

# Prostate Cancer Screening: Outcomes and Risk Prediction

Avdelningen för urologi, kliniska vetenskaper vid Sahlgrenska akademien

Göteborgs Universitet

## AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien vid Göteborgs Universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Sahlgrenska Akademien, Göteborg, fredagen den 18 januari 2019, kl 9:00

av

*Maria Frånlund, leg läkare*

### Fakultetsponent:

Docent Lars Henningsohn, Institutionen för klinisk vetenskap, Karolinska institutet, Stockholm

Avhandlingen baseras på följande delarbeten:

- I. **The absence of voiding symptoms in men with a prostate-specific antigen (PSA) concentration of  $\geq 3.0$  ng/mL is an independent risk factor for prostate cancer: results from the Gothenburg Randomized Screening Trial**  
Maria Frånlund, Sigrid Carlsson, Johan Stranne, Gunnar Aus and Jonas Hugosson.  
*BJU Int.* 2012 Sep;110(5):638-43. doi: 10.1111/j.1464-410X.2012.10962.x.
- II. **Prostate cancer risk assessment in men with an initial PSA below 3 ng/mL: results from the Göteborg randomized population-based prostate cancer screening trial**  
Maria Frånlund, Rebecka Arnsrud Godtman, Sigrid Carlsson, Hans Lilja, Marianne Måansson, Johan Stranne and Jonas Hugosson *Scand J Urol.* 2018 Sep 21:1–7. doi: 10.1080/21681805.2018.1508166 [Epub ahead of print]
- III. **Improving Prostate Cancer Screening: 22-Year Follow-up in a Randomized Trial**  
Maria Frånlund, Marianne Måansson, Rebecka Arnsrud Godtman, Gunnar Aus, Erik Holmberg, Pär Lodding, Carl-Gustav Pihl, Johan Stranne, Hans Lilja and Jonas Hugosson (*submitted*)
- IV. **Prostate Cancer Risk after Stop Age in Men Participating in a Long-Term Screening Programme: Results from the Göteborg Randomised Population-Based Screening Trial**  
Maria Frånlund, Marianne Måansson, Rebecka Arnsrud Godtman, Anna Grenabo, Johan Stranne, Hans Lilja and Jonas Hugosson (*in manuscript*)

# Prostate Cancer Screening: Outcomes and Risk Prediction

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## ABSTRACT

The Göteborg Randomized Population-Based Prostate Cancer (PC) screening trial was started in 1995 to evaluate prostate-specific antigen (PSA) screening and its long-term impact on PC-specific mortality and PC incidence. The four papers included in this thesis present the outcomes of PSA-based screening and also describe aspects of the risk of PC at initial screening, during the 22-year follow-up of the programme, and after termination of screening.

In this trial, 10,000 men born 1930–1944 were randomized and thereafter invited to PSA screening every second year from 1995 to 2014. An additional 10,000 men were randomized to the control group (i.e., not invited). The complete incidence of PC was ascertained by linkage to the Swedish Cancer Register and the Swedish Population Register. All relevant medical documentation was retrieved continuously for every man with PC. In our first study (**Paper I**), we investigated whether men with an elevated PSA level ( $\geq 3$  ng/mL) and voiding symptoms were at higher risk of PC; the results showed no association between such symptoms and an increased risk of PC. Thereafter (**Paper II**), we evaluated the long-term outcome in men with an initial PSA of  $< 3$  ng/mL. We concluded that men died from PC despite “normal” baseline PSA and regular participation in the programme. Baseline PSA was strongly associated with long-term PC risk. Free-to-total PSA had no additive value to PSA in this PSA range.

In our third study (**Paper III**), we assessed PC mortality and incidence in the screening and the control group after 22 years of follow-up, which showed that screening reduced PC-specific mortality by 29%. The absolute risk reduction has increased over the years, and the number needed to diagnose is now 9, which is an all-time low (NND=9). High risk of PC death was found in men who did not attend to the programme, men who started testing after the age of 60, and men who had a long life expectancy and terminated screening too early. **Paper IV** describes our evaluation of outcomes in men who stopped PSA screening after the age of 67–70. We found that participants with a PSA  $> 1.5$  ng/mL (at their final screen) had a non-negligible risk of a future Gleason score of  $\geq 7$  cancer, and later PC death. Notably, approximately 80% of these cases could have been detected and additional PC deaths prevented, if less than half of all men in the cohort had been offered additional testing (or other diagnostics).

**Keywords:** prostate cancer, screening, prostate-specific antigen, mortality, prediction

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