

# Time from Booking Until Appointment and Healthcare Utilization in Hand Surgery Patients with Discretionary Conditions

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**Abstract** Delaying treatment for benign musculoskeletal conditions may allow patients to learn self-efficacy and develop coping strategies, leading to less medical intervention and reduced cost. We tested the hypothesis that time from booking until appointment is not associated with healthcare costs. We further tested the secondary hypothesis that time from booking to appointment is not associated with specific healthcare utilizations. We identified 16,750 patients (55 % women; mean age 50 years) making first clinic visits to hand surgeons at our hospital between January 1, 2003 and December 31, 2012. Booking time was defined as the time between the scheduling of an appointment and the actual visit. Imaging procedures, injections, nerve conduction studies, occupational therapy visits, surgery, and referrals were determined up until the patient's second visit with the surgeon, or 90 days. Costs were determined in Relative Value Units. Duration between

booking and office visit was not associated with higher cost (regression coefficient [ $\beta$ ] 0.0023,  $P = 0.77$ ). Duration between booking and office visit was associated with a higher rate of nerve conduction studies (odds ratio [OR] 1.02,  $P < 0.001$ ) and a lower rate of occupational therapy (OR 0.98,  $P < 0.001$ ). There was substantial variation between surgeons. Greater wait time was not therapeutic, but is associated with different diagnostic and treatment measures that suggest people that are willing to wait have different types of problems. The variation by surgeon may make variation based on other factors, including time between booking and appointment, difficult to discern.

**Keywords** Cost · Utilization · Variation · Wait time

## Introduction

Many musculoskeletal illnesses are self-limiting. Most are benign although pain rarely feels benign because the normal human response to pain is to feel protective and prepare for the worst (i.e., catastrophic thinking). A delay in medical evaluation might be therapeutic in that the patient learns management strategies and grows self-efficacy; learns that most pains are nonspecific, benign, self-limiting, and do not benefit from medical attention; and avoids unnecessary testing and interventions that can cause iatrogenic harm [1]. Such a potentially therapeutic delay occurs in the interval between scheduling a clinic visit and seeing a hand surgeon—a delay that can be quite long in a national health service, but is generally quite short currently in the United States.

This study tested the primary null hypothesis that time from booking until appointment is not associated with healthcare costs, accounting for patient demographics, anatomic site, and treating surgeon. Additionally, we assessed the relationship

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between booking time to appointment and healthcare utilization, including imaging procedures, injections, nerve conduction studies, occupational therapy visits, surgery, referrals, and second opinions, accounting for patient demographics, anatomic site, and treating surgeon.

## Materials and Methods

### Patient Selection

This study was approved by our institutional review board and a waiver of informed consent was granted. All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. We retrospectively examined a database containing clinical encounters with hand surgeons at our institution [2]. We included patients whose first clinic visit to the hand and upper extremity service was between January 1, 2003 and December 31, 2012, the range for which complete data was available ( $n = 37,997$ ). Patients were excluded from the study if there was missing procedure or diagnosis data ( $n = 1399$ ), they were seen for a nondiscretionary conditions (e.g., fractures or lacerations;  $n = 13,672$ ), or they had more than 30 days between booking their appointment and the actual clinic visit ( $n = 5,645$ ). We limited the analysis to the three busiest hand surgeons in our department. Our final cohort included 16,750 patients with an average age of  $50 \pm 17$  years; 45 % ( $n = 7,557$ ) of our cohort were men (Table 1).

### Outcome Measures

Booking time was defined as the number of days between when a patient scheduled their appointment and their actual office visit. Anatomic site of symptoms was determined by assigned International Classification of Disease, 9th Revision (ICD-9) codes after the visit. Patients with multiple locations were classified as “mixed,” and patients with ambiguous locations based on ICD-9 codes were classified as “nonspecific” (Online Resource 1). Cost was determined as the sum of the relative value units (RVUs) for all procedures and was defined using the 2012 Medicare Physician Fee Schedule (Online Resource 2) [3].

Using Current Procedural Terminology (CPT) codes we determined utilization of imaging procedures, injections, nerve conduction studies and electromyography, occupational therapy visits, and surgeries between the first and second visit by the treating surgeon (Online Resource 2). To prevent overlap between appointments, we captured procedures up to three days prior to the second encounter. If a patient had no second encounter, we included procedures up to 90 days after the first appointment. Imaging included all radiographs, computed

**Table 1** Baseline characteristics

Variables	Mean ( $\pm$ standard deviation)
Age (years)	50 ( $\pm$ 17)
Cost (RVU)	4.7 ( $\pm$ 8.6)
Booking time (days)	10.8 ( $\pm$ 8.2)
<b>Percentage (number; total = 16,750)</b>	
Men	45 % (7,557)
Anatomic location	
Hand/fingers	29 % (4,839)
Wrist	18 % (3,035)
Forearm	8.0 % (1,345)
Elbow	5.9 % (996)
Arm	3.0 % (507)
Shoulder	1.8 % (302)
Mixed	11 % (1,864)
Unspecified	23 % (3,862)
Surgeons	
Surgeon 1	23 % (3,789)
Surgeon 2	25 % (4,250)
Surgeon 3	52 % (8,711)
Utilization	
Imaging procedure	23 % (3,898)
Injection	7.7 % (1,287)
Nerve conduction study	8.0 % (1,341)
Occupational therapy	21 % (3,567)
Surgery	11 % (1,905)
Referral	0.8 % (128)
Second opinion	0.7 % (115)

tomography, magnetic resonance imaging, and arthrograms of the upper extremity. Aspiration of ganglion cysts was included with injections.

Referrals were determined by searching for CPT codes billed by other departments (neurology, rheumatology, and psychiatry) until three days before the next hand clinic visit or up to 90 days after the visit if the patient did not return to clinic. All referrals ( $n = 128$ ) were subsequently manually verified by reviewing notes in the electronic medical record; 11 records could not be verified because of missing electronic records and were excluded. Second opinions were defined as a patient seeing another hand surgeon in our department for the same symptoms within one year. All second opinions ( $n = 115$ ) were manually verified, and 19 patients with missing electronic notes were excluded.

### Reliability of Database

The final dataset used for analysis was manually compared against the medical records of one hundred randomly selected patients for accuracy. Imaging was identified correctly at a rate of

**Table 2** Multivariable analysis factors associated with cost and imaging

Cost (RVU) factors	$\beta$ regression coefficient	Standard error	95 % confidence interval	P value	Semi-partial R <sup>2</sup>	Adjusted R <sup>2</sup>
Male sex	0.55	0.13	0.29,0.80	<b>&lt;0.001</b>	0.0011	
Age	0.011	0.0040	0.0036,0.019	<b>0.004</b>	0.00049	
Booking Duration (Days)	0.0023	0.0080	-0.013,0.018	0.77	0.0000051	
<i>Anatomic Site</i>						
Hand/Fingers	<i>Reference Value</i>					
Wrist	4.1	0.19	3.7,4.4	<b>&lt;0.001</b>	0.026	
Forearm	0.47	0.26	-0.042,0.98	0.072	0.00019	
Elbow	-0.56	0.29	-1.1,0.0042	0.052	0.00023	
Arm	3.3	0.39	2.5,4.1	<b>&lt;0.001</b>	0.0043	0.094
Shoulder	-0.045	0.49	-1.0,0.91	0.93	0.00000051	
Mixed	4.2	0.22	3.8,4.6	<b>&lt;0.001</b>	0.020	
Nonspecific	0.96	0.18	0.60,1.3	<b>&lt;0.001</b>	0.0016	
<i>Surgeon</i>						
Surgeon 1	<i>Reference Value</i>					
Surgeon 2	-4.1	0.19	-4.5,-3.8	<b>&lt;0.001</b>	0.029	
Surgeon 3	-4.6	0.17	-4.9,-4.2	<b>&lt;0.001</b>	0.043	
<b>Imaging procedures</b>	<b>Odds ratio</b>	<b>Standard error</b>	<b>95 % confidence interval</b>	<b>P value</b>	<b>Pseudo R<sup>2</sup></b>	
Male sex	1.2	0.049	1.06,1.3	<b>0.001</b>		
Age	0.99	0.0013	0.988,0.993	<b>&lt;0.001</b>		
Booking Duration (Days)	1.0	0.0025	0.999,1.01	0.088		
<i>Anatomic Site</i>						
Hand/Fingers	<i>Reference Value</i>					
Wrist	0.24	0.020	0.20,0.28	<b>&lt;0.001</b>		
Forearm	2.2	0.16	1.9,2.6	<b>&lt;0.001</b>		
Elbow	0.42	0.046	0.34,0.52	<b>&lt;0.001</b>	0.22	
Arm	2.1	0.23	1.7,2.6	<b>&lt;0.001</b>		
Shoulder	1.2	0.17	0.90,1.6	0.24		
Mixed	2.6	0.17	2.3,3.0	<b>&lt;0.001</b>		
Nonspecific	0.59	0.036	0.52,0.66	<b>&lt;0.001</b>		
<i>Surgeon</i>						
Surgeon 1	<i>Reference Value</i>					
Surgeon 2	0.49	0.025	0.45,0.54	<b>&lt;0.001</b>		
Surgeon 3	0.12	0.0062	0.11,0.13	<b>&lt;0.001</b>		

**Bold** indicates statistically significant difference

99 %, injection 96 %, nerve conduction tests and electromyography 96 %, occupational therapy visits 96 %, and surgery 99 %.

### Statistical Analysis

All utilization measures except cost are summarized dichotomously. Dichotomous and categorical variables are summarized with number and percentage, interval variables as mean ( $\pm$  standard deviation).

Multivariable linear regression was used to test for independent influence of all independent variables on cost, after converting categorical variables into indicator variables, with the first category as the reference value. We conducted

multivariable logistic regression analyses to test for independent influence of independent variables on each utilization measure in a similar fashion.

For bivariate analysis of costs, we used Pearson's correlation for interval variables, Student t-test for dichotomous variables, and analysis of variance for categorical variables. Dichotomous utilization measures and interval variables were compared using the Student t-test, dichotomous variables using Fisher's exact, and categorical variables using Fisher's exact (surgeon) or Chi<sup>2</sup> (anatomic location). Bivariate analysis is reported in Online Resource 3.

In order to account for potential variation in costs over the duration of the study period, an additional multivariable

**Table 3** Multivariable analysis factors associated with injections & nerve conduction studies

Injection	Odds Ratio	Standard error	95 % confidence interval	P value	Pseudo R <sup>2</sup>
Male sex	0.88	0.054	0.78,0.99	<b>0.031</b>	
Age	1.03	0.0021	1.02,1.03	<b>&lt;0.001</b>	
Booking Duration (Days)	1.0	0.0037	0.999,1.01	0.099	
<i>Anatomic Site</i>					
Hand/Fingers	<i>Reference Value</i>				
Wrist	0.23	0.023	0.19,0.28	<b>&lt;0.001</b>	
Forearm	0.13	0.025	0.085,0.19	<b>&lt;0.001</b>	
Elbow	0.26	0.043	0.19,0.36	<b>&lt;0.001</b>	
Arm	0.074	0.031	0.033,0.17	<b>&lt;0.001</b>	0.14
Shoulder	0.019	0.019	0.0026,0.13	<b>&lt;0.001</b>	
Mixed	0.38	0.037	0.31,0.46	<b>&lt;0.001</b>	
Nonspecific	0.16	0.018	0.13,0.20	<b>&lt;0.001</b>	
<i>Surgeon</i>					
Surgeon 1	<i>Reference Value</i>				
Surgeon 2	1.1	0.093	0.96,1.3	0.13	
Surgeon 3	0.69	0.055	0.59,0.81	<b>&lt;0.001</b>	
<b>Nerve Conduction Studies</b>					
	<b>Odds Ratio</b>	<b>Standard error</b>	<b>95 % confidence interval</b>	<b>P value</b>	<b>Pseudo R<sup>2</sup></b>
Male sex	1.2	0.073	1.04,1.33	<b>0.010</b>	
Age	1.02	0.0019	1.02,1.02	<b>&lt;0.001</b>	
Booking Duration (Days)	1.02	0.0037	1.01,1.02	<b>&lt;0.001</b>	
<i>Anatomic Site</i>					
Hand/Fingers	<i>Reference Value</i>				
Wrist	43	7.0	31,59	<b>&lt;0.001</b>	
Forearm	2.2	0.59	1.3,3.7	<b>0.003</b>	
Elbow	1.5	0.52	0.78,3.0	0.22	0.19
Arm	5.7	1.5	3.3,9.6	<b>&lt;0.001</b>	
Shoulder	2.7	1.2	1.1,6.3	<b>0.027</b>	
Mixed	19	3.1	13,26	<b>&lt;0.001</b>	
Nonspecific	10	1.7	7.3,14	<b>&lt;0.001</b>	
<i>Surgeon</i>					
Surgeon 1	<i>Reference Value</i>				
Surgeon 2	0.77	0.065	0.65,0.91	<b>0.002</b>	
Surgeon 3	0.60	0.046	0.52,0.70	<b>&lt;0.001</b>	

**Bold** indicates statistically significant difference

analysis was conducted including indicator variables for each year during the study period (Online Resource 4).

P values <0.05 are considered significant; all statistical analyses were conducted using Stata 13.0 (StataCorp LP, Texas, USA).

**Results**

Accounting for potential confounding with other factors using multiple linear regression, duration between booking and office visit was not associated with higher cost (regression coefficient [ $\beta$ ] 0.0023, semipartial R<sup>2</sup> 0.0000051, 95 %

confidence interval [CI] -0.013 to 0.018, P = 0.77) but male sex ( $\beta$  0.55, semipartial R<sup>2</sup> 0.0011, 95 % CI 0.29 to 0.80, P < 0.001), age ( $\beta$  0.011, semipartial R<sup>2</sup> 0.00049, 95 % CI 0.0036 to 0.019, P = 0.004), specific anatomic sites, and specific surgeons were independently associated with higher costs (adjusted R<sup>2</sup> = 0.094, P < 0.001; Table 2).

Accounting for potential confounding with other factors using multiple logistic regression, longer time between booking and office visit was associated with a higher rate of nerve conduction studies (odds ratio [OR] 1.02, 95 % CI 1.01 to 1.02, P < 0.001) and a lower rate of occupational therapy (OR 0.98, 95 % CI 0.98 to 0.99, P < 0.001). Booking duration was not associated with imaging procedures (OR 1.0, 95 % CI

0.999 to 1.01,  $P = 0.088$ ), injections (OR 1.0, 95 % CI 0.999 to 1.01,  $P = 0.099$ ), surgery (OR 1.0, 95 % CI 0.996 to 1.01,  $P = 0.57$ ), referrals (OR 1.0, 95 % CI 0.98 to 1.0,  $P = 0.82$ ), or second opinions (OR 0.99, 95 % CI 0.96 to 1.0,  $P = 0.36$ ). Except for referrals and second opinions, all other utilization measures were associated with male sex and age. Male sex was associated with more imaging procedures, nerve conduction studies, and surgery. Older age was associated with more injections, nerve conduction studies, and surgery. Healthcare utilization differed per anatomical site and by specific surgeons (Tables 2, 3, 4, and 5). When accounting for variation over the duration of the study period, the OR of injection for booking duration (OR 1.01, 95 % CI 1.001 to 1.02,  $P = 0.019$ ) and surgeon 2 (OR 1.3, 95 % CI 1.1 to 1.6,  $P = 0.002$ ) became

significant. No previously significant values lost their significance (Online Resource 4).

## Discussion

Many musculoskeletal illnesses are self-limiting and a delay in seeing a doctor might be therapeutic in that the patient learns management strategies and grows self-efficacy. Such a delay occurs when time between scheduling an appointment and seeing a hand surgeon increases. Our study tested if time between scheduling an appointment and seeing a hand surgeon was associated with healthcare costs and utilization. We found no association between costs and

**Table 4** Multivariable analysis factors associated with occupational therapy & surgery

Occupational Therapy	Odds Ratio	Standard error	95 % confidence interval	<i>P</i> value	Pseudo R <sup>2</sup>
Male sex	0.74	0.030	0.68,0.80	<0.001	
Age	0.997	0.0012	0.994,0.999	<b>0.010</b>	
Booking Duration (Days)	0.98	0.0025	0.98,0.99	<0.001	
<i>Anatomic Site</i>					
Hand/Fingers	<i>Reference Value</i>				
Wrist	0.85	0.050	0.75,0.95	<b>0.004</b>	
Forearm	0.83	0.066	0.71,0.97	<b>0.020</b>	
Elbow	1.3	0.11	1.1,1.6	<b>0.001</b>	
Arm	0.57	0.078	0.44,0.74	<0.001	0.080
Shoulder	1.4	0.18	1.0,1.8	<b>0.029</b>	
Mixed	1.4	0.088	1.2,1.6	<0.001	
Nonspecific	0.46	0.029	0.41,0.52	<0.001	
<i>Surgeon</i>					
Surgeon 1	<i>Reference Value</i>				
Surgeon 2	2.4	0.13	2.1,2.6	<0.001	
Surgeon 3	0.60	0.032	0.54,0.67	<0.001	
<b>Surgery</b>					
	<b>Odds Ratio</b>	<b>Standard error</b>	<b>95 % confidence interval</b>	<b><i>P</i> value</b>	<b>Pseudo R<sup>2</sup></b>
Male sex	1.2	0.059	1.1,1.3	<b>0.003</b>	
Age	1.01	0.0016	1.00,1.01	<0.001	
Booking Duration (Days)	1.0	0.0030	0.996,1.01	0.57	
<i>Anatomic Site</i>					
Hand/Fingers	<i>Reference Value</i>				
Wrist	2.1	0.14	1.8,2.3	<0.001	
Forearm	0.62	0.074	0.49,0.78	<0.001	
Elbow	0.21	0.048	0.14,0.33	<0.001	
Arm	1.1	0.16	0.85,1.5	0.42	0.078
Shoulder	0.32	0.010	0.17,0.59	<0.001	
Mixed	1.4	0.11	1.1,1.6	<0.001	
Nonspecific	1.2	0.085	1.0,1.3	0.058	
<i>Surgeon</i>					
Surgeon 1	<i>Reference Value</i>				
Surgeon 2	0.14	0.013	0.11,0.17	<0.001	
Surgeon 3	0.49	0.028	0.44,0.55	<0.001	

**Bold** indicates statistically significant difference

**Table 5** Multivariable analysis factors associated with referral & second opinion

Referral	Odds ratio	Standard error	95 % confidence interval	P value	Pseudo R <sup>2</sup>
Male sex	0.93	0.17	0.65,1.3	0.69	
Age	1.0	0.0055	0.998,1.02	0.12	
Booking duration (Days)	1.0	0.011	0.98,1.0	0.82	
<i>Anatomic site</i>					
Hand/Fingers	<i>Reference value</i>				
Wrist	1.4	0.42	0.78,2.5	0.26	
Forearm	3.1	0.98	1.6,5.7	<b>0.001</b>	
Elbow	0.78	0.42	0.27,2.3	0.64	
Arm	1.0	0.75	0.24,4.3	0.99	0.046
Shoulder	2.7	1.5	0.92,7.9	0.070	
Mixed	2.0	0.62	1.1,3.7	<b>0.023</b>	
Nonspecific	2.1	0.56	1.2,3.5	<b>0.008</b>	
<i>Surgeon</i>					
Surgeon 1	<i>Reference value</i>				
Surgeon 2	3.8	1.0	2.3,6.5	<b>&lt;0.001</b>	
Surgeon 3	1.1	0.3	0.60,1.9	0.82	
<b>Second opinion</b>	<b>Odds ratio</b>	<b>Standard error</b>	<b>95 % confidence interval</b>	<b>P value</b>	<b>Pseudo R<sup>2</sup></b>
Male sex	0.92	0.18	0.63,1.3	0.66	
Age	1.0	0.0059	0.995,1.02	0.29	
Booking duration (days)	0.99	0.013	0.96,1.0	0.36	
<i>Anatomic site</i>					
Hand/Fingers	<i>Reference value</i>				
Wrist	1.5	0.46	0.82,2.7	0.19	
Forearm	2.7	0.99	1.3,5.5	<b>0.008</b>	
Elbow	1.5	0.66	0.63,3.5	0.36	0.038
Arm	6.7	2.6	3.2,14	<b>&lt;0.001</b>	
Shoulder	0.83	0.85	0.11,6.2	0.85	
Mixed	1.6	0.58	0.75,3.2	0.24	
Nonspecific	1.8	0.52	1.0,3.2	<b>0.047</b>	
<i>Surgeon</i>					
Surgeon 1	<i>Reference value</i>				
Surgeon 2	5.0	2.3	2.1,12	<b>&lt;0.001</b>	
Surgeon 3	6.6	2.8	2.8,15	<b>&lt;0.001</b>	

**Bold** indicates statistically significant difference

the time between scheduling an appointment and seeing a hand surgeon.

Our study has some limitations. First, the RVU from the Medicare Physician Fee Schedule reflects relative healthcare use costs but does not account for nonmedical costs such as time from work; therefore, the Fee Schedule does not reflect total healthcare costs. Secondly, we could not track patients leaving our system after referral to another hospital or outside second opinion. These resultant costs and utilizations are not measured in our study.

In our study, healthcare costs were not associated with time between scheduling an appointment and seeing a hand surgeon. One study found that immediate surgery for patients

undergoing total hip arthroplasty revision reduced healthcare expenditure [4]. Another study found that waiting more than 6 months for total hip arthroplasty resulted in higher overall costs (including medical, personal, and societal) [5]. These studies differ considerably from ours in that the patients in those studies were in a queue for surgery, whereas our study was aimed at determining costs immediately after initial orthopaedic evaluation.

Longer time between booking and office visit was associated with a higher rate of nerve conduction studies and a lower rate of occupational therapy. We found no association with imaging procedures, injections, surgery, referrals, or second opinions. In our offices the average time from phone call to

appointment was 10.8 days (median 8.2 days). In a system with easy access, it may be that people well-adjusted to long-standing problems request later visits out of convenience and because they are at ease with their problem. Perhaps those patients are more likely to be offered tests in planning for surgery. Our intention was to measure the effect of wait time on the more common transient acute or intermittent and remittent musculoskeletal problems. For example, a previous study found that patients with knee injuries who waited longer for treatment had improved coping strategies [1]. The reduced need for occupational therapy observed in our study might reflect patient adaptation when waiting longer before seeing a doctor, but it might also reflect a prevalence of illnesses less responsive to occupational therapy among later presenters or even that they had already tried those treatments. Another study in rheumatology randomized patients into a ‘fast track’ group (mean waiting time 45 days) and an ‘ordinary’ group (mean waiting time 105 days) [6]. More patients in the ‘fast track’ group were prescribed analgesics or underwent routine lab testing. There was no difference between groups in terms of non-analgesic prescriptions, radiology, or referrals. Like our study, there was no difference in radiology or referral rates based on waiting time. Our study, however, did not measure rates of medication prescription or routine lab testing.

Increased use of imaging procedures, nerve conduction studies, and surgery were associated with male sex. Increased use of injections, nerve conduction studies, and surgery were associated with older age. This might simply reflect an increasing burden of disease with age. But a study focused on newly diagnosed hand osteoarthritis patients found that younger age was associated with more healthcare utilization the year after diagnosis [7]. Our study included a larger variety of conditions. Previous studies of hip, knee, and hand osteoarthritis found that male sex was associated with a higher rate of surgery [7, 8]. This might be explained by differences in attitudes toward surgery between men and women, because some data suggest that women are more fearful of surgery and more concerned about the postoperative recovery time, postoperative pain, risks of anesthesia, and complications [9]. One study found women are more willing to delay surgery in order to prevent the disruption of their caregiving roles [10].

The variation in utilization by anatomical site is probably related to a higher rate of diagnosis with a higher likelihood of surgery, e.g., carpal tunnel syndrome. We also found a difference in utilization between surgeons. Surgeon-to-surgeon variations in care are well documented [7].

In a setting with relatively short wait times, our findings do not support a therapeutic effect of a longer time between scheduling an appointment and seeing a hand surgeon. Rather, our data raise the possibility that when access is readily available there may be differences between people that schedule appointments several weeks in advance and those that take the first available appointment. Since data on patient

preferences for appointment time are not available, determining this would necessitate an additional study. As in prior studies, we observed wide variations in cost and resource utilization based on provider, patient sex, and patient age. In particular, the variation by surgeon seems to outweigh variation based on other factors including time between booking and appointment.

### Compliance with Ethical Standards.

**Potential Conflicts of Interest** One of the authors (DR) certifies that he, or a member of his immediate family, has or may receive payments or benefits during the study period from Wright Medical (USD less than 10,000) (Memphis, TN, USA); Skeletal Dynamics (USD less than 10,000) (Miami, FL, USA); Biomet (USD less than 10,000) (Warsaw, IN, USA); AO North America (USD less than 10,000) (Paoli, PA, USA); and AO International (USD less than 10,000) (Dubendorf, Switzerland).

**Research Involving Human Participants** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** For this type of study formal consent is not required.

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