PhD project proposals for the UKHSA-LSHTM PhD studentship 2025

Summary

Mathematical modelling of pertussis transmission dynamics and pertussis vaccination programmes in England

Supervisors:

John Edmunds **(LSHTM), Yoon Choi (UKHSA), Liz Miller (LSHTM)**

Advisory panel:

Gayatri Amirthalingam (UKHSA), Helen Campbell (UKHSA), Sharif Ismael (UKHSA)

Description:

Pertussis is a highly transmissible respiratory infection which remains endemic despite longstanding immunisation programmes that have achieved high coverage. Infants too young to be vaccinated are most at risk of severe disease but there is also a substantial burden of illness in older children and adults who are important contributors to transmission. In response to a resurgence in pertussis cases and infant deaths in 2012, the UK introduced a maternal pertussis immunisation programme which was highly effective at preventing pertussis cases and associated deaths in vulnerable infants. We developed an age-structured compartmental model of pertussis transmission dynamics fitted to notification and coverage data to 2012 to investigate the potential cause of the 2012 pertussis resurgence in England. The results indicated that the resurgence was likely due to the change from whole cell to acellular pertussis vaccine in 2004 with the latter generating poorer protection against infection and more rapid waning, though estimates of these key model parameters had considerable uncertainty.

There is now a pressing need to further develop the existing model in order to refine the key acellular vaccine parameters by fitting to more recent pertussis notification data, and to allow incorporation of the maternal pertussis vaccination programme which began in 2012 and the changes in population mixing that have occurred since the COVID-19 pandemic. This updated model would provide much needed insights into the cause of the pertussis resurgence that began in 2024 and allow evaluation of the effect on pertussis control of adding boosters to the existing vaccination programme, including the planned 18 month booster dose. It would also allow evaluation of the potential benefit of using a live attenuated pertussis vaccine that is currently at a late stage of development and is designed to provide better protection against infection than the current generation of acellular vaccines. Additional insights into the key model parameters underlying pertussis transmission could also be obtained by household transmission studies using oral fluid testing for elevated levels of IgG antibodies to pertussis toxin which are established diagnostic markers of recent pertussis infection.

The aims of the PhD project are therefore to develop a realistic compartmental pertussis transmission model that:
1. Incorporates a maternal immunisation programme and changes in mixing patterns post-COVID-19
2. Allows more precise estimation of the degree and duration of acellular pertussis vaccine efficacy against infection by fitting to pertussis notification data that incorporates the resurgence in England in 2024, and informed by epidemiological studies.
3. Allows the effect of planned and potential changes to the pertussis vaccination programme to be predicted and the cost-effectiveness of such interventions to be evaluated.
4. Provides the ability to evaluate the potential impact and cost-effectiveness of using a live attenuated pertussis vaccine to replace one or more doses of the current acellular pertussis vaccine.

The PhD would provide the successful candidate with experience in (i) developing and fitting a compartmental transmission dynamic model and using it to predict the impact of future changes to the national vaccination programme; (ii) assisting in the design and execution of epidemiological studies on pertussis; (iii) costing the burden of pertussis disease using data sources such as Hospital Episode Statistics, intensive care and general practice databases; (iv) conducting cost-effectiveness analyses including analysis of the QALY data currently being collected by UKHSA in teenagers with pertussis; (v) the processes underpinning policy development by the UK Joint Committee on Vaccination and Immunisation.

Modelling the patient pathways that lead to increased risk of healthcare-associated infection

Supervisors:

Gwen Knight **(LSHTM), Stephanie Evans (UKHSA), Edwin VanLeeuwen (LSHTM/UKHSA)**

Advisory panel

Diane Pople (UKHSA), Julie Robotham (UKHSA)

Description:

Hospital-acquired infections (HAIs) are a significant burden on the NHS accounting for 21% of NHS England's bed capacity in 2022 due to overstaying patients, costing Â£2.7 billion. These infections are typically associated with a higher mortality rate and hospital length of stay than infections generated in the community and measures implemented following the detection of ward outbreaks provide additional operational pressures on an already strained health service.

EDs are increasingly at risk of becoming sites for nosocomial transmission due to longer waiting times and higher numbers of patients mixing, and patients that are admitted through EDs have been demonstrated to be the source of multiple ward outbreaks of hospital-associated COVID-19. However, risk factors for, and the impact of, disease transmission in the ED on these patients and the rest of the hospital through onward transmission has not been well quantified. Moreover, it has been suggested that the different demographics of ED entry hospital patients could explain some of the variation seen in HAI and drug-resistant infection burden.

This PhD project will develop statistical and computational models to describe and simulate patterns of pathogen transmission in EDs as well as the subsequent patient pathways and transmission opportunities through the hospital and back into the community or a care home. This will improve understanding of where the risk of infection is greatest and explore the reciprocal link between the hospital and community environments. The model will be used to estimate the impact of increasing ED waiting times on the risk of future ward outbreaks of hospital-associated infections as well as the cost-effectiveness of interventions to reduce transmission such as repeated testing of patients that have spent time in EDs for preventing new outbreaks on wards.

Machine learning for infectious disease forecasting during epidemics and pandemics

Supervisors:

Sebastian Funk **(LSHTM), Daniela de Angelis (UKHSA)**

Description:

Background
Predicting the near future of infectious disease outbreaks is crucial to inform the policy response. During the COVID-19 pandemic an enormous variety of models incorporating varying levels of detail on infection mechanisms and integrating different amounts and types of epidemiological data were used in order to provide infectious disease forecasts. To date it is not clear how best to combine such mechanisms with the data available for maximising utility for decision making.

Nowcasts and short-term forecasts were a key component to the modelling response to the COVID-19 pandemic and are likely to be in high demand during future incidents. Advancing the methodology for better situational awareness, as well as a better understanding of the role that different data streams can play and development of tools implementing such methods would all improve future pandemic preparedness in UKHSA.

Questions to be addressed
Among the questions that could be addressed with this PhD are:

- How are state-of-the-art methods of machine learning best applied to spatially resolved infectious disease data in order to make granular predictions of the near future?
- Can mechanisms of transmission be learned from available data streams and beused to inform forecast and scenario models?
- What is the value of different data streams in informing the learning of mechanisms of transmission that inform forecasts?

General Methods
The project will investigate the use of machine learning methods applied to infectious disease case counts, informed by other available data streams such as behavioural data, environmental surveillance data or individual-level measurements. They will be implemented in R, Julia, python or a similar programming language.

Housing and Infections in Homeless People: a modelling and health economics study

Supervisors:

Lara Gosce **(LSHTM & UCL), Rein Houben (LSHTM); Neha Batura (UCL)**

Description:

Background: Approximately one in every 200 individuals is homeless in England. Homelessness is strongly associated with increased morbidity and mortality across a wide range of conditions, including infectious diseases such as tuberculosis (TB), HIV, HCV, COVID19 and influenza-like illnesses (ILI). Studies show that homeless individuals are at elevated risk for epidemic outbreaks, especially in settings such as shelters, because of overcrowding and shared hygiene facilities. Access to safe, secure, and affordable housing, can address some of the health disparities that exist among homeless individuals, but can be costly. At the same time, homeless individuals use about four times more acute hospital services than the general population, resulting into high resource and financial implications for the National Health Service (NHS).

Stable supported housing interventions therefore have the potential to ease the economic burden caused by homelessness on the NHS. The potential short-term benefit of stable housing policies in improving health among homeless people is gaining prominence, but the potential long-term health impact and cost-effectiveness, e.g. through prevention of ongoing transmission of infectious diseases, remain unexplored.

Questions: This project aims to generate evidence on the long-term impact and cost-effectiveness of stable housing interventions through the reduction of infectious diseases in homeless individuals. This will be achieved through the following three objectives:

1. Estimate epidemiological impact of housing interventions in reducing transmission of infection in order to estimate the long-term effect of these interventions on homeless and general population health.
2. Determine the implementation costs of current housing interventions to estimate the economic implications of providing housing to London's homeless population.
3. Quantify thresholds of stable housing interventions' cost-effectiveness through infectious disease reduction, to estimate the economic implications of scaling-up these interventions in terms of cost averted by the NHS.

Importance and relevance: The scope of the project is important, timely and highly relevant to UKHSA: homelessness is a growing problem in England, local authorities do not secure accommodation for all homeless individuals, leading to gaps in care. The candidate will generate evidence on the long-term epidemiological impact and budgetary benefits and risk/burden of housing interventions and share results with policy makers and the public. To maximise the value of these findings they will disseminate results through a series of workshops aimed at homelessness services organisations and their clients, and dissemination meetings aimed at academics, local authorities and policy makers, through existing connections.

Modelling the cost-effectiveness of Epstein-Barr virus vaccination in England

Supervisors:

Lara Gosce **(LSHTM & UCL), Helen Stagg (LSHTM)**

Description:

Epstein-Barr virus (EBV) is a gamma herpes virus and one of the most common human viruses; it is estimated that about 90% of the world's adult population is infected. Infection is usually asymptomatic, but in some instances it may cause infectious mononucleosis (IM), which can result in life-threatening acute complications and post-viral syndromes, or particular cancers such as Hodgkin's lymphoma, Burkitt's lymphoma, gastric cancer, nasopharyngeal carcinoma and diffuse large B cell lymphomas.

In previous work[1] we presented the first mathematical model of EBV transmission, parameterised using data from England, and used it to compare hypothetical prophylactic vaccines with different characteristics and the impact of vaccinating different age groups. However, EBV vaccines are now being developed and are currently undergoing clinical trials, thus a window of opportunity presented for parametrising the model using real vaccine-specific data and study the cost-effectiveness of EBV vaccination campaigns in England.

The PhD candidate will lease with colleagues at the German Center for Infection Research (DZIF) performing a cGMP (current Good Manufacturing Practice)-compliant manufacturing process for a novel EBV vaccine candidate. They will collect data and model the impact of this and potentially other vaccine candidates. Additionally, they will perform a cost-effectiveness analysis to estimate the most value-for-money EBV vaccination strategy in England.

This project fits within UKHSA's remit, especially its strategic priorities of improving health outcomes through vaccines and improve action on health security through data and insight.

References

1. Goscé L, Winter JR, Taylor GS, Lewis JE, Stagg HR. Modelling the dynamics of EBV transmission to inform a vaccine target product profile and future vaccination strategy. Scientific reports. 2019 Jun 26;9(1):9290.

Populations at risk of antimicrobial resistance

Supervisors:

Simon Procter **(LSHTM), Edwin van Leeuwen (UKHSA/LSHTM), Gwen Knight (LSHTM)**

Advisory panel

Julie Robotham (UKHSA), Stephanie Evans (UKHSA),

Description:

Populations at risk of acquiring antimicrobial resistance (AMR) bacteria/pathogens may be linked by a variety of factors. These include socio-economic differences that influence living conditions and contact patterns that affect the underlying transmission rates of pathogens, as well as disparities in the health outcomes of infections related to comorbidities, access to healthcare, and patterns of antimicrobial consumption. Additionally, uptake rates of other health interventions such as vaccination may shape patterns of resistance acquisition. The introduction of resistant pathogens through importation due to travel or migration could also be a significant driver of AMR. A better understanding of these factors would help to identify high-risk populations, inform targeted interventions to reduce the burden of AMR and address inequalities.

This knowledge gap is highlighted in the UK National Action Plan on AMR, with a focus on better understanding health disparities and health inequalities. By improving the information available to identify where the AMR burden and rates of acquisition or resistance development of AMR is greatest, this work will help to optimise future interventions. It also complements ongoing UK Health Security Agency (UKHSA) efforts to analyze and address drivers of AMR and inequalities across different population groups.

Within this PhD project, the student will develop statistical and computational models to explore the relationship between socio-economic factors, population characteristics, and the transmission dynamics of AMR in England. These models will be used to quantify the burden and transmission routes of AMR across different population groups (e.g. men versus women), investigate the role of importations, and evaluate the (cost-) effectiveness of interventions to reduce the rate of resistant infections, such as improved antibiotic stewardship or vaccination programs. The results will contribute to an improved evidence base for policy decisions aimed at reducing health inequalities and minimizing the burden of AMR in the UK.

Investigating the effect of influenza on the risk of progression to tuberculosis

Supervisors:

Palwasha Khan **(LSHTM), Nicky McCreesh (LSHTM), Tom Sumner (LSHTM)**

Description:

Tuberculosis (TB), is a complex and preventable disease caused by *Mycobacterium tuberculosis (M. tuberculosis)*. Most individuals infected with *M. tuberculosis* remain well by containing the pathogen immunologically. Five to ten percent of infected persons develop disease, leading to onward transmission of *M. tuberculosis*. It is well known that HIV infection increases the risk of progression to TB, but the effect of other viral infections on the natural history of TB remains ill-defined. Identifying modifiable factors that increase the risk of progression to TB in those already infected could lead to innovative interventions to curtail the epidemic. An under-researched area to date is the role of non-HIV viral triggers.[1]

The public health benefit of identifying common viral infections, such as influenza, which increase the risk of TB, and which can be targeted with vaccine interventions, may be substantial. In the UK, TB incidence could be reduced in key risk groups (e.g. household contacts of people with TB) through targeted vaccination. In higher burden countries such as South Africa, reductions in community-wide *M. tuberculosis* transmission could be achieved through larger scale vaccination of people in high-risk populations (e.g. people living with HIV).

Our hypothesis is that influenza trigger progression to TB, and that vaccination-induced prevention of influenza reduces the risk of TB.

Research questions

1. Does influenza increase the risk of TB in the UK?
2. Does prevention of influenza through vaccination reduce the risk of TB in the UK?
3. What would be the impact on TB incidence in South Africa of increased influenza vaccine coverage?

Research questions 1 and 2 will be addressed using the UK Clinical Practice Research Datalink (CPRD), which includes routinely-collected anonymised longitudinal primary care data on 11.3 million patients who are representative of the UK population for age and sex. Widely validated data on demographics, diagnoses, prescriptions, immunisations, investigations, and referrals are available. Data linkages to episodes of admitted patient care in all NHS hospitals in England and Wales (Hospital Episode Statistics) and death certificate data from Office for National Statistics are available.

1. Does influenza increase the risk of TB in the UK?
   Study population: Patients aged ≥ 15 years included in the CPRD
   Exposure: Influenza-like illness (ILI)
   Outcome: TB
   Study design: (i) Longitudinal cohort study (ii) Self-controlled case series (SCCS)[2,3]

2. Does prevention of influenza through vaccination reduce the risk of TB in the UK?
   Study population: Patients aged ≥ 15 years included in the CPRD and eligible for the influenza vaccination as per guidance at the time
   Exposure: Influenza vaccination
   Outcome and *study design as above*.

For research question 3, the student will develop and calibrate a mathematical model of tuberculosis and influenza transmission in South Africa, incorporating the impact of influenza on the risk of developing TB. They will model different levels of influenza vaccine coverage in different risk groups, and estimate the impact on TB incidence and mortality.

References

1. Cobelens F, Nagelkerke N, Fletcher H. The convergent epidemiology of tuberculosis and human cytomegalovirus infection. *F1000Res.* 2018;7:280.

2. Whitaker HJ, Farrington CP, Spiessens B, Musonda P. Tutorial in biostatistics: the self-controlled case series method. *Stat Med.* 2006;25(10):1768-1797.
3. Whitaker HJ, Hocine MN, Farrington CP. The methodology of self-controlled case series studies. *Stat Methods Med Res.* 2009;18(1):7-26.

Quantifying the impact and mitigation of climate change on tuberculosis in migrant and displaced populations

Supervisors:

Finn McQuaid **(LSHTM), Lara Gosce (LSHTM), Rein Houben (LSHTM)**

Topic submitter:

Finn McQuaid

Description:

Importance of the topic:
Tuberculosis remains a critical infectious disease of risk, with reported notifications in England increasing by 11% in 2023 compared to the previous year. Meanwhile, climate change acts as a threat multiplier to nearly all sustainable development goals, including health. A wide body of evidence exists revealing a concerning association between TB burden and key risk factors likely to be affected by climate change. However, the potential scale of the effect of the climate crisis on TB burden via these pathways is still unclear. This project will generate evidence on the potential impact of climate change on TB, using innovative TB models to capture climate-sensitive TB risk factors for migrants from countries most likely to be affected.

Questions to be addressed:
We need to know how migration, particularly forced displacement, could drive TB transmission in order to understand how climate-induced displacement could increase risk of new TB infections. We also need to know how changes in undernutrition and other key risk factors in migrants could affect progression from TB infection to disease, in order to understand how climate-mediated stress could increase TB burden. Finally, we need to know how disrupted access to healthcare and increased vulnerability to TB could affect TB diagnosis and cure, in order to understand how climate-driven crises could increase unsuccessful TB treatment and death in migrant populations.

General methods:
To achieve this, this project will develop TB models linking climate change to key risk factors, mapping the pathways from climate change to TB burden. The objectives will cover 3 broad areas:
i) The student will integrate models of climate-vulnerable populations and known migration routes with TB burden estimates, in order to estimate how migration could drive TB transmission;
ii) The student will develop risk-explicit TB transmission models linked to projections in risk factors (such as BMI), in order to estimate how changes in undernutrition could affect progression from TB infection to disease in populations;
iii) Finally, the student will generate cohort models of TB diagnosis and treatment linked to risk factors, in order to estimate how disrupted access to healthcare and increased vulnerability to TB could affect TB diagnosis and cure.

This will allow the student to quantitate and project key potential effects of climate change on TB, and model the potential effect of different intervention adaptation and mitigation measures, which will be used to support decision-making for the development of a climate-resilient TB programme.

Modelling and economic evaluation of future norovirus vaccines in the UK

Supervisors:

Kaja Abbas **(LSHTM) and Juan F Vesga (UKHSA)**

Description:

Background

Norovirus is the leading cause of acute infectious gastroenteritis globally and results in over 2,600 laboratory-confirmed cases annually in the UK. Norovirus has a seasonal presentation and a disproportionate burden among young children and the elderly, causing outbreaks in hospital wards, care homes, and childcare facilities. The overall impact on the UK's economy of an average norovirus season has been estimated at £107 million in healthcare costs but the widest societal impact is still to be estimated. No vaccine has been licensed yet but the development pipeline has at least two formulations in Phase III trials. However, the evidence on these new norovirus vaccines' health and economic impact and strategies for their introduction (upon licensure) and implementation are unclear.

Proposed project

The research will involve reviewing the epidemiology of norovirus infections and developing mathematical models to understand their spread and multistrain dynamics. This work builds on previous research led by UKHSA on modelling the multistrain transmission of norovirus in the UK. The overall aim is to explore the complexities of population dynamics in immune responses to viral strains, while advancing understanding of how future norovirus vaccines might be used to control infections—such as responding to outbreaks or incorporating them into routine immunisation programmes. Additionally, the project will estimate the public health impact and cost-effectiveness of future norovirus vaccines. Expected outcomes include generating new knowledge on norovirus epidemiology and dynamics, as well as the economic impact of vaccine candidates in development, which could inform vaccine policy in the UK

The role of UKHSA and LSHTM in this collaborative project

- The PhD candidate will be able to access the surveillance data collected by UKHSA through the Second-Generation Surveillance System. The candidate will leverage the expertise and professional development activities offered by the Centre for Mathematical Modelling of Infectious Diseases, Vaccine Centre, and Global Health Economics Centre at LSHTM.
- Juan Vesga's research focus is on applying mathematical and statistical methods to assess the dynamics of infectious disease and the impact of interventions at the interface of health systems and infectious disease epidemiology.
- Kaja Abbas's research is on vaccine impact modelling with a focus on estimating the health, economic, and equity impact of vaccination programmes to support evidence-based decision-making on vaccination strategies in collaboration with partners and stakeholders at the global, regional, and national levels.

Particular prior educational requirements for a student undertaking this project

- Essential: Knowledge of infectious disease epidemiology
- Desired: Experience in vaccinology and infectious disease modelling; programming skills (R, Python, C++ or MATLAB)

Skills we expect a student to develop/acquire whilst pursuing this project

- Vaccine impact modelling
- Vaccine economics

References

- Sandmann FG, Shallcross L, Adams N, Allen DJ, Coen PG, Jeanes A, Kozlakidis Z, Larkin L, Wurie F, Robotham JV, Jit M, Deeny SR. Estimating the Hospital Burden of Norovirus-Associated Gastroenteritis in England and Its Opportunity Costs for Nonadmitted Patients. Clin Infect Dis. 2018 Aug 16;67(5):693-700.

- Gaythorpe KAM, Trotter CL, Lopman B, Steele M, Conlan AJK. Norovirus transmission dynamics: a modelling review. Epidemiol Infect. 2018 Jan;146(2):147-158. https://doi.org/10.1017/s0950268817002692
- Gaythorpe KAM, Trotter CL, Conlan AJK. Modelling norovirus transmission and vaccination. Vaccine. 2018 Sep 5;36(37):5565-5571. https://doi.org/10.1016/j.vaccine.2018.07.053
- WHO guide for standardization of economic evaluations of immunization programmes, 2nd edition. Geneva: World Health Organization; 2019. https://www.who.int/publications/i/item/who-guide-for-standardization-of-economic-evaluations-of-immunization-programmes-2nd-ed
- Hasso-Agopsowicz M, Hwang A, Hollm-Delgado MG, Umbelino-Walker I, Karron RA, Rao R, Asante KP, Sheel M, Sparrow E, Giersing B. Identifying WHO global priority endemic pathogens for vaccine research and development (R&D) using multi-criteria decision analysis (MCDA): an objective of the Immunization Agenda 2030. EBioMedicine. 2024 Dec;110:105424. https://doi.org/10.1016/j.ebiom.2024.105424

The effect of weather and humidity on the impact of school closures

Supervisors:

Punam Mangtani **(LSHTM), Emilia Vynnycky (UKHSA/LSHTM)**

Advisory panel:

Charlotte Jackson (UCL)

Description:

School closures and mitigation measures such as improved ventilation are sometimes used as control measures to limit of the transmission of infections. They were used during the recent Covid pandemic in the UK and elsewhere and studies have found that the contact parameter (the per capita rate of effective contact between two specific individuals) is reduced for several infections, such as measles and chickenpox during school holidays as compared with term time. It is plausible that the impact of school closures is also affected by temperature and humidity as these factors may also affect transmission of different infections.

This project will extend previous work [1,2] to use primary care data from England over the last few decades to identify regional variations in the incidence of several infections such as influenza and chickenpox. It will use TSIR and transmission dynamic models to calculate regional estimates of the amount of contact among children during the course of a year and the difference in the amount of contact during term-time compared to that during school holidays. The work will explore whether any regional and temporal differences are consistent with differences in temperature and humidity. The role and relative benefits of mitigation measures such as ventilation or UVE light treatment [3] will be explored. The findings will be relevant for guiding policy on school closures for limiting infection transmission for the infections studied.

References

1. Jackson C, Vynnycky E, Mangtani P. The Relationship Between School Holidays and Transmission of Influenza in England and Wales. Am J Epidemiol. 2016 Nov 1;184(9):644-651
2. Jackson C, Mangtani P, Fine P, Vynnycky E. The effects of school holidays on transmission of varicella zoster virus, England and Wales, 1967-2008. PLoS One. 2014 Jun 16;9(6):e99762
3. Gráinne Brady, Fiona Bennin, Rosaline De Koning, Cecilia Vindrola-Padros, Sigrún Eyrúnardóttir Clark, Manish K. Tiwari, Simon Watt, Andrea Ducci, Ryo Torii, Danielle Morris, Elizabeth Lloyd-Dehler, Jerry Slann, Fiona Stevenson, Zarnie Khadjesari, Hakim-Moulay Dehbi, Lena Ciric, Ruth Epstein, John Rubin, Catherine F. Houlihan, Rachael Hunter, Laurence B. Lovat, Interventions used to reduce infectious aerosol concentrations in hospitals—a review, eClinicalMedicine,Volume 79,2025,102990,ISSN 2589-5370,https://doi.org/10.1016/j.eclinm.2024.102990.