Total hip arthroplasty is a cost-effective surgical procedure undertaken to relieve pain and restore function to the arthritic hip joint. More than 1 million arthroplasties are done every year worldwide, and this number is projected to double within the next two decades. Symptomatic osteoarthritis is the indication for surgery in more than 90% of patients, and its incidence is increasing because of an ageing population and the obesity epidemic. Excellent functional outcomes are reported; however, careful patient selection is needed to achieve best possible results. The present economic situation in many developed countries will place increased pressure on containment of costs. Future demand for hip arthroplasty, especially in patients younger than 65 years, emphasises the need for objective outcome measures and joint registries that can track lifetime implant survivorship. New generations of bearing surfaces such as metal-on-metal, ceramic-on-ceramic, and metal-on-ceramic, and techniques such as resurfacing arthroplasty have the potential to improve outcomes and survivorship, but findings from prospective trials are needed to show efficacy. With the recall of some metal-on-metal bearings, new bearing surfaces have to be monitored carefully before they can be assumed to be better than traditional bearings.

Introduction
Hip arthroplasty has evolved from a salvage procedure with poor long-term outcomes reserved for the most infirm patients, to one of the most successful and frequently undertaken elective surgeries. The era of modern total hip arthroplasty began in the 1970s, after widespread use of the Charnley prosthesis. More than 500 000 procedures are done each year in the UK and USA, with excellent clinical outcomes showing greater than 95% survivorship at 10-year follow-up, and greater than 80% implant survivorship at 25-year follow-up. However, in the present climate of tightening health-care budgets and debate about fiscal austerity, the implications of increasing demand for hip arthroplasty have led to intense discussion about the cost-effectiveness of new technologies. This Seminar is presented as an update of what is new in the specialty of total hip arthroplasty since this topic was last reviewed in The Lancet in 2007.

Epidemiology
Total hip arthroplasty is common, with more than 1 million procedures undertaken worldwide. Rates for primary and revision total hip arthroplasty have been increasing; between 1990 and 2002, the rate of primary total hip arthroplasties in the USA increased 50% from 47 per 100 000 population to 69 per 100 000 population. Between 2005 and 2010, the number of total hip arthroplasties in the UK increased 16%. Slightly higher utilisation rates have been reported in Finland and Norway, whereas lower rates are noted in South Korea. Between 2005 and 2030, the number of primary total hip arthroplasties in the USA is projected to increase 174% to 572 000 procedures every year. Similarly, the revision rate in the USA increased 60% from 9·5 per 100 000 to 15·2 per 100 000, and is projected to increase 137% by 2030.1,3

Utilisation rates are 1·5–2 times higher for women than for men, with the greatest disparity occurring in South Korea, where women undergo total hip arthroplasty seven to eight times as frequently as do men. Utilisation rates have been increasing equally for both sexes. The greatest proportion of procedures (65%) is in patients aged 65 years and older. However, the proportion of patients younger than 65 years is projected to increase to 50% of all arthroplasties by 2030.4

The indications for surgery in the UK are osteoarthritis (93%), osteonecrosis (2%), femoral neck fracture (2%), developmental dysplasia of the hip (2%), and inflammatory arthritis (1%). Risk factors for osteoarthritis include female sex, advanced age (>65 years), and obesity. The reported age-standardised incidence (20–89 years) of osteoarthritis is 88 per 100 000 patient-years, whereas the prevalence of symptomatic osteoarthritis is 9% in men and 11% in women. The cause of osteoarthritis is multifactorial, but findings from several studies have implicated femoroacetabular, cam, or pincer-type impingement, especially in young men. Prevalence of any type of congenital or acquired hip malformation is 4–3% in men and 3–6% in women. Of patients with symptomatic osteoarthritis, 71% of men and 36% of women have concomitant malformation of the hip joint. Many surgical procedures are being used to address impingement to forestall or obviate the need for total hip arthroplasty.
Surgical indication

Surgical indications for hip arthroplasty are guided by pain, functional impairment, physical examination, and radiographic findings (figure 1). However, an initial course of conservative therapy should always be attempted with analgesia, activity modification, ambulatory aids, and weight loss. Intra-articular injections can be useful to differentiate arthritic pain from referred sources, such as back pain, knee pain, or hernia.

The US National Institutes of Health 1995 position statement for total hip arthroplasty recommended surgery for patients with chronic pain and significant functional impairment. However, no international consensus position exists for surgical indications. The Global Orthopaedic Registry has shown that patient selection criteria varies between practitioners, surgeons, and referring physicians, and between countries. Wait time can be an important factor in patient outcomes since poor function before and after the operation are correlated. Early functional improvement is lower in patients who wait 6 months than in those who wait less than 3 months, which has implications for resource use and patient prioritisation.

Optimum surgical results are obtained through careful patient selection. Obesity, advanced age, and medical comorbidities are not absolute contraindications. However, a 40% increased risk for complications is noted for every decade above the age of 65 years. Conversely, total hip arthroplasty in patients younger than 50 years presents a unique set of challenges related to implant survivorship because of the possibility of increased wear and early implant failure in this group of more active patients. Although a broad range of patients benefit from total hip arthroplasty, preoperative education should aim to align patient expectations with the risks and benefits of the procedure.

Patient and implant assessment

Assessment of patient and implant outcomes is necessary to identify which implant designs or surgical techniques provide the best patient benefit. Several studies have focused on the economics of total hip arthroplasty, long-term patient functional outcomes, patient satisfaction, results, and patient perceptions. The appendix provides further discussion about these topics.

National registries

National joint registries have revolutionised the assessment of patient outcomes, implant survivorship, and surgical techniques. By surveying large samples, the statistical power provided to studies using comparative registry data can be used to record differences in outcomes with otherwise extremely low incidence. Cases of product recall, changes in treatment protocol, and decreases in revision surgeries have been attributed to registry-based studies.

Registries are available in the UK, Canada, Australia, New Zealand, Sweden, Norway, and Denmark (among others). The USA does not have a national registry, although some states and health-care organisations maintain such data. Some joint registries, such as those in the UK and Australia are funded by fees levied on orthopaedic implant manufacturers, with fund disbursement under the discretion of the registry steering committee. Although the cost associated with development and maintenance of national joint registries varies, these registries are considered to be one of the most cost-effective medical developments. However,
the amount of representation that orthopaedic surgeons have on the steering committees, and the implications that these databases have for patient confidentiality, have been debated.\(^{21,24}\) Furthermore, prospective registry data are not randomised, and could be susceptible to bias. Survivorship rates are particularly sensitive to competing risks of death and tend to underestimate the actual survivorship, which might skew the data of implants that are used in elderly patients.\(^{25}\)

An early success of joint registries was the identification of high rates of early failure of the DePuy ASR total hip and hip resurfacing system (DePuy Orthopaedics, Leeds, UK). Initial evidence of early failure was first identified in the Australian National Joint Replacement Registry. This finding was subsequently confirmed by National Joint Registry data in the UK, and several follow-up studies.\(^{26,27}\)

Use of national joint registries allows for long-term surveillance of implant survivorship and patient outcomes. The large number of patients enrolled in these databases allows for adequately powered analysis of outcomes, and could lead to assessment of cost-effective treatment options and improved implant survivorship.

**Clinical outcomes**

**Revision setting**

Total hip arthroplasty has shown excellent short-term and long-term outcomes, but despite advances in surgical technique and implant design, the revision burden has remained unchanged over the past several decades. In one study of primary total hip arthroplasties,\(^{28}\) the most common cause for revision surgery was instability (22% of revision cases), followed by mechanical loosening (20%), infection (15%), implant failure (10%), osteolysis (7%), and periprosthetic fracture (6%). In the revision setting, infection was the most common cause of revision failure (30%), followed by instability (25%), and loosening (19%).\(^{29}\) Retrieval analysis of failed components and examination of implants in situ at autopsy have expanded understanding of the mechanisms of failure.\(^{30}\) Factors affecting long-term survivorship include material wear properties, component positioning, and patient-related factors such as medical comorbidities and activity levels.

**Long-term survivorship**

The Charnley low-friction arthroplasty was the first widely accepted design to be used, and provides the basis of comparison to new designs (figure 2). Excellent implant survivorship has been reported for the Charnley prosthesis at greater than 20-year follow-up (>80%) and 35-year follow-up (78%).\(^{31,32}\) Hybrid total hip arthroplasty typically uses a cemented stem and non-cemented cup. Rasquinha and colleagues\(^{33}\) noted 100% survivorship at mean 15-year follow-up in a prospective series of 215 patients using third-generation cementing techniques. Cementless stems have been used most often and have shown favourable results. 60–90% of total hip arthroplasties done in the USA use cementless components. The theoretical benefit of cementless fixation is the ability of the bone-implant interface to remodel. Survivorship is greater than 95% in many implant types at 10-year follow-up, with some stem designs maintaining this survivorship at 20-year follow-up.\(^{34}\) High 10-year survivorship has also been reported with reverse hybrid total hip arthroplasty, which has a cemented cup and cementless stem. In studies of patients in the Swedish and Norwegian joint registries,\(^{35,36}\) this fixation method had similar clinical results to cemented fixation, but lower revision rates were noted for aseptic acetabular cup loosening than for cementless designs. Although several newer cementless designs are available, data to show
clear superiority over older designs are scarce. High rates of failures associated with newer stem designs, such as the first generation anatomically shaped stems or the initial short-stem designs,35,36 emphasise the importance of using tried and true designs.36

Clinical follow-up

Implants should be assessed for radiographic signs of loosening, migration, or failure every year. Although no studies have examined the benefit of specific follow-up frequencies, the National Institutes of Health recommend continued periodic follow-up; a survey of members of the American Association of Hip and Knee Surgeons showed that 80% of respondents recommended clinical follow-up in asymptomatic patients either every year or every 6 months.37,38 Radiostereometric analysis allows for precise quantification of any migration; however, direct visual interpretation and surgeon experience are the most commonly used ways to assess radiographs.39 The early detection of lesions that may place the implant at risk is more cost effective than is assessment of patients when pain or loss of function is present.37,38

Instability

Instability and dislocation are the most common reasons for revision surgery, and the second most common cause of failure of revision total hip arthroplasty. Prevalence of dislocation ranges between 0·3% and 10% for primary total hip arthroplasty, and as high as 28% for revision total hip arthroplasty.39,40,41 The most common reasons for instability are component malpositioning and abductor deficiency; however, age, previous fracture, surgical volume, surgical approach, component sizing, polyethylene wear, and patient compliance are also contributory factors.42–44

Treatment options for recurrent dislocation include revision with constrained polyethylene liners, larger diameter femoral heads, or dual mobility devices. Use of large diameter femoral heads increases the distance that the head must travel before dislocation, without decreasing hip range of motion, and thus increasing stability.45 This effect has been confirmed by UK registry data for femoral heads greater than 36 mm in diameter,46 and by Medicare data reported by Malkani and colleagues,47 who showed a decrease in the dislocations rate from 4% to 2% as larger diameter heads began to be used. Another option is a constrained liner, which offers increased stability but at the cost of smaller range of motion. Consequently, implant designs such as dual-mobility cups, which have two articulating surfaces, have been designed to overcome this drawback. As a result of these advances, recurrent late dislocation remains a major source of total hip arthroplasty failure. More prospective, randomised studies are needed to establish the optimum treatment for these patients.

Aseptic loosening and osteolysis

Aseptic loosening is a common cause of late failure in total hip arthroplasty. It arises because of osteoclast-mediated bone resorption at the bone-implant interface, which can lead to loosening, implant migration, implant failure, or periprosthetic fracture.48 Component malpositioning is a major cause of severe wear and osteolysis, but it is also affected by activity level and material and component design.49 It is diagnosed clinically by patient-reported start-up pain; however, clinicians should consider the possibility of infection since the reported prevalence of occult infection ranges from 4% to 13%.50–52

Radiographs are used for visualisation and preoperative planning, but might underestimate the amount of bone loss. Osteolysis was first classified in the femur by Gruen and colleagues53 and in the acetabulum by DeLee and Charnley.54 CT and MRI are generally reserved for complex cases.55,56 Positron emission tomography is a newer imaging method; early results have shown improved sensitivity and specificity compared with bone scanning, and the ability to distinguish between aseptic and septic loosening.57,58

Aseptic loosening is treated with replacement of loose components and correction of any component malalignment. Femoral stem revision with long-stem cementless femoral components has shown favourable results.54,55 Acetabular revisions, particularly in the setting of massive bone loss, may need additional techniques including the use of jumbo cups, bone grafting, acetabular cages, or highly porous metallic augments.59–61 Outcomes after revision surgery are generally good, with reported mechanical failure rates less than 5% at midterm follow-up.62

Periprosthetic fracture

Periprosthetic fracture is a major complication after total hip arthroplasty and is associated with increased morbidity and mortality. Risk factors for periprosthetic fracture include revision surgery, component malalignment, age, osteoporosis, previous fracture, and minor trauma.54,63 The mortality rate is similar to that for hip fractures, and the incidence of these fractures has been increasing.64–66 6% of the revision burden is attributable to periprosthetic fracture.66 The Vancouver classification is often used to classify fracture patterns and guide treatment. Findings from several multicentre studies have validated reliability and reproducibility of this system, even among non-specialists.67–70

Periprosthetic fractures are either intraoperative or postoperative, and frequency varies with method of fixation.77,78 Berry79 noted an intraoperative fracture rate of 0·3% in 20859 cemented arthroplasties and 5·4% in 3121 cementless primary total hip arthroplasties. Revision surgery was associated with a ten-fold increased risk of periprosthetic fracture with cemented components and a four-fold increase with cementless components.
Furthermore, the postoperative periprosthetic fracture rate was 1·1% for primary total hip arthroplasty and 4% for revision surgery. Treatment for most periprosthetic fractures is usually surgical. Dependent on the fracture pattern, treatment options include open reduction internal fixation with or without cortical strut allografts, longer femoral stems or augments in the setting of acetabular fractures, or tumour prostheses.

Infection
Periprosthetic infection is a devastating complication of total hip arthroplasty that results in increased morbidity, mortality, and health-care use. As more total hip arthroplasties are done, the absolute number of deep infections is likely to increase. Analysis of US Medicare data has shown a rate of infection of 1·67% at 2 years and 0·59% at 10 years, which is similar to data from the European joint registries. Risk factors for infection include age, obesity, comorbidities, and American Society of Anesthesiologists (ASA) score. Longer operative times, reoperation within 90 days, and use of laminar flow operating theatres and space suits (which were originally introduced to decrease infection rates) have been implicated as risks.

The most common infecting organisms are Staphylococcus aureus and Staphylococcus epidermidis. The appendix provides details of the prevention, diagnosis, and treatment of infection.

Current trends and controversies
Minimally invasive surgery and minimal incision total hip arthroplasty
Minimally invasive total hip arthroplasty is a fairly new approach that has paralleled general interest in less invasive orthopaedic surgery. The theoretical benefits of smaller incisions include less surgical trauma, decreased postoperative pain, and more rapid recovery than with standard techniques. The difference between surgery with minimal incisions and minimally invasive surgery is not only semantic—minimally invasive surgery aims to spare soft tissues, and emphasises mobilisation rather than surgical soft-tissue releases. In practice, the distinction between these two approaches has blurred since many practitioners attempt to spare soft tissues and minimise incisions even if they do not overtly proclaim to be undertaking minimally invasive surgery. Investigators of several studies have noted a significant clinical or functional differences between standard and minimally invasive approaches, possibly because of the positive effects of improved analgesia; however, there is a risk for component malposition and muscle fraying with minimally invasive surgery, which could temper its use.

Postoperative pain management
Pain management has shifted away from purely opioid-based therapies, with findings from studies showing increased patient satisfaction, fewer opioid-related side-effects, and better performance in physical therapy when multimodal therapy is used in combination with traditional pain control regimens. Commonly used analgesics include long-acting opioids, non-steroidal anti-inflammatory drugs, and neuromodulating agents (eg, gabapentin). Periarticular injections of anaesthetic or steroids and cold compressive devices have also been used, with varying success.

In a randomised controlled trial, Lee and colleagues analysed a comprehensive protocol for perioperative multimodal pain control that used oral therapy and periarticular injections. In the intervention group, early postoperative pain, as measured on a visual analogue scale, was significantly lower and patients were able to participate in rehabilitation sooner than were those in the control group who received on-demand intravenous narcotics only for perioperative pain control. However, in a randomised, double-blind, placebo controlled trial, intra-articular doses of anaesthetic (local infiltration analgesia) did not improve pain control at 8 h and 48 h postoperatively in patients already receiving a multimodal analgesic regimen.

Fast-track total hip arthroplasty
Attempts to streamline total hip arthroplasty to decrease the time that patients are in hospital have led to the development of fast-track programmes in many hospitals, particularly in Europe. Patients are perioperatively optimised, which includes nutritional optimisation, pre-emptive pain control, and early participation in physical therapy, to allow for rapid convalescence and early participation in physical therapy, while hospital logistics are optimised to eliminate barriers to early patient discharge. Examples of such barriers are non-homogeneous wards (eg, general surgical patients together with orthopaedic patients), or no clear discharge policy for length of stay in hospitals (eg, all patients are discharged after 3 days if they reach specific goals in physical therapy and pain control). In experienced centres, patient stay is often half as long as in less experienced centres, with findings from several reports showing no difference in readmission rates, low incidence of thromboembolic complications, and good patient-reported health-related quality-of-life outcomes.

Perioperative anaemia and prophylaxis of venous thromboembolism
Perioperative anaemia is caused by preoperative anaemia, intraoperative blood loss, or postoperative bleeding complications. The prevalence of preoperative anaemia has been estimated to be 24–49%, whereas postoperative anaemia can be as high as 51–87%. The costs of bleeding complications are estimated to be slightly lower than that of venous thromboembolic events. However, the incidence of postoperative bleeding complications is low (<1%). Attempts have been made to minimise the need for blood transfusions because of the cost and increased patient morbidity associated with allogeneic blood.
Techniques to decrease blood loss include cutaneous warming, gentle soft-tissue handling during surgery, use of newer bipolar electrocautery devices, and pharmacological management including discontinuation of anticoagulation unless contraindicated (eg, recent cardiac stents) and preoperative use of tranexamic acid. The appendix provides a discussion of venous thromboembolism and prophylaxis.

Physical therapy and gait
Physical therapy in the inpatient and outpatient setting has become the standard of care. Inpatient physical therapy promotes early ambulation and decreases patient length of hospital stay. Furthermore, outpatient physical therapy improves function and range of motion in the short term (<1 year), but these potential clinical benefits have not been studied at long-term follow-up.

Patients who have undergone total hip arthroplasty have shown improved gait dynamics compared with those with late-stage osteoarthritis who have been managed non-operatively. Improved gait speed, step length, and cadence has been reported after total hip arthroplasty in patients who participate in a home exercise programme.

Computer navigation
Improper component positioning is associated with instability, increased wear, and early failure after total hip arthroplasty. Computer navigation increases the accuracy and precision of component placement, with findings from several studies showing a reduction in the proportion of radiographic outliers. In a meta-analysis of three randomised trials of 250 patients, Gandhi and colleagues reported a significant decrease in the number of outliers in acetabular cup positioning when navigation was used compared with traditional cutting guides (odds ratio 0.285, 95% CI 0.14–0.57).

Despite evidence supporting improved acetabular component positioning, studies have not conclusively shown long-term clinical benefit in functioning or implant survivorship. Furthermore, concerns have been raised about cost of the technology, partially increased operative time, and the morbidity of extra pin placement. However, further study is needed to establish whether potentially lower revision rates would decrease lifetime costs. Despite these criticisms, navigation might be suitable when combined with minimally invasive surgery when direct visualisation is difficult.

Bearing surfaces
Metal-on-metal articulations have less linear wear than do traditional metal-on-polyethylene bearings and might be an option for selected younger, more active patients. The use of larger head sizes improves stability and range of motion compared with the smaller head diameters that are used with other bearing surfaces. However, the use of metal bearings has been controversial. Alison Smith and colleagues’ analysis of data from the National Joint Registry of England and Wales showed that stemmed (non-resurfacing) metal-on-metal articulations failed at higher rates than did other bearings. Rates of failure were increased with the implantation of large-diameter femoral heads, and implant survival was poor in women. The effect of metallic wear debris is believed to cause a local soft tissue response, which may lead to premature implant failure. Schmalzried used the term adverse local tissue reaction to describe the range of disease that encompasses metal allergy, lymphocytic infiltrates, metallosis, and pseudotumour formation.

The US Food and Drug Administration (FDA), the UK Medicines and Healthcare Products Regulatory Agency (MHRA), and the British Orthopaedic Association have released statements of concern about metal-on-metal articulations. Much of this concern stemmed from the 2010 recall of the ASR total hip system and the ASR hip resurfacing system (DePuy Orthopaedics, Leeds, UK). In a study of 505 arthroplasties, Langton and colleagues showed a 25% failure rate for the resurfacing system and 49% failure rate for the acetabular system at 6 years.

Metallic wear debris can lead to excessive serum ion concentrations of chromium and cobalt. Although some correlation between serum and synovial ion concentrations has been noted in failed arthroplasties, the relation between serum ion concentrations and bearing wear is less clear. Potential sources of wear include cup malpositioning (particularly high inclination angles—ie, greater than normal angles of 45° inclination and 20° anteverision), and very large or small diameter femoral heads, which can lead to changes in lubrication dynamics, edge loading, and increased wear of the acetabular rim. However, investigators of several studies have disputed the effect of small femoral heads. Another source of wear is the taper junction (also known as trunion-head interface) in modular femoral components. The observed fretting and stem corrosion is thought to be caused by mechanical deformation resulting from very large femoral heads.

Present recommendations for patients with metal-on-metal bearings include yearly measurements of serum ion concentrations in at-risk patients and radiographic assessment of the painful hip joint to exclude adverse local tissue reactions as the source of pain. Radiographic assessment can be done with ultrasound, CT, or MRI. Ultrasound is a useful screening method, but its sensitivity decreases with very obese patients and it is less effective than CT or MRI at detection of medially located lesions. MRI has high sensitivity and is able to detect osteolysis. Resurfacing arthroplasty is a bone-conserving option that is suited to younger, more active, male patients. Despite reported 10-year survivorship ranging from
88% to 95%, the use of resurfacing is very controversial. Component positioning in resurfacing is inherently no more challenging than total hip arthroplasty; however, because most surgeons do not undertake the resurfacing procedure, a learning curve is involved. Serum ion concentrations, however, are lower than those with metal-on-metal total hip arthroplasty. Favourable outcomes are noted with well defined patient selection criteria. Johnson and colleagues reported 100% survivorship at 5-year follow-up in 93 patients (95 arthroplasties) identified with narrow selection criteria. The investigators noted that the best results were in male patients younger than 50 years, with a primary diagnosis of osteoarthritis, and native femoral head greater than 50 mm in diameter. In meta-analyses, Smith and coworkers and Springer and colleagues showed that patients who had resurfacing arthroplasty had improved function outcomes, but an increased risk of aseptic loosening and revision surgery compared with patients who had total hip arthroplasty. The appendix provides details of other bearing interfaces, including ceramic bearings and highly cross-linked polyethylene.

**Total hip arthroplasty in elderly patients**

Use of total hip arthroplasty has increased in elderly patients with hip fractures since it gives better outcomes than does internal fixation in displaced femoral neck fractures. Previously, most displaced femoral neck fractures were treated with hemiarthroplasty because the hip did not have overt osteoarthritis and fracture; however, patients who undergo internal fixation need further additional surgery compared with those initially treated with arthroplasty. In randomised, prospective studies investigators showed that lucid patients with displaced femoral neck fractures had less pain and better functional outcomes with a total hip arthroplasty than with hemiarthroplasty. At 4-year follow-up after hip fracture, results of the total hip arthroplasty group were better than those for patients treated with hemiarthroplasty. These results have led to some controversy in the appropriate treatment of hip fractures in elderly patients. Because many of these patients are cared for by general orthopaedic surgeons who do not routinely undertake total hip arthroplasty, higher risks of complications could arise in the arthroplasty group. Further study is needed as practice patterns for treatment of hip fractures evolve.

**Conclusions**

Total hip arthroplasty has fulfilled the promise of pain relief and restored function to millions of patients with end-stage degenerative joint disease. In the past several decades, advances have been made in implant design, manufacturing, bearing surfaces, surgical technique, technology for component positioning, and long-term postoperative implant surveillance. Nowadays most patients can expect their prosthesis to last well over 20 years. Although there have been failures in both prosthetic design and after improper alignment, most patients can expect no complications to arise from their prosthesis. The future challenge will be the shift in focus towards younger and more active patients, which will put emphasis on design of novel implants with better wear properties, ideal and consistent component positioning (possibly with the assistance of computer navigation), and the use of soft-tissue preserving surgical techniques.

**Contributors**

All authors contributed equally to the preparation of this Seminar.

**Conflicts of interest**

MAM has received research and/or grant support from the National Institutes of Health, Stryker, Sage Products, Ongoing Care Solutions, Janssen Pharmaceuticals, Wright Medical, and TissueGene; is a consultant for Stryker, Sage Products, Janssen Pharmaceuticals, Salient Surgical, Ongoing Care Solutions, and TissueGene; and is on the editorial board of the Journal of Bone and Joint Surgery and American Journal of Orthopaedics. SCM is on the editorial board of Journal of Geriatric Orthopaedics and Rehabilitation, Arthritis and Rheumatism. AJJ is a consultant for Sage Products and Ongoing Care Solutions. RP declares that he has no conflicts of interest.

**Acknowledgments**

We thank Joy D Marlowe for her expertise and contribution in undertaking the artistic conceptualisation and illustration of the figures in this manuscript.

**References**


