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REVIEW

# The Study of Active Monitoring in Sweden (SAMS): A randomized study comparing two different follow-up schedules for active surveillance of low-risk prostate cancer

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**Abstract**

*Objective.* Only a minority of patients with low-risk prostate cancer needs treatment, but the methods for optimal selection of patients for treatment are not established. This article describes the Study of Active Monitoring in Sweden (SAMS), which aims to improve those methods. *Material and methods.* SAMS is a prospective, multicentre study of active surveillance for low-risk prostate cancer. It consists of a randomized part comparing standard rebiopsy and follow-up with an extensive initial rebiopsy coupled with less intensive follow-up and no further scheduled biopsies (SAMS-FU), as well as an observational part (SAMS-ObsQoL). Quality of life is assessed with questionnaires and compared with patients receiving primary curative treatment. SAMS-FU is planned to randomize 500 patients and SAMS-ObsQoL to include at least 500 patients during 5 years. The primary endpoint is conversion to active treatment. The secondary endpoints include symptoms, distant metastases and mortality. All patients will be followed for 10–15 years. *Results.* Inclusion started in October 2011. In March 2013, 148 patients were included at 13 Swedish urological centres. *Conclusions.* It is hoped that the results of SAMS will contribute to fewer patients with indolent, low-risk prostate cancer receiving unnecessary treatment and more patients on active surveillance who need treatment receiving it when the disease is still curable. The less intensive investigational follow-up in the SAMS-FU trial would reduce the healthcare resources allocated to this large group of patients if it replaced the present standard schedule.

**Key Words:** *Biopsy, patient selection, prostatic neoplasm, randomized clinical trial, watchful waiting.*

## Introduction

*Overdiagnosis and overtreatment of prostate cancer*

For the past 20 years, early diagnosis of prostate cancer has been based on a blood test for prostate-specific antigen (PSA). The widespread PSA testing of men without clinical symptoms or signs of prostate cancer has resulted in a dramatic increase in the incidence of the disease (Figure 1). It has been estimated that up to half of the prostate cancers detected after PSA testing are "overdiagnosed", i.e. would not

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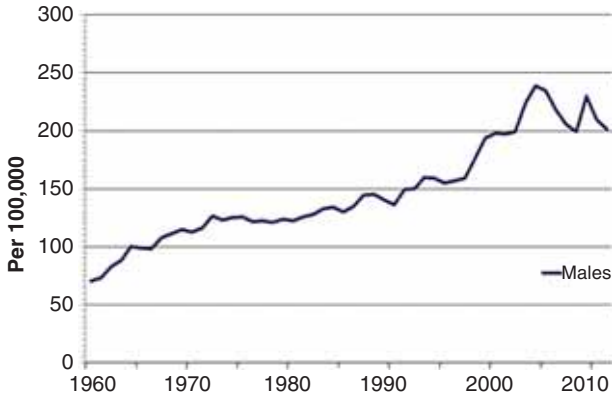


Figure 1. Age-standardized incidence of prostate cancer in Sweden. (From the National Board of Health and Welfare: Official Statistics of Sweden, Health and Medical Care, Cancer Incidence 2011.)

have caused clinical disease [1]. Many of these overdiagnosed prostate cancers are treated with surgery or radiotherapy, i.e. "overtreatment" [2]".

In Sweden, 28% of the prostate cancers diagnosed in 2011 were classified as low risk (T1–2, Nx/N0, Mx/M0, Gleason score ≤ 6 and PSA < 10 ng/l) [3]. For most men with low-risk prostate cancer treatment with curative intent causes side-effects and reduced quality of life without prolonging life. The disease-specific mortality of low-risk prostate cancer managed without curative intent is only 9% after 15 years, whereas the mortality from competing causes of death is 50% [4]. The randomized PIVOT study did not find even a trend towards a survival benefit from radical prostatectomy compared with watchful waiting for low-risk prostate cancer [5]. Is it ethical to harm so many men (with overdiagnosis and overtreatment) to prevent a few deaths from prostate cancer?

On a group level it is reasonable to manage all men with low-risk prostate cancer conservatively. However, some men with prostate cancer categorized as low risk harbour more aggressive cancer, which is not detected by the diagnostic biopsies [6–9]. The clinical challenge for urologists is to identify men with such cancers, as they can benefit from curative therapy, while sparing men with genuinely low-risk prostate cancer the side-effects of curative treatment. The best available method for doing so is active surveillance with selective, delayed intervention with curative intent for men with signs of progressive disease. The follow-up during active surveillance is based on repeated PSA tests, digital rectal examination (DRE) and prostate biopsies, although the protocols vary somewhat between different institutions [10].

The aim of this article is to describe the rationale, design and setting of a prospective study on active surveillance.

*Present experience of active surveillance*

Four large cohort studies have been published [11–14]. The results are remarkably uniform: after 5.7–7.4 years of follow-up the disease-specific survival was 99% in all four cohorts. In total, 13 of the 1863 patients died from prostate cancer and 269 from other causes. One-third (36%) received some kind of therapy during follow-up, most commonly with curative intent.

A computer simulation based on 5202 patients estimated that immediate radical prostatectomy for low-risk prostate cancer would decrease the mortality by 1.2% after 20 years and on an average prolong the life of patients by 1.8 months, compared with active surveillance and selective, delayed curative treatment [15].

Although the harm of treating low-risk prostate cancer at the time of diagnosis clearly exceeds the benefits on a group level, and active surveillance is the only realistic alternative, many clinical and scientific questions remain to be answered. Some of them are discussed below.

*How can the cancers best managed by active surveillance be identified?*

Adequate selection of patients for active surveillance is crucial. It is not acceptable to diagnose cancer and advise against potentially curative treatment, if the patient actually has an aggressive cancer. However, the prevailing criteria for defining the cancers best managed with active surveillance are based on expert opinion only.

Most urologists and oncologists agree that patients with a life expectancy of more than 10 years should be recommended immediate treatment if a substantial amount of cancer with Gleason pattern 4 or 5 is present in the prostate biopsies, and active surveillance if only one or two minimal foci of Gleason grade 3 are detected. Centres reporting on active surveillance use somewhat different selection criteria, based on Gleason score, cancer extent in biopsies and PSA values [10]. Some include all patients with low-risk prostate cancer, whereas some only include patients with "very low-risk" cancer, defined by cancer in one or two biopsy cores [10]. At the Royal Marsden Hospital, patients older than 65 years with Gleason score 3 + 4 = 7 cancers are also included [14].

The cancer-specific mortality at 15 years for patients aged less than 65 years at the time of diagnosis of intermediate-risk prostate cancer is only 17% with conservative management [4]. The favourable prognosis suggests a role for active surveillance also for some patients with intermediate-risk cancers, but the experience is still limited [11,14,16].

Recent research indicates that Gleason grade 3 adenocarcinomas do not have the biological potential to metastasize [17]. Gleason grade 3 may thus be regarded more as a risk factor for concomitant Gleason grade 4–5 than as an indication for treatment. It has been suggested that Gleason grade 3 should not even be considered as cancer [18,19]. The amount of Gleason grade 3 in the biopsies is related to the risk of more aggressive cancer [20], but the optimal cut-off is not known. These recent findings indicate that the selection criteria for active surveillance should include also patients with Gleason score 3 + 3 = 6 in multiple biopsy cores, provided that concomitant Gleason grade 4–5 has been excluded with reasonable certainty.

The optimal number of biopsies and the location of these for accurate sampling of the prostate prior to active surveillance are still to be defined. It is now clear that most aggressive cancers detected during active surveillance were present, but undetected, at the time of diagnosis [10]. It is not uncommon that large cancers with Gleason pattern 4 are located in the anterior part of the prostate [21–23], where they are not detected by standard diagnostic biopsies. A confirmatory repeat biopsy, including anterior sampling, is therefore now commonly recommended before deciding on active surveillance [10].

The PSA kinetics (if available at diagnosis), PSA density and possibly the ratio of free to total PSA predict aggressive prostate cancer, but the optimal cut-off values for recommending active surveillance are not known [14,24–26].

The value of multimodal magnetic resonance imaging (MRI) for assessing the cancer and guiding the biopsies in potential candidates for active surveillance is not clear, but recent results are promising [27–29].

*Which parameters should be followed during active surveillance?*

It is not acceptable to recommend surveillance of cancer if this results in the "window of curability" closing before curative therapy is initiated. It is likely that the chance for cure is decreased substantially when cancer progression is detected by DRE or transrectal ultrasound. Little is known of the cancer dedifferentiation process over time. Repeat biopsies are incorporated in most follow-up schedules for active surveillance, but how they should be performed and how the results should be interpreted has not been studied systematically. Some advocate repeat biopsies guided by multimodal MRI instead of sampling according to predefined biopsy templates [30].

Increasing PSA is the most common reason for conversion to curative treatment [11–14]. One problem with PSA as a marker of cancer progression is that poorly differentiated cancers produce less PSA than slowly growing, well-differentiated cancers. Another problem is that many patients with low-risk prostate cancer also have benign prostatic hyperplasia, which may contribute to most of the PSA measured in blood plasma. A small, but comparatively rapidly progressing cancer in a large gland may therefore not be heralded by a short PSA doubling time before it metastasizes. Furthermore, PSA may fluctuate for various reasons, which may lead to unnecessary intervention or anxiety. The PCPT and REDUCE studies indicate that 5α-reductase inhibitors may be used to stabilize the PSA derived from the benign hyperplasia and enhance the utility of PSA in detecting progressive cancer [31,32].

*Which are the optimal assessment intervals during active surveillance?*

In the majority of cases, cancer progression is probably so slow that biannual or even annual assessment is adequate. The crucial issue is how short the intervals must be to detect more rapid progression during the "window of curability" for the small minority of patients with lethal cancers. Clinicians still cannot give a reliable answer to patients asking: "What is the risk that my prostate cancer will progress to an incurable stage during active surveillance and then kill me?"

*What is the role of 5α-reductase inhibitors?*

The 5α-reductase inhibitors may have several favourable effects for patients on active surveillance. The evidence is more substantial for dutasteride than for finasteride in this group of patients. As mentioned above, the utility of PSA for detecting progressive cancer has improved [31–34]. The 5α-reductase inhibitors delay progression and time to treatment for patients on active surveillance [35,36]. Since most patients on active surveillance have benign prostatic enlargement [11,14], the well-documented effects on symptoms and progression of the benign hyperplasia are also valuable.

However, based on findings in the PCPT study [37], there is concern that 5α-reductase inhibitors may induce high-grade prostate cancer [38]. The increased incidence of high-grade cancer among men treated with finasteride in the PCPT study may be caused by improved detection only, but more studies with long-term follow-up are needed to clarify this issue, as well as to investigate the other potentially beneficial effects for patients on active surveillance for prostate cancer.

*How does active surveillance affect quality of life?*

Although active surveillance reduces the risk of physical side-effects of treatment, there may be mental side-effects of not being treated. Some studies on this topic have been published, but most questions remain unanswered. What is the impact of having an

Table I. Inclusion and exclusion criteria in the Study of Active Monitoring in Sweden (SAMS).

| Inclusion criteria | Exclusion criteria |
|---|---|
| Age 40–75 years | Cancer in prostate biopsy cores sampling exclusively the anterior parts of the gland* |
| Expected remaining lifetime of > 10 years | Cancer diagnosed at TURP* |
| Diagnosis of prostate cancer within the previous 6 months | Evidence of metastatic cancer |
| Peripheral zone prostate cancer diagnosed with a set of biopsies including 6–12 cores* | Any previous therapy for prostate cancer |
| Local therapy with curative intent is planned if progression during follow-up | Treatment with 5α-reductase inhibitors during the previous 12 months* |
| The patient has understood the concept of active surveillance and signed informed consent | Additional sets of prostate biopsies within the previous 12 months* |
| PSA < 13 μg/l | Recurrent urinary tract infection or bacterial prostatitis |
| PSA doubling time > 3 years during the last 2 years (if PSA history available) | Anorectal disease interfering with digital rectal examination or ultrasound |
| PSA increase of < 2 μg/l during the last 2 years (if PSA history available) | Any other disease or circumstance that may interfere will study-related procedures |
| PSA density < 0.2 μg/l/ml* | |
| Cancer stage (UICC 2002) T1c or T2a* | |
| Prostate volume < 90 ml* | |
| Gleason score ≤ 6* with no grade 4* or 5 | |
| ≤ 33% of cores with cancer* | |
| ≤ 6 mm cancer in any one biopsy* | |

All criteria apply for the randomized SAMS-FU, whereas patients with T1–2, Gleason score ≤ 7 cancers can be included in the observational study (SAMS-ObsQoL) even if the criteria marked with an asterisk are not fulfilled.
PSA = prostate-specific antigen; TURP = transurethral resection of the prostate; UICC = International Union Against Cancer.



untreated cancer, of slowly rising or fluctuating PSA values, and of the uncertainty of what the next scheduled visit will lead to? To what extent is delayed treatment associated with more side-effects than immediate curative treatment? How are patients affected when deferred treatment with curative intent turns out to be initiated too late, at a time when the disease has already spread?

*Rationale for the Study of Active Monitoring in Sweden (SAMS)*

As made clear above, the challenge to the scientific community is not to study *whether* active surveillance is an option for men with low-risk prostate cancer, but to study *to whom* it should be recommended and *how* it should be performed. With so many unanswered questions it is unethical not to include patients on active surveillance in studies.

Preferably, patients should be included in randomized studies that address specific unsolved issues of active surveillance, but few such studies are being conducted. However, data from prospective, observational studies, such as the Toronto study [13], PRIAS [39] and the Royal Marsden Study [14], help us to answer the questions "to whom?" and "how?"

The rationale for the Study of Active Monitoring in Sweden (SAMS) was primarily to offer an easily accessible observational study to Swedish urologists, so that a large proportion of the Swedish patients could contribute to the scientific basis for future refinement of active surveillance. Practising active surveillance within a defined protocol might also improve the quality of care, and perhaps reduce anxiety for both patients and urologists.

The need for improved knowledge on the quality of life for patients on active surveillance was obvious. A longitudinal assessment of quality of life was thus included in the SAMS and a group of patients receiving immediate treatment added for comparison.

Furthermore, a growing body of evidence suggested that a substantial proportion of patients with cancers classified as low risk actually had significant amounts of Gleason grade 4 cancer in parts of the prostate not sampled by the diagnostic biopsies [6,7]. In the SAMS a mandatory rebiopsy was therefore included, as well as a randomized evaluation of the number and location of the biopsy cores.

The healthcare resources allocated to active surveillance of men with low-risk prostate cancer are increasing rapidly. If the patients needing treatment were identified shortly after diagnosis, instead of after several years of surveillance, surveillance for the remaining patients could be less intensive. Healthcare

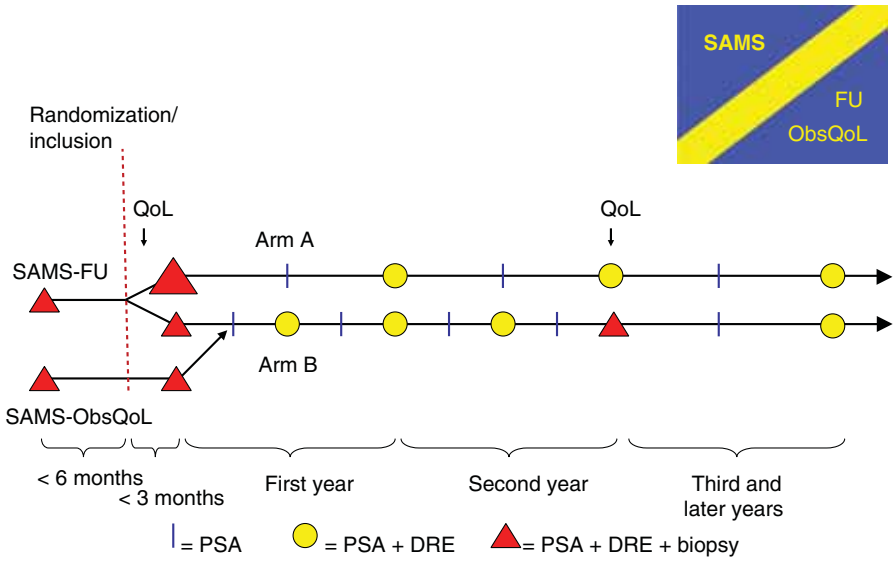


Figure 2. Flowchart for the first 3 years of the Study of Active Monitoring in Sweden (SAMS). Patients in SAMS-ObsQoL are managed similarly to patients randomized to standard follow-up in SAMS-FU. The larger red triangle represents an extensive rebiopsy and the smaller standard biopsies (Table II). QoL = Quality of life and symptom questionnaire; PSA = blood sample for prostate-specific antigen; DRE = digital rectal examination.



resources could be saved and the number of unpleasant procedures for the patients reduced. The experimental arm of the randomized part of SAMS was therefore linked to a less intensive follow-up, presuming that most of the aggressive cancers would be detected by the more extensive, immediate repeat biopsies.

## Material and methods

The initiative for the SAMS came from the National Prostate Cancer Register (NPCR) of Sweden, and the study is conducted in close collaboration with the NPCR. SAMS has two parts that are partially overlapping and partially separated: SAMS-FU and SAMS-ObsQoL. Both are prospective, multicentre studies conducted in Sweden only. SAMS-FU and SAMS-ObsQoL were approved on 5 December 2010 by the Regional Ethical Review Board at Lund University (EPN 2010/598). Patients planned for active surveillance can be included within 6 months after a diagnosis of prostate cancer. The inclusion and exclusion criteria are listed in Table I. They are in agreement with the range of criteria used in similar studies [10]. Multimodal MRI was considered for the initial assessment and during follow-up, but only a few centres in Sweden have the resources and the competence needed. Use of multimodal MRI and whether the results affected the management of the patient are registered. Detailed information in Swedish about the SAMS can be obtained at http://www.cancercentrum.se/INCA/Om-inca2/SAMS/

### *The randomized SAMS-FU*

The international standard randomized controlled trial number for SAMS-FU is ISRCTN64891728. Patients with "very low-risk" prostate cancer (Table I) are randomized 1:1 either to the investigational arm A, with an extensive rebiopsy and less intensive follow-up, including no further scheduled biopsies, or to arm B, with standard follow-up (Figure 2). Restricted randomization with permuted-block design is used, stratified for age (above or below 65 years) and local stage (T1c or T2a). The two different templates for biopsies are described in Table II. The biopsy protocol is a compromise between optimal sampling and clinical feasibility.

To reach 80% power with a two-sided alpha of 0.05 to detect a difference in the proportion treated with curative intent within 5 years (the primary endpoint) between 20% or less in the investigational arm A and 30% in the standard arm B, 220 patients are needed in each arm. To compensate for patients lost to follow-up and for protocol violations, the intention is to include 500 patients in SAMS-FU during 5 years.

### *The observational SAMS-ObsQoL*

Patients not fulfilling the criteria for randomization (Table I) or not accepting randomization are included in the observational SAMS-ObsQoL. The aim is to include at least 500 patients in SAMS-ObsQoL. The initial procedures and the follow-up in SAMS-ObsQoL are identical to the standard arm B of

Table II. Biopsy protocol in the Study of Active Monitoring in Sweden (SAMS).

| | SAMS-FU investigational arm A | SAMS-FU standard arm B and SAMS-ObsQoL |
|---|---|---|
| Prostate volume < 30 ml | 15–18 cores: | 9–12 cores: |
| | 8 cores in the periphery of the peripheral zone | 8 cores in the periphery of the peripheral zone |
| | 2 paramedian cores in the peripheral zone | |
| | 4 paramedian cores in the anterior part of the gland | |
| | 1–2 extra cores from each area with cancer in the diagnostic set of biopsies | 1–2 extra cores from each area with cancer in the diagnostic set of biopsies |
| Prostate volume 30–59 ml | 19–22 cores: | 11–14 cores: |
| | 10 cores in the periphery of the peripheral zone | 10 cores in the periphery of the peripheral zone |
| | 4 paramedian cores in the peripheral zone | |
| | 4 paramedian cores in the anterior part of the gland | |
| | 1–2 extra cores from each area with cancer in the diagnostic set of biopsies | 1–2 extra cores from each area with cancer in the diagnostic set of biopsies |
| Prostate volume 60–89 ml | 23–26 cores: | 13–16 cores: |
| | 12 cores in the periphery of the peripheral zone | 12 cores in the periphery of the peripheral zone |
| | 4 paramedian cores in the peripheral zone | |
| | 6 paramedian cores in the anterior part of the gland | |
| | 1–2 extra cores from each area with cancer in the diagnostic set of biopsies | 1–2 extra cores from each area with cancer in the diagnostic set of biopsies |

In SAMS-FU the second set of biopsies (the first being the diagnostic) is performed within 3 months from randomization. In SAMS-ObsQoL the second set of biopsies should be obtained within 6 months from diagnosis. In the experimental arm A of SAMS-FU no further sets of biopsies are scheduled following the initial rebiopsy, but biopsies should be obtained if PSA increases above the level for the intervention criteria but the patient is not treated. In SAMS-ObsQoL and in the standard arm B of SAMS-FU further sets of biopsies are scheduled every second year with the same pattern of sampling as for the initial repeat biopsy.



SAMS-FU. All the data from these two groups of patients will be merged when analysing the SAMS-ObsQoL study. Quality of life, symptoms of prostate cancer and side-effects of treatment are assessed with questionnaires. Prognostic factors correlating with the endpoints (treatment, symptoms, distant metastases, mortality), such as cancer extent, PSA (levels, density, kinetics), age, comorbidity and physical activity, will be studied, as will the effect of 5α-reductase inhibitors.

### *Data management and follow-up in SAMS-FU and SAMS-ObsQoL*

All patients will be followed according to the protocol for 10–15 years or until death, whichever comes first. The plan is to conduct the first analysis of the primary endpoint of SAMS-FU in 2018 (1 year after completed inclusion) and the principal analysis in 2022. The final analyses of the secondary endpoints of both studies are planned for 2027. The analyses will be stratified according to age at diagnosis of prostate cancer (older versus younger than 65 years), local stage (T1c versus T2a) and treatment with 5α-reductase inhibitors (none versus < 1 year versus > 1 year).

Patient data are registered via the Internet in INCA (Information Network for Cancer Care) software, which is used throughout Sweden for registration and data management in the NPCR. INCA is administered by the six Swedish Cancer Centres on a non-profit basis. The study data are subjected to external monitoring by CROAC AB.

### *Treatment with 5α-reductase inhibitors*

Patients with symptomatic benign prostatic hyperplasia (prostate volume ≥ 30 ml) should be counselled about the possible benefits and side-effects of 5α-reductase inhibitors. Treatment decisions are then made by the investigating urologist and the individual patient. Dutasteride is recommended because of evidence for decreased progression of low-grade prostate cancer and enhanced sensitivity for detecting high-grade prostate cancer among men with PSA 3—10 μg/ml [31,36], but treatment with finasteride is an alternative. The criteria for intervention differ for patients with and without medication with 5α-reductase inhibitors (Table III).

### *Assessment of quality of life, side-effects of treatment and pelvic symptoms*

The quality of life is assessed at baseline, after 1 year, and then every second year. The questionnaires are filled in by the patients via the Internet. They consist of three parts: the first part assesses attitudes to and experiences of active surveillance, the second part various aspects of quality of life including the Hospital Anxiety and Depression Scale (HADS), and the third

Table III. Criteria for initiating therapy with curative intent in the Study of Active Monitoring in Sweden (SAMS).

| DRE or TRUS indicates progression | |
|---|---|
| Pathological progression | > 33% positive cores (additional cores from previous cancer site excluded) |
| | > 6 mm cancer in any biopsy core |
| | Any Gleason grade 4 or 5 |
| PSA increase (patients not taking dutasteride or finasteride) | To total PSA > 15 μg/l |
| | PSA density > 0.3 μg/l/ml |
| | PSA doubling time < 3 years during the last 2 years |
| | PSA increase of > 2 μg/l during the last 2 years |
| PSA increase (patients taking dutasteride or finasteride) | PSA density > 0.2 μg/l/ml |
| | PSA increase of > 1 μg/l above nadir |
| Physician's recommendation for other reasons | |
| Patient's request | |

Since prostate-specific antigen (PSA) values may fluctuate considerably owing to infection and other benign causes, treatment decisions should always be based on three or more PSA measurements. Unexpected rises of PSA should prompt a new PSA test within 1–3 months.
DRE = digital rectal examination; TRUS = transrectal ultrasound.



part pelvic symptoms, including possible side-effects of local therapy. The first part is based on the experience from previous studies on patients with localized prostate cancer [40]. The third part is identical to the NPCR questionnaire ("Sverige-enkäten"), a validated instrument used all over Sweden for patients receiving treatment with curative intent.

For comparison, 500 patients receiving treatment with curative intent shortly after diagnosis will be evaluated with the same Internet-based questionnaire at the same time intervals.

### *Economic issues*

The study is financed by several non-profit research foundations, none of which influenced the protocol. Participating centres receive reasonable economic compensation for their work during the study.

## Results

Inclusion started in October 2011. In March 2013, 148 patients had been included at 13 urological centres, of which 45 were randomized in SAMS-FU. The currently participating centres are, from south to north: Helsingborg Hospital, Ängelholm Hospital, Kalmar Hospital, Växjö Hospital, Department of Urology in Jönköing County, Sahlgrenska University Hospital in Gothenburg, Örebro University Hospital, Liljeholmen Urology Centre in Stockholm, Karolinska University Hospital in Solna, Karlstad Hospital, Uppsala Academic Hospital and Umeå University Hospital. Patients from Stockholm with low-risk prostate cancer detected in the STHLM3 study will be included from May 2013. SAMS welcomes additional Swedish centres wishing to join the study.

## Discussion

It is hoped that the results of SAMS will contribute to that fewer patients with indolent, low-risk prostate cancer receiving unnecessary treatment and that more patients on active surveillance who need treatment will receive it when the disease is still curable. If the investigational schedule for follow-up in the randomized SAMS-FU trial turns out to be acceptable, the efficacy of active surveillance can be increased and the healthcare resources allocated to this large group of patients can be reduced. It is possible that the patients' stress and anxiety will be reduced with the less frequent follow-up in the investigational arm A of the SAMS-FU trial.

SAMS will increase our knowledge on the outcome, including psychological aspects and quality of life, and on prognostic factors for patients with low-risk prostate cancer on active surveillance. It is expected that specific psychological issues related to patient anxiety will be identified that are not addressed in today's clinical care. Better understanding of these issues may improve the way patients are informed and how they are supported, with the goal of reducing the mental side-effects of active surveillance.

As a secondary effect, it is hoped that this study will increase knowledge among Swedish urologists and urology nurses about active surveillance, which after all is a relatively new treatment strategy. Some patients have probably been managed with "passive surveillance", jeopardizing the chance of detecting cancer progression in time. The authors' experience is that merely discussing the study in general, and the biopsy strategy in particular, is a catalyst for better care for this patient group. SAMS may thus lead to more uniform and diligent active surveillance in Sweden.

Several other studies related to active surveillance are currently being prepared by the SAMS steering committee, including studies on circulating tumour cells, a qualitative study of the treatment decision process for patients with low-risk prostate cancer, and a study of the stress caused by the visits during active surveillance.

SAMS is the first clinical trial using INCA as a study platform. The experience gained from developing the clinical report forms and the randomization module in INCA will be valuable for the planning and execution of future clinical cancer studies. INCA is available in all public healthcare units in Sweden, and many professionals are already used to reporting data in INCA. INCA is thus an ideal study platform for academic, clinical trials.



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