

A

Activation - The preparation of a molecule or a cell for a specific activity. For example, a receptor molecule will be activated to transmit signals to a cell when its target molecule becomes attached to it.

Adhesion molecules – *Proteins* situated on the surface of the *cell* that facilitate attachment of the cell to another cell or to the external *extracellular matrix*.

Adjuvant induced arthritis - An experimental *animal model* of arthritis induced by the injection of a stimulator or the immune response, such as heat-killed bacteria.

Adverse event - An unfavourable outcome that occurs during or after the use of a drug or other intervention, but is not necessarily caused by it.

Agonist - A molecule that attaches, or binds, to a structure on the surface of a cell, triggering a response from the cell.

Algorithm – A precise, sequential set of computer rules put in place to solve a problem.

Allele – One of two (or more) variant forms of a particular *gene* that occurs at a specific site on a *chromosome*.

Amino acids - Small molecules with a common basic structure that, when joined in chains, form the building blocks of *proteins*. There are 20 different amino acids, and each protein is defined by its unique amino acid sequence.

Anabolic – Metabolic process that builds, large, more complex molecules from simpler, smaller molecules.

Anaemia - A shortage of haemoglobin (oxygen-carrying pigment) in the blood resulting in a decrease in the ability of the blood to carry oxygen around the body. Anaemia may be caused by chronic *inflammatory arthritis*.

Analgesics - A wide range of drugs used to relieve pain.

Aneuploidy – An abnormal number of *chromosomes*; missing or extra chromosomes.

Animal model - An animal that has a disease (naturally occurring or experimentally induced), or injury that is similar to a human condition. The use of animal models allows researchers to investigate diseases in ways which would be impractical or unethical in humans.

Ankylosing Spondylitis - A form of inflammatory arthritis characterised by inflammation of the spinal joints and ligaments, leading to back pain and stiffness and eventual fusion of the vertebrae. Its cause is unknown, but there is a strong genetic association.

Anterior cruciate ligament, ACL – One of the four major *ligaments* of the knee that joins the thigh bone to the bones of the lower leg, helping to limit joint mobility and stabilise the knee joint.

Anti-inflammatory - A substance or treatment that reduces *inflammation*.

Anti-nuclear antibodies (ANA) - *Auto-antibodies* that are directed against *DNA*. They indicate the presence of certain auto-immune diseases and are present in 80-90% of people with SLE.

Anti-TNF - Drugs which block the action of a *protein* in the blood called tumour necrosis factor (TNF), which causes inflammation when present in excessive amounts. Adalimumab, Etanercept and Infliximab are all anti-TNF drugs.

Antibodies - Blood *proteins* which are usually formed by cells of the immune system in response to bacteria, viruses or any other substances which the body recognises as foreign or dangerous. The role of antibodies is to attack these foreign invaders and make them harmless.

Antigen - Any substance that can trigger the production of *antibodies* and cause an immune response.

Antigen presenting cell (APC) - A cell that can break down large *protein* molecules into smaller fragments, and display these fragments, or *antigens*, on its surface for presentation to cells of the immune system.

Antiphospholipid antibody - An *auto-antibody* against phospholipids (a type of fat molecule that is a major constituent of the cell membrane), causing anti-phospholipid syndrome, a disease characterised by blood clot formation in arteries and veins and strongly implicated in complications of pregnancy.

Apatite – Term for various calcium phosphate crystals that are present in bones but can also form in joints, tendons and occasionally other tissues.

Apoptosis - Also known as ‘programmed cell death’. A series of orchestrated biochemical events in the cell that lead to its death. Apoptosis is integral to growth and development, and is an important control mechanism in healthy tissues. Impairment of apoptosis is implicated in some cancers.

Arm - Refers to a group of participants allocated to a particular treatment. In a randomised controlled trial, allocation to different arms is determined by the randomisation procedure. Many controlled trials have two arms, a group of participants assigned to an experimental intervention (sometimes called the treatment arm) and a group of participants assigned to a control (the control arm). Trials may have more than two arms.

Arthroscopy - Keyhole surgery procedure where small (less than 1 cm) incisions are used to allow the insertion of a light and camera to view the inside of a joint.

Articular cartilage – See *cartilage*.

Assay - A test to determine the amount or concentration of a specific molecule in a mixture.

Auto-antibody - A type of *antibody* made by the immune system and directed against one of the body’s own *proteins*. Normally, the immune system ignores the body’s own proteins, and recognises and makes antibodies in response only to invading foreign substances.

Auto-antigen - A molecule resident in the body (i.e. not foreign) that stimulates the production of *auto-antibodies*.



Autoimmune disease - A disorder of the immune system, in which antibodies (*auto-antibodies*) and other components of the immune system are directed against the body's own tissue rather than against foreign invaders.

Azathioprine - A drug used to help prevent rejection of transplanted organs and also in the treatment of *rheumatoid arthritis*. It works by suppressing the body's immune system so it will not attack the transplanted organ or the joints.



B

B cell - Cell of the immune system whose main function is to produce *antibodies*.

Basic research – Research carried out, often in the laboratory, to gain understanding of the fundamental biological processes occurring in health and disease.

Behcet's syndrome – A syndrome caused by over-activity of the immune system, leading to *inflammation* of the small blood vessels (*vasculitis*) and painful ulcers in the mouth and genitals, skin problems and *inflammation* of the eye.

Bias - A systematic error or deviation in results or inferences from the truth. In studies of the effects of health care, the main types of bias arise from systematic differences in the groups that are compared (selection bias), the care that is provided, exposure to other factors apart from the intervention of interest (performance bias), withdrawals or exclusions of people entered into a study (attrition bias) or how outcomes are assessed (detection bias). Reviews of studies may also be affected by reporting bias, where a biased subset of all the relevant data is available.

Biochemical pathway - A linked series of chemical reactions, inside or outside a *cell*, that converts one molecule into another.

Bioinformatics – The use of computers to analyse biological information. It involves the creation of large databases of information on *genes* or *proteins*, and is used to model complex biological systems.

Biologic – A therapeutic agent that is derived from a living organism; an animal, bacterium or virus. Examples of biologics are vaccines and *monoclonal antibodies*, such as *Anti-TNF*.

Biomarker, Biochemical marker - A substance in the body that can be used to measure a normal biological state, the progression of a disease, or the effects of a drug.

Biomechanics – The study of the forces acting on various areas of the human body, for example the joints, and the effects of these forces on the tissues (*bone* and *cartilage*)

Bioreactor - A vessel or system which supports a biological process. This may be a chemical process involving organisms such as cells or bacteria, or the substances derived from such organisms.

Bisphosphonate - A class of drugs used to prevent bone loss, and commonly used to treat *osteoporosis*.

Blinding - The process of preventing those involved in a trial from knowing which comparison group a participant belongs to. The risk of bias is minimised when fewer people know who is receiving the experimental intervention or the control intervention. Participants, caregivers, outcome assessors, and analysts are all candidates for being blinded. Blinding of certain groups is not always possible, for example, surgeons in surgical trials.

Blockade - Blockage of the activity of one molecule (usually harmful) with another.

Bone density, Bone mass - The amount (or mass) of bone tissue in a certain volume of bone.

Bursa – A pouch or sac of soft tissue that is present between a bone and the tendons that move over it.



C

C-reactive protein (CRP) - A *protein* in the blood which can be measured to indicate *inflammation* or disease activity.

Calcific tendinitis - Pain and *inflammation* caused by the deposit of calcium phosphate crystals onto a *tendon*, most commonly in the shoulder.

Calcium pyrophosphate - The crystal which is the most likely to be deposited in cartilage (*chondrocalcinosis*). Shedding of these crystals causes *pseudogout*.

Capsule – The tough, fibrous sleeve of *ligaments* that encloses a joint. It is lined with a thin layer of *cells* called the *synovium*.

Cartilage – A layer of tough, gristle-like tissue that covers the ends of the bones in a joint, and acts as a ‘shock-absorber’ when force is applied. Its smooth, slippery surface allows the bones to glide over each other without friction.

Cell - The smallest unit of life in the body. Each cell is a self-contained unit, taking in nutrients and converting them to energy, carrying out specialised functions, and reproducing.

Cell culture, tissue culture -The process of growing *cells* or tissue derived from organisms (often humans) under controlled conditions in the laboratory.

Cell signalling - The complex system of *cell* to cell communication that controls cellular activity. Signalling often occurs via ‘*chemical messenger*’ molecules in the external environment of the cell making contact with ‘*receptor*’ molecules on the surface of the cell, thereby triggering, through a chain of subsequent chemical reactions, a change in the activity of the cell.

Cell surface marker - A molecule found on the surface of a *cell*, and often characteristic of a particular cell type.

Cell therapy - The transplantation of new cells into a tissue to treat a disease. These cells may originate from the patient (autologous), or from a donor (allogenic). The cells may be mature and specialised (differentiated) or immature (stem cells), with the potential to renew themselves into a range of different cell types depending on how they are stimulated.

Chemical messenger - A molecule that transmits a message within a *cell* or from one cell to another.

Chemokine – A family of *proteins* that lures immune cells such as *monocytes* and *neutrophils* to sites of *inflammation*.

Chondrocalcinosis - The deposition of calcium crystals within cartilage. The crystal which usually causes this is *calcium pyrophosphate*.

Chondrocyte - The resident cell of the *cartilage*. Chondrocytes produce and maintain the cartilage ‘matrix’, the tough but flexible material of cartilage comprised mainly of *collagen* and *proteoglycan*.



Chondrodysplasia – Inherited disease that affects the *cartilage* and causes arrested development, deformity and shortening of the limbs.

Chromosome – A single, thread-like piece of *DNA* containing many *genes*, as well as other molecules associated with the control of DNA. Human cells contain 46 chromosomes, arranged in 23 pairs.

Citrullinated protein - A *protein* that has been modified to contain the *amino acid* citrulline. Citrullination occurs in response to *inflammation* or *apoptosis*. *Antibodies* to citrullinated proteins are found in most patients with *rheumatoid arthritis*, and they are measured in the laboratory as a diagnostic *marker* of the disease.

Clinical Studies Groups (CSGs) – Seven expert groups assembled on behalf of the charity that exist to determine the priority areas for funding and to provide expert clinical advice as needed.

Clinical trial - A test of a drug or treatment in a group of people to determine whether or not it is safe and effective for use in the general population.

Clinical Trials Unit (CTU) – an independent institution or part of a university/hospital that exists to assist in the running of a clinical trial/study – typical staff include Trial Managers, Trial Coordinators, Statisticians, Health Economists, Data Managers, Administrative staff

Clone - A population of genetically identical *cells* originating from a single parent cell.

Cluster randomised trial - A trial where clusters of individuals (e.g. clinics, families, geographical areas), rather than individuals themselves, are randomised to different arms.

Cohort - A group of human subjects defined by a particular characteristic, e.g. year of birth, for the purposes of a research study.

Cohort study - An observational study in which a defined group of people (the cohort) is followed over time. The outcomes of people in subsets of this cohort are compared, to examine people who were exposed or not exposed (or exposed at different levels) to a particular intervention or other factor of interest. A prospective cohort study assembles participants and follows them into the future. A retrospective (or historical) cohort study identifies subjects from past records and follows them from the time of those records to the present.

Collaborator - an organization other than the Sponsor that provides support for a clinical study. This support may include funding, design, implementation, data analysis, or reporting.

Collagen - A long *protein* molecule, that when bundled into fibres, forms the main component of the *connective tissue* and *cartilage*. It is the most abundant protein in mammals, and is responsible for the tensile strength of cartilage.

Collagen-induced arthritis (CIA) – The most commonly used *animal model* of *inflammatory arthritis*. It is induced by immunization of mice with type II *collagen*, resulting in an *auto-immune* process typical of *rheumatoid arthritis*.

Collagenase - A type of *enzyme* molecule that breaks down and destroys *collagen*. Collagenases are key players in the destruction of cartilage in arthritis.

Complement – A complex system of at least 19 separate *proteins* that plays an important part in the body's immune system. It allows foreign particles or micro-organisms to be made



harmless, but also generates *inflammation*. The blood can be tested to find how much of each of the major elements of complement is present.

Computer model - A computer programme or network that attempts to simulate a biological system.

Confidence interval - A measure of the uncertainty around the main finding of a statistical analysis. Wider intervals indicate lower precision and narrow intervals indicate greater precision.

Confounder - A factor that is associated with both an intervention and the outcome of interest. For example, if people in the experimental group of a controlled trial are younger than those in the control group, it will be difficult to decide whether a lower risk of death in one group is due to the intervention or the difference in age. Age is then said to be a confounder, or a confounding variable. Randomisation is used to minimise imbalances in confounding variables between experimental and control groups. Confounding is a major concern in non-randomised trials.

Connective tissue - Fibrous tissue occurring throughout the body that supports, separates and provides a structural framework to the more specialised organs and tissues of the body.

Control - A participant in the arm that acts as a comparator for one or more experimental interventions. Controls may receive placebo, no treatment, standard treatment, or an active intervention, such as a standard drug.

Cortical bone – Compact and dense layer of bone tissue that forms the hard outer layer of bones.

Corticosteroids, steroids - Drugs which have a very powerful effect on *inflammation*, and are often used to treat early *inflammatory arthritis*.

Cross-over design - Describes a clinical trial in which groups of participants receive two or more interventions in a particular order. For example, a two-by-two cross-over design involves two groups of participants. One group receives drug A during the initial phase of the trial, followed by drug B during a later phase. The other group receives drug B during the initial phase, followed by drug A. So during the trial, participants "cross over" to the other drug. All participants receive drug A and drug B at some point during the trial but in a different order, depending on the group to which they are assigned

CT (Computer Tomographic) scan - A type of X-ray that records images of 'slices' of the body. Computer software then transforms these slices into a 3-D image of the body.

Cytokine - A large and diverse family of *protein* molecules that are involved in *cell signalling*. Some cytokines interact with cells of the immune system in order to regulate the body's response to disease and infection, and are implicated in *inflammatory arthritis*. Other cytokines regulate normal cell activity to maintain health.

Cytology – Study of the structure and function of *cells*, as found in their natural environment.



D

Data Monitoring Committee (DMC) – A committee that may be established by the sponsor (the funding institution) to assess at intervals, the progress of a clinical trial, the safety data, and the critical efficacy (effectiveness) endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

Degenerative arthritis - Another term for *osteoarthritis*.

Dendritic cell - A type of *antigen-presenting cell* that processes and ‘presents’ foreign, invading *proteins* to other cells of the immune system so that an immune response specific to that protein can be initiated.

Differentiation - The process, over many cycles of cell division, that transforms a less specialised cell into a more specialised one.

Disease-modifying anti-rheumatic drugs (DMARDs) – Drugs which reduce pain and stiffness in *rheumatoid arthritis*.

DNA - The molecule situated in the nucleus, or ‘brain’, of the *cell* that holds the genetic instructions for the production of *amino acids* and *proteins* necessary for the development and functioning of all living organisms.

DNA sequence - The pattern of letters (A, C, G and T) representing each of the four small nucleotide molecules that comprise *DNA*. The many possible sequences of these nucleotides in long chains determine the varied types of information held by the DNA molecule which, in their entirety, are unique for each individual.

Dysplasia - A disruption to the normal sequence of maturation of *cells* in a tissue, resulting in an increase in number of immature cells, with a decrease in mature cells. Dysplasia is often a precursor to cancer.



E

Effect size - A generic term for the estimate of treatment effect for a study.

Efficacy - The extent to which an intervention produces a beneficial result under ideal conditions. Clinical trials that assess efficacy are sometimes called explanatory trials.

Electroencephalography (EEG) – A technique for recording the electrical activity from different parts of the brain.

Eligibility criteria - The key standards that people who want to participate in a clinical study must meet or the characteristics they must have. Eligibility Criteria include both inclusion criteria and exclusion criteria. For example, a study might only accept participants who are above or below certain ages.

Endocrine – A system of glands that manufactures and secretes *hormones* into the bloodstream.

Endothelium – Thin layer of *cells* lining the inside surfaces of the body's closed internal organs, such as the blood vessels.

Enzyme - A type of *protein* molecule that can catalyse, or speed up, the rate of a chemical reaction.

Epidemiology - The study of population and community health, not just individuals.

Epigenetic - Changes in the way that a gene is *expressed* that are due to molecules that modify or influence *DNA*, but are not part of the sequence of the *DNA* molecule itself.

Epithelium – Thin layer of *cells* that covers the surface of the body's internal and external organs. Skin is an example of an epithelial tissue.

Equipoise - A state of uncertainty where a person believes it is equally likely that either of two treatment options is better.

Erythrocyte sedimentation rate (ESR) – A test which indicates the level of *inflammation* in the body and can assist in the diagnosis of *rheumatoid arthritis*. It is based on the speed at which *red blood cells* settle in a sample of blood.

Excrete – To discharge waste products from the *cell*.

Ex-vivo - Short-term experimentation carried out in the laboratory on living tissue removed from an organism, with minimal alteration of conditions. The aim is to mimic the natural growing environment of the tissue allowing experimentation not possible within the organism, under highly controlled conditions.

Expression - A term referring to the general process of transforming information encoded in the *DNA* molecule into specific *proteins* that carry out the many different functions required in *cells*, tissues and organs. The term may also refer to the actual presence of a protein.

Extracellular - The space outside the *cell*. This space may be occupied by fluid or by solid *extracellular matrix*.

Extracellular matrix (ECM) - A complex material produced by *cells*, comprised principally of a network of *collagen* fibres embedded in a gel-like substance. The extracellular matrix



surrounds the cells, providing protection, anchorage and structural support, and regulates cell metabolism and communication from other cells and from the cellular environment.



F

Feasibility studies - This is a definition that has been agreed by the EME, PHR, HTA and RfPB programmes. Feasibility Studies are pieces of research done before a main study in order to answer the question “Can this study be done?”. They are used to estimate important parameters that are needed to design the main study. For instance:

- standard deviation of the outcome measure, which is needed in some cases to estimate sample size;
- willingness of participants to be randomised;
- willingness of clinicians to recruit participants;
- number of eligible patients, carers or other appropriate participants
- characteristics of the proposed outcome measure and in some cases feasibility studies might involve designing a suitable outcome measure;
- follow-up rates, response rates to questionnaires, adherence/compliance rates, ICCs in cluster trials, etc.
- availability of data needed or the usefulness and limitations of a particular database
- time needed to collect and analyse data

Fibroblast - The most common cell found in *connective tissue* and responsible for producing the *extracellular matrix*, principally the protein *collagen*.

Fibrocartilage - Tough, fibrous *cartilage* that occurs in some joints as loose 'spacers', for example, the meniscus cartilage in the knee.

Fibrosis - The development of *excessive connective tissue* in an organ, often as a result of *inflammation* or injury. Thickening and scarring of the tissue may lead to loss of function in various organs.

Finite element analysis – A mathematical modelling technique adapted from the field of engineering, used to solve complex problems in biological research.

Follow-up -The observation over a period of time of study/trial participants to measure outcomes under investigation.

FPFV (First Person First Visit) – In a clinical study, the term used to refer to the first visit to the first recruited participant; this is important as marks the date when the trial has officially started recruiting.

FPLV (First Person Last visit) – In a clinical study, the term used to refer to the last visit to the first recruited participant.

Fragility fracture - A bone fracture that occurs after a simple fall and is usually indicative of a weakened skeleton resulting from *osteoporosis*. Common fragility fractures are those occurring in the vertebrae, the neck of the femur (thigh) bone, or wrist.

Fusion protein - A *protein* molecule that is produced as a result of the joining of two different *genes* which originally coded for two different proteins.



G

Gene - A short stretch of *DNA* that provides the template for the production of one *protein*.

Gene therapy - Insertion of a working *gene* into an individual's *DNA* to replace an absent or faulty gene, so that the correct *protein* can be produced and the cause of the disease eliminated.

Genetic marker - A *gene* or section of *DNA* that can be associated with a particular disease or characteristic in an individual. Can be used as an experimental aid in the laboratory.

Genetic modification - Artificial alteration of genetic material in a living organism so that a new substance or function can be produced.

Genome – The entire genetic code of an organism.

Genome-wide association study (GWAS) – a study comparing the *genomes* of a large group of people with a certain disease to the genomes of people without the disease, in order to find the genetic variants, or *single nucleotide polymorphisms*, that are responsible for the disease.

Genotoxic – Any agent capable of causing damage to *DNA*.

Genotype – The genetic makeup of an organism.

Glenohumeral joint – The main ball-and-socket joint of the shoulder.

Gold standard - The method, procedure, or measurement that is widely accepted as being the best available, against which new developments should be compared.

Gout - *Inflammation* caused by uric acid crystals deposited in the joint.

Growth factor - A substance made in the body that stimulates cell growth, *differentiation* and survival. Typical examples are *hormones* and *cytokines*.

Growth plate – A layer of *cartilage* found at each end of a growing bone, that serves to form new bone tissue adjacent to it, allowing the bone to gradually lengthen. When growing ceases, the growth plate closes and is replaced with solid bone.



H

Heterogeneous - A mixture of different, easily distinguishable components.

HLA B27 – Human leukocyte antigen B27. People who have the *gene* that codes for this *antigen* are more likely to have conditions such as *reactive arthritis*, *psoriatic arthritis* or *ankylosing spondylitis*.

Homogeneous - A mixture of similar components.

Hormone - A *chemical messenger* molecule produced and released by *cells* that transfers '*signals*' to cells elsewhere in the body, influencing functions such as metabolism, reproduction and growth.

Homeostasis - Maintenance of a constant and stable state in a cell, tissue, organ or biological system.

Hyaline cartilage - The smooth, tough but deformable and elastic *cartilage* that covers the ends of the bones in free moving joints and forms other organs such as the trachea.

Hypothesis - A tentative or suggested explanation for a set of observed events. Scientific research sets out to test hypotheses.

Hypoxia - Deprivation of an organ, tissue or cell of adequate oxygen.



Imaging - Techniques used to create images of the human body or its tissues to aid diagnosis, for example, X-ray or *MRI*.

Immune-suppression - The natural or induced suppression of the immune response.

Immune response - The complex and variable reactivity of the *immune system* to an *antigen*.

Immune system – A network of *cells*, tissues, organs and processes that protect the body from disease by working together to identify and attack invaders such as bacteria, viruses and tumour cells.

Immune tolerance – Process where the *immune system* does not mount a response to an *antigen*. A type of immune tolerance is self-tolerance; this protects the body's own *proteins* from attack from the immune system. Failure of self-tolerance may lead to *auto-immune* disease.

Infective arthritis – A serious infection of the joints, also known as *septic arthritis*, caused by a bacterial, fungal or viral infection, and characterised by pain, swelling and *inflammation*. It may occur in isolation, or as a complication of joint surgery or *rheumatoid arthritis*.

Inflammation – The reaction of a tissue to infection or irritation, characterised by heat, swelling and redness.

In-vitro - Experimentation in an artificial, controlled environment outside a living organism.

In-vivo - Experimentation in a whole, living organism.

Interleukin - A group of *proteins* within the *cytokine* family, produced by cells of the immune system in response to a stimulus. The many different interleukins control the immune response by regulating the proliferation and *differentiation* of specifically responsive cells.

Interventional Studies – in general, this refers to a clinical study type where participants are randomly assigned to one of two groups: the experimental group receiving the intervention (drug, device, etc) that is being tested and a comparison group (controls) which receives a conventional/existing accepted treatment or placebo (e.g. a sugar pill or sham device)

Intervertebral disc - A shock-absorbing 'cushion' situated between each of the spinal bones (vertebrae). Each disc is comprised of a thick and fibrous outer layer, enclosing a gel-like centre.

Intra-articular - Within the joint.



J

Jaccoud's arthropathy – A rare form of *lupus* disease in which the joints of the fingers become deformed.

Juvenile idiopathic arthritis (JIA) - Arthritis occurring in children before the age of sixteen, and with no defined cause. The disease takes several forms, and may be transient and short-lived, or chronic and disabling with permanent damage as a consequence.



K

Kinase – A type of *enzyme* that facilitates that transfer of a small chemical, the phosphate group, from one *protein* molecule to another.

Kinematics – Study of the motion of an object, without taking into consideration the mass of the object or the forces acting on it.



L

Lesion - An area of diseased or traumatised tissue.

Ligaments - Tough, fibrous bundles of *connective tissue* that connect one bone with another in the skeleton, forming a joint. Ligaments align and stabilise the joint, and safely restrict its range of motion.

Ligand – A substance that is able to bind, or attach to, another specific target molecule to trigger a biological reaction; for example, the binding of a ligand to a *receptor* on the surface of a *cell*.

Loading – See *Mechanical loading*.

Longitudinal study - A study of the same group of people at several time-points over a long period.

Loss to Follow up (LTF) - The loss of participants during the course of a study. Also called 'Attrition'

LPFV (Last person first visit) – In a clinical study, the term used to refer to the first visit to the last recruited participant; this is important as marks the date when the trial has completed recruitment.

LPLV (Last person last visit) – In a clinical study, the term used to refer to the last visit to the last recruited participant; this is important as marks the date when the trial has completed collection of participant data and can begin the next step of analysis.

LTFU (Long term follow up) – Referring to the action of observing clinical study participants over a period of time after the study ends to obtain data on long term effects of the intervention

Lupus - A shortened term for *systemic lupus erythematosus*.

Lupus anticoagulant test - A blood test used to diagnose *anti-phospholipid syndrome*, measuring the effect of the antiphospholipid antibodies on the time that it takes the blood to clot.

Lymphocyte - One of the main cell types of the *immune system*. Lymphocytes respond specifically to each foreign invader that they encounter. They are found in the bloodstream and in lymphoid tissues such as the lymph nodes and spleen. There are two main types of lymphocyte; *B cells* and *T cells*.



M

Macrophage - A type of immune system cell that devours and helps destroy invaders such as bacteria, parasites and tumour cells. Unlike *lymphocytes*, a macrophage's activity is not specific to a particular target. Macrophages also produce substances that help other cells of the immune system, as well as presenting molecules from foreign invaders to lymphocytes in order to stimulate a specific immune response.

Magnetic resonance imaging (MRI) – A type of scan which uses radio waves in a strong magnetic field to build up images of the inside of the body. It works by detecting water molecules in the body's tissue which give out a characteristic signal in the magnetic field.

Matrix metalloproteinase - A group of *enzymes* that break down the *proteins* that make up the *extracellular matrix*. They are essential to the normal processes of wound healing and blood vessel formation and are over-active in arthritis, contributing to the destruction of *cartilage* and bone.

Mechanical loading – The force applied to the bones or joints during movement.

Mediate - The action of one molecule indirectly facilitating the activity of another.

Menisci (singular '*meniscus*') – Loose 'spacers' of *fibrocartilage* contained in some joints such as the knee. They act as shock absorbers and help the movement of the joint.

Mesenchymal cells - Stem cells that differentiate to form all of the *connective tissue* cells of the body.

Meta-analysis - Combining data from multiple independent studies. May be undertaken in evidence syntheses.

Methylation - Modification of a *DNA* or *protein* molecule by the addition of a small chemical (methyl) group. Methylation of DNA may contribute to *epigenetic* inheritance.

Microarray - A large set of miniature chemical reaction areas, used to test many fragments of *DNA* or *proteins* simultaneously.

MicroRNA - Small *RNA* molecules that influence the way that *DNA* is *expressed*.

Mitochondria - Structures within the *cell* that generate the energy required for the cell to carry out its many functions. They are also involved in cell reproduction, growth, *differentiation* and death.

Molecular pathway - A connected series of reactions between molecules that lead to a certain event in the *cell* or tissue.

Monoclonal antibody - A highly specific *antibody* preparation, produced in the laboratory from a single *clone* of immune cells, and therefore reactive against only one *antigen*. Monoclonal antibodies are useful tools for laboratory analyses, and are also used therapeutically; for example, *anti-TNF*.

Monocyte - Immune system cells that circulate in the bloodstream and migrate to sites of *inflammation* in the tissues, where they mature into *macrophages*.

Morbidity - Illness or disease.



Morphometry – Study of the change in size and shape of organisms, or tissue structures within organisms.

Multicentre trial - A trial conducted at several geographical sites. Trials are sometimes conducted among several collaborating institutions, rather than at a single institution - particularly when large numbers of participants are needed.

Mutagen – Any substance capable of causing a permanent genetic change, or *mutation*, in the *DNA*.

Mutation - A permanent change in the *DNA* sequence of a *gene*, leading to an alteration in the *protein* encoded by the *gene*.

Myopathy – General term for any disease of the muscle that leads to weakness and loss of function, and is not attributable to a nerve disorder.



N

Natural killer cells (NK cells) - A type of immune *cell*, one of the *lymphocyte* family, that forms a front-line defence against cancer cells and cells infected by viruses. Unlike other lymphocytes, the NK cell does not need prior sensitisation to its target, and will attach itself to and destroy any cell that it recognises as foreign.

Neurotransmitter - A chemical released from a nerve *cell* that transmits or amplifies a message or impulse across the gap from one nerve cell to another, triggering a biological effect in the 'receiving' nerve cell.

Neutrophil - A type of immune cell, normally found in the bloodstream, that forms an early line of defence against bacterial invaders. *Neutrophils* engulf bacteria, then kill and digest them with *enzymes* contained in granules within the cell.

Non-inferiority trial - A trial designed to determine whether the effect of a new treatment is not worse than a standard treatment by more than a pre-specified amount.

NSAID, non-steroidal anti-inflammatory drug – Class of pain-relieving, temperature-lowering *anti-inflammatory* drugs often used to treat arthritis. Examples of NSAIDS are aspirin and ibuprofen.

Nucleus - The 'brain' of the cell that contains the *DNA* and all of the other material that forms the *chromosomes*.

Nucleus pulposus - Water-rich, jelly-like material in the centre of the *intervertebral discs* between the vertebrae that helps to distribute pressure when the spine is put under *load*.



O

Observational Study – Like Interventional studies, observational studies attempt to understand cause-and-effect relationships. However, unlike interventional studies, the researcher is not able to control how subjects are assigned to groups and/or which treatments each group receives.

Orthotic - Shoe insert used to correct an abnormal walking pattern by altering the angle at which the foot strikes a surface.

Osteoarthritis - A degenerative disease of the joints that is associated with age or joint injury, and is characterised by wearing away of the *cartilage* and thickening and hardening of the surrounding bone.

Osteoblast - *Cell* responsible for bone formation.

Osteoclast - Type of bone *cell* that dissolves and absorbs bone during the normal processes of growth and development of the skeleton and in fracture repair. Increased *osteoclast* activity may lead to *osteoporosis*, and is a feature of the malignant bone disease multiple myeloma.

Osteopaenia - Lower than normal *bone density*. May be a precursor to *osteoporosis*.

Osteophytes – Overgrowths of new bone at the edges of *osteoarthritic* joints, that occur as a deranged reparative response to the disease. *Osteophytes* may alter the shape of the joint and induce pain.

Osteoporosis – Disease of reduced *bone density* and disrupted bone structure, leading to an increased risk of fracture.

Outcome - A component of a participant's clinical and functional status after an intervention has been applied, that is used to assess the effectiveness of an intervention.

Outcome Measure - A planned measurement described in the protocol that is used to determine the effect of interventions on participants in a clinical trial.



P

Parallel design - Describes a clinical trial in which two or more groups of participants receive different interventions. For example, a two-arm parallel design involves two groups of participants. One group receives drug A, and the other group receives drug B. So during the trial, participants in one group receive drug A "in parallel" to participants in the other group, who receive drug B.

Participant - An individual who is studied in a trial, often, but not necessarily, a patient.

Pathogen - Any agent that causes a disease, such as a bacterium or virus.

Pathology, pathobiology - The study of the various functional manifestations of disease as well as its causes, development and consequences.

Peptide - A chain of 2 or more (up to around 50) *amino acids*. Longer chains are generally referred to as *proteins*.

Periarthritis – *Inflammation* near to, but just outside, a joint.

Peripheral blood cells – Cells found in the circulating blood stream; *red blood cells*, *white blood cells* and *platelets*.

Pharmacology – Field of science concerned with the discovery, composition, use and biological effects of drugs.

Phase 1 clinical trial - Small scale trial to test the safety of a drug.

Phase 2 clinical trial - Small scale trial after *phase 1* to test the effectiveness of a drug, and to find out more about side-effects and safety.

Phase 3 clinical trial - Larger scale trial after *phase 2* to compare the effectiveness of a drug against a standard treatment and to determine most appropriate dose.

Phase 4 clinical trial - Carried out on a licensed drug to ascertain longer term risks and benefits and to test effectiveness in different clinical settings.

Phenotype – The observable characteristics, such as appearance, behaviour, biochemical properties or presence of disease, that occur as a consequence of an individual's genetic make-up, or *genotype*, in combination with its environment.

Phospholipids – A type of fat found throughout the body, particularly in the outer coating of cells such as the *white blood cells* called *platelets*.

Pilot study - a smaller version of the main study used to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure that recruitment, randomisation, treatment, and follow-up assessments all run smoothly. It resembles the main study in many respects, including an assessment of the primary outcome. In some cases, this will be the first phase of the substantive study and data from the pilot phase may contribute to the final analysis; this can be referred to as an internal pilot. Or, at the end of the pilot study, the data may be analysed and set aside, a so-called external pilot

Platelets – Disc-shaped blood *cells* which help the blood to clot at sites of bleeding.



Polymorphism - The natural variability of *DNA* within a population.

Power, statistical power - The ability of a study that is reliant on the analysis of a number of samples to produce a statistically convincing outcome. Power analysis is used to calculate the minimum number of subjects required in order to accept the outcome of a statistical test with a particular level of confidence.

Pragmatic trial - A trial that aims to test a treatment policy in a 'real life' situation, when many people may not receive all of the treatment, and may use other treatments as well.

Pre-clinical study – The testing of a drug or procedure in animals, primarily to determine safety, before critical trials can begin in humans.

Precursor cell - A type of late *stem cell* that has developed to the stage where it is capable of *differentiating* into only one or two final, fully specialised cell types.

Primary outcome - The outcome of greatest importance

Pro-inflammatory cytokine - A *cytokine* that promotes *inflammation*.

Progenitor cell - A type of *stem cell* that has the capacity to *differentiate* into several specialised cell types, but is not able to reproduce itself indefinitely, as the most primitive stem cells are able to do.

Prognostic – An indicator, for example, a symptom or a test, that indicates the future course of a disease.

Prosthetic joint - An artificial replacement for a surgically removed joint.

Protease - A group of *enzymes* that is able to hydrolyse, or breakdown, *proteins* into their constituent *peptides* or *amino acids*.

Protein - A long chain of *amino acids*. The particular *amino acid* sequence of each protein, along with its 3 dimensional structure, determines its very specific function.

Protein folding – The formation of a *protein's* final, complex 3-dimensional shape from its original 2-dimensional linear chain.

Proteoglycan – Group of molecules containing a *protein* 'backbone' to which is attached many carbohydrate molecules. In *cartilage*, proteoglycans are important components of the *extracellular matrix*, holding large volumes of water within the cartilage and endowing it with strength and stiffness.

Protocol - The plan or set of steps to be followed in a study.

Pseudogout ('acute pyrophosphate arthritis') – Severe joint *inflammation* which occurs suddenly, caused by deposition of *calcium pyrophosphate* crystals.

Psoriatic arthritis - *Inflammatory* joint disease associated with the skin disease psoriasis.



Q

Quantitative research – Scientific investigation that gathers and analyses data that can be measured; (numerical data), or data that can be converted into numbers.

Quantitative research – Scientific investigation collecting non-numerical information that is interpreted in a more subjective, observational manner. It seeks to understand the processes that underlie behaviour, and looks for patterns and themes rather than statistical output.



R

Randomised controlled trial – *Clinical study* where people are assigned randomly to either receive or not receive the drug or clinical intervention being tested.

Randomisation is an attempt to balance out any factors that may bias selection of people to different treatment groups, possibly confounding the results of the trial.

Raynaud's phenomenon – A circulatory disorder that causes the blood supply to certain areas of the body to be greatly reduced, turning the fingers and toes temporarily cold, discoloured and numb. Raynaud's phenomenon can also occur with the condition *scleroderma*.

Randomisation - There are two components to randomisation: the generation of a random sequence, and its implementation, ideally in a way so that those entering participants into a study are not aware of the sequence (concealment of allocation).

Randomised Controlled Trial (RCT) - A study in which people are allocated at random (by chance alone) to receive one of several clinical interventions. One of these interventions is the standard of comparison or control. The control may be a standard practice, a placebo ("sugar pill"), or no intervention at all.

Reactive arthritis - *Inflammation* in the joints that can develop following a bacterial or viral infection elsewhere in the body.

Reagent – A substance used in a chemical reaction.

Receptor - A molecule usually embedded in the outer membrane of the *cell* that acts to receive and transmit 'signals' from other molecules that attach or bind to it.

Recombinant – An organism that contains genetic material from another organism within its *genome*.

Red blood cell – The most common type of cell in the *peripheral blood* stream. Red blood cells are disc shaped and easily deformable to allow them to squeeze through narrow capillaries. Their main function is to deliver oxygen to the tissues. They owe their colour to the large amount of the oxygen binding molecule, haemoglobin, that they contain.

Regulatory pathway - A series of connected chemical reactions that will proceed down a particular route depending on the type of genetic or biochemical stimulation present in the cell, or a biochemical pathway that influences the *expression* of a particular *gene*.

Regulatory proteins - Specialised *proteins* that act to 'switch' particular *genes* on and off.

Regulatory T cell, T reg - One of several different types of *T cell* that regulates the activity of another T cell.

Remodelling - The biological process of shaping and forming the skeleton during growth, disease and after injury, through the removal of old bone and its replacement with new bone.

Repressor - A protein molecule that can bind to *DNA* and block the *transcription* of a *gene*.

Resorption - Breakdown of the bone structure by *osteoclasts*, and release of bone minerals into the bloodstream.



Retrospective study - A study in which the outcomes have occurred before the study commenced. Case-control studies and cohort studies can be retrospective, but randomised controlled trials never are.

Rheumatoid arthritis - *Inflammatory* disorder that principally affects the tissues of the joints, but may affect many other tissues and organs.

Rheumatoid factor – An *auto-antibody* that forms complexes with other antibodies and contributes to the disease process in *inflammatory arthritis*. It is detectable in the blood of around 80% of people with arthritis, and is often used, in conjunction with other physical indicators, to diagnose the disease.

Risk factor – Anything that is likely to increase the likelihood of infection or disease.

RNA, ribonucleic acid – Molecule similar in structure to *DNA*, that serves to *translate* and *transcribe* the information encoded in the DNA template, so that the cell machinery can produce the necessary *proteins*.



S

Secondary outcome - An outcome used to evaluate additional effects of an intervention deemed as being less important than the primary outcomes.

Secretion - The production and release of a substance such as a *cytokine*, *hormone* or *enzyme* by a cell.

Scleroderma - Autoimmune disease characterised by the formation of excessive scar tissue in the skin and other body organs, leading to thickness, deformation and loss of function.

Signal, signal transduction - Transfer of information within *cells* or between cells using a *chemical messenger* molecule.

Single nucleotide polymorphism – A change in a single sub-unit of *DNA* that may be associated with a particular disease.

Spondylosis - *Osteoarthritis* of the small joints in the neck and back.

Statistically significant - A result that is unlikely to have happened by chance.

Stem cell - Unspecialised cell that is able to divide and reproduce indefinitely, and has the capacity to *differentiate* into a wide range of specialised cells.

Sub-group analysis - An analysis in which the intervention effect is evaluated in a defined subset of the participants in a trial, or in complementary subsets, such as sex or age.

Substrate - A molecule that is acted on and changed by an *enzyme*. The *enzyme* molecule will attach specifically to its substrate or substrates to form a complex, facilitating the transformation of the substrate into one or more different molecules.

Synovial fluid - Fluid produced within the joint *capsule* which helps to nourish the *cartilage* and lubricate the joint.

Synovium - The inner membrane of the joint *capsule* that produces *synovial fluid*.

Systematic review - A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.

Systemic lupus erythematosus (SLE) - A chronic *auto-immune* disease of *connective tissue*, causing *inflammation* and damage to many organs including the joints, skin, kidneys and nervous system.



T

T cell, T lymphocyte - One of the immune system cells that initiates and controls the body's response to infection or malignancy through recognition of specific 'foreign' molecules. There are several types of T cell.

Tendon - Tough, fibrous cord that anchors muscles into bones.

Tendinitis - Disease or *inflammation* of tendons.

Tenocyte - The resident *cell* of the *tendon*.

Tetraploidy – Four sets of *chromosomes* per *cell*, instead of the single set.

Thrombosis - A blood clot that occurs in an artery or vein.

Tissue engineering – Scientific field using the principles of engineering, biology and materials science to help replace and repair damaged tissue such as bone and *cartilage*.

Trabecular bone - The internal structure of the bones, comprising an interconnecting, open meshwork. The trabecular bone is surrounded by a dense outer shell of *cortical* bone.

Transcription factor - A *protein* that binds, or attaches, to specific areas of *DNA* and controls the transfer (*transcription*) of information from *DNA* to *RNA*, early in the process of protein formation in the cell.

Transgenic - An organism that has genes from another organism inserted into its *genome*.

Translation - Process of decoding the information that is transferred to *RNA* during the *transcription* process into *protein* molecules.

Translational research – Application of the fundamental understanding acquired from *basic*, laboratory research to the study of biological systems in whole organisms. A bridge between 'bench' and 'bedside'.

Translocation – Transfer of a segment of a *chromosome* to another chromosome.

Trialist - Used to refer to a person conducting or publishing a controlled trial.

Tribology - The study of friction and wear between interacting surfaces in motion.



U

Ultrasound scan – Imaging technique that uses high-frequency sound waves to visualise the internal organs of the body.



V

Vasculitis – *Inflammation* of the walls of blood vessels causing reduction in blood flow. Vasculitis can occur in isolation (primary vasculitis) or secondary to established diseases such as Sjögren's syndrome, *rheumatoid arthritis* and *lupus*.

Vacuole – A bubble-like structure within the *cell* containing a watery solution of molecules. The vacuole has a variety of functions, including digestion of nutrients and waste storage.

Virulence – The ability of any infective agent, or *pathogen*, to cause a disease, or a measure of the severity of the disease that the pathogen causes.



W

White blood cell - General term for the cells that defend the body against infection, foreign invaders and cancer. *Lymphocytes*, *neutrophils*, *monocytes* and *macrophages* are all types of white blood cell.



X



Y



Z

