Modélisation des infections sexuellement transmissibles
Modeling sexually transmitted infections

Groupe de travail de l'Action Coordonnée Modélisation (AC49)
de l'ANRS—MIE

org. : Samuel Alizon, Samuel Soubeyrand, Laura Témime

5 avril 2024, CNAM, Paris (France)
`https://sti2024.sciencesconf.org/`

Oratrices invitées

— Tara D Mangal, Imperial College, London, UK
— Debra ten Brink, Burnet Institute, Australia
— Irene Man, IARC, Lyon, France
— Lilith Whittles, Imperial College, UK

Détails pratiques

Lieu

Amphithéâtre Abbé Grégoire

Conservatoire National des Arts et Métiers (CNAM)

292 rue Saint-Martin

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Métros : Réaumur Sebastopol (lignes 3 et 4), Strasbourg St Denis (lignes 8 et 9) ou Arts et Métiers (lignes 3 et 11).

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Horaires

— Accueil à partir de 8h30

— Introduction à 8h45

— Fin des discussions à 18h

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	Fri. 05
08:00	
	Welcome
	Symposium introduction
09:00	Public health impact and cost-effectiveness of gonorrhoea vaccination in UK MSM: an integrated transmission-dynamic health-economic modelling analysis
	Behavioral changes in the 2022 MPOX epidemic in MSM in Île-de-France
10:00	Coffee break
	Optima HIV: maximizing epidemiological impact of HIV spending
11:00	
	Modelling HIV epidemic in the UK
	Development and evaluation of a method to produce migration-adjusted HIV epidemic indicators
12:00	Lunch
13:00	
	The Ripple Effect: HIV's influence on Multidimensional Health Landscapes
14:00	
	Building resilient cervical cancer prevention through gender-neutral HPV vaccination: a modelling study
15:00	
	Dynamic modelling of genital human papillomavirus (HPV) infections and co-infections and the long-term impact of HPV vaccination
	Break
	Anogenital herpes in France, 2022-2023: a spatiotemporal multivariate disease mapping approach
16:00	
	Generalised infinite dimensional SIS model
	Non-selective distribution of infectious disease prevention may outperform risk-based targeting
	Research on STI modeling
17:00	

Public health impact and cost-effectiveness of gonorrhoea vaccination in UK MSM: an integrated transmission-dynamic health-economic modelling analysis

Dr Lilith Whittles[a*†]

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Abstract

Gonorrhoea is a rapidly growing public health threat in the UK, with rising incidence and increasing drug resistance, particularly among men who have sex with men (MSM). Observational evidence that the vaccines designed against *Neisseria meningitidis* may offer partial cross-protection against gonorrhoea has created interest in using four-component serogroup B meningococcal (4CMenB) vaccines for this purpose, and raised prospects for developing gonorrhoea-specific vaccines. We developed an integrated transmission-dynamic health-economic model, calibrated to surveillance data on MSM in England using Bayesian methods. We quantified the potential impact and cost-effectiveness of vaccination of MSM, comparing three realistic approaches to targeting. We found that even under conservative assumptions, 4CMenB administered using a risk-targeted strategy would likely be cost-saving at its current National Health Service price, averting an estimated mean 110,200 cases (95% credible interval 36,500–223,600), gaining a mean 100.3 QALYs (31.0–215.8), and saving a mean GBP 7.9 million (0.0–20.5) over 10 years.

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Behavioral changes in the 2022 MPOX epidemic in MSM in Île-de-France

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Résumé

Background & aims of study The first case of mpox in the Île-de-France, the region of Paris, was confirmed on May 19, 2022, then leading to a growing epidemic. Most of the cases were among men who have sex with men (MSM), the majority of whom have multiple sexual partners. The outbreak started declining at the end of June, before that the mpox vaccination campaign was launched. We investigated whether the decline was attributed to the dwindling of susceptible MSM, behavioral changes, or the post-exposure prophylaxis (PEP) vaccination campaign for at-risk subjects.

Methods & results Using survey data on Parisian MSM sexual habits, we built a temporal sexual contact network and informed an agent-based model for mpox transmission. We fitted the model to the data on mpox cases in Île-de-France. We included the effect of the PEP vaccination campaign, the smallpox vaccine, and behavioral changes with the reduction of sexual activity due to risk awareness. We showed that PEP vaccination had no effect in curbing the wave. The dwindling of susceptible individuals affected the outbreak evolution, but cannot explain the decline alone. Considering a detection rate of 50% of the cases, the decline is explained by 13% of high-risk MSM reducing their sexual activity by 92% from mid-June to mid-July. These percentages are estimated to be respectively 49% and 98% if the change of sexual behavior occurred randomly among MSM, independently of their activity.

Implications The rapid decline of the mpox wave in Île-de-France observed in July 2022 was likely favored by behavioral changes in the MSM population driven by risk awareness, combined with building immunity in the population. This was later confirmed by the 2023 ERAS survey and by WHO.

*Intervenant

Optima HIV: maximizing epidemiological impact of HIV spending

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Abstract

Introduction. Human immunodeficiency virus (HIV) does not yet have a cure, and there is a need to provide ongoing treatment for the increasing number of people living with HIV, despite reductions in available funding. The Optima HIV model can assess the most effective distribution of scarce national HIV resources.

Methodology. Optima HIV is dynamic compartmental population-based model, overlaid with an optimization algorithm. Epidemiological, behavioral and programmatic data inform the risks of transmitting, acquiring, and dying from HIV, and can vary across the population, across partnerships, and over time.

Results. The flexible Optima HIV model can be adapted to different contexts, and the results of the optimization reflect the need to tailor programs to the key population with the highest risk of acquiring HIV. We work together with the HIV modelling consortium in multi-modelling projects to enhance certainty around projections.

Conclusion. Mathematical modelling can be a key part of evidence-informed decision-making, and applying multiple models at the same time can help strengthen evidence.

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Modelling HIV epidemic in the UK

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Résumé

The information collected from the HIV drug resistance tests carried out in the UK since 1996 is available in the UK HIV Drug Resistance Database. The database stores protease and reverse transcriptase HIV sequences from dozens of thousands of tests, accounting for about 50% of infected individuals in the UK. This is a unique and valuable resource for HIV researchers allowing us to answer questions about the HIV spread and detect clusters of public health interest via mathematical modelling.
In the talk I will present phylodynamic methods and models for analysis of the mechanisms of HIV epidemic spread using large sequence datasets. I will then talk about lessons learnt about the UK HIV B spread from applying these methods to the UK HIV Drug Resistance data.

*Intervenant

Development and evaluation of a method to produce migration-adjusted HIV epidemic indicators

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Résumé

Background: A Bayesian model based on CD4, clinical stage, previous negative test, and date of migration has previously been used to identify the proportion of HIV infections diagnosed in Europe that were likely acquired prior to migration (1). We aimed to adapt this existing model to produce overall estimates of HIV incidence and the size of the undiagnosed HIV epidemic accounting for place of infection and to evaluate the model's performance using a simulated dataset.
Methods: We used a slightly modified version of the existing Bayesian migration model to generate individual-level posterior distributions of infection times for each individual diagnosed from 2012-2022 in a simulated database of MSM born in France based on the HIVSynthesis model (2). To estimate HIV incidence, draws from these posterior distributions were combined with methods previously developed to estimate AIDS reporting delays (3). The size of the undiagnosed population at the end of 2022 was estimated by summing the number of HIV incident cases each year from 2012-2022 expected to still be undiagnosed and projecting forward from 2023-2042 the yearly number of diagnoses among people infected prior to 2012. A cohesive approach for estimating HIV incidence in France, the number of arriving migrants with undiagnosed HIV infection, and the size of the undiagnosed population in France is proposed.

Results: Yearly numbers and trends in HIV incidence produced by these methods are very similar to the true, simulated values. Estimates of the size of the undiagnosed population are also similar to the simulated values, though the number of individuals infected in 2019-21 and still undiagnosed at the end of 2022 is slightly underestimated due to a simulated drop in diagnoses during the COVID pandemic.

Discussion: The proposed methods for estimating HIV incidence and the size of the undiagnosed population in France perform well on simulated data. Next steps include finalizing these methods and applying them to the French surveillance data to produce migration-adjusted indicators.

References

*Intervenant

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2. Cambiano V et al. The effect of combination prevention strategies on HIV incidence among gay and bisexual men who have sex with men in the UK: a model-based analysis. Lancet HIV. 2023;10(11):e713-e22.

3. Brookmeyer R, Liao JG. The analysis of delays in disease reporting: methods and results for the acquired immunodeficiency syndrome. Am J Epidemiol. 1990;132(2):355-65.

Building resilient cervical cancer prevention through gender-neutral HPV vaccination: a modelling study

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Résumé

The COVID-19 pandemic has disrupted HPV vaccination programmes worldwide. Using an agent-based model, EpiMetHeos, recently calibrated to Indian data, we illustrate how shifting from girls-only (GO) to gender-neutral (GN) vaccination strategy could improve the resilience of cervical cancer prevention against disruption of HPV vaccination. In the base case of 5-year disruption with no coverage, shifting from GO to GN strategy under 60% coverage (before disruption) would increase the resilience, in terms of cervical cancer cases still prevented in the disrupted birth cohorts per 100,000 girls born, by 2.8-fold from 107 to 302 cases, and by 2.2-fold from 209 to 464 cases under 90% coverage. Furthermore, shifting to GN vaccination helped in reaching the WHO elimination threshold. Under GO vaccination with 60% coverage, the age-standardised incidence rate (ASIR) of cervical cancer in India in the long-term with vaccination decreased from 11.0 to 4.7 cases per 100,000 woman-years (above threshold), as compared to 2.8 cases (below threshold) under GN with 60% coverage and 2.4 cases (below threshold) under GN with 90% coverage. In conclusion, GN HPV vaccination is an effective strategy to improve the resilience to disruption of cancer prevention programmes and to enhance the progress towards cervical cancer elimination.

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Dynamic modelling of genital human papillomavirus (HPV) infections and co-infections and the long-term impact of HPV vaccination

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Résumé

Human papillomaviruses (HPV) are common sexually transmitted infections, with prevalence peaking at ages 20-24 years. HPV is characterized by a broad diversity of genotypes, some of which are causal for cervical cancer. Because available vaccines target a subset of genotypes only, it is essential to monitor the transmission dynamics of vaccine (V) and non-vaccine (NV) genotypes while accounting for their potential intra-host interactions. This work was based on the development of an individual-based model that makes it possible to reproduce both the heterogeneity of sexual behaviors and the transmission dynamics of V and NV genotypes as functions of age. The model assumed that the interaction between genotypes results in the reduction (competition) or extension (synergy) of the duration of infection by an NV genotype in the event of prior infection by a V genotype. Calibration of transmission parameters for various interaction strengths showed that several of them are compatible with pre-vaccine epidemiological data on infection and co-infection. In the simulations, after introduction of vaccination into the population, we observed that the prevalence of NV genotypes increased in the case of competition and decreased in the case of synergy, especially when the interaction was strong. In the event of competition, the increase in the prevalence of NV could lead to a slight decrease or even an increase in the overall prevalence of all genotypes despite vaccination. The simulations highlighted variations in NV prevalence before and after vaccination which were more marked in less sexually active individuals. In addition, the model was used to emulate epidemiological studies in order to determine the conditions (number of subjects, time after the introduction of the vaccine) necessary to detect a decrease or increase in HPV prevalence following vaccine introduction in the population. A systematic review of the literature identified two observational study designs comparing the prevalence of infection either in two populations in the pre- and post-vaccination eras, or in vaccinated and unvaccinated individuals in the post-vaccination era. The results obtained suggested that the studies published to date, regardless of the design, lack statistical power to detect variation in NV prevalence. Based on the development of a model validated to reproduce realistic sexual behaviors and prevalence of HPV infection, this work contributes to the improvement of epidemiological knowledge on HPV infections and co-infections and allows us to anticipate the impact of vaccine prevention measures on the prevalence of HPV infection.

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Anogenital herpes in France, 2022-2023: a spatiotemporal multivariate disease mapping approach

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Résumé

Background: Anogenital herpes represents a noticeable public health burden. Past studies remained
silent on the spatial heterogeneity of this burden in France.

Methods: We used 21,650 HSV-1 and 2 RT-PCRs performed in France between 2022 and 2023. Both tests
were performed on the same lesions. We used these data within a hierarchical Bayesian multivariate
disease mapping approach to identify areas in which the number of observed anogenital herpes was
greater than expected given the sociodemographic composition of sampled patients. We accounted for
model structure uncertainty through Bayesian model averaging via stacking weights. We measured
the correlation between the standardised number of HSV-1 and 2 positive RT-PCR through correlation
distance.

Results: HSV-1 was isolated in 18.66% of anogenital lesions analysed, against 13.49% for HSV-2. HSV-1
and 2 were isolated in less than 1% of sampled lesions. HSV-2 represented 42.09% of all detected
anogenital herpes.

*Intervenant

For HSV-1, North and East of France appeared to be areas with greater than expected number of
detected anogenital herpes whereas Paris appeared to get a relatively lower than expected burden. For
HSV-2, we identified a strong North-East/South-West gradient and found. Paris regions was one of
the key areas in terms of unexpected burden for HSV-2. We also found a positive dynamic. Support
towards a positive temporal dynamic was found for HSV-1 and 2 although a substantial amount of
uncertainty remained for HSV-1.

Countrywide, the correlation distance between the standardised number of positive HSV-1 and 2
RT-PCRs was found to be likely in the interval (0.11,0.47). The joint posterior distributions favored a
negative relation, supporting the assumption of a negative spatial correlation between the expected
number of standardised positive HSV-1 and 2 RT-PCR. Last but not least, the posterior distribution for
the correlation distance remained stable between the years.

Limits: The analysis focused on the relative burden of genital herpesvirus among individuals tested for
genital lesions. The statistical approach focused on identification and description of spatiotemporal
patterns.

Implication: We identified areas with an unusually high number of detected genital herpes. This result
could help in planning any future intervention campaigns which would aim to reduce the public
health burden associated with genital herpes.

Generalised infinite dimensional SIS model

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Résumé

The SIS epidemic model, first introduced by Kermack and McKendrick, models the spread of an epidemic where infected individuals recover with no immunity, and thus are susceptible again to the disease. This model is usually used for gonorrhea. Many ways to generalize the basic Kermack-McKendrick SIS exist in the literature, we focus in this talk on two of them:
- Adding heterogeneity to the model. One can assume that the spreading and recovery rates depend on some parameters, for instance some specific health conditions, geographic position of the individuals, ...

- Considering another model for the infection rate than the law of mass-action. It is usually assumed that the infection rate in a population with S susceptible individuals and I infected individuals is proportional to SI. This assumption does not always fit epidemiological data.

The model we propose in this talk unites all these two aspects. Using some elements of operator theory, we prove that, for any initial condition, the proportion of infected individuals converges to an endemic equilibrium.

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Non-selective distribution of infectious disease prevention may outperform risk-based targeting

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Résumé

Epidemic control often requires optimal distribution of available vaccines and prophylactic tools, to protect from infection those susceptible. Well-established theory recommends prioritizing those at the highest risk of exposure. But the risk is hard to estimate, especially for diseases involving stigma and marginalization. We address this conundrum by proving that one should target those at high risk only if the infection-averting efficacy of prevention is above a critical value, which we derive analytically. We apply this to the distribution of pre-exposure prophylaxis (PrEP) of the Human Immunodeficiency Virus (HIV) among men-having-sex-with-men (MSM), a population particularly vulnerable to HIV. PrEP is effective in averting infections, but its global scale-up has been slow, showing the need to revisit distribution strategies, currently risk-based. Using data from MSM communities in 58 countries, we find that non-selective PrEP distribution often outperforms risk-based, showing that a logistically simpler strategy is also more effective. Our theory may help design more feasible and successful prevention. REF: Steinegger, et al. (2022) Nat. Commun. 13 (3028) https://www.nature.com/articles/s41467-022-30639-3

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