

# Prostate Cancer Screening

## – Aspects of Overdiagnosis

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs

universitet, kommer att offentligen försvaras i sal Hjärtats aula,

Vita stråket 12 Sahlgrenska Universitetssjukhuset, onsdagen den 10 december 2014 kl. 13:00

av

Rebecka Arnsrud Godtman

Fakultetsopponent:

Professor Per-Anders Abrahamsson

Institutionen för kliniska vetenskaper, Lunds Universitet, Lund

Avhandlingen baseras på följande arbeten:

- I. **Godtman R**, Holmberg E, Stranne J, Hugosson J. High accuracy of Swedish death certificates in men participating in screening for prostate cancer: a comparative study of official death certificates with a cause of death committee using a standardized algorithm. *Scand J Urol Nephrol*. 2011;45(4):226-32.
- II. **Arnsrud Godtman R**, Holmberg E, Khatami A, Stranne J, Hugosson J. Outcome following active surveillance of men with screen-detected prostate cancer. Results from the Göteborg randomised population-based prostate cancer screening trial” *Eur Urol*. 2013;63(1):101-7.
- III. **Arnsrud Godtman R**, Holmberg E, Lilja H, Stranne J, Hugosson J. Opportunistic testing versus organized prostate-specific antigen screening, outcome after 18 years in the Göteborg Randomised Population-Based Prostate Cancer Screening Trial. *Submitted*
- IV. **Arnsrud Godtman R**, Carlsson S, Holmberg E, Stranne J, Hugosson J. Age at termination of screening – the most important risk factor for (over) diagnosis in screening for prostate cancer. Results from the Göteborg Randomised Population-based Prostate Cancer Screening Trial. *In manuscript*.



UNIVERSITY OF GOTHENBURG

Göteborg 2014

# Prostate Cancer Screening

## -Aspects of Overdiagnosis

Rebecka Arnsrud Godtman

Department of Urology, Institute of Clinical Sciences  
Sahlgrenska Academy at University of Gothenburg  
Göteborg, Sweden

### ABSTRACT

The overall aim of this thesis is to explore aspects of overdiagnosis, i.e. the diagnosis of a tumor that in the absence of screening would never have been diagnosed, in prostate cancer (PC) screening. The four papers in this thesis all emerge from the Göteborg randomized population-based PC screening trial, in which 10,000 men were invited to biennial prostate-specific antigen (PSA)-screening between 1995 and 2014 and 10,000 non-invited constituted a control group. In paper I, the accuracy of cause of death (COD) certificates, for men with PC, is evaluated by comparison with the COD as assigned by an independent committee after blinded review of medical records. Paper II assesses outcomes for men with screen-detected PC managed with, so called “active surveillance”. In paper III, organized screening is compared with opportunistic screening with respect to effectiveness in reducing PC mortality, measured as the number needed to invite (NNI) to screening and overdiagnosis, measured as number needed to diagnose (NND) to prevent one man from dying from PC. Paper IV investigates the risk of being diagnosed with PC depending on age at screening and the number of screens. The overall agreement between COD certificates and the committee was 96%. A large proportion of men screen-detected PC has low-risk PC (60%) and could safely be managed with active surveillance, at least with intermediate follow-up. Organized screening was more effective in reducing PC mortality and was associated with less overdiagnosis than opportunistic screening (NNI 139, NND 13 versus NNI 493, NNI 23). The risk of being diagnosed with PC increased dramatically with age but there was no apparent relation to the number of screens. From this thesis it can be concluded that Swedish COD certificates have a high accuracy and can be used for COD determination for men with PC, at least in the age-range studied (50-64 years old at the start of screening). Active surveillance appears safe for men with low-risk PC and should be used as a treatment strategy in order to reduce overtreatment. In order to reduce overdiagnosis and improve the benefit harm ratio of PC screening, screening should be conducted within the frameworks of an organized program where “younger” men could be screened relatively intense but where “older” men are screened more selectively.

**Keywords:** active surveillance, age, cause of death, opportunistic, organized, overdiagnosis, prostate cancer, prostate-specific antigen, risk factors, screening, screening interval