PhD studentship proposal: In silico *studies in HTA* (M Soares, D Glynn)

Medical developments are increasingly made using advanced computation, including artificial intelligence methods, modelling and simulation. An important advancement in this area relates to *in-silico* clinical trials (ISTs), trials performed on cohorts of virtual patients using individualised computer simulations. A recently published exemplar is the FD-PASS study [https://doi.org/10.1038/s41467-021-23998-w], that evaluated flow diverters (a medical device) in the treatment of unruptured intracranial aneurysms. This work showed that the *in silico* replicated the results of *in vivo* randomised controlled trials, and even offered additional information about populations more likely to experience device failure.

By contributing with evidence on the effectiveness of health care technologies, ISTs have the potential to replace/augment the current *in vivo* clinical research portfolio, and even extend it, for example, by examining treatment effects over a range of patient subgroups. This may have a number of implications for Health Technology Assessment (HTA), including early HTA supporting Research and Development (R&D). For example, ISTs could be used alongside early modelling to optimise product development and support the design of *in-vivo* clinical research, generating better-targeted, higher value products and ensuring a higher chance of success for clinical research. ISTs could also be used as evidence within HTA assessments supporting Regulation and Reimbursement (R&R), accelerating patients' access to innovative technologies.

ISTs therefore have the potential to be transformative to HTA policy and practice but to date there has been no research exploring the expected economic and societal value of these studies within an HTA framework. This PhD aims to use decision modelling to start developing this area, exploring methodological aspects of relevance to ISTs, including the need to reflect judgements over the validity of these studies explicitly as decision uncertainty.