SGIM Foundation
Solothurnerstrasse 68
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Project Funding 2014/2015 «OVERDIAGNOSIS»

The award of CHF 50'000.-- is granted to the following project:

Risk-stratified prostate cancer screening: Development of a risk score for informed decision-making and preventing overdiagnosis in primary health care

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Abstract

Project summary
Early detection and treatment of prostate cancer are the goals of PSA screening. However, PSA screening is associated with overdiagnosis of prognostically irrelevant tumours. Otherwise healthy men will suffer from erectile dysfunction and incontinence associated with biopsies and unnecessary treatments, and from emotional distress associated with being labelled with a cancer diagnosis. Ideally, screening should detect only clinically significant prostate cancers, which will eventually lead to distant metastasis or death due to prostate cancer, without creating overdiagnosis. If men can be stratified according to their risk of developing distant metastases or death due to prostate cancer, and the decision to undergo or repeat PSA screening is based on an understanding 01 the risk 01 developing clinically significant prostate cancer, the problem of overdiagnosis and overtreatment may be reduced.

We propose to develop a clinical risk score based on patient history, which quantifies the long-term risk of developing clinically significant prostate cancer that will lead to distant metastases or death. The score can be used as a basis for discussion of PSA screening with patients and combined with subsequent information from digital rectal examination and PSA screening (if the patient decides to have it performed) to derive a more definite estimate of the long-term risk 01 suffering from distant metastases or death due to prostate cancer. Men at low risk, an estimated 50 to 80% of the male population, could be advised not to undergo PSA

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screening ever (again), which could in turn strongly reduce the risk 01 overdiagnosis.

We will develop a clinical risk score based on risk factors such as family history, ethnicity, age, BMI, smoking and other factors using high quality data from the randomized Prostate, Lung Colorectal, and Ovarian (PLCO) Cancer Screening Trial. We will fit univariable Cox regression models to identify clinical characteristic variables that are associated with the outcomes and then multivariable Cox regression models based on a hierarchical step-wise backward selection 01 risk factors.

Recent research has shown that early and once-only measured PSA concentration may be a reliable predictor for clinically significant prostate cancer later in life. By analysing the PLCO dataset, we will try to replicate the approach of once-only PSA screening in males with low PSA levels at the initial test.

We will calculate sensitivity, specificity, positive predictive value, negative predictive value, as well as positive and negative likelihood ratios by using Cox regression models and logistic regression models by estimating the area under the curve for ail outcomes in relation to different PSA concentrations and age. To test whether results of digital-rectal examination and the clinical risk score can add to predictions of distant metastases and death, these are also integrated into calculations.

If successful, the risk score in combination with results from digital rectal examination and PSA testing, if available, and can be used a decision-making tool to decide upon future PSA testing. It has the potential 01 significantly reducing overdiagnosis and associated overtreatment.