Fluoroquinolone associated disability – *recognise and refer*

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Funding Sources:
No funding sources were involved in preparing this manuscript and is written as an independent commentary by all the authors.

Conflicts of interest:
NLM has received honoraria or research funding to his University from Novartis, Stryker.
SS has received honoraria or research funding to his University from Novartis, Celgene, Janssen, Pfizer, Abbvie, UCB, Boehringer Ingelheim, BMS
IBM has received honoraria or research funding to his University from Novartis, Celgene, Janssen, Pfizer, Abbvie, UCB, Boehringer Ingelheim, BMS

All authors take equitable responsibility for the content and ideas proposed herein.

The European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has completed its findings from its public hearing on fluoroquinolone and quinolone antibiotics incorporating the views of patients, healthcare professionals and academics, including our group, which recommended restricted use of systemic/inhaled (fluoro)quinolones[1].

Quinolone antibiotics were first developed in the 1960s and now account for 29.7 million antibiotic prescriptions in the United States. In the 1980s fluorine molecules were added to facilitate better penetration of tissues (central nervous system/musculoskeletal), while enhancing their effectiveness against a range of bacterial infections. However, they may also impair mitochondrial function, trigger oxidative stress or result in epigenetic changes in tissues[2]. For many years, the regulatory agencies and medical profession were sceptical of reports suggesting that a brief course of such antibiotics could mediate long term tissue damage with consequent clinical impact. Nonetheless, persistent campaigning by patient groups internationally led the US Food and Drug Administration (FDA) in 2008 to announce the first of what would be a series of alerts about the serious side effects including tendon rupture, musculoskeletal joint pain and irreversible nerve damage[3] while in 2016 the agency accepted the existence of a potentially permanent syndrome; *fluoroquinolone-associated disability* (FQAD)[4].

We became increasingly concerned about this issue upon starting a dedicated tertiary complex tendon disease clinic in Scotland some 5 years ago. Our practice made clear the significant musculoskeletal disabilities evident in FQAD patients, while we anecdotally observed that our patients with existing spondyloarthritis occasionally report worsening of these symptoms following fluoroquinolones. Importantly, we along with others[5] have come to recognise that these patients require a multidisciplinary approach with input from specialist physiotherapists, rheumatologists, orthopaedic surgeons, neurologists, musculoskeletal radiologists and occupational therapists. This prompted us to give evidence to the PRAC and highlight the *recognise and refer* mentality that should be adopted for this difficult-to-treat and under-recognised patient group.

The EMA's Committee for Medicinal Products for Human Use (CHMP) has recently adopted the PRAC recommendations, which will be ratified by the European Commission in early 2019. We believe this process and subsequent guidance will finally add weight to the scientific evidence surrounding FQAD, providing sufferers the recognition they longed and a treatment pathway they were commonly denied. It is vital that practising clinicians acknowledge this debilitating drug adverse reaction and in doing so recognise and refer to appropriate musculoskeletal or neurological specialist services, depending on the predominating symptoms.

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