

**Title:** Does Calcium Pyrophosphate Deposition associate with low bone mineral density, and does it affect the outcome of Osteoarthritis (OA)?

PhD project (Available to self-funded Home & EU / international students)

**Supervisors:** Professor Michael Doherty, Dr Weiya Zhang, Dr A Abhishek, Academic Rheumatology, University of Nottingham.

**Theme:** Rheumatology

**Keywords:** CPPD, Osteoarthritis, Osteoporosis, epidemiology.

Fee band: Home EU: £3996; International - £13,470

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**Background:** Recent research shows that Calcium Pyrophosphate Crystal Deposition (CPPD) may associate with osteoporosis. This is a novel association, and may be mediated by high pyrophosphate levels, which inhibit hydroxyapatite crystal nucleation and growth. CPPD also associates with OA. Although this association is well established, there is conflicting evidence as to whether CPPD associates with rapidly progressive OA.

**Objectives:** The objectives of this PhD project are to examine:

1. the association between CPPD and prevalent osteoporosis
2. the association between CPPD and incident osteoporosis
3. whether there is a higher risk of total knee or hip replacement in those with CPPD + OA compared to OA alone.

**Methods:** This will be a population based nested case-control and cohort study. Data from the UK Clinical Practise Research Datalink (CPRD) will be used for this purpose. CPRD contains prospective healthcare data on over 650 general practices (14 million people) throughout the UK, and is a nation-wide primary care database. Doctors record full details of patient characteristics including all consultations on their practice computers. These details are coded using a system of classification (Read codes). Read codes will be used to identify patients with OA, CPPD (chondrocalcinosis or pseudogout), osteoporosis, and matched controls.

A cross-sectional study will be carried out using data from all eligible patients to examine if CPPD associates with prevalent and with incident osteoporosis. If an association is found, further analysis will be carried out to examine if CPPD increases the risk of fragility fractures. Odds ratio (OR) and 95% CI will be used to examine the prevalent associations. A prospective cohort study design will be used to examine if CPPD associates with incident osteoporosis. Hazard ratio (HR) and 95% CI will be used to examine the association between CPPD and incident osteoporosis. A prospective study design will also be used to examine if CPPD associates with increased risk of knee or hip joint replacement in those with OA.

**Training/supervision:** A standard PhD training package will be provided including training in epidemiology, STATA, literature review, study design, analysis and writing up of the thesis. Additional training will be added according to individual needs. The successful applicant will be jointly supervised by Professor Michael Doherty (Professor of Rheumatology), Dr Weiya Zhang (Reader in Musculoskeletal Epidemiology) and Dr A Abhishek (Associate Professor in Rheumatology), and will work in the team including clinicians, nurses, academics and other PhD students.