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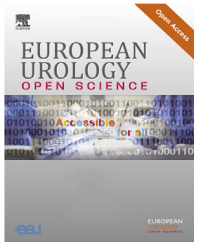

European Association of Urology

Prostate Cancer

Prospective Implementation and Early Outcomes of a Risk-stratified Prostate Cancer Active Surveillance Follow-up Protocol

Vineetha Thankapannair[a], *Alexandra Keates*[b], *Tristan Barrett*[c], *Vincent J. Gnanapragasam*[a,b,d,*]

[a] *Department of Urology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK;* [b] *Cambridge Urology Translational Research and Clinical Trials Office, Cambridge Biomedical Campus, Addenbrooke's Hospital, Cambridge, UK;* [c] *Department of Radiology, University of Cambridge, Cambridge, UK;* [d] *Division of Urology, Department of Surgery, University of Cambridge, Cambridge, UK*

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Abstract

Background: Active surveillance (AS) is a major management option for men with early prostate cancer. Current guidelines however advocate identical AS follow-up for all without considering different disease trajectories. We previously proposed a pragmatic three-tier STRATified CANcer Surveillance (STRATCANS) follow-up strategy based on different progression risks from clinic-pathological and imaging features.
Objective: To report early outcomes from the implementation of the STRATCANS protocol in our centre.
Design, setting, and participants: Men on AS were enrolled into a prospective stratified follow-up programme.
Intervention: Three tiers of increasing follow-up intensity based on National Institute for Health and Care Excellence (NICE): Cambridge Prognostic Group (CPG) 1 or 2, prostate-specific antigen density, and magnetic resonance imaging (MRI) Likert score at entry.
Outcome measurements and statistical analysis: Rates of progression to CPG $\geq$3, any pathological progression, AS attrition, and patient choice for treatment were assessed. Differences in progression were compared with chi-square statistics.
Results and limitations: Data from 156 men (median age 67.3 yr) were analysed. Of these, 38.4% had CPG2 disease and 27.5% had grade group 2 disease at diagnosis. The median time on AS was 4 yr (interquartile range 3.2–4.9) and 1.5 yr on STRATCANS. Overall, 135/156 (86.5%) men remained on AS or converted to watchful waiting and 6/156 (3.8%) stopped AS by choice by the end of the evaluation period. Of the 156 patients, 66 (42.3%) were allocated to STRATCANS 1 (least intense follow-up), 61 (39.1%) to STRATCANS 2, and 29 (18.6%) to STRATCANS 3 (highest intensity). By increasing STRATCANS tier, progression rates to CPG $\geq$3 and any progression events were 0% and 4.6%, 3.4% and 8.6%, and 7.4% and 22.2%, respectively (p = 0.019). Modelling resource usage suggested potential reductions in appointments by 22% and MRI by 42% compared with current NICE guideline recommendations

* Corresponding author. Division of Urology, Department of Surgery, University of Cambridge, Cambridge, UK. Tel. +44 7712655419.
E-mail address: vjg29@cam.ac.uk (V.J. Gnanapragasam).

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(first 12 months of AS). The study is limited by short follow-up, a relatively small cohort, and being single centre.
Conclusions: A simple risk-tiered AS strategy is possible with early outcomes supporting stratified follow-up intensity. STRATCANS implementation could de-escalate follow-up in men at a low risk of progression while husbanding resources for those who need closer follow-up.
Patient summary: We report a practical way to personalise follow-up for men on active surveillance for early prostate cancer. Our method may allow reductions in the follow-up burden for men at a low risk of disease change while maintaining vigilance for those at a higher risk.

1. Introduction

Active surveillance (AS) is now the preferred management option for men with favourable-prognosis prostate cancer [1,2]. Multiple guidelines have endorsed its use in this setting, and the rate of uptake is growing [1–4]. In the UK, the National Institute for Health and Care Excellence (NICE) guidelines recommend that AS should be the first option for men with Cambridge Prognostic Group (CPG) 1 (comparable with low risk) disease, and men with CPG2 (comparable with favourable intermediate risk) disease should be offered it in parallel with radical treatment options [1]. AS or conservative management is estimated to be the initial management option for 20–25% of men diagnosed with prostate cancer [5,6]. Unlike surgery or radiotherapy, however, there is no quality metric for inclusion, exclusion, follow-up, or triggers for treatment. As such, clinical practice varies tremendously between and within practitioners, units, hospitals, and countries [7–9]. Both nationally and internationally, there are now active working groups seeking to attain consensus, and this is a work in progress [8,10].

One key area of unmet need is how to follow up men on AS. Currently, guidelines usually recommend the same follow-up regime for all men regardless of disease type or the risk of progression [1,3,4];. To date, there is little evidence base to guide how frequent AS follow-up should be or whether current recommendations are appropriate and warranted. This results in potential overinvestigation and morbidity (eg, from repeat biopsies) and is a significant health resource burden. Less intense follow-up is also more patient friendly in terms of time and travel costs. Thus, there is a need for a way to risk stratify AS follow-up events and potentially de-escalate follow-up in appropriate AS subgroups. Most importantly, to do this in a cost-neutral or cost-effective way in an increasingly resource-poor health economy.

In our previous work, we demonstrated how starting prognostic group (based on the CPG prognostic criteria) and prostate-specific antigen (PSA) density (PSAd) could be used, in conjunction with magnetic resonance imaging (MRI) visibility, to identify men at three different risks of progression and hence potentially tailor the intensity of follow-up [6,11]. Here, we report the implementation and early outcomes of this tiered strategy STRATified CANcer Surveillance (STRATCANS) programme, based on that proposal. Our goals were to assess progression event rates, attrition from AS, and model the potential for resource savings.

2. Patients and methods

2.1. Cohort description

Commencing in March 2019, men with early prostate cancer and on AS were enrolled into a prospective stratified follow-up programme. The standard diagnostic workup and entry criteria for AS in our institution have been described previously [11,12]. Briefly, the inclusion criteria were the following: men otherwise fit for curative therapy and with disease suitable for AS defined as CPG $\leq$2 (clinical stage T1-T2, PSA $\leq$20 ng/ml, and histological grade group $\leq$2) [1]. The CPG criteria is the UK standard for prognostic classification and treatment recommendation for newly diagnosed prostate cancer (NICE) and can be accessed at https://www.nice.org.uk/guidance/NG131. All men were investigated by multiparametric MRI prebiopsy, which was used to guide biopsies (sectoral and targeted), or sectoral only if there were no lesions. Patients underwent MRI on a 3-T Discovery MR750 HDx or a 1.5-T MR450 scanner (GE Healthcare) with a Prostate Imaging Reporting and Data System (PI-RADS)-compliant protocol performed as a multiparametric study at baseline and as a biparametric study without dynamic contrast enhancement in AS follow-up as described previously [13,14]. Prostate volume was estimated by MRI measurements using the ellipsoid formula, and changes were reported using the Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) criteria [15]. At diagnosis, all had been counselled on risk-benefit using the NICE CPG recommendations and individual prognosis estimates using the Predict Prostate tool (https://prostate.predict.nhs.uk). Men already on AS were transferred to the STRATCANS programme as they came up for routine review. Figure 1 summarises our pathway from cancer diagnosis, personalised risk stratification, and entry into AS and subsequent risk-based follow-up. For this study, we confined the analysis to those men who were on AS for <3 yr so as to minimise disease stability influencing outcomes. Evaluation time was from the start of entry into STRATCANS and censored at the time of an event or on March 1, 2022 for those remaining on AS. The implementation and evaluation had institutional review board approval and oversight (Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; registration number: ID3059 PRN9059). No additional administrative, personnel, or set-up costs were used.

2.2. Allocation to follow-up and criteria for early review

Based on CPG, PSAd (PSA divided by MRI-derived prostate volume), and presence of an MRI lesion, men were included into STRATCANS-tiered groups as previously described and outlined in Table 1 [11]. In brief, men in the lowest tier had de-escalated follow-up at 18-months inter-

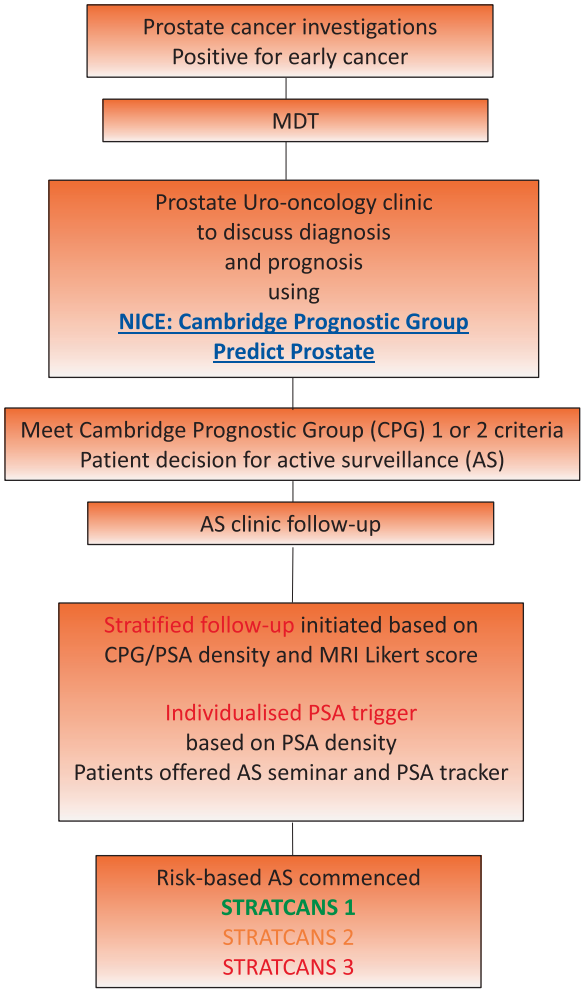

Fig. 1 – Schema of the diagnostic, risk stratification, and counselling process for men with new prostate cancer and the onward pathway for men who select active surveillance (AS) in the Stratified Cancer Surveillance (STRATCANS) programme. CPG = Cambridge Prognostic Group; MDT = metastasis-directed therapy; MRI = magnetic resonance imaging; NICE = National Institute for Health and Care Excellence; PSA = prostate-specific antigen.

vals, while those in the highest tier had 6 monthly follow-ups and those in the middle tier had annual follow-ups. Repeat MRI was risk scheduled based on the presence of no lesion (PI-RADS Likert 1–2) every 3 yr, an equivocal lesion (Likert 3) every 18 months, or a positive lesion (Likert 4–5) every 12 months (Table 1). Men in the highest-risk STRATCANS group had annual MRI regardless of lesion positivity. PSA was repeated every 3 months regardless of the follow-up tier. A personalised PSA threshold for earlier review was defined for each man based on their individual PSAd at the start of AS: if the starting PSAd was <0.15, then a PSA level that breached 0.15 on two separate occasions 3 months apart was used as a trigger for an early review. If the PSAd was ≥0.15, then a PSAd threshold of 0.20 was used. Higher PSA thresholds were decided on a case-by-case basis. Digital rectal examination (DRE) was not required as part of the follow-up protocol. Protocol repeat biopsies were mandated only at 3 yr for STRATCANS 2 and 3, with the option for the patient to not proceed if other features were favourable (Table 1). For STRATCANS 1, a biopsy was only recommended if triggered by a change in PSA or MRI. In dealing with suspected progression, we used the following steps: PSA increases triggered repeat MRI; if this showed a change, a repeat biopsy was recommended. MRI changes similarly triggered a recommendation for rebiopsy. Neither PSA changes alone nor MRI changes were automatic triggers for a change to treatment recommendation.

Table 1 – Risk-stratified follow-up schedule and intervals of outpatient appointments, PSA testing, MRI scans, and recommendations for biopsy

STRATCANS group	Inclusion criteria	Follow-up schedule
1	Cambridge Prognostic Group 1 and PSAd <0.15	3 monthly PSA 18 monthly outpatients telephone
		MRI Likert 1–2—repeat at 3 yr MRI Likert 3—repeat at 18 mo MRI Likert 4–5—repeat at 12 mo
		No routine rebiopsy Triggered rebiopsy if any change
2	Cambridge Prognostic Group 2 or PSAd ≥0.15	3 monthly PSA 12 monthly outpatients telephone
		MRI Likert 1–2—repeat at 3 yr MRI Likert 3—repeat at 18 mo MRI Likert 4–5—repeat at 12 mo
		Rebiopsy at 3 yr [a] Triggered rebiopsies if any change
3	Cambridge Prognostic Group 2 and PSAd ≥0.15	3 monthly PSA 6 monthly outpatients telephone MRI (any Likert)—repeat at 12 mo Rebiopsy at 3 yr [a] Triggered rebiopsies if any change

MRI = magnetic resonance imaging; PSA = prostate-specific antigen; PSAd = PSA density; STRATCANS = STRATified CANcer Surveillance.
[a] Option to omit and discuss with patient.

2.3. *Patient education and support*

Prior to enrolment into STRATCANS, men were informed of the rationale and plan of transfer to the programme by letter, and asked to contact if they had any concerns or declined to enrol. Men were also invited to attend an AS seminar explaining how the programme would work. Men were also encouraged to keep a record of their own PSA in paper form, using the Expanded Prostate Cancer Index Composite MyChart facility or by access to the patient-maintained electronic tracker (trackmypsa.com), and to self-report changes in PSA if they breached preset thresholds. Formal patient feedback was not collated and assessed for this current report, but is being planned.

2.4. *Outcomes reported*

The main outcome measure was the rates of objective progression to CPG ≥3 disease (unfavourable intermediate-risk disease), which is consistent with a change in NICE guideline recommendation to consider treatment rather than surveillance [1]. This could be reached by upgrade on biopsy to grade group ≥3 or upstage to ≥T3. PSA increases only without a pathological change were not considered progression for this study. We also assessed for any other pathological progression (defined as grade group 1–2 increase, increase in core involvement, or any increase in the PRECISE score), conversion to watchful waiting (WW), patient choice for treatment, or death from other causes. Conversion to WW was decided on a case-by-case basis, though in general, this was because of advanced age or a new significant comorbidity, making the person ineligible for any future radical treatment. As the study was primarily descriptive, we reported on event rates as percentages. Differences in progression rates between follow-up groups were compared using chi-square statistics ($p < 0.05$).

3. Results

3.1. Cohort description and overall outcomes

A total of 156 men were included for this analysis. The median age was 67.3 yr, and the median PSA and PSAd were 6.1 ng/ml and 0.12 ng/ml^2, respectively (Table 2). In this cohort, one in three men (38.4%) had CPG2 disease and 27.5% had grade group 2 at the start of AS. The median time in years on AS from diagnosis to the end of the evaluation period (March 2022) was 4 yr. No man declined transfer to the tiered follow-up programme. The median follow-up on STRATCANS was 1.5 yr, with 13/156 (8.3%) of men reaching a full 36 mo of follow-up on the new programme. One man (0.6%) died of other causes and six (3.8%) had treatment out of patient choice. Of 156 men, 14 (8.9%) developed pathological progression, but only four (2.6%) progressed to CPG ≥3. No man developed metastasis (Table 2). Across this cohort, a total of 135/156 (86.5%) men remained on AS or had converted to WW (n = 8) by the time of evaluation. Compliance with the STRATCANS schedule was good. Of the 156 men, 117 (75%) adhered to all planned visits without additional intervals, appointments, or scans. Twenty-four men had additional visits: seven were seen early for PSA rises, four for changes in the MRI, and 13 at the patients' request to rediscuss options or other concerns. The final 15 men were those who had chosen treatment, died of other causes, or switched to WW.

Table 2 – Demographics and outcomes of men enrolled into the STRATCANS programme

	Cohort (n = 156)
Age (yr)	
Mean	66.1
Median	67.3
Interquartile range	62–71.1
PSA (ng/ml)	
Mean	6.5
Median	6.1
Interquartile range	4.51–7.9
Prostate volume (ml)	
Mean	53.5
Median	45.5
Interquartile range	33.9–70.0
PSA density	
Mean	0.14
Median	0.12
Interquartile range	0.08–0.17
Cambridge Prognostic Group	
CPG1	96
CPG2	60
Grade group	
GG1	113
GG2	43
STRATCANS group	
1	66
2	61
3	29
Days on AS since diagnosis to end of review (mo)	
Mean	1466.9 (47.3)
Median	1447 (46.7)
Interquartile range	1176.5–1787.5 (37.9–57.7)
Days on STRATCANS (mo)	
Mean	543.8 (17.5)
Median	575 (18.6)
Interquartile range	413–686 (13.2–22.1)
Outcome, n (%)	
Still on AS or change to WW	135 (86.5)
Any pathological progression (pathology/imaging)	14 (8.9)
Progression to CPG3 (grade or stage increase)	4 (2.6)
Pt choice to stop AS or management elsewhere	6 (3.8)
Other-cause mortality	1 (0.6)
Progression to metastasis	0 (0)

AS = active surveillance; CPG = Cambridge Prognostic Group; GG = grade group; Pt = patient; PSA = prostate-specific antigen; STRATCANS = STRATified CANcer Surveillance; WW = watchful waiting.
All men were on active surveillance for ≤3 yr before inclusion. Pathological progression defined as a change in histology or ≥T3 disease.

3.2. Outcome by STRATCANS tier

Of 156 men, 66 (42.3%) were allocated to STRATCANS 1, 61 (39.1%) to STRATCANS 2, and 29 (18.6%) to STRATCANS 3 follow-ups (Table 3). Men in the highest-intensity follow-up (STRATCANS 3) had the greatest risk of any pathological progression or progression to CPG ≥3 (6/27, 22.2% and 2/27, 7.4%, respectively; Table 3). Nevertheless, 70% of men remained on AS or had converted to WW during this study period. In contrast, men in the lowest follow-up tier (STRATCANS 1) had the least likelihood of progression, with over 95% remaining on AS or converting to WW. Only three men (4.6%) showed evidence of progression, with none progressing to CPG ≥3. Subclassification by MRI lesion visibility further revealed that, in STRATCANS 1 only those with Likert 3–5 experienced progression (Table 3). Men in the intermediate group (STRATCANS 2) had, not unexpectedly, more events, but still 91% remained free from progression. Of the five men % who progressed, only two (3.4%) developed CPG ≥3 disease. In this group, there was again difference in progression rates between MRI-visible and MRI-invisible men (Table 3). The definitions of what constituted progression for each event by each tier (MRI progression or biopsy upgrade) are detailed in Supplementary Table 1. The differences across the three STRATCANS groups were statistically significant for overall progression rates (p = 0.019). These

Table 3 – Active surveillance continuance or progression outcomes by STRATCANS tier

Classification	Still on AS or change to WW (%)	Any progression [a] (%)	Progression to CPG3 [a] (%)
STRATCANS group and numbers (excluding death from other cause, patient choice for treatment)			
1: n = 66 (64)	61 (95.3%)	3 (4.6%)	0 (0%)
1A: MRI no lesion, n = 27 (26)	26 (100.0%)	0 (0%)	0 (0%)
1B: MRI Likert 3–5, n = 39 (38)	35 (92.1%)	3 (7.9%)	0 (0%)
2: n = 61 (58)	53 (91.3%)	5 (8.6%)	2 (3.4%)
2A: MRI no lesion, n = 20 (20)	19 (95.0%)	1 (5.0%)	0 (0%)
2B: MRI Likert 3–5, n = 41 (38)	34 (89.4%)	4 (10.5%)	2 (5.2%)
3: n = 29 (27)	19 (70.3%)	6 (22.2%)	2 (7.4%)

AS = active surveillance; CPG = Cambridge Prognostic Group; MRI = magnetic resonance imaging; STRATCANS = STRATified CANcer Surveillance; WW = watchful waiting.
Numbers of men in each risk stratified group are shown as well as the numbers of men still on AS or converted to WW or had progressed to CPG3 or any pathological progression.
[a] Based on any pathological progression compared with baseline.

Table 4 – Modelling scenario comparing outpatients and MRI use for the first 12 mo of follow-up required by STRATCANS strategy versus UK NICE–recommended schedule

Events follow-up	STRATCANS scheduled	NICE guidelines Recommended [a]	Difference (%)
Clinic visit	98	126	–22%
MRI	73	126	–42%
DRE	–	126	No DRE

AS = active surveillance; DRE = digital rectal examination; MRI = magnetic resonance imaging; NICE = National Institute for Health and Care Excellence; STRATCANS = STRATified CANcer Surveillance.
Numbers here are based on the 126 men who had at least 12 mo of follow-up and assuming the scenario that all these men were newly enrolled into AS and in their 1st year of follow-up.
[a] Based on NICE guidelines recommendation of MRI at 12-mo interval and annual clinic review and DRE for all (https://www.nice.org.uk/guidance/ng131/chapter/Recommendations#localised-and-locally-advanced-prostate-cancer).

data recapitulate our earlier findings and justify the notion of using different-intensity follow-up based on progression risk.

3.3. *Resource utilisation modelling*

To estimate the potential resource use of the STRATCANS approach, we modelled its use against following the current NICE guideline recommendations for AS, that is, an annual clinical review with DRE and repeat MRI at 12 mo, and a similar PSA repeat interval (Table 4). To make this comparable, we modelled the scenario to include only cases with at least 12 months of follow-up and assumed a scenario where all men were new to AS. In this exercise following the NICE schedule, men would have required a total of 126 clinic visits and 126 MRI scans by the first 12 mo of follow-up (Table 4). STRATCANS follow-up for this cohort instead required 98 scheduled clinic appointments and 73 MRI scans (Table 4), representing 22% fewer clinic visits and 42% fewer MRI scans. The estimated cost savings were £1518 per 100 men in outpatient visits (HRG code RD101, based on £69 per follow-up) and £6027 per 100 men in MRI costs [16,17]. As repeat DRE is not part of the STRATCANS initiative, all follow-up appointments in STRATCANS were also done remotely without the need for face–to-face evaluation.

4. Discussion

In this paper, we report on the prospective implementation of a pragmatic stratified follow-up protocol for men on AS. We demonstrate that using a previously proposed simple model, men can be divided into three follow-up schedules and recapitulate different rates of disease progression. We show that implementation of de-escalated follow-up for suitable men appears to be appropriate and likely to be resource effective.

It is well known that AS practice is extremely heterogeneous, with disparate approaches to inclusion, exclusion, exit criteria, and how men are followed up [18–20]. There are very few on-going trials to compare follow-up protocols with notable ones from Scandinavian countries recruiting into the SAMS and SPCG17 studies [21,22]. These are focused on addressing fundamental questions on the value of MRI and optimal biopsy schedules, and are recruiting men with grade group 1 disease, which differs from more contemporary AS practice. Some studies comparing protocols have been conducted in non-trial settings, and these so far suggest no differences in stricter versus more relaxed protocols in low-risk (CPG1) patients [23]. Currently, the main focus of predictive modelling in AS is to identify the optimal timing for repeat biopsies with a number of calculators already produced [24–27]. Most of these initiatives have mainly included men with classical low-risk disease with progression to grade group 2 as the end point. However, there is increasing recognition that grade group 2/favourable intermediate-risk/CPG2 disease is also suitable for management with AS, and this has been endorsed by national guidelines [1,4,28–30]. These men have a higher risk of progression (as we have shown in this study) and hence require closer follow-up, but the majority will do very well. In a recent study from the Veterans Health Administration, for example, men on AS with favourable intermediate-risk/CPG2 disease had a 90.4% metastasis-free survival rate at 10 yr [31]. In the same study for men with low-risk/CPG1 disease, this rate was 98.5%. Therefore, it is reasonable that CPG2 can be managed by AS, it is clear that these men do need close follow-up. The same however cannot be said for men with low-risk features given the extremely low event rates. Applying the same protocol to both groups may be either not sufficient or overly intrusive, depending on which AS subgroup is being considered [29,32].

AS guidelines currenlty do not differentiate between the types of prostate cancer in prescribing follow-up intervals, but the identification of potential progression risk factors has attracted significant research interest. Novel imaging and genomic biomarkers/panels have been proposed, but have not yet found a place in routine clinical practice [33,34]. In terms of readily available clinical factors, the most consistent predictors of progression are initial prognostic (risk) category, PSAd, and MRI lesion visibility. It is no surprise that initial biopsy grade/prognostic group is a strong predictor of progression. Men with grade group 1/CPG1 disease in our study had a very low risk of progression, which probably does not justify intensive clinic reviews or repeat DRE as advocated by current guidelines [1–4]. In our study, no patient progressed to grade group 3/CPG3 disease, and only 5.9% progressed to grade group 2 and arguably could have continued on AS. PSAd has also emerged as a powerful predictor of the future behaviour of disease. Studies have shown that in AS, it is a useful predictor of biopsy upgrading, aids MRI in predicting early reclassification, and informs repeat biopsy interval [35–37]. Remarkably, both our work and others' works have demonstrated the key threshold of PSAd of $\geq$0.15 in differentiating future behaviour [11,38,39]. MRI is now an indispensable aspect of AS management, with some advocating that it can even replace biopsy in future [40]. Systematic reviews however are more nuanced on this and show that MRI alone is insufficient to detect all progressions (negative predictive value of 0.80 and positive predictive value of 0.39) [41]. It is undoubtedly an important tool to noninvasively detect changes and trigger reassessment, particularly when standardised using the PRECISE scoring system [15].

However, MRI is a resource-intensive tool, and husbanding this is going to be crucial for sustainability in any AS programme. In this study, men with MRI-visible lesions (especially Likert 4–5) were conferred an additional higher risk of progression within the subgroups. Conversely, we found, similar to others, that MRI invisibility is a favourable marker for non-progression [40]. Uniquely, within the STRATCANS framework, we have combined all three of these important elements to underpin a strategy to tailor follow-up by progression risk. This allows a more rational use of resources and reduces the burden of investigations for patients. Of note, we did not embed formal health economics into this programme, and our resource calculations should therefore be treated as exploratory.

Our study has the limitation of being a single-centre prospective and comparatively small observational cohort. Our cohort is however well characterised, with all men being diagnosed and risk assessed through a high-quality MRI-guided diagnostic pathway [13]. Our follow-up is short, and event rates were relatively low. In addition, as men were transferred into STRATCANS and already on AS, they may represent a particularly good performing group as they had not progressed before entering into STRATCANS. Of note, all newly diagnosed men and those who select AS are now automatically included into the STRATCANS protocol, and we look forward to reporting larger numbers and longer follow-ups in due course. Nevertheless, we believe that our main finding, in the current study, of safe lower-intensity follow-up for men in the lowest-risk tiers is not affected by this heterogeneity. Moreover, the median time on AS before STRATCANS was only 2.5 yr, which is relatively short in terms of AS. Another potential criticism is that the differences observed in progression rates could be due to the varying intensities of follow-up, that is, we looked more intensely in STRATCANS 3 and less so in STRATCANS 1. However, we do not believe that this affected our outcomes for a number of reasons. Firstly, all groups had the PSA check intervals; hence, biochemical changes would have been detected at the same time regardless of the STRATCANS group. Secondly, we had previously reported different progression risks (which led to the development of STRATCANS) in cohorts that had the same follow-up intensity, and this current prospective report recapitulates the clear differences in event rates [11]. Finally, the progression rate differences are logically supported by the expected biological variations in behaviour when comparing CPG1 versus CPG2, low and high PSAd, and MRI-visible and MRI-invisible lesions, as discussed above. We acknowledge that only a formal randomised controlled trial of STRATCANS versus other protocols can definitely address these limitations. Here, we have also not looked at all outcomes from protocol (non-triggered) biopsies, as follow-up was short, so it is possible that some progression may occur, which is not detected by PSA or MRI changes. We also did not look at negative biopsy rates and what factors may allow us to refine further selection for biopsies. Continuous data collection will inform how these risk strata perform over an extended period of follow-up, including protocol and nonprotocol rebiopsy events. We note that practice is increasingly exploring triggered rather than protocol biopsies, which is consistent with the approach that we have employed here [20,42].

5. Conclusions

In conclusion we present early outcomes of a risk-stratified follow-up schema with the potential to de-escalate follow-up in men at the lowest risk of progression while on AS. Implementation of STRATCANS has the potential to reduce resource utilisation and maintain high levels of patient compliance. The STRATCANS model is also pragmatic enough to be emulated in any AS clinic that uses clinical prognostic classification and MRI in routine practice without any added costs or tests. This aspect also lends itself to protocol-driven nurse-led follow-up, and we are actively exploring this in our centre. In addition, we have disseminated our protocol and outcomes to our regional cancer alliance (East of England), and are currently in discussion on how this can be adopted by different units given the simplicity of the clinical criteria we have used. Future studies will report on longer-term outcomes and explore additional factors to further refine follow-up and potentially a formal multicentre trial to test its efficacy against the current standards of care.

***Author contributions*:** Vincent J. Gnanapragasam had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gnanapragasam.
Acquisition of data: Thankapannair, Keates, Gnanapragasam, Barrett.
Analysis and interpretation of data: Gnanapragasam, Keates.
Drafting of the manuscript: Gnanapragasam, Barrett.
Critical revision of the manuscript for important intellectual content: Gnanapragasam, Thankapannair, Keates, Barrett.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.12.013.

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