n = 1,748, 6% of all patients), 56–65 years (n = 6,152, 19%), and > 65 years (n = 24,119, 75%). These cut-off points were used because 55 years has been used in many earlier studies as the cut-off for younger patients (Crowder et al. 2005, Eskelinen et al. 2005, Gioe et al. 2007) whereas 65 years is a common retirement age in several European countries.

**Outcome**

The primary outcome was the prosthesis survival rate, which was defined as the proportion of prostheses surviving without revision (removal, exchange, or addition of any prosthesis component) during the follow-up time. Revisions for reasons other than infection were subjected to a separate subgroup analysis.

**Statistics**

For comparisons of patient characteristics and operative data between different age groups, chi-squared test or Fisher’s exact test was used for categorical variables and analysis of variance was used for continuous variables. Kaplan-Meier survival analysis was used to construct the survival probabilities of TKRs at 1, 3, and 5 years postoperatively.

The comparisons between the age groups ≤55 years, 56–65 years, and > 65 years and the analyses of contributory factors were performed using Cox regression analysis. The effect of the following contributory factors was studied: sex, reason for the primary operation (primary or secondary osteoarthritis), TKR type (based on the type of the femoral component: constrained designs and cementless fixation were slightly more common in the younger age groups. Constrained designs and cementless fixation were slightly more common in the younger age groups. Demographic and perioperative data for the 3 age groups are presented in detail in Table 1.

**Revision operations**

During follow-up, 909 (2.8%) of the 32,019 primary TKRs were revised. The mean time until revision was 1.9 years (1 day to 7.8 years). 205 prostheses (23% of all revisions) were revised due to infection. The predominant non-infectious reasons for revision were patellar complications (n = 139), malposition of the prosthesis (n = 109), aseptic loosening (n = 78), and other, unspecified reasons (n = 320), which included revisions due to polyethylene wear and instability (Tamminen et al. 2007). The remaining revisions were performed for periprosthetic fracture (n = 28), dislocation (n = 23), and fracture of the prosthesis (n = 7). Infections accounted for 19%, 15%, and 26% of all revisions among patients aged ≤55 years, 56–65 years, and > 65 years, respectively (p = 0.002).

**Prosthesis survival**

The age of the patient was a strong determinant of prosthesis survival. The overall prosthesis survival improved with increasing age in the 5-year age categories (p < 0.001) (Figure 1). This was also seen in a separate analysis using aseptic failure as endpoint (data not shown). With septic failures, there was no clear correlation between the age of the patient and prosthesis survival (data not shown).

Figures 2 and 3 show the Kaplan-Meier survival curves for the 3 age groups (≤55 years, 56–65 years, and > 65 years) with respect to prosthesis failure for any reason and failure
At 5 years, TKRs implanted into patients ≤ 55 years showed an overall survival rate of 92% (95% CI: 89.7–93.3). In the 56–65-year-old patients, the corresponding survival rate was 95% (95% CI: 94.8–96.0) and in patients over 65 years it was 97% (95% CI: 96.9–97.3). When only aseptic reasons were considered as endpoints, the respective survival rates were 93% (95% CI: 91.8–95.0), 96% (95.6–96.8), and 98% (97.7–98.1). Compared to patients aged more than 65 years, the risks of prosthesis failure for any reason and for aseptic failure were higher in both younger patient groups during the whole course of follow-up (Table 2). There were no differences in the survival rates for different operation years (data not shown).

### Predictors of prosthesis survival

Apart from age (the two younger age groups compared to the oldest group), secondary osteoarthritis, lack of a patellar component, and fixation method other than fully cemented fixation were associated with a higher probability of prosthesis failure for any reason and for reasons other than infection in the adjusted analysis during the first 3.6 years of follow-up (Table 3). The effect of these contributory factors on prosthesis survival was of approximately the same magnitude in different age groups (data not shown), although they were more prevalent in the younger age groups (Table 1). Adjustment for these variables and prosthesis type reduced the overall hazard ratios slightly in the youngest age groups compared to the results of univariate analysis (HR for any revision = 2.4 (95% CI: 2.0–3.0) vs. 2.8 (2.3–3.4); HR for aseptic revision = 2.9 (2.3–3.6) vs. 3.2 (2.5–4.0) (Tables 2 and 3).

There was still a strong association between age group and revision performed for any reason, and for reasons other than infection, in the adjusted analysis also (Table 3).

### Sensitivity analyses

The 3 most frequently used prostheses were Duracon (n =
11,970), AGC v2 (n = 7,690), and PFC Sigma (n = 3,416), which together accounted for 72% of all implants. There were slightly fewer revisions with PFC Sigma (2.2%) than with Duracon and AGC v2 (3.0% and 3.3%, respectively), but the difference did not reach statistical significance in the adjusted analysis.

Antibiotic cement was associated with fewer revisions compared to cemented and hybrid prostheses without antibiotic cement (2.6% vs. 4.9%, adjusted HR = 1.5 (95% CI: 1.3–1.8). Compared to the 7 hospitals with highest volume (> 1,000 operations in 1997–2003), the revision rate for reasons other than infection in the 48 lowest-volume hospitals (< 500 operations) was 1.3-fold increased (95% CI: 1.0–1.5) according to adjusted Cox analysis. Altogether, 76 hospitals performed the operations.

Adjustment for the use of antibiotic cement or hospital volume had no effect on the comparison between the age groups in the adjusted analysis. The results also remained unchanged when the analyses were run in the groups of the 3 most commonly used prostheses (all 3 separately), in the group of prostheses used less than 2,000 times during the observation period, for prostheses fixed with the 2 most commonly used bone cements (Palacos cum gentamycin and Simplex antibiotic), and separately for hospitals with different operation volumes.

Exclusion of patients with secondary osteoarthritis and exclusion of patients who had had both knees operated during the observation period (either simultaneous or staged bilateral operation) (n = 11,010) had no effect on the results of the adjusted analyses (data not shown).

Discussion
This is by far the most detailed register-based study to systematically compare the survival rates of primary TKR between different age groups in osteoarthritis. In general, our findings support the earlier pioneering register-based studies showing high failure rates in younger patients even with short-term follow-up. In addition, our study demonstrates a

Table 2. The effect of age group on prosthesis survival, proportion of aseptic failures, and the results of regression analyses

| Age group | n (knees) | Prosthesis survival, % (95% confidence interval) | Overall risk of prosthesis failure | Hazard ratio (95% confidence interval) |
|-----------|----------|-----------------------------------------------|-----------------------------------|----------------------------------------|
|           |          | At 1 year | At 3 years | At 5 years | Follow-up in total | Follow-up ≤ 3.6 years | Follow-up > 3.6 years | Follow-up in total | Follow-up ≤ 3.6 years | Follow-up > 3.6 years |
| ≤ 55 years | 1,748    | 98       | 95        | 92        | 2.8            | 2.1               | 5.0               | 3.2            | 2.5              | 4.8                     |
| (97.6–98.8) | (93.7–95.7) | (89.7–92.3) | (97.6–98.8) | (93.7–95.7) | (89.7–92.3) | (97.6–98.8) | (93.7–95.7) | (89.7–92.3) | (97.6–98.8) | (93.7–95.7) | (89.7–92.3) |
| 55–65 years | 6,152    | 99       | 97        | 95        | 1.5            | 1.4               | 2.0               | 1.7            | 1.6              | 2.0                     |
| (98.6–99.0) | (96.4–97.2) | (94.8–96.0) | (98.6–99.0) | (96.4–97.2) | (94.8–96.0) | (98.6–99.0) | (96.4–97.2) | (94.8–96.0) | (98.6–99.0) | (96.4–97.2) | (94.8–96.0) |
| > 65 years  | 24,119   | 99       | 98        | 97        | 1              | 1                 | 1                 | 1              | 1                | 1                       |
| (98.8–99.2) | (97.5–97.9) | (96.9–97.3) | (98.8–99.2) | (97.5–97.9) | (96.9–97.3) | (98.8–99.2) | (97.5–97.9) | (96.9–97.3) | (98.8–99.2) | (97.5–97.9) | (96.9–97.3) |
clear relationship between the age of the patients in 5-year age categories and the crude (unadjusted) prosthesis survival rates. Patients in the younger age groups were more prone to undergo revision knee replacements for reasons other than infection and the difference between age groups increased during the follow-up.

The patient population consisted of a large and unselected series of primary TKRs performed for osteoarthritis. As a result of obligatory reporting of joint replacement procedures, the Finnish Arthroplasty Register covers approximately 96% of primary knee replacements performed in Finland (Jämsen et al. 2009). Because this study is based on nationwide register data and because emigration from Finland is minor, loss to follow-up is negligible.

Prosthesis survival rates in our study are similar to those in some earlier register-based regional (Gioe et al. 2007) and nationwide studies (Robertsson et al. 2001, Himanen et al. 2005). There were, however, some limitations in these earlier studies: Gioe et al. reported survival rates only for the youngest cohort (75% at 14 years), Robertsson et al. did not differentiate the patients ≤ 55 years from the total cohort of patients aged < 65 years, and in the study by Himanen et al. the analysis was restricted to only one specific prosthesis type.

Compared to the figures reported in register-based series, much better survival rates have been described for young TKR patients in some smaller series. Ritter et al. (2007) reported a survival rate of 97.6% in a 9-year follow-up, and Duffy and co-workers (1998) reported a 99% survival rate in a 10-year follow-up. These survival rates were unadjusted and can probably be explained (at least to some extent) by patient selection and bias arising from the use of specialized clinics. These sources of bias are avoided in nationwide population-based series like ours.

Although secondary osteoarthritis is a relatively rare indication for TKR, it accounted for 15% of operations in patients aged ≤ 55 years and it was found to have a considerable effect on the prognosis of TKRs. The adjusted risk ratio was 1.9 (95% CI: 1.5–2.5) for secondary osteoarthritis compared to primary osteoarthritis. Secondary osteoarthritis has also been found to be a risk factor for revision in another study (Lonner et al. 1999), which suggests that the factors leading to secondary osteoarthritis, e.g. instability, may also strain the prosthetic joint in some patients. On the other hand, this result may also be due to more complicated surgery and possible soft tissue deficiencies related to secondary and posttraumatic osteoarthritis.

Cemented TKR prostheses had somewhat better survival rates than cementless or hybrid prostheses. Gioe et al. (2007) reported similar results, suggesting that cement fixation may improve prosthesis survival in younger patients. In a randomized study in which more elderly patients were included, cemented and cementless prosthesis fixation had a similar 15-year survival (Baker et al. 2007a). Although constrained prostheses are typically used in complex cases with ligamentous incompetence and instability, and considering that using constrained devices increases transmission of forces to the bone-cement interface and thereby predisposes to loosening, constrained TKR designs had short-term survival that was as

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### Table 3. Adjusted hazard ratios (HRs) for revision for any reason and only for reasons other than infection. Adjustments were made for gender, diagnosis, patellar component, TKR type, and fixation method. The values are adjusted hazard ratios (95% CI)

|                        | Any reason for revision |                        | Reasons other than infection |                        |
|------------------------|-------------------------|------------------------|-----------------------------|------------------------|
|                        | Follow-up in total ≤ 3.6 years | Follow-up > 3.6 years | Adjusted hazard ratio (95% CI) | Follow-up in total ≤ 3.6 years | Follow-up > 3.6 years |
| Age group              |                         |                        |                             |                         |                        |
| ≤ 55 years             | 2.4 (2.0–3.0)           | 1.8 (1.4–2.3)          | 4.6 (2.8–7.4)               | 2.9 (2.3–3.6)           | 2.2 (1.7–2.8)          | 4.5 (2.6–7.8)          |
| 56–65 years            | 1.5 (1.3–1.7)           | 1.3 (1.1–1.6)          | 2.0 (1.4–2.9)               | 1.7 (1.4–2.0)           | 1.6 (1.3–1.9)          | 2.0 (1.3–3.0)          |
| > 65 years             | 1                       | 1                      | 1                           | 1                       | 1                      | 1                        |
| Gender                 |                         |                        |                             |                         |                        |
| female                 | 1.1 (1.0–1.3)           | 1.0 (0.9–1.2)          | 1.0 (0.7–1.4)               | 1.0 (0.9–1.2)           | 0.9 (0.8–1.1)          | 1.1 (0.7–1.6)          |
| male                   | 1                       | 1                      | 1                           | 1                       | 1                      | 1                        |
| Diagnosis              |                         |                        |                             |                         |                        |
| primary osteoarthritis | 1.9 (1.5–2.5)           | 2.5 (1.9–3.3)          | 1.6 (0.9–3.0)               | 1.7 (1.3–2.3)           | 2.3 (1.7–3.3)          | 1.1 (0.5–2.4)          |
| secondary osteoarthritis | 1                       | 1                      | 1                           | 1                       | 1                      | 1                         |
| Patellar component     |                         |                        |                             |                         |                        |
| installed              | 1.2 (1.1–1.4)           | 1.2 (1.0–1.35)         | 1.1 (0.8–1.5)               | 1.4 (1.2–1.7)           | 1.4 (1.1–1.7)          | 1.1 (0.7–1.6)          |
| not installed          | 1                       | 1                      | 1                           | 1                       | 1                      | 1                         |
| TKR type               |                         |                        |                             |                         |                        |
| condylar               | 1.0 (0.8–1.3)           | 0.8 (0.6–1.0)          | 1.0 (0.5–2.2)               | 0.9 (0.6–1.2)           | 0.6 (0.4–0.9)          | 1.1 (0.5–2.6)          |
| hinge                  | 1.5 (0.9–2.8)           | 1.9 (1.0–3.6)          | 1.0 (0.2–4.3)               | 1.8 (0.9–3.4)           | 2.1 (1.1–4.4)          | 1.5 (0.4–6.3)          |
| Fixation               |                         |                        |                             |                         |                        |
| both components cemented | 1.4 (1.1–1.8)           | 2.6 (2.0–3.3)          | 1.2 (0.8–7.4)               | 1.4 (1.1–1.8)           | 2.7 (2.0–3.6)          | 1.1 (0.6–1.9)          |
| hybrid fixation        | 1.4 (1.0–1.9)           | 2.5 (1.7–3.5)          | 0.8 (0.4–1.9)               | 1.3 (0.9–1.9)           | 2.3 (1.5–3.4)          | 1.0 (0.4–2.3)          |
| both component cementless | 1.4 (1.0–1.9)           | 2.5 (1.7–3.5)          | 0.8 (0.4–1.9)               | 1.3 (0.9–1.9)           | 2.3 (1.5–3.4)          | 1.0 (0.4–2.3)          |
Although register-based studies provide a lot of useful information, they also have their limitations, as discussed above and elsewhere (Paavolainen et al. 1991, Kim et al. 2002, Eskelinen et al. 2005). First of all, the Finnish Arthroplasty Register has not been validated. The reliability of the factors analyzed in this study is, however, probably good as the data on implanted components include serial numbers. The reliability of the diagnoses appears to be acceptable when compared to national Hospital Discharge Register data (Esa Jämsen, unpublished data).

Selection of the main reason for revision from the options provided in the official Arthroplasty Register Reporting Form is not always unambiguous. Moreover, revisions due to polyethylene wear and instability are classified in the group “other, unspecified reasons” and comprise approximately two-thirds of this large group of revisions (Tamminen et al. 2007). Thus, in our study all revisions performed for reasons other than infection were lumped into one category. The deep infections reported most likely represent true cases (Jämsen et al. 2009), but it is acknowledged that some low-grade infections may have been falsely classified as aseptic failures. However, it is improbable that this would have substantially affected the present results.

Some confounding factors not reported in the Finnish Arthroplasty Register, such as functional demand, body mass index, and physical activity may interfere with more detailed data interpretation. Moreover, early prosthesis failure due to patellar complications, instability, and prosthesis malalignment is often a result of poor surgical technique, inappropriate prosthesis selection, or technical errors (Fehring et al. 2001, Mulhall et al. 2006). These provider-related factors could not be analyzed in our study but it is improbable that they would explain the differences between age groups.

In conclusion, in the short-term follow-up the relatively young age of ≤ 55 years was associated with a higher risk of revision, especially for aseptic failure. With increasing age at surgery, the prosthesis survival rates continuously improved. In the category of 56–65 year old patients, the results were already better than in the youngest age group and they were improved further in patients over 65 years of age. The underlying mechanisms require further investigation, but current knowledge indicates that in patients who are less than 55 years old, total knee replacement should only be used in selected cases when there are no other satisfactory means of giving relief from pain and dysfunction.

JJ planned the study and analyzed the data with EJ, wrote the first draft of the manuscript, and took care of revisions. EJ, TP, YTK, and TM contributed to interpretation of the results and writing of the manuscript. EJ and TM supervised JJ’s work.

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