ANESTHESIOLOGY

Postoperative Pain and Age: A Retrospective Cohort Association Study

Jacqueline F. M. van Dijk, Ph.D., Ruth Zaslansky, Ph.D., Regina L. M. van Boekel, Ph.D., Juanita M. Cheuk-Alam, Sara J. Baart, Ph.D., Frank J. P. M. Huygen, M.D., Ph.D., Mienke Rijsdijk, M.D., Ph.D.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Worldwide populations are aging, leading to larger numbers of elderly patients receiving surgery
- Reports of associations between age and postoperative pain have been conflicting

What This Article Tells Us That Is New

- Data from the PAIN OUT registry involving more than 11,000 patients undergoing spinal surgery, joint replacement, and laparoscopic cholecystectomy were used in a retrospective cohort analysis
- Pain reported postoperative day 1 declined slightly with age
- Severe postoperative pain was prevalent regardless of age or surgical type

ABSTRACT

Background: As the population ages, the number of elderly people undergoing surgery increases. Literature on the incidence and intensity of postoperative pain in the elderly is conflicting. This study examines associations between age and pain-related patient reported outcomes and perioperative pain management in a dataset of surgical patients undergoing four common surgeries: spinal surgery, hip or knee replacement, or laparoscopic cholecystectomy. Based on the authors' clinical experience, they hypothesize that pain scores are lower in older patients.

Methods: In this retrospective cohort, study data were collected between 2010 and 2018 as part of the international PAIN OUT program. Patients filled out the International Pain Outcomes Questionnaire on postoperative day 1.

Results: A total of 11,510 patients from 26 countries, 59% female, with a mean age of 62 yr, underwent one of the aforementioned types of surgery. Large variation was detected within each age group for worst pain, yet for each surgical procedure, mean scores decreased significantly with age (mean Numeric Rating Scale range, 6.3 to 7.3; $\beta = -0.2$ per decade; $P \leq 0.001$), representing a decrease of 1.3 Numeric Rating Scale points across a lifespan. The interference of pain with activities in bed, sleep, breathing deeply or coughing, nausea, drowsiness, anxiety, helplessness, opioid administration on the ward, and wish for more pain treatment also decreases with age for two or more of the procedures. Across the procedures, patients reported being in severe pain on postoperative day one 26 to 38% of the time, and pain interfered moderately to severely with movement.

Conclusions: The authors' findings indicate that postoperative pain decreases with increasing age. The change is, however, small and of questionable clinical significance. Additionally, there are still too many patients, at any age, undergoing common surgeries who suffer from moderate to severe pain, which interferes with function, supporting the need for tailoring care to the individual patient.

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In the overall surgical population, 30 to 55% of all patients report moderate or severe pain on the first postoperative day.[1–3] Poorly managed acute pain can lead to complications and prolonged hospital stay, and increases the risk of developing chronic pain.[4,5] Therefore, adequate postoperative pain treatment is important. Within our aging patient population, adequate postoperative pain management is increasingly challenging. The challenge lies in the fact that elderly patients more often have contraindications for analgesic drugs such as nonsteroidal anti-inflammatory drugs and a greater susceptibility to adverse effects of analgesics.

In the literature, the incidence and intensity of postoperative pain in the elderly are conflicting. Some studies suggest that elderly patients report pain to be of a lower intensity than younger patients,[6,7] while other studies do not find differences.[8,9] Studies demonstrate that pain in older patients is underrecognized and undertreated due to lack of pain assessment and concern of increased risks of adverse effects.[10] To be able to improve postoperative pain management in this group, it is important to have more information on the experience of postoperative pain in elderly patients. Since the experience of pain is

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multidimensional and described on several levels—sensory (intensity and character of pain), affective (emotional component), and impact (ability to function)[11]—all these items should be assessed to obtain a comprehensive evaluation of this experience. Additionally, the cultural influence on pain expression should be considered. Using the International Pain Outcome Questionnaire,[12] which assesses these different dimensions of pain, the experience of pain was measured in the unique international PAIN OUT registry.[13] In current study, the objective is to analyze associations between age and a diverse range of pain-related patient reported outcomes and treatments, studying a large sample of patients undergoing spinal surgery, hip replacement, knee replacement, or laparoscopic cholecystectomy. We hypothesize, based on clinical practice, that older patients have lower postoperative pain scores than younger patients.

Materials and Methods

PAIN OUT Registry and Network

The analysis presented here relies on data collected prospectively by the PAIN OUT registry. PAIN OUT (www.pain-out.eu), an international registry and research project, aims at improving postoperative pain management in the clinical routine. PAIN OUT was established with funding from the European Community's Seventh Framework Program. PAIN OUT is registered in ClinicalTrials.gov (NCT02083835). Approval for participation is obtained by each site from its local ethics committee. Informed consent from patients for participation in the survey can be oral or written, depending on requirements of the local ethics committee.

The current analysis is based on data contributed by patients cared for in 268 hospital wards from 26 countries worldwide. Inclusion criteria require that the patient was of consenting age (18 yr or older, in most countries); was on the first postoperative day, back on the ward from the recovery room for at least 6 hours; and agreed to participate in the survey. Patients were approached for participation in the survey by research assistants who could be students, nurses, or medical residents, and they underwent training for approaching patients, collecting data, and entering it into a Web-based password secure portal. As far as possible, research assistants did not have clinical duties on wards from which they collected data.

A standardized postoperative questionnaire, the International Pain Outcomes Questionnaire, which has been validated in English and has been translated using standardized methods into 29 different languages,[12] is used in PAIN OUT. This patient outcome questionnaire is based on the revised American Pain Society Patient Outcome Questionnaire. The construct validity of the International Pain Outcomes Questionnaire is confirmed by the Bartlett test ($P < 0.001$). The factor analysis resulted in a three-factor structure explaining 53.6% of the variance. Chronbach's alpha of the total scale was high (0.86).[12] Patients are asked to evaluate different facets of pain. This includes pain intensity and its duration, pain interference with doing activities in bed, or taking a deep breath or coughing, or sleep, side effects (such as nausea and drowsiness), emotions (anxiety and helplessness), satisfaction with pain treatment, and preoperative presence of chronic pain and its intensity (appendix 1). Patients fill out the International Pain Outcomes Questionnaire in their respective language on the first day after surgery. The International Pain Outcomes Questionnaire uses 11-point Numeric Rating Scale (where 0 = none and 10 = worst imaginable) or binary items (appendix 1). To reduce interviewer bias, patients complete the questionnaire independently with no assistance from family or staff. If a patient requests help, the research assistant can assist. Patient characteristics, sex, age, comorbidities related to pain, use of opioids before admission and clinical data, perioperative analgesics administration, and type of surgery (International Classification of Diseases, Ninth Revision surgical procedure codes) are collected from the medical record by the research assistant. For spinal surgery, International Classification of Diseases, Ninth Revision codes 81.00, 81.04 to 81.08, and 81.62 are used; for hip replacement, 81.51, and partial hip replacement, 81.52; for knee replacement, 81.54; and for laparoscopic cholecystectomy, 51.23 and laparoscopic partial cholecystectomy, 51.24.

Study Design and Variables Used in the Current Study

After approval from the PAIN OUT publication board, an anonymized dataset of patients who underwent spinal surgery, hip replacement, knee replacement, and laparoscopic cholecystectomy between 2010 and 2018 was made available for analysis. The dataset contained records from patients from Europe, Middle East, Asia, and South America. Culture is a complex construct to measure. In this study, we used language as a surrogate measure.

Outcome

The primary outcome was the worst pain on the first postoperative day experienced for each type of surgery. Secondary outcomes were the worst pain in male and female patients, pain interference with physical function and sleep, anxiety, helplessness, side effects (nausea and drowsiness), and opioid consumption before and after surgery in the recovery room and on the ward. Additionally, "wish for more pain treatment" (yes/no) was analyzed in patients speaking different languages subdivided to patients below and above 65 yr old.

Statistical Analysis

A statistical analysis plan was formalized before accessing the data for the primary outcome. Predictors used in the regression model were *a priori* selected based on literature. No data-driven variable selection models were used. A *post hoc* analysis was performed in the review process, and two possible confounders, "year of data collection" and "anesthesia type," were added to the model. We also performed *post hoc* analyses after initial examination of the data on opioid administration, wish for more treatment, and language.

No statistical power calculation was conducted before the study. The sample size was based on the available data. Datasets were included without setting a minimum number per ward. Datasets were excluded from the analysis when age was missing, or worst pain was lower than least pain. A maximum of 12% of data for a variable was missing (year of data collection, 0%; sex, 0.2%; worst pain score, 3%; presence of chronic pain before surgery, 3%; use of opioids before admission, 6%; presence of comorbidities related to pain, 12%; and anesthesia type, 12% [in imputation sequence]). Using a fully conditional specification multiple imputation technique, 12 imputed datasets were created to be used for the multiple regression models. The pooled results and standard errors are presented in the results section.

Continuous data were expressed as mean ± SD, and categorical data as absolute numbers with percentages for the available data.

Associations between age and worst pain, interference of pain with doing activities in bed, breathing deeply and coughing, sleep, nausea, drowsiness, anxiety, and helplessness for each type of surgery was first assessed using linear regression (on the imputed dataset). We corrected for sex, presence of comorbidities related to pain, presence of chronic pain before surgery, use of opioids before admission, year of data collection, and anesthesia type as they may be confounders.[14] Using a Bonferroni correction, a P value of 0.001 or below was regarded as statistically significant. A logistic regression was performed for the relation between age and wish for more treatment for each type of surgery using the same set of predictors. To avoid effect modification, linear regression analysis was not performed to assess the relationship between age and the interference of pain with activities out of bed because younger patients (less than 65 yr) were out of bed significantly more often than older patients (65 yr or more).

Locally estimated scatterplot smoothing lines were used to fit a smooth curve through the scatterplot with age on the x-axis and a Numeric Rating Scale on the y-axis. It is a nonparametric strategy to find a curve of best fit without assuming the data must fit some distribution shape and enables the reader to visualize the relation between age and Numeric Rating Scale. This approach was also carried out separately for male and female patients, in light of the literature that indicates that there may be differences in pain reports between the sexes.[14]

To further explore the nonlinear patterns of age and worst pain score, we estimated regression models for the four types of surgery separately, adding restricted cubic splines to the model. Using Akaike's Information Criterion, we determined whether cubic splines were a better fit of the data and how many knots would provide the best fit (limited to two, three, or four knots). The knots were placed automatically on the corresponding percentiles of the data. The R package *splines* was used to estimate the models, and *effects* and *ggplot* were used for the visualizations.

Opioids administration and wish for more pain treatment, both dichotomous variables, were expressed as frequencies and calculated for young and older patients (less than 65 yr and 65 yr or more) per surgery category. Wish for more pain treatment of young and older patients was subdivided by language. Differences in means between young and older patients were expressed as effect sizes. This is a quantitative measure of the strength of a phenomenon and is classified as small (d = 0.2 to 0.4), medium (0.5 to 0.7), or large (greater than 0.8).[15] To measure the effect size, we used the Cohen d coefficient with 95% CI. In this study, values were considered clinically relevant when Cohen d was 0.5 or greater. The effect size of the difference in percentages between young and older patients was expressed as risk ratio and is classified as small, 2 to 3; medium, 3 to 4; and large, 4 or more. The cutoff for clinical relevance is 3 or more.[16] Effect sizes are measured with the Practical Effect Size Calculator.[17]

For all analyses, unless indicated otherwise, P values of less than 0.05 were considered statistically significant, and two-sided statistical tests were performed. Statistical analyses were performed using either SPSS Statistical Software, version 20.0 (SPSS Inc, USA), or R version 4.0 (R Studio, USA).

Results

Research assistants approached 15,051 patients for inclusion in the PAIN OUT database. We excluded 3,080 cases who did not undergo one of the four types of surgery. Additionally, 220 cases were excluded due to lack of registered informed consent, 65 because age was missing, and 176 cases because least pain scores were higher than worst pain scores (fig. 1). Of the 11,510 included patients, 3,941 patients received hip replacement, 3,691 knee replacement, 2,894 laparoscopic cholecystectomy, and 984 a spinal fusion.

Patient Characteristics

The mean age of the total cohort was 62 yr, and 59% were female. In table 1, patient characteristics are presented for each type of surgery.

Of patients undergoing hip or knee replacement or spinal fusion, 83 to 90% reported preoperative chronic

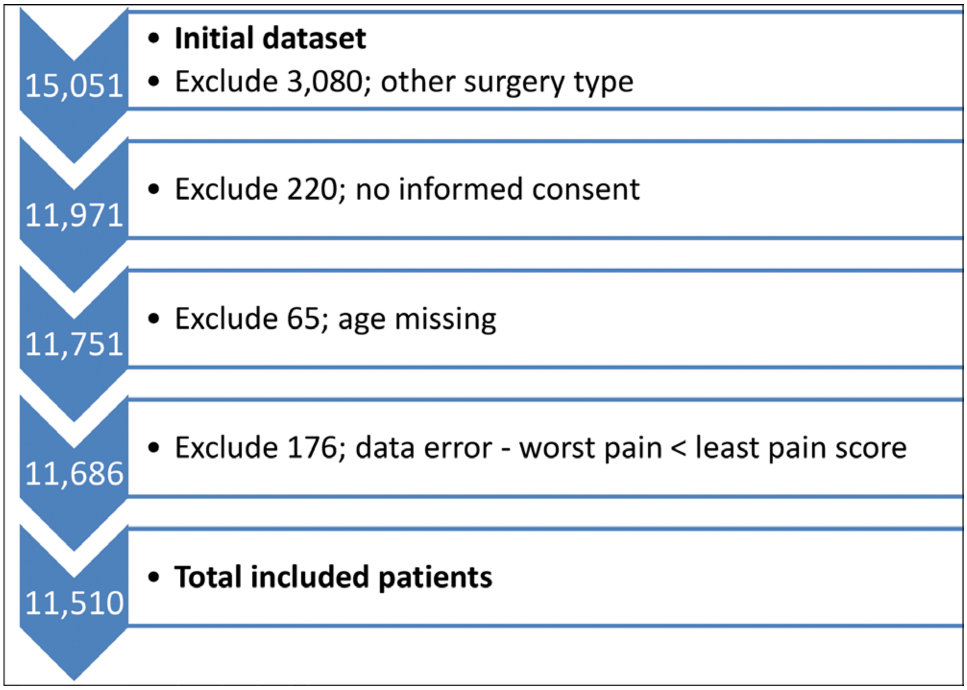

Fig. 1. Study flowchart. Numbers represent patients in the dataset.

Table 1. Patient Characteristics

	Hip Replacement, N = 3,941	Knee Replacement, N = 3,691	Spinal Fusion, N = 984	Laparoscopic Cholecystectomy, N = 2,894
Age, yr, mean ± SD	65 ± 13	67 ± 10	59 ± 13	52 ± 15
≥ 65 yr, No. (%)	2,082 (53)	2,258 (61)	379 (39)	717 (25)
Sex, female, No. (%)	2,140 (54)	2,341 (63)	520 (53)	1,887 (65)
Body mass index, mean ± SD	27.7 ± 5.5	30.8 ± 6.5	28.3 ± 5.6	27.8 ± 5.2
Presence of ≥ 1 comorbidities related to pain, No. (%)*	2,469 (72)	2,621 (80)	672 (73)	1,308 (53)
Presence of preoperative chronic pain, No. (%)*	3,151 (83)	3,215 (90)	785 (83)	1,278 (46)
Intensity of preoperative chronic pain Numeric Rating Scale score, mean ± SD	6.6 ± 2.2	6.7 ± 2.1	7.5 ± 1.8	7.0 ± 2.5
Opioid use before admission, No. (%)*	482 (13)	389 (11)	274 (29)	37 (1)

*Percentages calculated on available data.

pain with average score of 6.6, 6.7, and 7.5, respectively. Opioid use before admission was present in 11 to 29% of cases. Preoperative pain was reported by 46% of patients undergoing laparoscopic cholecystectomy, it was rated with an average of 7.0, and 1% of patients used opioids before admission (table 1).

Age was significantly correlated with presence of comorbidities related to pain, presence of chronic pain before surgery, and use of opioids before admission, with older patients more frequently having comorbidities related to pain, and having chronic pain before surgery and more frequently using opioids before admission.

Postsurgical Pain and Related Symptoms

Patients undergoing spine surgery reported the highest scores for worst pain, interference of pain with moving in bed, sleep, and doing activities out of the bed. Patients after laparoscopic cholecystectomy experienced the highest pain scores with deep breathing or coughing. Most patients

Table 2. Numeric Rating Scale Scores for Worst and Least Pain, Time in Severe Pain, the Interference of Pain, Side Effects, Anxiety, and Helplessness per Type of Surgery

	Hip Replacement, N = 3,941	Knee Replacement, N = 3,691	Spinal Fusion, N = 984	Laparoscopic Cholecystectomy, N = 2,894
Worst pain score	5.7 ± 2.7	6.1 ± 2.8	6.6 ± 2.7	5.0 ± 2.6
Male	5.4 ± 2.6	5.8 ± 2.7	6.3 ± 2.7	4.5 ± 2.5
Female	5.9 ± 2.8‡	6.3 ± 2.8‡	6.9 ± 2.5†	5.3 ± 2.6‡
Least pain score	1.9 ± 1.9	2.2 ± 2.1	2.7 ± 2.1	1.8 ± 1.8
Time in severe pain	29% (25)	33% (27)	38% (28)	26% (23)
Deep breathing/coughing	1.0 ± 1.9	0.8 ± 1.8	3.0 ± 3.1	3.7 ± 3.0
Moving in bed	4.9 ± 3.2	4.6 ± 3.2	6.2 ± 3.0	4.3 ± 2.8
Sleep	3.1 ± 3.1	3.5 ± 3.2	3.9 ± 3.4	2.4 ± 2.7
Out of bed, yes, No. (%)*	1,815 (53)	1,923 (59)	510 (57)	2,186 (89)
Pain out of bed	4.6 ± 3.1	4.7 ± 3.1	4.8 ± 3.0	3.4 ± 2.6
Nausea	2.0 ± 2.9	2.0 ± 3.0	2.3 ± 3.2	2.1 ± 3.0
Drowsiness	2.7 ± 2.9	2.8 ± 3.0	3.1 ± 3.2	3.0 ± 3.0
Itch	0.6 ± 1.7	0.8 ± 1.8	0.8 ± 2.0	0.4 ± 1.3
Dizziness	1.5 ± 2.4	1.6 ± 2.5	2.0 ± 2.7	2.0 ± 2.6
Anxiety	2.3 ± 2.8	2.6 ± 3.0	3.0 ± 3.2	2.1 ± 2.6
Helplessness	2.4 ± 3.1	2.6 ± 3.2	3.3 ± 3.5	1.8 ± 2.6

Results are presented as mean ± SD Numeric Rating Scale score or as otherwise specified. Time in severe pain refers to the percentage of time in severe pain since surgery.
*Percentages calculated on available data. †$P \leq 0.01$. ‡$P \leq 0.001$.

scored below a Numeric Rating Scale of 3 on side effects. Patients after spine fusion scored highest on anxiety and helplessness (table 2).

Age-related Effects on Postsurgical Pain

For all four types of surgery, maximum pain scores decreased significantly with increasing age (table 3). Maximum pain scores were higher when there was use of opioids before admission (β range: 0.9 to 1.0; $P < 0.001$) and in female patients (β range: –0.4 to –0.7; $P \leq 0.008$). When there was presence of chronic pain before surgery, maximum pain scores were higher for knee replacement, spinal fusion, and laparoscopic cholecystectomy (β range: 0.4 to 0.9; $P \leq 0.001$). Locally estimated scatterplot smoothing lines show an age-related decrease of worst pain score for all four surgery types with a stabilization of the worst pain score around the age of 70 yr in patients after laparoscopic cholecystectomy and knee and hip replacement (fig. 2).

Exploring the nonlinear patterns of age and worst pain score for hip replacement, spinal fusion, and laparoscopic cholecystectomy, cubic splines with three knots demonstrated the best fit and also showed an age-related decrease of worst pain. For knee replacement surgery, cubic splines did not improve model fit, and a linear decrease in worst pain scores with advancing age remained to be the best model (appendix 2).

Age-related Effects on Pain Interference with Moving in Bed, Breathing, Coughing, Sleep, and Side Effects

The interference of pain with doing activities in bed decreases significantly with age, as does interference of pain with sleep, with breathing deeply or coughing, nausea, drowsiness, anxiety, and helplessness (table 3). As scores were lower for total hip and knee replacement compared to spinal surgery, the association with age was less robust. When plotting worst pain scores and pain interference with moving in bed, a similar age-related decrease is observed for all types of surgery except for knee replacement (fig. 3). Also, worst pain scores and pain while breathing have a similar age-related decrease for laparoscopic cholecystectomy (fig. 3).

Opioid Treatment in Patients Aged Less than 65 yr or 65 yr and Older

Older patients were less often administered opioids in the recovery room and ward than younger patients for all procedures. Older patients less often had a wish for more pain treatment compared with younger patients for three procedures, not for laparoscopic cholecystectomy. Young patients undergoing hip and knee replacement surgery received opioids more often before surgery compared with older patients (table 4).

Pain and Wish for More Treatment in Patients Speaking Different Languages

Lower maximum pain scores after hip and knee surgery in patients above the age of 65 yr were observed in Spanish-, Dutch-, and German-speaking patients. (table 5). Serbian-, Spanish-, German-, and French-speaking patients above the age of 65 yr less often had a wish for more treatment after hip or knee surgery. In English-speaking patients above the age of 65 yr, the wish for more treatment was higher. In the remaining language groups, no age-related difference was

Table 3. Linear Regression of Relation of Age to Pain, Side Effects, Anxiety, and Helplessness for All Procedures

	Constant*	Age β per Decade (Standard Error)	*P* Value	Numeric Rating Scale Score Difference over a Time Span of 60 yr
Worst pain score				
Spinal fusion	7.2	−0.2 (0.06)	< 0.001	1.3
Hip replacement	6.8	−0.2 (0.04)	< 0.001	1.3
Knee replacement	7.3	−0.2 (0.05)	< 0.001	1.3
Laparoscopic cholecystectomy	6.3	−0.2 (0.04)	< 0.001	1.3
Pain interference with moving in bed				
Spinal fusion	7.5	−0.3 (0.07)	< 0.001	1.9
Hip replacement	4.6	−0.04 (0.04)	0.315	
Knee replacement	3.3	0.1 (0.05)	0.021	
Laparoscopic cholecystectomy	6.2	−0.3 (0.04)	< 0.001	1.9
Pain interference with breathing/coughing				
Spinal fusion	6.8	−0.5 (0.08)	< 0.001	3.2
Hip replacement	1.2	−0.04 (0.03)	0.161	
Knee replacement	0.9	−0.01 (0.03)	0.699	
Laparoscopic cholecystectomy	5.9	−0.4 (0.04)	< 0.001	2.2
Pain interference with sleep				
Spinal fusion	5.9	−0.4 (0.08)	< 0.001	2.6
Hip replacement	3.8	−0.2 (0.04)	< 0.001	1.3
Knee replacement	4.4	−0.2 (0.06)	< 0.001	1.4
Laparoscopic cholecystectomy	4.0	−0.2 (0.04)	< 0.001	1.3
Drowsiness				
Spinal fusion	5.0	−0.4 (0.08)	< 0.001	2.3
Hip replacement	4.1	−0.3 (0.04)	< 0.001	1.6
Knee replacement	5.2	−0.3 (0.05)	< 0.001	2.0
Laparoscopic cholecystectomy	4.5	−0.2 (0.04)	< 0.001	1.4
Nausea				
Spinal fusion	3.8	−0.2 (0.08)	0.019	
Hip replacement	3.7	−0.2 (0.04)	< 0.001	1.1
Knee replacement	2.5	−0.07 (0.05)	0.181	
Laparoscopic cholecystectomy	3.4	−0.2 (0.04)	< 0.001	1.0
Anxiety				
Spinal fusion	5.4	−0.4 (0.08)	< 0.001	2.4
Hip replacement	2.8	−0.2 (0.04)	< 0.001	1.2
Knee replacement	3.3	−0.2 (0.05)	< 0.001	1.3
Laparoscopic cholecystectomy	3.2	−0.2 (0.04)	< 0.001	1.4
Helplessness				
Spinal fusion	6.5	−0.4 (0.08)	< 0.001	2.2
Hip replacement	3.6	−0.2 (0.04)	< 0.001	1.4
Knee replacement	4.4	−0.3 (0.05)	< 0.001	2.0
Laparoscopic cholecystectomy	3.1	−0.2 (0.03)	< 0.001	1.4

Using a Bonferroni correction, we regarded a P value ≤ 0.001 as statistically significant.

*The constant is interpreted at the reference level of the covariates; female sex, no presence of comorbidities related to pain, no presence of chronic pain before surgery, no use of opioids before admission, year of data collection starting at 2010 and general anesthesia type.

observed. The effect sizes were small and did not meet the level of clinical significance.

Discussion

The current study assessed the association between age and postoperative pain after hip replacement, knee replacement, laparoscopic cholecystectomy, or spinal fusion using the international PAIN OUT database. The reported maximum pain levels decreased significantly with increasing age. However, this decrease in Numeric Rating Scale (less than 2 Numeric Rating Scale points) over a lifespan is defined as not clinically relevant.[18,19] A decrease in Numeric Rating Scale with increasing age is also observed for interference of pain with doing activities in bed, breathing deeply, coughing, sleep, side effects (nausea and drowsiness), and emotions (anxiety and helplessness). Older patients were less often administered opioids and less often had a wish for more treatment. Our observations correspond with literature showing that younger age is a risk factor for the occurrence of early postoperative severe pain in surgical patients.[14,20,21]

Also important to note is that all patients, independent of surgery type, spent about a third of the first postoperative day in severe pain; a sizeable proportion did not get out of bed; pain during movement indicated moderate to severe levels of pain. Thus, discussing these findings together, we may conclude that although mean worst postoperative pain scores decrease with

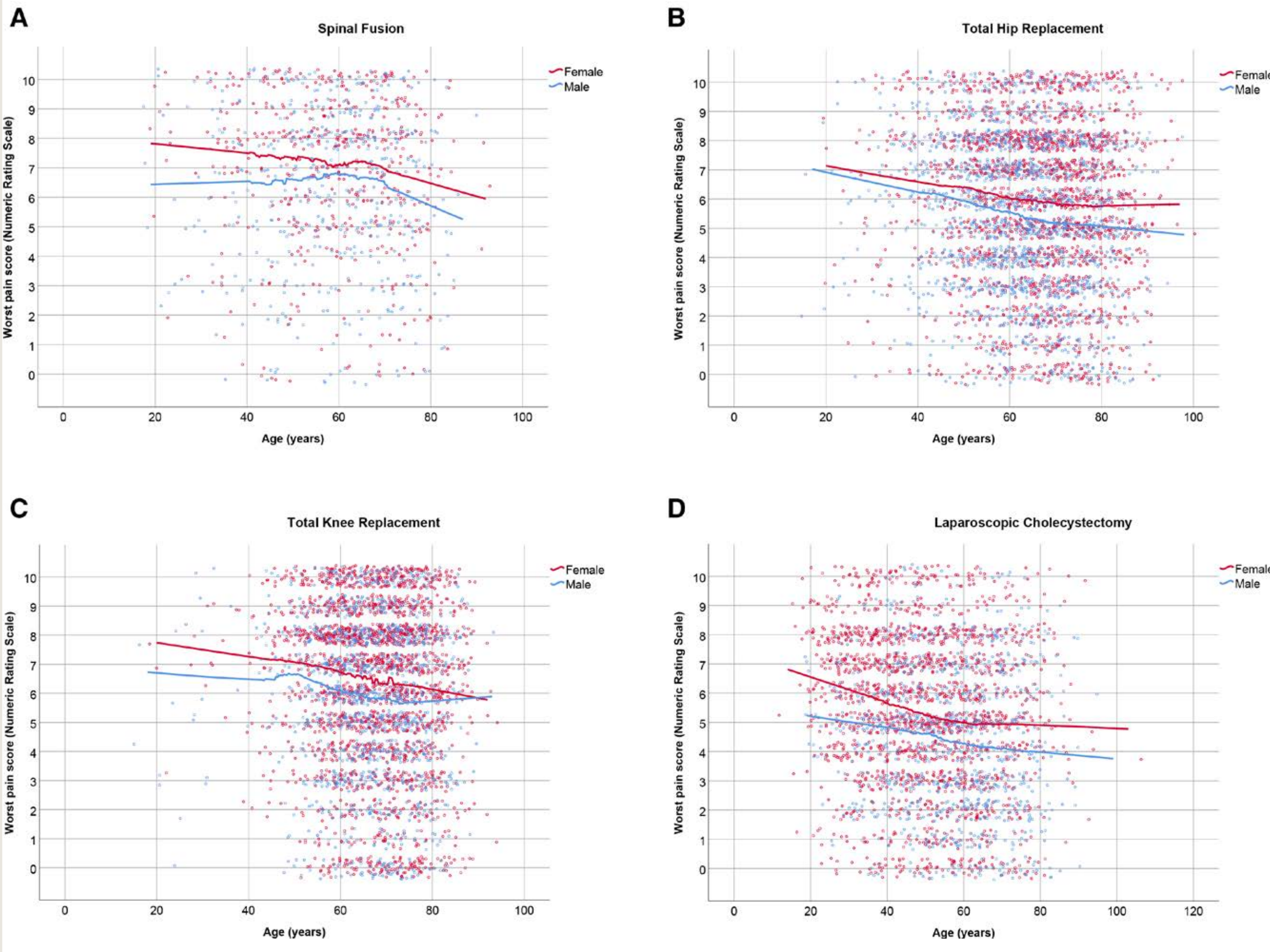

Fig. 2. Association between worst postoperative pain score and age. Numeric Rating Scale for worst pain score (*y-axis*) and age in years (*x-axis*) with locally estimated scatterplot smoothing for female (*red*) and male (*blue*) patients for (*A*) spine surgery, (*B*) hip replacement, (*C*) knee replacement, and (*D*) laparoscopic cholecystectomy. To improve data visualization, a jittering technique was applied.

age, Numeric Rating Scale scores are still in the moderate to severe range for all ages, and do not relieve us clinicians from our obligation to improve postoperative pain management.

There are more observations in this study that are worth mentioning in an effort to improve postoperative pain management. A high percentage of patients receiving regional anesthesia (79%) for a total knee replacement have high pain scores on the ward and receive opioids on the ward in over 80% of cases. This should alert the healthcare providers that it is not enough to provide anesthesia according to guidelines, but management needs to be continued on the ward. Also, female sex, presence of chronic pain before surgery, and use of opioids before admission are related to increased postoperative pain. We argue that current standardized analgesic dosing in adult postsurgical patients is often not sufficient for patients at risk for severe postoperative pain, *e.g.*, a young female patient with preoperative chronic pain on opioids. We therefore encourage clinicians to base their postoperative pain management on the individual patient, taking these risk factors into account, and not solely rely on the current standardized dosing in adult postsurgical patients.

Emphasizing that there is still room for improvement in the postoperative pain management for elderly patients, we also want to discuss the interesting finding that there seems to be an age-related effect on postoperative pain. We hypothesize that there is a multifactorial explanation for the effect of age on postoperative pain. Postoperative pain may be influenced by age-related changes in the structure and function of peripheral sensory pathways, hormonal changes, and/or pharmacokinetic changes, but the assessment of pain and its integration by the elderly patients influenced by psychologic factors (catastrophizing, anxiety, earlier life experiences), cultural, and generational influences may also contribute to this finding. Below we will discuss these factors in more detail.

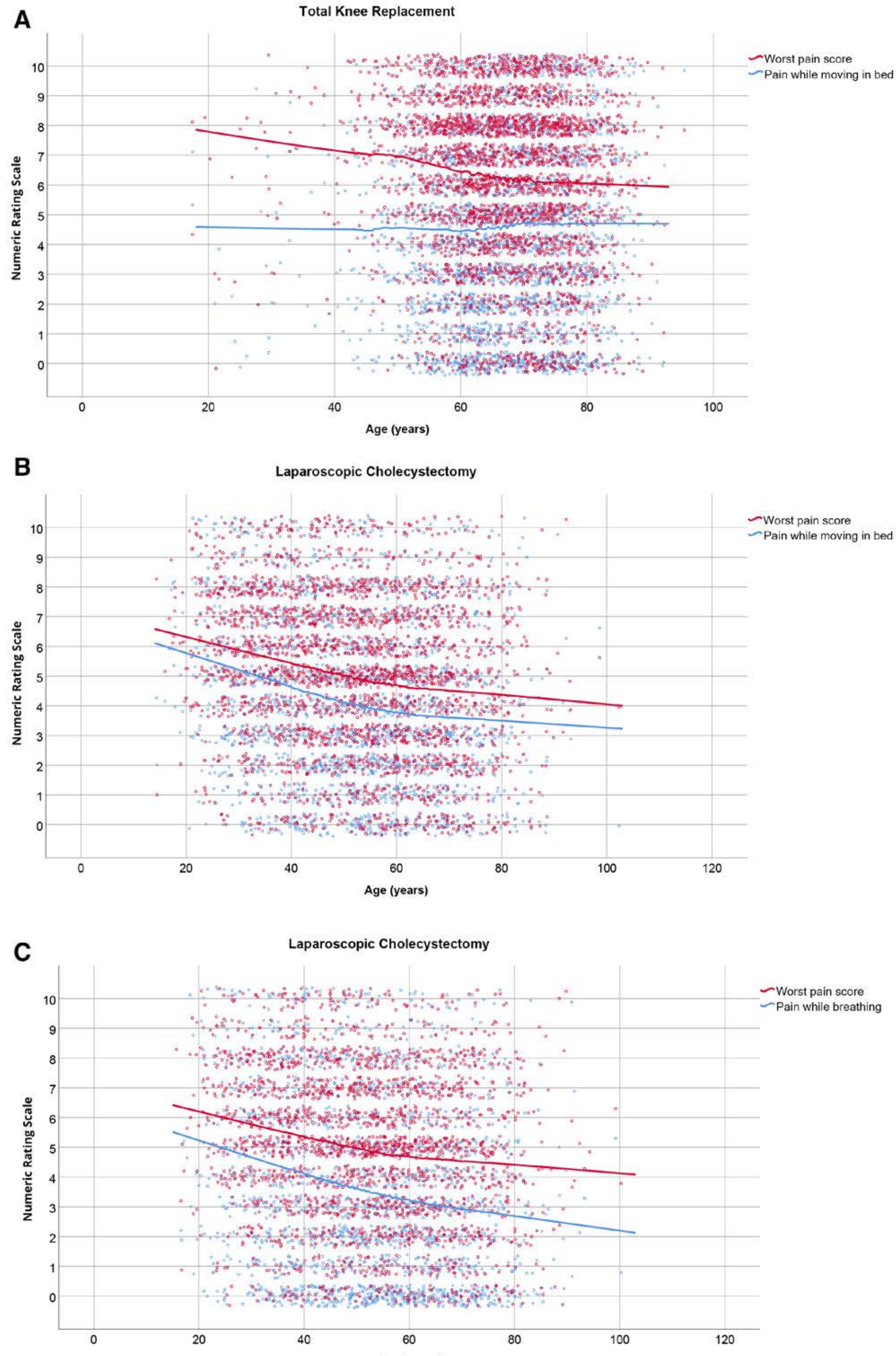

Fig. 3. Association between pain interference and age. (*A* and *B*) Numeric Rating Scale for worst pain score (*red*) and pain while moving in bed (*blue*; *y-axis*) and age in years (*x-axis*) with locally estimated scatterplot smoothing for (*A*) knee replacement and (*B*) laparoscopic cholecystectomy. (*C*) Numeric Rating Scale for worst pain score (*red*) and pain while breathing (*blue*; *y-axis*) and age in years (*x-axis*) with locally estimated scatterplot smoothing for laparoscopic cholecystectomy. To improve data visualization, a jittering technique was applied.

Table 4. Opioid Use and Wish for More Pain Treatment of Young and Elderly Patients per Surgery Type

	< 65 yr, N = 6,074	≥ 65 yr, N = 5436	Effect Size Relative Risk* (CI)
Sex, female, No. (%)	3,566 (59)	3,290 (61)†	0.96 (0.93–1.01)
Spinal fusion, No. (%)	605 (62)	379 (38)	
Opioids before admission	164 (28)	110 (30)	0.93 (0.64–1.36)
Opioids recovery room	452 (76)	257 (69)†	1.10 (0.10–1.21)
Opioids ward	505 (85)	296 (79)†	1.08 (1.00–1.15)
Wish for more treatment	157 (27)	71 (20)‡	1.35 (0.79–2.30)
Hip replacement, No. (%)	1,859 (47)	2,082 (53)	
Regional anesthesia	701 (43)	787 (44)	0.98 (0.87–1.10)
Opioids before admission	252 (15)	230 (12)†	1.25 (0.79–1.97)
Opioids recovery room	1,310 (72)	1,267 (62)§	1.16 (1.10–1.23)
Opioids ward	1,462 (79)	1,508 (74)§	1.07 (1.03–1.11)
Wish for more treatment	362 (20)	278 (14)§	1.43 (1.00–2.04)
Knee replacement, No. (%)	1,433 (39)	2,258 (61)	
Regional anesthesia	1,053 (79)	1,569 (79)	1.00 (0.96–1.04)
Opioids before admission	200 (15)	189 (9)§	1.67 (0.95–2.92)
Opioids recovery room	1,080 (77)	1,518 (69)§	1.12 (1.06–1.17)
Opioids ward	1,254 (88)	1,770 (79)§	1.11 (1.08–1.15)
Wish for more treatment	344 (25)	466 (22)†	1.14 (0.88–1.46)
Laparoscopic cholecystectomy, No. (%)	2,177 (75)	717 (25)	
Opioids before admission	22 (1)	15 (2)†	0.5 (0.001–117.8)
Opioids recovery room	763 (37)	216 (31)‡	1.19 (0.96–1.49)
Opioids ward	899 (42)	280 (40)	1.05 (0.89–1.24)
Wish for more treatment	337 (16)	89 (13)	1.23 (0.68–2.22)

*Risk ratio. †$P \leq 0.05$. ‡$P \leq 0.01$. §$P \leq 0.001$.

Innervation of soft tissue (*e.g.*, skin) and bone tissue changes with advancing age both in animals[22,23] and in humans.[24,25] Age-related changes in nerve conduction, studied in caudal and digital nerves, are represented by a parabolic curve with highest conduction speed during adolescence, decreasing again with advanced age.[22,23,26] Increased thermal and mechanical thresholds measured on the skin using quantitative sensory testing have been observed in the elderly.[27,28] A contradicting finding is that there is also increased temporal summation of pain and reduced pain inhibitory function in older adults, increasing the risk for chronic pain.[29] We hypothesize, taking these preclinical and clinical studies into account, that the net effect of age-related changes in the function and structure of the peripheral sensory pathways may contribute to a decreased pain sensation after surgery.

Hormonal changes and their effect on postoperative pain is a challenging relation to study as menopause coincides with the age that pain is reported most often and with highest pain scores. In studies on chronic pain syndromes and menopause, there is no consensus that menopause itself is related to higher pain scores.[30,31] In current study, we did not observe a peak in reported pain intensity in women aged between 40 and 60 yr after surgery. Men and women showed a comparable age-related decrease in maximum pain score, with slightly higher scores in women compared to men. Female sex is a known risk factor for moderate to severe postoperative pain.[14]

Opioid consumption was lower in older patients in current study. The elderly also less often had a wish for more pain treatment compared to younger patients. This observation corresponds with previous studies.[21,32] There are several explanations for this finding. First, older patients may receive less opioids because of increased risk of adverse events and contraindications for opioid drug treatment due to comorbidities. Second, opioid clearance may be reduced with advancing age.[33] In current study, however, older patients experienced less nausea and drowsiness compared with younger patients.

Catastrophizing, anxiety, and depression are well-known risk factors for development of chronic pain.[34] Also, for acute pain, anxiety has been related to postoperative pain intensity.[21] In current study, older patients had lower anxiety and helplessness scores compared with younger patients, which could very well contribute to the lower postoperative pain scores reported by elderly patients. Many elderly patients believe that pain is a normal part of aging and that pain is something they must live with or endure in silence.[35] Older adults are more often stoic, believing that they should tolerate unnecessary pain, and should not ask for or self-administer analgesia until pain is more severe.[36,37] Resilience, a psychologic construct that allows adults to improve the ability to adapt positively when faced with adversity, is demonstrated to be higher in women than in men, and in older women more so than in younger women. Higher resilience might also be a potential contributor to lower pain scores in older patients.[38,39] Finally, older patients may report less pain because previous painful experiences may cause them to interpret any noxious stimulus in an age-dependent context that decreases perception of severity.[40]

Table 5. Wish for More Pain Treatment and Worst Pain Score in Patients after Hip or Knee Replacement Speaking Different Languages, Subdivided for Patients below and above 65 yr

Language	N = 7,632	No. (%) of Patients ≥ 65 yr	Wish for More Pain Treatment, %: All Patients, No. (%)	< 65 yr, No. (%)	≥ 65 yr, No. (%)	Effect Size (CI) Relative Risk*	Maximum Pain Score Mean: < 65 yr	≥ 65 yr	Effect Size (CI) Cohen's d
Spanish—Mexican	373	194 (52)	78 (40)	69 (39)	80 (41)	1.05 (0.71 to 1.56)	4.9	5.6	−0.21 (−0.41 to −0.01)
Hebrew	153	104 (68)	52 (34)	22 (42)	30 (30)	1.40 (0.67 to 2.92)	7.8	7.5	0.11 (−0.21 to 0.44)
Serbian	566	326 (58)	163 (29)	84 (35)	79 (24)‡	1.46 (0.89 to 2.38)	5.5	5.6	−0.04 (−0.20 to 0.13)
Chinese	147	62 (42)	40 (27)	22 (26)	18 (29)	0.90 (0.33 to 2.46)	4.4	4.3	0.04 (−0.28 to 0.36)
English	1,055	306 (29)	236 (22)	152 (20)	84 (28)‡	0.71 (0.45 to 1.14)	6.5	6.6	−0.08 (−0.21 to 0.05)
Spanish	983	727 (74)	204 (21)	80 (31)	124 (17)§	1.82 (1.10 to 3.03)	6.1	5.3§	0.26 (0.12 to 0.40)
Swedish	274	139 (51)	49 (18)	22 (16)	27 (19)	0.84 (0.25 to 2.84)	5.9	5.3	0.20 (−0.03 to 0.44)
Dutch	497	356 (72)	82 (17)	29 (21)	53 (15)	1.40 (0.54 to 3.63)	6.5	5.7‡	0.32 (0.12 to 0.51)
German	1440	825 (57)	203 (14)	100 (16)	103 (13)†	1.23 (0.63 to 2.41)	6.2	5.6§	0.23 (0.13 to 0.34)
Italian	188	133 (71)	30 (16)	10 (17)	20 (16)	1.06 (0.19 to 5.80)	4.8	5.1	−0.10 (−0.41 to 0.20)
French	1,348	820 (61)	162 (12)	75 (14)	87 (11)†	1.27 (0.56 to 2.89)	6.0	5.7	0.12 (0.01 to 0.23)
Other language or missing	608								

*Risk ratio. †$P \leq 0.05$. ‡$P \leq 0.01$. §$P \leq 0.001$.

In the current study, we observed differences in worst pain scores and in the wish for more pain treatment in the different language groups. Cultural differences have been described for pain beliefs/appraisals, coping, and catastrophizing.[41] A recent study on pain in American elderly shows that today's midlife Americans have had more pain throughout adulthood than today's elderly.[42] They find that for those with less education, each successive birth cohort has a higher prevalence of pain at each age. They state that this phenomenon is not observed in other rich countries. Finally, cultural differences may also be present in the way healthcare providers manage pain.[43,44]

The current study is unique due to its large study population, the multinational data collection in a highly standardized manner, and combining patient reports on pain and related symptoms with perioperative data. We focused on four frequently performed surgical procedures, both soft tissue (laparoscopic cholecystectomy) and bone surgery (hip and knee replacements and spinal surgery). Since the mean age differed between the procedures with the youngest patients in the laparoscopic cholecystectomy group and the oldest in the total knee replacement group, and there was variation in the presence of comorbidities, presurgical chronic pain, and opioid use, this selection of procedures, all showing a similar age-related decrease in maximum pain reports, strengthens our conclusion.

There are, however, also limitations. Although the dataset included data from different countries, data from northern America, Africa, and Australia/New Zeeland are missing. Potentially larger cultural differences may hinder the generalizability of the study. Second, within the timeframe of this study (2010 to 2018), changes in pain management have been implemented (*e.g.*, enhanced recovery protocols). We have corrected for "year of data collection," and as changes were implemented for all ages at the same time, we are of the opinion that the primary outcome is not influenced by changes in pain management over the years. Third, we have chosen to relate the worst pain score after surgery to aging, but one may argue that this is not always the best representative of pain suffering. However, our hypothesis still holds for patients after spinal fusion, hip replacement, and laparoscopic cholecystectomy when time in severe pain is used as composite endpoint (*post hoc* analysis, appendix 3). Finally, we only show an association between age and pain on the first operative day and cannot extrapolate these findings to pain developing in the trajectory after surgery.

Conclusions

This study assesses the association between age and postoperative pain after hip replacement, knee replacement, laparoscopic cholecystectomy, or spinal surgery. When looking on a population level, postoperative pain decreases with increasing age. Older patients experience less interference of pain with doing activities in bed, breathing deeply, coughing, sleep, side effects (nausea and drowsiness), and emotions (anxiety and helplessness), and were less often administered opioids and less often had a wish for more treatment. However, we want to stress that on an individual patient level, at any age, there are still too many patients undergoing common surgeries who suffer from moderate to severe pain, which interferes with function. We therefore encourage clinicians to base their postoperative pain management on the individual patient, taking risk factors such as age, being female, presence of chronic pain before surgery, and use of opioids before admission into account and not solely rely on the current standardized dosing in adult postsurgical patients.

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Competing Interests

Dr. Huygen reports grants and personal fees from Abbott (Lake County, Illinois); nonfinancial support from the Pfizer advisory board (New York, New York); and nonfinancial support from the Boston Scientific advisory board (Marlborough, Massachusetts), outside the submitted work. The other authors declare no competing interests.

Correspondence

Address correspondence to Dr. Rijsdijk: Pain Clinic, Department of Anesthesiology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands. m.rijsdijk-2@umcutrecht.nl. Anesthesiology's articles are made freely accessible to all readers on www.anesthesiology.org, for personal use only, 6 months from the cover date of the issue.

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Appendix 1: Questions in the International Pain Outcomes Questionnaire and Answer Options

Questions	Numeric Rating Scale	Percentage	Binary
The worst pain since surgery	X		
The least pain since surgery	X		
How often in severe pain since surgery		x	
Pain interference with doing activities in bed	X		
Pain interference with breathing deeply or coughing		x	
Pain interference with sleeping		x	
Out of bed since surgery			x
Pain interference with doing activities out of bed	X		
Nausea since surgery	X		
Drowsiness since surgery	X		
Itching since surgery	X		
Dizziness since surgery	X		
Feelings of anxiety because of the pain	X		
Feelings of helplessness because of the pain	X		
Wish for more pain treatment			x
Persistent painful condition for 3 months before surgery			x
Pain score of chronic pain	X		
Comorbidities (pain-related)			x

Appendix 2: Nonlinear Relation between Age and Worst Pain Score

Models	β	Standard Error	*P* Value
Spinal fusion			
(Intercept)	6.95	0.53	< 0.001
Knots:			
Age 1	0.16	0.39	0.673
Age 2	–1.72	1.27	0.174
Age 3	–2.04	0.67	0.002
Total hip replacement			
(Intercept)	6.11	0.42	< 0.001
Knots:			
Age 1	–1.06	0.24	< 0.001
Age 2	–0.40	0.95	0.673
Age 3	–0.27	0.39	0.496
Total knee replacement			
(Intercept)	7.56	0.31	< 0.001
Age	–0.02	0.005	< 0.001
Laparoscopic cholecystectomy			
(Intercept)	6.27	0.33	< 0.001
Knots:			
Age 1	–1.87	0.24	< 0.001
Age 2	–2.22	0.84	0.008
Age 3	–0.69	0.59	0.241

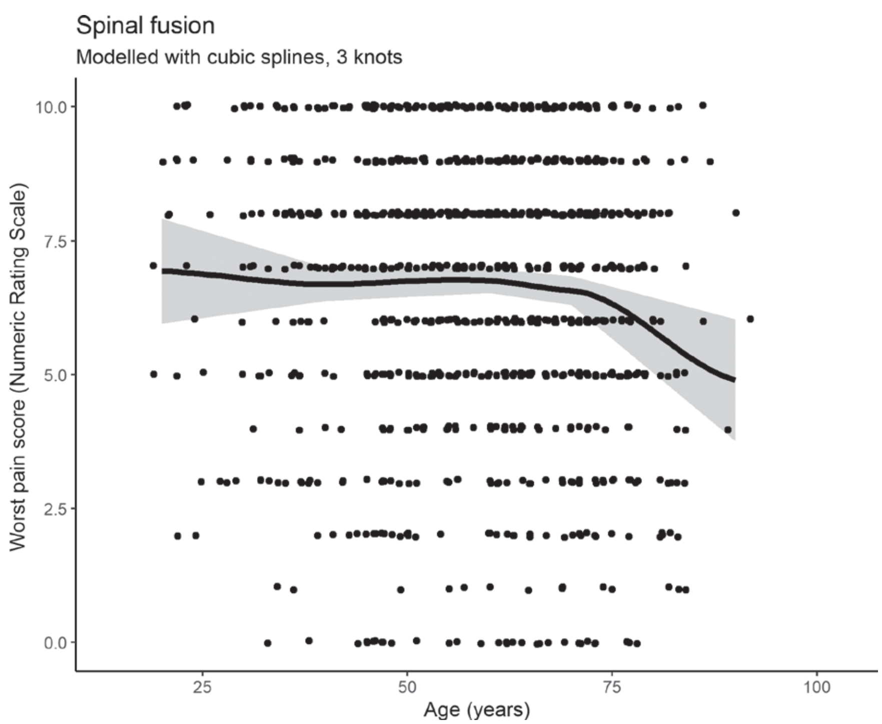

Fig. A2.1. Spinal fusion. Modeled with cubic splines, three knots. *Shaded area* indicates 95% confidence intervals.

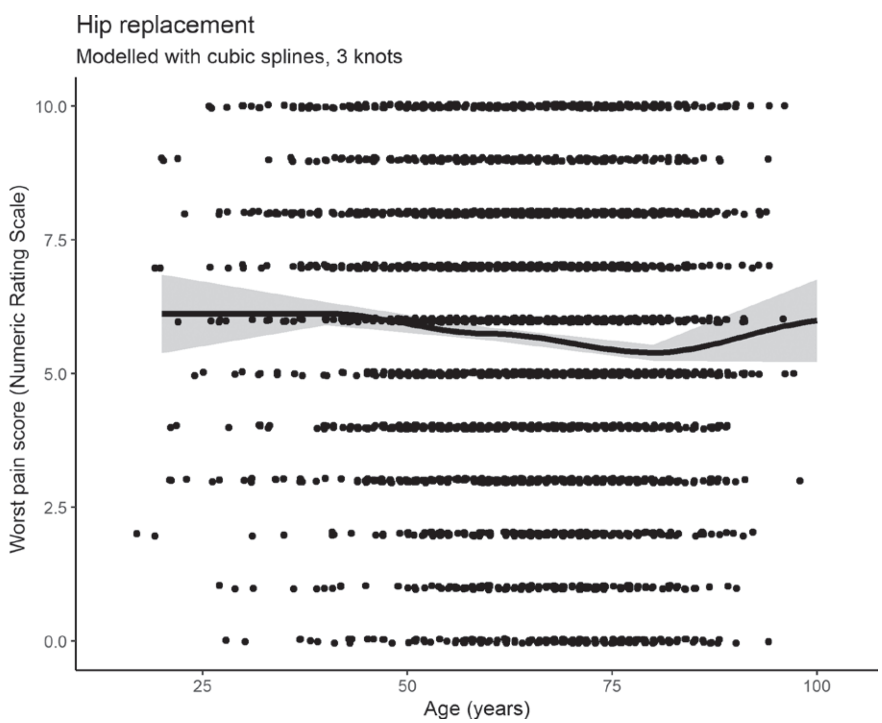

Fig. A2.2. Hip replacement. Modeled with cubic splines, three knots. *Shaded area* indicates 95% confidence intervals.

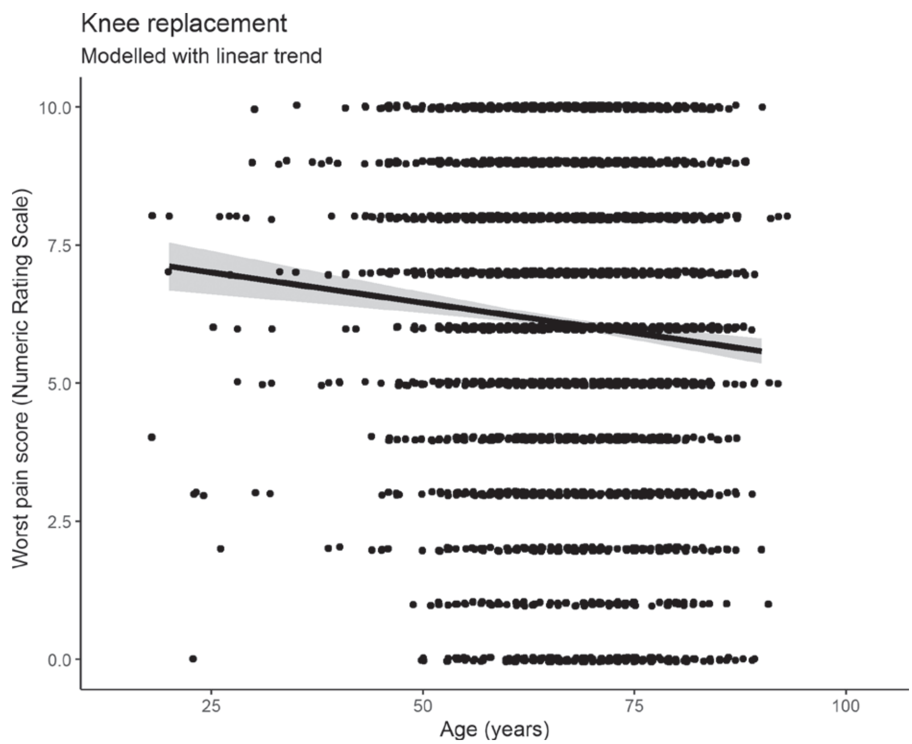

Fig. A2.3. Knee replacement. Modeled with linear trend. *Shaded area* indicates 95% confidence intervals.

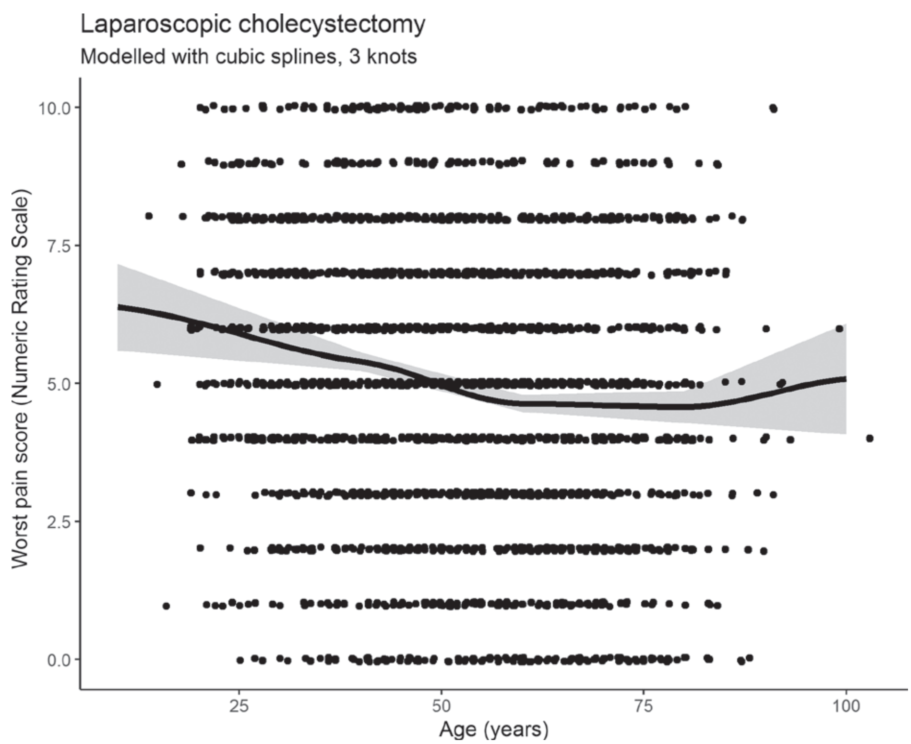

Fig. A2.4. Laparoscopic cholecystectomy. Modeled with cubic splines, three knots. *Shaded area* indicates 95% confidence intervals.

Appendix 3: *Post hoc* Analysis with Composite Endpoint: Time in Severe Pain

Regression Models	Constant	Age β per Decade (CI)	*P* Value
Primary endpoint: worst pain score			
Spinal fusion	7.2	−0.22 (−0.36 to −0.11)	< 0.001
Hip replacement	6.8	−0.22 (−0.30 to −0.15)	< 0.001
Knee replacement	7.3	−0.21 (−0.26 to −0.07)	< 0.001
Laparoscopic cholecystectomy	6.3	−0.22 (−0.28 to −0.13)	< 0.001
Composite endpoint: worst pain score * time in most severe pain			
Spinal fusion	4.2	−0.19 (−0.36 to −0.08)	0.002
Hip replacement	2.2	−0.13 (−0.21 to −0.07)	< 0.001
Knee replacement	1.6	0.02 (−0.08 to 0.13)	0.662
Laparoscopic cholecystectomy	2.2	−0.13 (−0.22 to −0.10)	< 0.001

We performed an additional *post hoc* analysis to verify our hypothesis that postoperative pain scores decrease with age. In our primary analysis, our endpoint is worst pain score. In the *post hoc* analysis, we created a composite endpoint by adding the factor "time in most severe pain" to the primary outcome, resulting in "worst pain score

*time in most severe pain." The association between age and worst pain score

*time in most severe pain shows a less robust but still significant decrease of pain with advancing age for spinal fusion, hip replacement, and laparoscopic cholecystectomy.