PROPOSAL INTERNSHIP  
[26/11 / 2015]

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<tr>
<td>Title of research/project</td>
<td>Estimating the adenoma dwell time from doubly censored data.</td>
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**Short description of research proposal**

**Scientific background of research**

With over 1.3 million incident cases and almost 700,000 deaths worldwide in 2012, colorectal cancer (CRC) is a serious health problem, especially in developed countries[1]. CRC has a long preclinical course and therefore, is an excellent target for population screening.

The duration from a precursor lesion, i.e. an adenoma, to CRC is unknown. This adenoma dwell time is an important parameter in determining the optimal screening strategy and strongly influences projected screening effectiveness[2]. Since adenomas are removed upon detection, it is not possible to observe the adenoma dwell time. However, cross-sectional data can be used to infer this dwell time, as has been demonstrated in the case of cervical cancer[3]. A challenge in using cross-sectional data to estimate the adenoma dwell time is to account for left censored data. That is, the exact moment of development of adenomas and CRC is not observed.

**References**


### Research question/ Aim of research

To estimate the duration from a small adenoma to an advanced adenoma and from an advanced adenoma to clinically detected colorectal cancer.

### Research methods and design

A statistical model will be set up describing the disease process from adenoma initiation and adenoma growth to the development of colorectal cancer. Age-specific adenoma incidence will be modeled assuming either a constant hazard or a slightly increasing hazard. The duration from small to advanced adenomas will be modeled with a negative exponential distribution. Adenomas will be assumed not to regress in size. Duration between advanced adenomas and CRC will be modeled using a mixture of gamma distributions, to take into account the likely existence of slow versus fast progressing advanced adenomas.

Data for model estimation will come from the colonoscopy arm of the Dutch COCOS trial. This source will provide input on the prevalence of small and advanced adenomas in individuals aged 50 to 75 years old. It will be assumed that the prevalence is zero at age 20 and increases from that age onwards. Data on the prevalence of CRC will be obtained from the Dutch cancer registry. The statistical model will take into the account the left-censored nature of the data.

### Work to do

- Set up the data for modeling fitting
- Build the statistical model in R
- Estimate the parameters of the model using Monte Carlo simulation methods.

### Expected result

This study will estimate the duration from small to advanced adenoma and from advanced adenoma to colorectal cancer. The estimated durations will be used as an input for an existing colorectal cancer screening model; ASCCA<sup>4</sup>. The ASCCA model is used to predict the effectiveness and cost-effectiveness of CRC screening. Since the durations between disease stages are important parameters in these models, the results of this study will lead to more accurate predictions of the impact of screening. The final product of this study will be a scientific article concerning the estimation of the duration from adenoma initiation to CRC.

### Time Schedule

The internship will last 6 months.

### Competences needed

- Statistical modeling
- Data analysis
- Monte Carlo simulation for parameter inference.

### Further information

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