

PhD research activity

2nd Annual progress report

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PhD cycle XXIX (start date: 14 February 2014)
PhD course Medical Sciences And Biotechnology
Locations Department of Health Sciences and Department of Translational Medicine (Novara - Italy)
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Supervisors

Aims

Develop an ad-hoc software suite that dynamically simulates the potential impact public health measures aiming at reducing the burden of chronic diseases in the population. The present project will be developed from the perspective of two study cases: a) primary and secondary prevention of cervical cancer consequent to carcinogenic Human Papilloma Virus (HPV) infection, and b) implementation of tobacco control measures. The models developed for the present project will be based on high-performance programming, i.e. programmed using "low level" computing languages (e.g. C/C++), efficient data structures and algorithms, and advanced statistical methods/libraries (e.g. GNU Scientific Library [GSL]) and software (e.g. R).

Activity description

During this second year of my PhD I compared the current vaccination program for HPV infection in Sweden versus alternatives vaccination strategy using my transmission HPV model. This work related a collaboration with Karolinska Institute led to an article named *"Human Papillomavirus Vaccination of Boys and Extended Catch-up Vaccination: Effects on the Resilience of Programs"* published in July 2015. This article indicate the reduction attributable to vaccination of HPV16/18 prevalence by vaccination strategy but above all what happens in case of a temporary drops in vaccination coverage (halved for 2 or 5 years). Alternative vaccination strategies that we tested provided more resilient than current national Swedish program, we found a clear evidence that the inclusion of males increased resilience of vaccination program. During this second PhD year I also contributed to two other articles not yet published. The first one is related to a project that want estimate, using a transmission model of HPV16 infection, the potential impact of a population's sexual behaviour on the age-specif prevalence of the infection and whether it may influence the effectiveness of HPV vaccination programmes. This report shows for the first time that a population's sexual behaviour, instead to a reactivation of HPV infection, helps to explain the different age-specif HPV prevalence observed across different world population.

Furthermore, there is another submitted article related to a collaboration with Rwandan Ministry of Health with the purpose to acquire data from HPV prevalence and determinants (HIV status, number of sexual partner, sex for money,...). Rwanda is the first African country to have implemented a national HPV vaccination programme. This country as many sub-Saharan African countries, cervical cancer represents by far the most common cancer among females and our study is setting a robust baseline for future evaluations of vaccine impact.

Over this second year of my PhD I created a new compartmental,

dynamic, population-based model that is able to simulate cervical cancer progression and screening strategies. This new model start from an dump (photography) of HPV prevalence distribution by age and by time since infection. Eventually this source data can be dynamic over the time in order to handle a changing in sexual behaviors with a different HPV prevalence. We are able to create a pipeline between our previous infection model and this new one or use a specific HPV distribution provides by each countries. This model is able to manage different screening categories, useful to simulate the propensity of various people to undergo at screening tests. The next step is use this model in order to identify best cervical cancer strategies to optimize the combination of vaccination and screening.

Lastly, there is another model related transmission HPV that I created in this second year. Aim of this new one is to separate vaccinated cohort to unvaccinated cohort with the purpose to model an ad-hoc screening programme for these two category.

Attended seminars

- 10/11/2014; IARC Lyon; Prof. Henrik Møller; Prostate cancer incidence, clinical stage and survival in relation to obesity: a prospective cohort study in Denmark;
- 09/12/2014; IARC Lyon; Dr François Fuks; Cancer Epigenetics & Epigenomics are Coming of Age;
- 11/12/2014; IARC Lyon; Prof Andreas Stang; Epidemiologic insights into causes of testicular cancer;
- 13/01/2015; IARC Lyon; Dr. Michail Fragkos; DNA replication enters the world of RNA: non-coding RNA as a tool to treat cancer;
- 29/01/2015; Faculté de Médecine Lyon; Dr Nicolas Voirin; Modélisation de l'exposition aux maladies infectieuses;

- 24/02/2015; IARC Lyon; Dr Silvia Franceschi & Dr Salvatore Vaccarella; Increased incidence of differentiated thyroid carcinomas - an epidemic of diagnosis or an epidemic of disease?
- 24/02/2015; IARC Lyon; Dr Caroline Relton; Causal inference in epigenetic epidemiology - defining the role of DNA methylation in disease prediction, prevention and treatment;
- 27/02/2015; IARC Lyon; Dr Peter Mulligan; Epigenetic Regulatory Complexes in Development and Cancer
- 24/03/2015; IARC Lyon; Prof Steve Horvath; Epigenetic clock and biological age
- 28/04/2015; IARC Lyon; Dr Isidro Sánchez-García; The Etiology of Childhood Leukaemia
- 12/05/2015; IARC Lyon; Prof Jessica Zucman-Rossi; Sequencing liver tumors: mechanism of malignant transformation, therapeutic targets and signatures of exposition
- 08/06/2015; A.O.U. Citta della Salute e della Scienza di Torino; Dr.ssa Silvia Franceschi; Tiroide: epidemia di tumori o di diagnosi?
- 08/09/2015; IARC Lyon; Dr Rosa Karlić; Using chromatin organization to predict cancer cell-of-origin

Attended meeting/workshop

- 03/11/2014; Torino, A.O.U. Città della Salute e della Scienza di Torino; Programma Regionale di Screening per il Cervicocarcinoma "Prevenzione Serena"
- 05/12/2014; IARC Lyon; Round table related modelling project with London School of Hygiene & Tropical Medicine (LSHTM);
- 20/02/2015; Novara, Università Piemonte Orientale; Riunione rete sanità pubblica
- 26-27/01/2015; IARC Lyon; Quinquennial Review Panel for Section of Infections (INF)

- 26/03/2015; IARC Lyon; WHO: The Global Hepatitis Programme;
- 29/07/2015; Novara, Università Piemonte Orientale; Riunione della "rete di epidemiologia" del quadrante NE del Piemonte

Scientific Congress: 30th International Papillomavirus Conference & Clinical and Public Health Workshops (HPV 2015), Lisbon Portugal - September 17-21, 2015.

- Lazzarato F, Elfström K.M., Franceschi S, Dillner J, Baussano I; Gender-neutral HPV vaccination and extended catch-up vaccination: effects on the resilience of programs;
- Baussano I, Lazzarato F, Franceschi S; HPV transmission modelling in the international hpv faster consortium;
- Brisson M, Bénard É, Drolet M, Baussano I, Berkhof J, Boily M-C, Canfell K, Chesson H, Jit M, Vänskä S, Bogaards J, Burger E, Choi Y, De Blasio B, De Vlas S, Guzzetta G, Hontelez J, Horn J, Jepsen M, Kim J, Lazzarato F, Matthijsse S, Mikolajczyk R, Pavelyev A, Pillsbury M, Shafer LA, Smith M, Tully S, Turner H, Usher C; Population-level impact, herd immunity and elimination after HPV vaccination: A systematic review & Meta-analysis of predictions of 16 transmission-dynamic models.

Publication with affiliation: Department of Translational Medicine, University of Piemonte Orientale Avogadro, Novara, Italy

- Elfström KM*, Lazzarato F*, Franceschi S, Dillner J, Baussano I. (2015) Human papillomavirus vaccination of boys and extended catch-up vaccination: Effects on the resilience of programs. J Infect Dis. 2015 Jul 3; (* KM.E. and F.L. contributed equally to this work)

Other submitted publication:

- Baussano I, Lazzarato F, Brisson M, Franceschi S; Human Papillomavirus Vaccination at a time of changing sexual behaviors (to Emerging Infectious Diseases)
- Ngabo F, Franceschi S, Baussano I, Umulisa C, Snijders P, Lazzarato F, Tenet V, Gatera M, Binagwaho A, Clifford G; Human papillomavirus infection in Rwanda at the moment of implementation of a national HPV vaccination programme (to International Journal of Cancer)

Torino, 25 September 2015

Lazzarato Fulvio

A handwritten signature in black ink that reads "Lazzarato Fulvio". The signature is written in a cursive style and is placed on a light-colored rectangular background.