Developing methods to estimate HIV incidence and evaluate the role of prevention interventions in controlling transmission

Supervisors: - Daniela De Angelis, Paul Birrell (PHE) and Anne Presanis

The last two years have seen a sustained downturn in the number of new HIV diagnoses in Men who have Sex with Men (MSM) in England for the first time in the epidemic’s history. This could be explained by changes in propensity to test or a decrease in the number of new infections, or by both. Application of a Bayesian CD4-based back-calculation (Birrell et al, 2012, Brizzi et al, 2018) to diagnosis data to the end of 2016 has revealed that incidence of HIV infections in MSM had peaked around 2012. The decreasing trend in new diagnosis is therefore the result of decreasing HIV transmission, vindicating years of continued and intensified test and treat strategies amongst MSM.

Irrespective of its successful application to uncover the process underlying the recent observed fall in diagnosis, the back-calculation approach currently used suffers from a number of limitations. Firstly, it is the approximation of a closed system, with no inclusion of external (e.g. migration) processes. This prevents its application to diagnosis data on heterosexuals, which are particularly affected by migration patterns from countries with high historical HIV prevalence. Secondly, HIV diagnoses result from the combination of infection and testing processes and new diagnosis data inevitably suffer from a diagnosis delay, which is a limiting factor in the estimation of recent infection. Data on other recent infection biomarkers, of which CD4 count at diagnosis is an example, can be usefully exploited to improve incidence estimation. Thirdly, the progressive introduction of pre-exposure prophylaxis in MSM, and soon in heterosexuals, requires analytical approaches to quantify the contribution of the various infection prevention initiatives to changes in HIV transmission. The back-calculation model does not currently include a disease transmission component, so might be an inadequate tool for this purpose.

This project aims to address the above limitations by developing the back-calculation in three ways.

1. To include a migration process exploiting available data on migration patterns.

2. To incorporate additional surveillance data on the recency of infection in newly diagnosed individuals. These include information on biomarkers indicative of recent infection, which classify new diagnoses into recently infected and not recently infected; and information on most recent negative HIV test result. How to use these data most appropriately in the current back-calculation framework is not straightforward.

3. To extend the multi-state back-calculation to incorporate the mechanistic generation of new infections through the interaction of susceptible with infected individuals. This development would build on the extended model from 1. and 2. above and use ideas from the work in Presanis et al (2011) where incidence is estimated by using serial HIV prevalence in MSM together with population-level demographic data. The resulting model will combine all currently available sources of information and will provide a tool to estimate historical and current patterns in transmission and quantify the impact of the different prevention policies introduced over time. Given the model complexity, it is likely that parameter estimation will pose computational challenges, and computationally efficient methods (e.g. Goudie et al, 2018, Birrell et al, 2018) will be investigated.
This project would suit a student motivated to develop methods to solve substantive public health problems that will have a direct impact on the formulation and evaluation of public health policy. The project will be carried out in close collaboration with the HIV/STI and Statistics departments at Public Health England, who provide the relevant datasets.

**Start date:** Easter Term (April) or Michaelmas Term (October) 2019

All application queries regarding eligibility should be directed to phdstudy@mrc-bsu.cam.ac.uk

**How to Apply:** Applications should be made on-line via www.graduate.study.cam.ac.uk/applicant-portal selecting course details MDBI22 PhD in Biostatistics

**Deadline for applications:** 3rd January 2019