Structured chain when testing for prostate cancer shortens lead times

UPDATED EXPERIENCES FROM CAPIO ST. GÖRAN'S HOSPITAL SHOW ACCURATE DIAGNOSTICS AND GOOD HEALTH ECONOMY

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Each year, approximately 10,000 men in Sweden are affected by prostate cancer, of which approximately 2,000 die from the disease. Prostate cancer detected early is often curable, while late detection is associated with a poor prognosis. It is estimated that almost half a million PSA tests are performed annually in Sweden in order to detect prostate cancer early [1].

In 2018, we reported in Läkartidningen preliminary results from our model for early diagnostics at Capio St. Göran's Hospital. Much has happened since then. Two well-designed Swedish studies have shown that MRI and targeted tissue samples should be part of a modern chain of care for prostate cancer [2, 3]. Transperineal tissue sampling is now recommended in international guidelines to minimize risk of infection [4], and since 2022 the EU recommends member states to evaluate organised screening for prostate cancer [5]. Several Swedish regions have also started organised prostate cancer testing, which means that healthcare resources can be used more efficiently.

Despite progress, there are still major problems in current diagnostics. Availability and quality are variable, and organised prostate cancer testing still only covers a very small portion of diagnostics. Furthermore, there is a shortage of resources in urology, radiology and pathology, which results in long waiting times within standardised care processes for prostate cancer.

Here we describe our experiences of a structured and coherent model for early detection of prostate cancer that has been established at Capio St. Göran's Hospital. It is our hope that it can be a source of inspiration for ensuring equal care in Sweden and that we can make the best use of our limited resources.

In order to improve the possibility of early detection and at the same time avoid unnecessary MRI examinations and biopsies, our model uses the Stockholm3 test as a reflex test after PSA. The Stockholm3 test is, like the PSA test, a regular blood test.

KEY MESSAGE

- The Prostate Cancer Centre at Capio St. Göran's Hospital has implemented a model for structured and coherent prostate cancer diagnostics since 2017.
- The model utilises nurse-led diagnostics, the Stockholm3 test and magnetic resonance imaging (MRI) with targeted perineal tissue sampling.
- The model results in short lead times, high precision in diagnostics and good health economics.

Unlike the PSA test, which measures one protein marker, the Stockholm3 test combines more than 100 protein markers as well as genetic and clinical markers to calculate the risk of clinically significant prostate cancer (Gleason score 7 or higher). The Stockholm3 test has been tested in several major studies, indicating that it can reduce the risk of unnecessary MRI examinations, biopsies and treatments, while more cancers requiring treatment can be identified early compared to PSA [3].

The Capio St. Göran model

Capio St. Göran's Hospital has been commissioned by Region Stockholm to provide around 25 percent of prostate cancer care in Stockholm, which corresponds to about 500 new prostate cancer cases per year. In 2017, the Prostate Cancer Centre was established at Capio St. Göran's Hospital with the aim of providing cost-effective prostate cancer diagnostics using new diagnostic methods and efficient and structured processes.

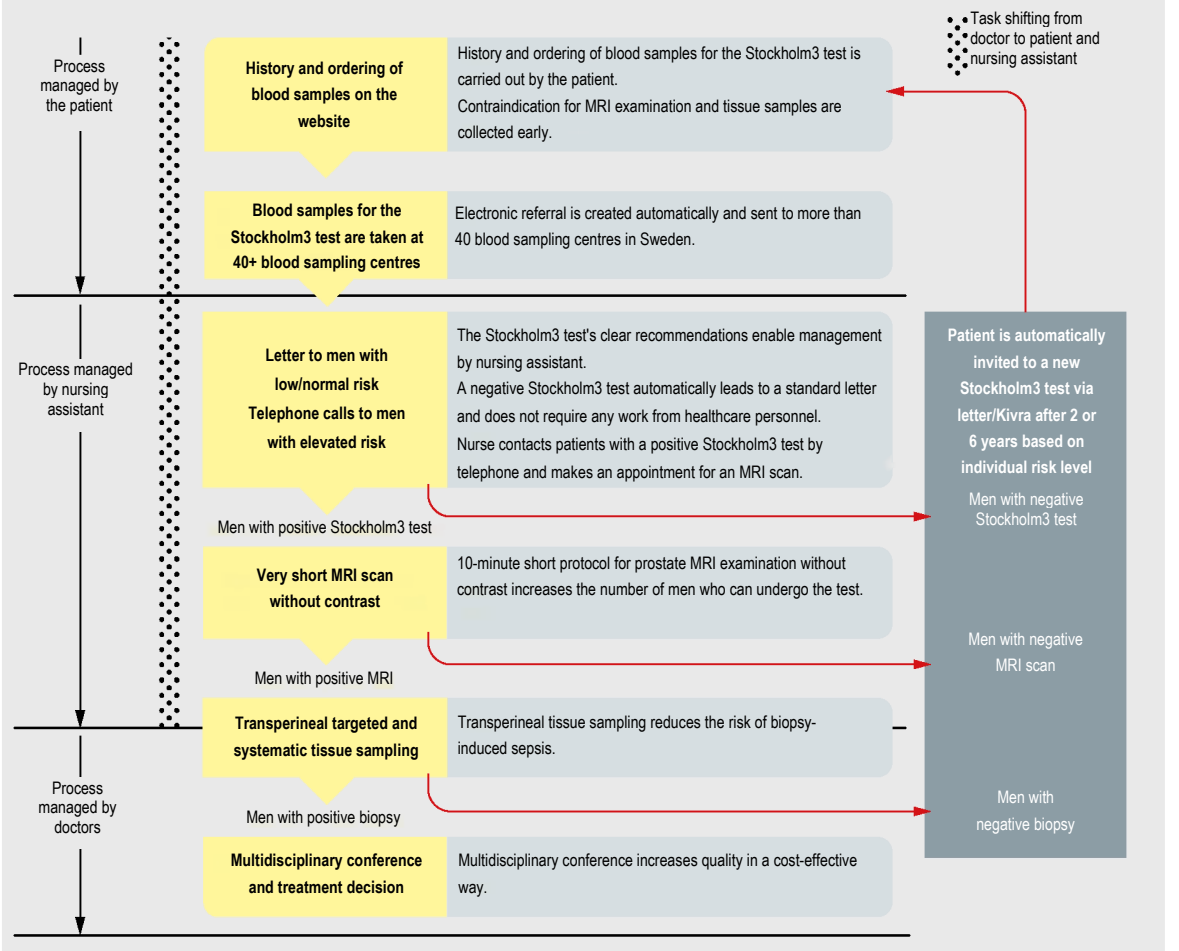
'To improve the possibility of early detection and at the same time avoid unnecessary MRI examinations and biopsies, our model uses the Stockholm3 test as a reflex test after PSA...'

The project has been reviewed and approved by the Swedish Ethical Review Authority.

Based on available knowledge, we have chosen to build a diagnostic chain structured as follows (Figure 1):

- Men between the ages of 45 and 75 who have not previously been diagnosed with prostate cancer and want to be tested are referred from the health centre or referred to the Prostate Cancer Centre's website.
- The man logs on to the website with mobile bank ID and creates his referral for testing. He answers questions about previous prostate cancer diagnosis (which leads to exclusion), reads information about the pros and cons of early diagnosis of prostate cancer and answers questions about co-morbidity and factors for the analysis of the Stockholm3 test.

FIGURE 1. **The Capio St Göran's model for prostate cancer diagnostics uses task shifting from doctor to nursing assistant and new diagnostic innovations with higher precision and digitisation**

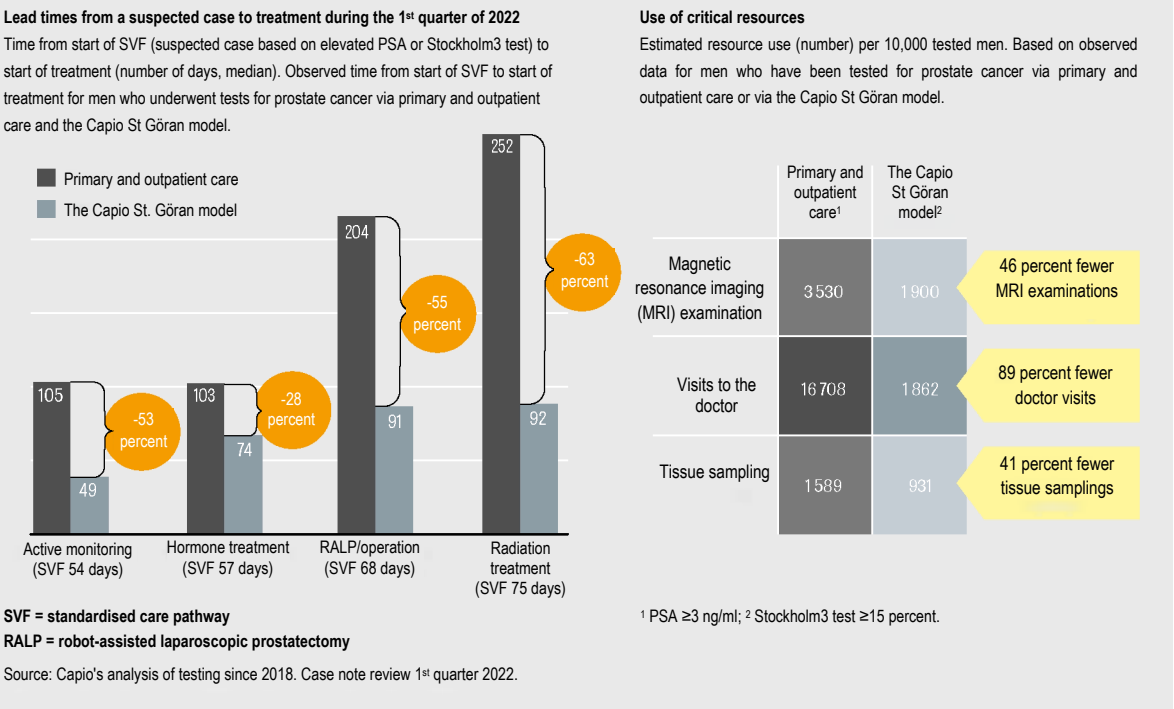


- The man provides a blood sample for analysis by the Stockholm3 test at one of Unilab's blood centres. The blood sample is first analysed for PSA. If the value is greater than 1.5 ng/ml, an analysis using the Stockholm3 test is automatically carried out on the same blood sample. This reflex analysis saves time for the patient while minimising healthcare costs. In the event of a significantly elevated PSA (>40 ng/ml), the patient is immediately fast-tracked for diagnostics within a week.
- Men with normal results on the Stockholm3 test receive information about when follow-up blood tests should take place sent home in a letter. The letter is generated automatically and does not require any work by healthcare professionals. Depending on the results from the PSA test and Stockholm3 test, follow-up after 2 or 6 years is recommended. The diary system automatically activates a reminder for the man to make contact after the recommended time interval.
- Men with an elevated result on the Stockholm3 test are contacted by a nurse by phone who books them in for a 10-minute MRI scan. This contains T2-weighted axial and sagittal as well as functional diffusion-weighted series without the addition of contrast.

The MRIs are classified in accordance with PI-RADS (Prostate imaging reporting and data system) version 2.1, and any abnormalities with PI-RADS (≥3) are segmented by the radiologist in the MIM software, which is used in BK Medical's ultrasound machines for MRI guided fusion biopsies.

- Men with a negative MRI (PI-RADS ≤2) receive a letter informing them of the result and that a follow-up blood test with the Stockholm3 test should be carried out in 2 years. They also receive an automatic reminder to take the test.
- Men with suspicious changes on MRI (PI- RADS ≥3) are contacted by a nurse by phone who books the man in for transperineal tissue sampling with MRI/fusion technology (BK Medical). Men with suspected tumour findings (PI-RADS 4-5) undergo both targeted and systematic tissue sampling, while men with more uncertain findings (PI-RADS 3) only undergo targeted tissue sampling to minimise the risk of overdiagnosis.
- All men who provided tissue samples are discussed in a multidisciplinary video conference, where decisions are made on treatment recommendations.

FIGURE 2. Lead times from a suspected case to treatment as well as use of resources for the Capio St. Göran model compared to the current clinical procedure in Stockholm with primary and outpatient urology.



- Men who have provided a tissue sample receive feedback from the urologist in charge. If the tissue sample is negative, feedback is given by phone, but if there are signs of cancer or if there are special circumstances, a physical meeting is arranged.

Medical results

We have compiled results from 16 May 2018 to 31 December 2021. Of 5,439 men tested, 29 percent (n = 1,592) underwent an MRI scan. In comparison, 35 percent (n = 1903) of the men had a PSA ≥3 ng/ml, illustrating that the use of the Stockholm3 test in addition to PSA testing reduces the number of MRI examinations.

47 percent (n = 744) of the men who underwent MRI were recommended tissue sampling.

In 56 percent (n = 414) of men with suspected findings on MRI, clinically significant prostate cancer was identified, while only 12 percent (n = 88) had low-grade prostate cancer (Gleason score 6). This means that roughly 8 percent of the men who underwent testing at the Prostate Cancer Centre were diagnosed with clinically significant prostate cancer. Unfortunately, there are no Swedish studies to compare with.

155 men with an elevated result in the Stockholm3 test had a negative PSA test (1.5-3 ng/ml). Of these, 75 men (48 percent) had a clinically significant prostate cancer on biopsy.

Continuous improvements based on new research

It is well known that transrectal tissue sampling of the prostate is associated with a risk of urosepsis [7]. Since 2019, we have therefore completely switched to transperineal tissue samples with local anaesthesia, which is now recommended internationally, and we expect that Swedish guidelines will soon do the same.

We have now also excluded routine antibiotic use during prostate biopsy and despite this only registered 3 cases of associated urosepsis (<0.5 percent).

In August 2021, the results of the STHLM3 MR study with 12,750 participants were presented in Lancet Oncology [3]. Based on these new research findings, since January 2022 the Prostate Cancer Centre uses the Stockholm3 test ≥15 percent as the cut-off point for further management with MRI.

Shorter lead times and better utilisation of resources

We have conducted a medical record review of all men who were diagnosed and treated at Capio St. Göran's Hospital during the period 1 January to 31 March 2022. In total, we have reviewed 218 patients, approximately half of whom have come via referral with established prostate cancer for treatment. Based on this review, we can compare lead times, resource utilisation and health economics in the Capio St. Göran model with traditional diagnostics initiated in primary care.

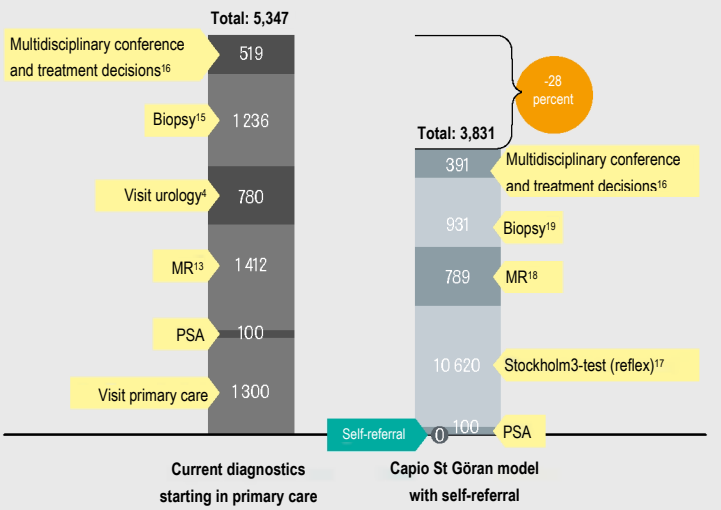
Compared to today's clinical procedure, with visits to primary care, the urologist and hospital, the Capio St. Göran model leads to the average times for standardised care processes, from suspected case (elevated PSA or Stockholm3 test) to treatment, being reduced by 53 percent for active monitoring, 28 percent for hormone therapy, 55 percent for surgery, and 63 percent for radiation therapy (Figure 2). This is also reflected in a report from the National Prostate Cancer Registry which compares the proportion of patients receiving PAD notification within 11 days of tissue sampling.

FIGURE 3. Costs for the Capio St. Göran model compared to today's clinical procedure

Input data and costs

Proportion PSA ≥1.5 ng/ml[1]	60 percent
Proportion PSA ≥3 ng/ml[1]	35.3 percent
Proportion Stockholm3 test ≥15 percent [1]	19 percent
Proportion positive MR PSA [2]	35 percent
Proportion positive MR Stockholm3 test[1, 3]	49 percent
Proportion high-risk cancer[1, 4]	20 percent
Visit primary care[5]	SEK 1,300
Visit urologist[6]	SEK 3,400
Management nurse[7]	SEK 150
Analysis PSA[8]	SEK 100
Analysis Stockholm3-test[9]	SEK 2,700
Magnetic resonance imaging (MRI)[10]	SEK 4,000
Biopsy and pathology[11]	SEK 10,000
Multidisciplinary conference[12]	SEK 4,000
Treatment decision[6]	SEK 3,400

Expected cost of diagnostics per person tested, SEK



▶ [1] Observed proportion in men tested at Capio St. Göran's Hospital. Breakpoint Stockholm3 test ≥15 percent is used since January 2022. [2] Proportion of positive MRI (PI-RADS ≥3) if only PSA is used. Data based on the Göteborg 2 study [2]. [3] Proportion of positive MRI (PI-RADS ≥3) if PSA followed by Stockholm3 test is used as a reflex. [4] Proportion of men with high-risk prostate cancer in biopsy. [5]Visits to primary care = doctor's monthly salary x wage cost surcharge x 'overhead' / (number of patients/day x 20 days/month) = 80,000 x 1.5 x 1.3 / (6 x 20) = SEK 1,300/visit. [6] Price list in Region Stockholm for visits to a urologist in hospital. [7] Management nurse = monthly salary nurse x wage cost surcharge x 'overhead' / (number of patients per day x 20 days/month) = 30,000 x 1.5 x 1.3 / (20 x 20) ≈ SEK 150/patient. [8] Estimate based on price list at Karolinska University Laboratory including sampling cost. [9]Price list A3P Biomedical. [10]Estimate based on price proposals from private radiology. [11]Estimate based on price list at urology at Region Stockholm and price list at Karolinska University Laboratory for handling and review of biopsy specimens. [12]Price list Region Stockholm for multidisciplinary conference in high-risk cancer. [13]Men with PSA ≥3 ng/ml. [14] Men with positive MRI based on PSA. [15]Only men with negative MRI (= 1 - proportion of positive MRI based on PSA). Men with a positive MRI see a urologist for a biopsy. [16]Men with positive MRI based on PSA. Men with high-risk cancer conduct multidisciplinary conference. All men see a urologist to obtain biopsy results. [17]Men with PSA ≥1.5 ng/ml. [18]Men with Stockholm3 test ≥15 percent. [19]Men with positive MRI based on Stockholm3 test.

The national average is 11 percent and the average for all hospitals in Stockholm is 17 percent, while Capio St. Göran's Hospital tops the list with 57 percent [8].

At the same time, resource utilisation decreased. In an analysis where we calculate resource needs based on 10,000 tested patients, resource utilisation was reduced by 46 percent for MRI, 89 percent for visits to the doctor and 41 percent for tissue sampling in the Capio St. Göran model compared to today's clinical procedure in Stockholm (Figure 2).

The Capio St. Göran model saves money

It is important that new care processes are introduced in a manner that is reasonable in terms of health economics. We have carried out a comprehensive evaluation of the healthcare system's direct costs for diagnostics up to treatment decisions. We have evaluated 2 different strategies:

- Strategy 1 mimics clinical procedure in Sweden. We have assumed that men with positive PSA (≥3 ng/ml) undergo MRI. Process-wise, this strategy begins with the patient seeing a general practitioner at a health centre when a first PSA sample is taken. Patients with elevated PSA (≥3 ng/ml) are referred to MRI and a urologist in hospital followed by targeted and systematic tissue sample tests if positive.
- Strategy 2 is the Capio St. Göran model and involves taking a Stockholm3 test as a reflex for PSA ≥1.5 ng/ml. Men with a positive Stockholm3 test (≥15 percent) undergo MRI. In terms of process, this strategy begins with the man himself creating a referral to Stockholm3 sampling. Logistics and administration are handled here by nurses up until the tissue sampling.

The health economy analysis indicates that the cost is lower with the Capio St. Göran model and that the diagnostic costs can be reduced by 28 percent for each man tested compared to the current clinical procedure based on the primary care physician. The reason for the lower cost is to avoid unnecessary visits to the primary care physician and urologist, unnecessary MRI examinations and unnecessary tissue samples (Figure 3).

Discussion

There is consensus that early diagnosis in an organised screening programme reduces prostate cancer mortality, but also that early diagnosis is associated with widespread diagnosis of harmless tumours (overdiagnosis) and complications caused by investigation and treatment (infections, treatment-induced incontinence and impotence). It is therefore important that diagnostics are improved.

We illustrate here a model in which more than half of the men biopsied have Gleason score 7, that is, a clinically significant prostate cancer, while the number of men with small non-treatment-requiring cancer is low.

The Capio St. Göran model is one of several possible strategies to improve prostate cancer diagnostics.

»We have shown here that in a structured and cohesive care chain it is possible to introduce important improvements continuously and in a short time.«

An example is using PSA and MRI without the addition of other blood tests [2]. Another example is the model introduced in Region Värmland's programme for organised prostate cancer testing, where the Stockholm3 test is used as a reflex for men with PSA >3 ng/ml. Additional options include combining PSA with prostate volume measurement (PSA density) or using alternative blood tests such as the 4K score, which is being studied in the Finnish screening study, Proscreen. If you are considering introducing new tools into clinical procedure, we believe that it is important that the scientific support is sufficient, that resource utilisation is investigated and that a health economic evaluation is carried out. Several of the proposed alternatives still fall short in this regard.

Read more!
English summary at Läkartidningen.se

Healthcare is constantly evolving. We have shown here that in a structured and cohesive care chain it is possible to introduce important improvements continuously and in a short period of time. For example, we have introduced digitised processes with elements of automation, which saves resources. Other examples are task shifting from doctor to nurse, the introduction of a new blood test, MRI and the transition to perineal biopsies. Our experience shows that a structured care of men who wish prostate cancer testing in a coherent care chain, where PSA is combined with the Stockholm3 test and MRI followed by targeted perineal tissue sampling, is

- feasible
- associated with high sensitivity for detecting prostate cancer
- leads to a cost-effective use of healthcare resources.

The feedback from patients has been good spontaneously, and the comments we have received relate to good accessibility, clear recommendations and short lead times.

We are also very happy about the demand for our experience among our colleagues. Since 2017, we have received over 40 Swedish and foreign study visits, which have been highly appreciated.

In summary, at Capio St. Göran's Hospital, through task switching, use of new diagnostic innovations with higher precision and smart digitisation, we have created a simpler, better and more efficient flow for diagnostics, which has led to lower costs for the principal, better use of critical resources, earlier detection of prostate cancer, shorter treatment time and fewer side effects.

• Potential conflicts of interest: Henrik Grönberg and Tobias Nordström have shares in A3P Biomedical AB, which sells the Stockholm3 test.

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SUMMARY

Improved prostate cancer diagnostics with a structured pathway including »Stockholm3« test, MRI and targeted perineal biopsies

The Prostate Cancer Centre at Capio St. Göran's hospital is located in Stockholm and offers testing for prostate cancer. The pathway applies task shifting from doctors to nurses and new and innovative test methods, and leverages digitalisation opportunities to enable a cost-efficient pathway with high specificity and sensitivity. In this article, we describe our experiences of the Capio St. Göran Model.