

BRITISH ORTHOPAEDIC FOUNDATION

RESEARCH AGENDA

- 1 ARTHRITIS AND ARTHROPLASTY
- 2 OSTEOPOROSIS AND FRAGILITY FRACTURES
- 3 MAJOR LIMB TRAUMA
- 4 SPINAL DISORDERS
- 5 SOFT TISSUE INJURIES
- 6 PAEDIATRIC ORTHOPAEDICS



Orthopaedic Research Appeal



INTRODUCTION

INTRODUCTION

This document summarises the burning questions about musculoskeletal disease and injury that must be answered if we are to address a range of problems that frequently threaten people's quality of life. With the increasing proportion of the elderly in the population and their very reasonable desire to live life to the full for as long as possible, these questions are more urgent than ever.

This research agenda is not exhaustive of all that can happen in the musculoskeletal system; it focuses on the priority areas that affect the largest number of people. In each section, we describe the burden of disease caused by each condition and then identify the new knowledge that is needed to improve our ability to reduce that burden.

We have derived the Research Agenda from previous work conducted by the Bone and Joint Decade, the British Orthopaedic Research Society and the American Academy of Orthopaedic Surgeons. In particular we acknowledge the work of Brian Freeman, Andrew McCaskie, Carlos Wigderowitz, Brigitte Scammell, Nicholas Clarke, Roger Atkins, David Marsh, Hamish Simpson and Nicola Maffulli in drafting the chapters under the aegis of BORS.

The British Orthopaedic Foundation aims to lead the process of developing the research base in UK orthopaedics and harnessing it systematically to address these vital questions. In past years, many important innovations in orthopaedic surgery have come from the UK, most notably the first reliable artificial hip joint, which has brought real improvement in the quality of many patients' lives. The collaborative relationships we have forged between orthopaedic surgeons, engineers and biologists will stand us in good stead to produce many more innovations, and to demonstrate that they are efficacious and cost-effective. Our main driver is, as it has always been, the burden of musculoskeletal disease as it affects our patients.

The British Orthopaedic Association is the professional body that represents nearly 4,000 orthopaedic surgeons. It launched The British Orthopaedic Foundation as its charitable fundraising arm in order to develop a programme of research into the areas addressed by this Research Agenda. This research has real potential to improve significantly the lives of many thousands of people throughout Britain, from the newborn through to the elderly.

RESEARCH AGENDA

The British Orthopaedic Foundation's Research Committee has worked closely with the British Orthopaedic Research Society, The British Geriatrics Society, the International Society for Fracture Repair, the National Osteoporosis Society and the International Osteoporosis Foundation and other relevant bodies in the development of this Research Agenda.

The Research Agenda maps out the direction for orthopaedic research both nationally and internationally. By focussing on these priority areas, the British Orthopaedic Foundation will be able to achieve maximum potential from its research grants for the benefit of orthopaedic patients throughout the country.

KEY EXPLANATIONS

- B** **Basic Research:** answers fundamental questions on the physical, chemical, and functional mechanisms of life processes and disease. It provides the building blocks upon which other types of research are based, but is not necessarily disease specific.

- T** **Translational Research:** translates knowledge from basic research into new or improved methods to treat and prevent disease; translates clinical insights into hypotheses that can be validated in the laboratory

- C** **Clinical Research:** is conducted with human subjects, or on material of human origin such as tissue and specimens, with an investigator who interacts directly with human subjects.

- H** **Health Services Research:** examines access to, and the use, costs, quality, delivery, organisation, financing, and outcomes of health care services to produce new knowledge about the structure, processes, and effects of health services for individuals and populations.

1 ARTHRITIS AND ARTHROPLASTY

BURDEN OF DISEASE

- Osteoarthritis (OA) accounts for half of all chronic conditions in people aged over 65.
- Some 25 % of people over the age of 60 have significant pain and disability from osteoarthritis.
- OA, also known as degenerative joint disease, leads to pain, deformity, and loss of joint motion as protective cartilage within the joint is damaged and diminished, leaving sensitive bone exposed and vulnerable to abrasion and destruction.
- OA is the most common form of arthritis and is a leading cause of disability worldwide. The incidence of OA increases with age, and disproportionately affects women.
- The economic consequences of osteoarthritis are enormous.

DIRECTIONS FOR FUTURE RESEARCH

- Investigate the pathogenic steps in arthritis that could be explored for potential preventative and symptomatic treatments for arthritis, in particular for;
 - Cartilage: Mechanisms of destruction (B,T)
 - Bone: Mechanisms of remodelling formation and destruction (B,T)
 - Soft tissue: Relevance of meniscal and ligament tissue to cartilage destruction (T,C)
- And in the fields of;
 - Biomechanics: Role of abnormal loading patterns (B,T)
 - Genetics: Relevance of certain genes to the mechanisms of arthritis (B)
 - Nutritional factors: Role of micronutrient antioxidants on incidence and progression (B,T)
 - Hormonal Status: Role of oestrogen levels. (B,T)
- Investigate whether arthritis can be prevented

- Populations at risk will include patients after trauma and injury. The effectiveness of treatment of injury (e.g. fracture, ligament and menisci tears) needs to be determined. (C)
 - Biomechanical abnormality, which may be due to obesity, joint injury or deformity, muscle weakness, occupational factors or sports participation, are risk factors for developing osteoarthritis and need to be identified before structural changes occur. (T)
 - Investigate the effectiveness of Physical Therapy for treating patients at risk using a combination of exercise, education, bracing, corrective footwear and walking aids where necessary. (R,H)
 - Investigate the effectiveness of pharmacological prevention methods such as Nutraceuticals. (B,T,C)
 - Determine the effect of dietary advice to promote weight loss for obese patients. (C,H)
 - Investigate additional preventative interventions will include: Education, Complimentary Therapy, and Behavioural Interventions to promote lifestyle change. (C,H)
- Explore the role of technology in improving the treatment of arthritis and the performance of arthroplasty. In particular:
 - To understand the biological and mechanical basis of implant loosening (B,T)
 - To use tribology approaches to improve bearing wear characteristics (B)
 - To optimise interface fixation, both for cemented fixation and cementless (B,T)
 - To produce improved biomaterial for implants (B)
 - To use tissue engineering – including the combination of biology and bioengineering in tissue repair and regeneration (B,T,C)
 - To use nanotechnology techniques to improve the treatment of arthritis (B,T)
 - To determine the role of gene therapy for treating arthritis (B,T)
 - Prevention requires understanding the problem using accurate population, health and lifestyle measures. This will lead to effective early arthritic case finding and intervention. (C)
 - To examine the most cost-effective way of providing surgical and non-surgical interventions (C,H)
- New techniques/implants will also impact on cost effectiveness, and in particular the following will need to be evaluated: (C,H)

- Pharmacological including biologics (C,H)
- Implant cost-effectiveness (C,H)
- Minimally invasive surgery/image guided/computer assisted/robotic. (C,H)
- To ensure that innovative surgical and medical treatments for arthritis are introduced safely and effectively, pre-clinical testing has to be undertaken to ensure the true clinical relevance. (T)
- To carry out high quality clinical trials. (C)
- To standardise outcome measures measuring function, structure, activities and participation, for implants, novel measures such as Roentgen Stereophotogrammetric Analysis and DEXA need to be further developed. (C,H)
- To ensure that innovation is brought into clinical practice safely and that registers continue to be developed and supported. (C,H)
- To record adverse reactions closely. (C)

KEY: B = BASIC RESEARCH T= TRANSLATIONAL RESEARCH C= CLINICAL RESEARCH
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2 OSTEOPOROSIS AND FRAGILITY FRACTURES

BURDEN OF DISEASE

- Osteoporosis is a progressive disease characterised by low bone mass and bone fragility that often leads to osteoporotic fractures, especially of the hip, spine and wrist. This serious and costly public health problem often results from minor trauma, especially in the elderly. Health care and social costs for osteoporosis and related fractures approach £1.7 billion annually in the UK.
- Approximately 3.2 million women over the age of 50 in the United Kingdom currently suffer from osteoporosis. Many more have low bone mass, leaving them susceptible to osteoporosis.
- In women 180,000 fractures each year are associated with osteoporosis, which can be a significant cause of deformity, disability and pain, and can lead to death.
- At least 80% of hip and spine fractures in those between 65 to 84 years of age, are attributable to osteoporosis.
- A woman's risk of hip fracture is equal to her combined risk of breast, uterine, and ovarian cancer.
- Women are 4 times more likely to suffer from osteoporosis than men and their rate of fracture is 2 to 3 times that of men, but death rates in men one year post fracture are higher.
- Falls are the second most common mechanism of injury due to trauma, following motor vehicle crashes. They account for 30% of emergency cases and are associated with the second largest number of hospital and ICU days.
- Hip fractures lead to 70,000 hospital admissions per year. Approximately 10% of hip fracture patients die within the first month following their fracture, initial hospitalisation, and 24% die within a year of injury.
- Only 50% of our patients return to independent living in their own home.

DIRECTIONS FOR FUTURE RESEARCH

- Explore the factors that contribute to the development of peak bone mass (B,C,T)
- Focus educational efforts on the maintenance of bone mass throughout life and secondary prevention such as medical therapies and physical activity training (C,T)
- Explore the use of emerging technology such as vertebroplasty and kyphoplasty in the treatment of vertebral compression fractures. (C,T)
- Improve injury prevention programmes for the elderly. (T)
- Improve the management of fractures once they have occurred including fracture fixation methods, improved inpatient management, and localised as well as systemic bone augmentation. (C,T,H)
- Improve measurement of osteoporosis and determination of fracture risk. (C,T,H)
- Determine gene and matrix factors that affect bone mechanical strength and optimal fracture healing. (B)
- Develop appropriate cost-effective methods to evaluate causes of secondary osteoporosis at the time of the hip fracture. (C,T,H)
- Identify essential services needed to optimise the outcomes, particularly in the context of the heterogeneous hip fracture population. (T,H)
- Identify the parameters to be used to determine appropriate length of stay in the acute and rehabilitative settings. Develop criteria to determine transfer to acute to sub-acute rehabilitation centres, skilled nursing facility, or discharge to home. These criteria should include milestones that determine when utilisation of these alternate care settings have been optimised and no further benefits can be anticipated. (H)

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3 MAJOR LIMB TRAUMA

BURDEN OF DISEASE

- Major limb trauma includes fractures, crushing injuries, dislocations, open wounds, amputations and damage to nerve and blood vessels.
- Injury is the leading cause of death up to the age of 45 years.
- Road traffic accidents each year in the UK result in:
 - 320,000 injuries
 - 40,000 serious injuries
 - 3,400 deaths.
- Worldwide, 25% of health care expenditure will be on trauma by 2010.

DIRECTIONS FOR FUTURE RESEARCH

- Understanding of mechanisms of injury. **(B,T)**
- Improve injury prevention by optimization of design of injury site, including motor car, work place and sports arena. **(H)**
- Investigate biological mechanisms underlying fracture repair, including mechanism by which inflammation leads to bone formation and the role of stem cells. **(B,T)**
- Understanding of the control of individual subparts of fracture healing, including endochondral and intramembranous ossification, direct bone healing and remodelling and develop biological and mechanical interventions for their acceleration. **(B,T)**
- Causes and biological mechanisms for delayed and non-union of fracture. **(B,C,T)**
- Development of methods for investigation of physical changes associated with fracture healing, including blood flow and mechanical strength. **(B,C,T)**
- Elucidation of pathological anatomy of fractures such as tibial pilon fractures. **(B,C)**
- Development of new implants for individual fractures. **(C,T)**
- Elucidate the local (CRPS) and systemic (SIRS) effects of uncontrolled inflammation associated with trauma and develop therapeutic strategies for their prevention and treatment. **(B,C,T)**
- Improvement in treatment of bone infection following trauma. **(C,H)**
- Optimisation of recovery of soft tissue injury in the context of severe trauma and sports injury. **(B,C,T,H)**
- Elucidation of the mechanisms and clinical applications of distraction histiogenesis and development of improved clinical techniques. **(B,C,T)**
- Optimisation of the organisation and delivery of trauma services. **(C,H)**

- Improving rehabilitation by determining optimal regimes and facilitation of re-entry to work. (C,H)

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4 SPINAL DISORDERS

BURDEN OF DISEASE

- The spine may be affected by trauma, tumour, infection, inflammatory disease, osteoporosis, deformity and degenerative conditions such as disc degeneration, spinal stenosis and spondylolisthesis.
- Over 70% of people in developed countries will experience low back pain at some point in their life.
- General Practice consultations for low back pain have been estimated at 14-15 million per year in the UK.
- Back pain is the second leading cause of sick leave in the United Kingdom.
- Disability resulting from low back pain has become a public health problem accounting for 119 million days of incapacity at a cost to the state of almost £ ½ billion.
- The annual incidence of spinal cord injury remains at 15-40 cases per million population.

DIRECTIONS FOR FUTURE RESEARCH

- Improve the understanding of basic mechanisms of pain production and the potential influence of the central nervous system on chronic pain. (C,T)
- Investigate the role of selective anti-inflammatory agents (eg. anti-tumour necrosis factor) in the treatment of sciatica. (B,C)
- Explore the role of autologous disc chondrocyte transplantation and gene therapy to reverse the process of disc degeneration. (B,C,T)
- Research and develop a compliant artificial disc replacement that will allow absorption and transmission of load both in the cervical and lumbar spine. (B)
- Complete comprehensive standardized biomechanical testing of all new spinal implants such as cervical and lumbar disc replacements. (B)
- Health education for the public and the medical profession in fear avoidance and beliefs about back pain to prevent the transition from acute to chronic back pain disability. (H)
- Predicting which patients with Internal Disc Disruption will do well following surgical intervention. (C,H)
- In clinical trials it is important to use valid and reproducible outcome measures. Further work on patient expectation and the 'Mean Clinically Important Difference' in outcome measures should continue. (C,H)
- Large multicentre randomised controlled trials to establish the most effective form of spinal fusion. (C)

- The role of bone graft substitutes and growth factors such as Bone Morphogenetic Protein-2 and Osteogenic Protein-1 in routine spinal fusion. (B,C)
- Three dimensional appreciation and role of the rib cage in scoliosis. Earlier diagnosis of scoliosis and work on prediction of curve progression through potential biochemical markers such as calmodulin and somatomedin. (B,C)
- The role of early spinal decompression and stabilisation in acute spinal cord injury should be clarified by large scale randomised clinical trials. (C)
- The use of growth factors, stem cells and olfactory glial cell grafts in inducing regeneration within the central nervous system. (B,C,T)
- Better define the role of radiotherapy, chemotherapy and / or surgical decompression and stabilisation for spinal cord compression secondary to spinal metastases. (C)

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5 SOFT TISSUE INJURIES

BURDEN OF DISEASE

- Soft tissues, including ligaments, tendons, muscles, nerves, and cartilage, can be injured in nearly every type of physical trauma, including violence, abuse, motor vehicle crashes, occupational accidents, sports and recreational injury, repeated overuse, and normal everyday activities in susceptible individuals.
- Soft tissue injuries include sprains, strains, contusions, tendonopathy, bursitis, lacerations, ruptures, crushing, and compression injuries.
- In the UK, soft tissue injuries and conditions have been estimated to account, annually, for:
 - 1/3 million hospitalisations, 1.5 million bed days,
 - 1 million outpatient visits,
 - 3 million emergency room visits, and
- There are an estimated 2 million sports injuries per year in the UK.: 95% involve soft tissues.
- More than 50% of knee injuries result from sports-related activities.
- The leading occupational injuries causing lost productivity include:
 - Sprains to the low back, knee, and upper arm;
 - Amputation, severance, or laceration of fingers.
- Cumulative trauma disorders, including carpal tunnel syndrome, synovitis, tendonitis tenosynovitis, repetitive strain injury and bursitis, account for 64% of all occupational illnesses.

DIRECTIONS FOR FUTURE RESEARCH

- To increase the understanding of the causes of peripheral nerve compression and develop alternatives to surgical treatment. (B,T)
- Increase our understanding of Charcot arthropathy and diabetic foot insensitivity complications. (T)
- Identify the links, if any, between factors that regulate microcirculation and those that mediate pain perception. (B,T)
- Develop improved methods of nerve repair and regeneration. (C)
- Develop synthetic replacements for muscle, ligament, tendon, and cartilage using tissue engineering techniques and or gene therapy. (B,T,C)
- Explore the knowledge of the interaction of the immune system and its role in transplantation of bone and ligaments. (B)
- Identify the signalling pathways involved with muscle, tendon, and ligament injury, repair, and hypertrophy. (B,T)
- Understand the role of physical activity in the development of tendon, ligament, and muscle. (B,T,C)
- Develop a better understanding of the particular fitness requirements for different genders, for different age groups and for individuals with different physical disabilities. (C,H)
- Develop a better understanding of the impact of inactivity with respect to common pathologic mechanisms in musculoskeletal and neurological diseases or disorders. (C)
- Develop training and conditions programs that improve muscle reaction time, protective muscle stiffness, and performance. (T,C)
- Analyse the forces in normal tissues and the healing of soft tissues during in vivo activities. Develop new designs based on this analysis, for improved repair and reconstruction procedures. (B,T,C)
- Study pathomechanics of joint injury focusing on prevention and the development of more effective protective devices for particular sports and jobs where risks of physical impairment exist. (T,C)

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6 PAEDIATRIC ORTHOPAEDICS

The cost of childhood musculoskeletal conditions is incalculable. Although some conditions can be treated, with a full restoration to active life, others can result in early death or progressive problems into adulthood, creating lifelong burdens for the individual and family.

BURDEN OF DISEASE

Hereditary and Congenital Problems in Childhood

- **Clubfoot** is a congenital foot deformity with an incidence of 1 in 735 births and with an incidence in males twice that of females. If a family has one child with clubfoot, the risk in subsequent siblings is 3% to 4%. If one parent and one child in a family have clubfoot, subsequent children have a 25% chance of having clubfoot.
- **Congenital Dislocation of the Hip** is a common orthopaedic condition in infants and children, affecting 1 in 750 children. Infants may be born with an 'unstable hip' which is often treated with splints. Outcome measures for early treatment are poor and there is a real problem in respect of screening for the disorder. Children whose hip displacement is diagnosed between the ages of one and five, if left untreated will eventually develop osteoarthritis which can necessitate teenage hip joint replacement. Despite strenuous efforts to improve diagnosis, the incidence of late presenting cases has largely remained unaltered.
- **Osteogenesis Imperfecta (Brittle Bone Disease)** is a genetic disorder of connective tissue causing bone fragility and multiple long bone fractures. There is a spectrum of severity of the disease. In its mildest form an apparently normal child may sustain few fractures and the distinction between osteogenesis imperfecta and non accidental injury may be unclear. In the severe types, there are progressive bowing deformities of long bones and the spine and growth retardation. In most individuals there is a genetically determined defect in type I collagen.
- **Perthes' Disease** affects 1 in 8,000 young people. It causes the femoral head (ball of the hip joint) to lose its blood supply leading to deformity of the femoral head and an increased risk of fracture. The aetiology is not fully understood and the question of treatment is open to debate. Originally patients were treated with bed rest, immobilisation and weight relief. The modern therapeutic approach embraces the concept of containment of the femoral head by operative or non-operative means.
- **Slipped Capital Femoral Epiphysis** is the most common hip disorder in young teenagers. It occurs when there is a period of rapid growth and

shearing stress, frequently from excessive body weight, causes the femoral epiphysis to displace. Urgent surgical treatment is needed to stabilise the epiphysis by screw fixation. There is a high incidence of late morbidity caused by residual deformity.

Neuromuscular Disorders in Childhood

- **Muscular Dystrophies** include Myotonic, Congenital Dystrophy, Becker, and Duchenne Muscular Dystrophy which the most common inherited muscle disease and affects 1 in 3,500 males. It causes progressive muscle weakness and degeneration of the muscles, with walking eventually becoming impossible around the age of ten. Becker Muscular Dystrophy is very similar to Duchenne's, but the age of onset is later, the progression of symptoms is slower and the ability to walk continues into the thirties and death tends to occur later.
- **Cerebral Palsy** is the most prevalent physical disability originating in childhood. It affects 150,000 individuals in the UK, including about 2,000 babies per year at birth. Cerebral palsy is a group of non-progressive motor function disorders caused by lesions or anomalies of the brain. Its aetiology is not well understood. It may occur from low birth weight, illness, infection or injury. Prevalence of 2.4 per 1,000 children aged 3-10 years is increasing due to survival of very low birth weight infants.
- **Hereditary Motor Sensory Neuropathies** include Dejerine-Sota and Charcot-Marie-Tooth disorder which causes weakness and wasting away of legs, feet and hands. It is the most common form of polyneuropathy and affects 1 in 2,500 people.

Diseases of the Spine

- **Scoliosis** is a common diagnosis, involving lateral (sideways) curvature of the spine, affecting 10% of adolescents. It may be the result of different diseases or conditions, including Spina Bifida, Cerebral Palsy, or Muscular Dystrophy, although in 90% of cases the cause is unknown. Treatment of the curves is required in 3 to 5 per 1,000.

Childhood Arthritis

- **Juvenile Rheumatoid Arthritis** is the most common form of arthritis in children, affecting 10,000 to 20,000 children under 16 years of age in the UK. It is an autoimmune disease in which the body attacks its own healthy cells and tissues.

Trauma and Non-Accidental Injury

- **Trauma** is the leading cause of mortality after the first year of life, exceeding all other causes of death in children combined. Every year 20% - 25% of children have an injury severe enough to require medical attention, absence

from school, and/or bed rest. The incidence of trauma is higher in boys than girls, and poverty increases injury rates. Mortality rates from injuries in children whose families have incomes below the poverty line is at least 2.6 times that of other children.

Cancer in Children

- **Osteosarcoma** is the most common type of primary bone cancer and the sixth most common type of cancer in children, accounting for 5% of all childhood cancers. It begins in the bone and eventually spreads. **Ewing's Sarcoma** is the second most common bone malignancy in children, accounting for 5% of bone tumours in children. The 5-year survival rate has increased from 5% to 50% in the last thirty years. **Osteochondroma** accounts for 20% to 50% of benign tumours and 10% to 15% of all tumours. It can become malignant. **Osteoid Osteoma** is a relatively common tumour in children, leading to pain.

Infections

- **Osteomyelitis** is an infection in bone, usually bacterial in origin, affecting about 1 in 10,000 children. Symptoms include pain, soft tissue swelling, bone tenderness, and malaise.
- **Septic Arthritis** is a common childhood condition in which bacteria settle into the joint. Its aetiology is unknown, but serious cases can result in joint destruction or death.

DIRECTIONS FOR FUTURE RESEARCH

- Identify and define the action of the genes that regulate skeletal formation, growth, and development. (B)
- Improvement in clinical screening techniques, particularly the efficiency of ultrasound examination in the early detection and management of congenital dislocation of the hip. (C)
- Centralisation of conservative treatment and surgical services to provide a consistency of expert management to reduce the incidence of avascular necrosis and multiple surgical interventions. (H)
- Osteogenesis Imperfecta research has shown that the use of intravenously administered bisphosphonate (pamidronate) improves complaints of generalised bone pain and fracture frequency. Further research is necessary to identify any long-term potential adverse affects. (B,T)
- The possibility of replacing the defective COL1A1 or COL1A2 gene needs to be investigated. (B)
- Major developments in the surgical correction of long bone deformity have recently been developed, particularly involving the use of the extensible intramedullary rod. Complex surgical techniques have produced good results but high complication rates. Additionally the lengthening of long bones over intramedullary rods have been reported and requires development. (T)

- Technological and molecular biological advances and the positional cloning of human genetic disease genes may allow a better understanding of the relationship between the limb growth disorders and defective genes. (B)
- Investigation of multifactorial causes to determine the role of coagulation abnormalities in Perthes' Disease. (B)
- Investigation into the possibility of anthropometric, nutritional and environmental factors in the development of Perthes' Disease, and its increased prevalence in urban areas (B,T)
- Longitudinal studies are required to compare the results of conservative and surgical interventions in order to determine the optimum treatment regimen for Perthes' Disease. (C,H)
- Delay in diagnosis of Slipped Capital Femoral Epiphysis contributes to many cases and is an important cause of morbidity. Education is urgently required to assist health professionals in their understanding of the disorder and to associate knee pain with hip pathology in the adolescent. (H)
- Longitudinal randomised studies are urgently needed to determine whether or not to reduce an acute unstable slip and its effect or otherwise on the rate of avascular necrosis. (C)
- Investigate the developmental biology of the musculoskeletal system with emphasis on bone and joint development and mechanism of regeneration.(B)
- Develop more physiologic interventions for the correction of skeletal deformities and neuromuscular conditions including cerebral palsy and muscular dystrophies (B,C,T)
- Design and conduct clinical trials to determine optimal therapeutic approaches to these conditions as new treatments are developed. (C,T)
- Improve childhood injury programmes. (C,H)
- Understand the molecular heterogeneity of bone and soft tissue tumours in terms of characterisation and response to therapy. (B,C,T)
- Investigate the role of genetics in bone tumours with emphasis on molecular staging, therapeutic targets, models development and use of gene chip (microarray) analysis. (B,C,T)
- Improve the use of bone allografts and prosthetic reconstruction in limb salvage for bone tumours. (C,T)
- Develop rapid diagnostic tools for musculoskeletal infection. (C)

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BRITISH ORTHOPAEDIC FOUNDATION

at the British Orthopaedic Association

35-43 Lincoln's Inn Fields

London WC2A 3PE

Tel: 020 7405 6507

Fax: 020 7831 32676

Email: secretary@boa.ac.uk

Website: www.boa.ac.uk

Steering Committee

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