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The Movember Foundation's GAP3 cohort: a profile of the largest global prostate cancer active surveillance database to date

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[a]The Movember Foundation's Global Action Plan Prostate Cancer Active Surveillance (GAP3) consortium members presented in Appendix A.

Objectives

The Movember Foundation launched the Global Action Plan Prostate Cancer Active Surveillance (GAP3) initiative to create a global consensus on the selection and monitoring of men with low-risk prostate cancer (PCa) on active surveillance (AS). The aim of this study is to present data on inclusion and follow-up for AS in this unique global AS database.

Patients and Methods

Between 2014 and 2016, the database was created by combining patient data from 25 established AS cohorts worldwide (USA, Canada, Australasia, UK and Europe). Data on a total of 15 101 patients were included. Descriptive statistics were used to report patients' clinical and demographic characteristics at the time of PCa diagnosis, clinical follow-up, discontinuation of AS and subsequent treatment. Cumulative incidence curves were used to report discontinuation rates over time.

Results

At diagnosis, the median (interquartile range [IQR]) patient age was 65 (60–70) years and the median prostate-specific antigen level was 5.4 (4.0–7.3) ng/mL. Most patients had clinical stage T1 disease (71.8%), a biopsy Gleason score of 6 (88.8%) and one tumour-positive biopsy core (60.3%). Patients on AS had a median follow-up time of 2.2 (1.0–5.0) years. After 5, 10 and 15 years of follow-up, respectively, 58%, 39% and 23% of patients were still on AS. The current version of GAP3 has limited data on magnetic resonance imaging (MRI), quality of life and genomic testing.

Conclusions

GAP3 is the largest worldwide collaboration integrating patient data from men with PCa on AS. The results will allow individual patients and clinicians to have greater confidence in the personalized decision to either delay or proceed with active treatment. Longer follow-up and the evaluation of MRI, new genomic markers and patient-related outcomes will result in even more valuable data and eventually in better patient outcomes.

Keywords

adenocarcinoma, guideline, evidence-based, #PCSM, #ProstateCancer

Introduction

Prostate cancer (PCa) is the second most common cancer in men, with nearly a million new cases diagnosed worldwide in 2008[1]. The number of men living with a diagnosis of PCa is likely to continue to increase as the population in many countries continues to age and as cancer is detected earlier, owing to the more widespread use of serum PSA testing [2,3]. As a result, active surveillance (AS) was introduced as a management strategy for men with low-risk PCa, with the intention to start curative treatment at the time of progression, and to avoid overtreatment and its associated morbidities. In recent years, AS has evolved from an experimental protocol to a broadly accepted management

strategy for men diagnosed with low-risk PCa [4]. Contemporary data suggest that use of AS has increased globally [5–7].

Nevertheless, identification of those men whose disease is at low risk for progression is a critical and much debated issue when deciding which men will benefit from AS for their PCa [8]. Numerous agencies have endorsed clinical practice guidelines for the management of low-risk PCa, which include criteria for enrolment of patients in AS programmes and their subsequent management [3]; however, there is currently no consensus in this area. There has been shown to be variability in enrolment criteria and follow-up in international and national series of AS [9]. Moreover, robust data from men with clinically insignificant PCa who are undergoing AS, especially from studies with long follow-up durations, are still limited. Hence, many important questions regarding AS remain unanswered, such as which newly diagnosed men should be considered suitable candidates for AS and what constitutes an appropriate follow-up regimen for AS [10]. There is a need for a worldwide consensus regarding the optimal criteria and protocols for AS and more comparative data on patient selection and testing protocols [11].

In August 2014, the Movember Foundation launched the Global Action Plan Prostate Cancer Active Surveillance initiative (GAP3). Milestones of the project include a global AS database for clinical, marker-related and imaging data. Its primary goal is to create a global consensus on the selection and monitoring of men with low risk PCa. Ultimately, worldwide uniform guidelines will be developed. The aim of the present study was to present data from this unique global dataset on inclusion and follow-up for AS in men with low-risk PCa.

Patients and Methods

Study Population

Between 2014 and 2016, a global database was created by combining patient data from established AS cohorts worldwide. To assemble existing cohorts into a large consortium of cohorts, a new collaborative framework was needed. The GAP3 partners therefore developed documentation required for sharing and use of clinical data within the global database. The database has been developed at the site of Philips Electronics Nederland B.V., Eindhoven, the Netherlands and is currently hosted by the Erasmus Medical Centre, Rotterdam, the Netherlands [12]. The GAP3 initiative was initiated and is coordinated by the Erasmus Medical Centre, Rotterdam, the Netherlands. The Movember Foundation is the sole funder of the project.

Funding has now been secured to provide sustainability of the GAP3 database until February 2019.

Requirements for participation in GAP3 included, among others, ethical approval for sharing digital patient data in a centralized global database, and an active registry of AS patients over the last 2 years or more, including at least ~50 patients annually. To date, 25 centres from the USA, Canada, Australasia, the UK and Europe fulfilled the requirements for participation and joined the initiative (Table S1). References to the individual AS cohorts can be found in Table S1. The global database currently comprises data on 15 101 patients (Table S1; database version 'gap3data_2.3', released in June 2017). A summary of the entry criteria for each individual AS cohort is included in Table S2.

Although many variations in protocols currently exist, most agree that the most suitable patients for AS are those aged >18 years, and those with pretreatment clinical stage T1–T2 PCa, serum PSA ≤10 ng/mL, a biopsy Gleason score of ≤6 or (3+4) 7, and a maximum of two tumour-positive biopsy core samples. Some protocols included PSA density (most often using a threshold of 0.2 ng/mL^2), the maximum extent of cancer per core (most often using a threshold of 50%) and life expectancy (>10 years) and adequate biopsy sampling as inclusion criteria for AS. As a result the following baseline host (e.g. age, body mass index, race, ethnicity, marital status, educational level, family history of PCa, smoking history and comorbidities/overall health status) and tumour characteristics (e.g. clinical stage, PSA, prostatic volume, biopsy Gleason score, PSA density, number of biopsy cores with PCa, and maximum cancer extent per core) were recorded.

In addition to baseline information, follow-up information was key for the entire GAP3 project; it will allow us to shed light on current practice and outcomes, with the final goal of providing consensus guidelines. A summary of the monitoring strategy for each individual AS cohort is included in Table S3. After initiation of AS, almost all protocols recommend serial measurement of serum PSA levels, DRE and surveillance biopsy sampling in order to identify pathological progression. Many uncertainties remain surrounding the optimum timing of these surveillance strategies. Some protocols recommend PSA measurements every 3 months, while others state that serum PSA monitoring should be implemented at intervals no more often than every 6 months after the start of AS. Some protocols recommend DRE every 6 months, whilst others do not include DRE in follow-up as a result of the use of MRI. Substantial variation exists in the recommended frequency at which rebiopsy procedures should be conducted. Further, several protocols consider MRI for routine use in AS, again with differences between the recommended frequency, although most protocols recommend a 12-month interval. PSA kinetics and quality-of-life data are less frequently recommended as methods to identify whether or not a patient's cancer has progressed. We therefore collected follow-up information on, for

example, PSA, PSA kinetics (PSA doubling time and PSA velocity), T stage by DRE, biopsy characteristics and MRI findings (e.g. suspicious lesions found on MRI). Finally, the database contains information on discontinuation of AS (e.g. the reasons for stopping AS), potential subsequent treatments (e.g. radical prostatectomy), and cause of death.

Statistical Analyses

Descriptive statistics were used to assess the clinical and demographic characteristics at time of PCa diagnosis for all men included in the GAP3 cohort, their clinical follow-up, discontinuation of AS and potential subsequent treatments. Cumulative incidence curves were used to report discontinuation rates over time [13]. R software was used to perform all analyses [14].

Results

The GAP3 database currently comprises data on 15 101 patients from 25 centres across 15 countries (database version 'gap3data_2.3', released in June 2017). At time of diagnosis, the median (interquartile range [IQR]) patient age was 65 (60–70) years, the median (IQR) PSA was 5.4 (4.0–7.3) ng/mL, the median (IQR) PSA density was 0.12 (0.09–0.17) ng/mL and the median (IQR) prostate volume was 43.2 (33–59) cc. Most patients had a clinical stage T1 (71.8%), a biopsy Gleason score of 6 (88.8%), one tumour-positive biopsy core (60.3%) and no comorbidity (25%; Table 1). Table S4 shows patient characteristics at time of PCa diagnosis for all patients included in the GAP3 cohort for each participating centre. Patients on AS had a median (IQR) follow-up time (i.e. the time until discontinuation or the time until the last known follow-up without discontinuation being reported) of 2.16 (1.02–4.47) years. The maximum follow-up time was 21.3 years. The median (IQR) number of years until patients' last follow-up while on AS was 1.99 (0.83–4.24) years (Table 2).

By the end of current follow-up, 45 patients (0.3%) had developed metastases and 566 patients (3.7%) had died, of whom 37 (0.2%) died from PCa (Table 2). The main clinical and demographic characteristics and clinical follow-up data for all patients who developed metastases during AS (n = 45) and for all patients who developed metastases and died from PCa (n = 17) are summarized in Table 3. Of the patients who had died from PCa by the end of current follow-up (n = 37), a total of 32 patients had switched to curative treatment, of whom 21 switched to androgen deprivation therapy, four to external beam radiotherapy, two to external beam radiotherapy and brachytherapy, one to external beam radiotherapy and androgen deprivation, and four to radical prostatectomy.

Table 1 Characteristics at time of prostate cancer diagnosis for all men included in the GAP3 cohort*.

Characteristics	Distribution of characteristics (N = 15 101)	Number of centres reported (N_{total} = 25)
Median (IQR) age, years	65 (60–70)	25
Age, *n* (%)		
≤55 years	1 547 (10.3)	25
56–60 years	2 402 (16.1)	
61–65 years	3 579 (23.9)	
66–70 years	4 002 (26.8)	
71–80 years	3 256 (21.8)	
>80 years	172 (1.1)	
Year of diagnosis, *n* (%)		
1992–1997	260 (1.8)	25
1998–2004	1 743 (11.6)	
2005–2008	3 011 (20.2)	
2009–2011	4 101 (27.5)	
2012–2014	4 228 (28.4)	
2015–2016	1 565 (10.5)	
Charlson comorbidity index, *n* (%)		
0	3 775 (25.0)	10
1	669 (4.4)	
2	761 (5.0)	
≥3	563 (3.7)	
Missing	9 333 (61.8)	
T stage (at DRE), *n* (%)		
T1	10 841 (71.8)	23
T2	2 034 (13.5)	
T3	11 (0.1)	
T4	1 (<0.1)	
Unknown	2 214 (14.6)	
Gleason grade group, *n* (%)		
<6	400 (2.7)	25
6	13 198 (88.8)	
>6	1 263 (8.5)	
Unknown	240 (1.6)	
PSA level, *n* (%)		
0–3.0 ng/mL	1 826 (12.6)	25
3.1–6.0 ng/mL	6 913 (47.8)	
6.1–10.0 ng/mL	4 511 (31.2)	
>10.0 ng/mL	1 207 (8.3)	
Median (IQR) PSA, ng/mL	5.4 (4.0–7.3)	
Missing PSA data, *n* (%)	644 (4.3)	
Prostate volume		
Median (IQR), cc	43.2 (33.0–59.0)	22
Missing, *n* (%)	4 069 (26.9)	
PSA density		
Median (IQR), ng/mL	0.12 (0.09–0.17)	22
Missing, *n* (%)	4 221 (28.0)	
Positive cores		
Median (IQR)	1 (1–2)	24
Missing, *n* (%)	1 305 (8.6)	
Positive cores		
0	78 (0.6)	24
1	8 321 (60.3)	
2	3 270 (23.7)	
≥3	2 127 (15.4)	
Percentage of cancer in any one core		
Median (IQR)	10 (5–20)	17
Minimum, maximum, %	0, 100	
Missing, *n* (%)	6 114 (40.5)	

*IQR, interquartile range. *Database version 'gap3data_2.3', released in June 2017.*

Table 2 Characteristics of clinical follow-up, discontinuation of active surveillance and subsequent treatment*.

	Patient age group at PCa diagnosis						
	50–55 years (*n* = 1 547)	56–60 years (*n* = 2 402)	61–65 years (*n* = 3 579)	66–70 years (*n* = 4 002)	71–75 years (*n* = 2 412)	>75 years (*n* = 1 016)	All† *N* = 15 101
Median (IQR) number of years on AS	2.38 (1.04–4.63)	2.21 (1.07–4.51)	2.17 (1.05–4.58)	2.23 (1.03–4.50)	2.12 (1.04–4.45)	1.91 (0.85–3.84)	2.16 (1.02–4.47)
Median (IQR) number of years until last follow-up while on AS	2.63 (1.00–5.04)	2.51 (1.02–5.07)	2.50 (1.02–5.22)	2.55 (1.02–5.19)	2.29 (1.02–4.85)	2.04 (0.87–4.32)	2.44 (1.01–5.02)
Remaining on AS, *n* (%)	1 083 (70.0)	1 584 (66.0)	2 236 (62.5)	2 379 (59.5)	1 460 (60.5)	607 (59.7)	9 476 (62.8)
Metastasis, *n* (%)	4 (0.3)	4 (0.2)	9 (0.3)	11 (0.3)	13 (0.5)	4 (0.4)	45 (0.3)
Death, *n* (%)							
Alive	1 535 (99.2)	2 371 (98.7)	3 481 (97.3)	3 808 (95.2)	2 273 (94.2)	927 (91.2)	14 535 (96.2)
Death from other causes	11 (0.7)	28 (1.2)	94 (2.6)	180 (4.5)	129 (5.3)	84 (8.3)	529 (3.5)
Death from PCa	1 (0.1)	3 (0.1)	4 (0.1)	14 (0.3)	10 (0.4)	5 (0.5)	37 (0.2)
Discontinuing AS for different reasons, n (%)							*N* = 5 625 (37%)
Progression	225 (14.5)	435 (18.1)	698 (19.5)	746 (18.6)	386 (16.0)	107 (10.5)	2 599 (46.2)
Pathological progression	150 (9.7)	276 (11.5)	383 (10.7)	401 (10.0)	190 (7.9)	52 (5.1)	1 452 (25.8)
Other progression	75 (4.8)	159 (6.6)	315 (8.8)	345 (8.6)	196 (8.1)	55 (5.4)	1 147 (20.4)
Converting to WW	4 (0.3)	10 (0.4)	22 (0.6)	38 (0.9)	63 (2.6)	42 (4.1)	180 (3.3)
Death	10 (0.7)	18 (0.8)	67 (1.9)	131 (3.3)	95 (3.9)	69 (6.8)	391 (7.0)
Patient anxiety	53 (3.4)	77 (3.2)	139 (3.9)	138 (3.5)	73 (3.0)	25 (2.5)	511 (9.1)
Lost to follow-up	46 (3.0)	72 (3.0)	106 (3.0)	151 (3.8)	105 (4.3)	50 (4.9)	531 (9.4)
Unknown	128 (8.1)	206 (8.6)	311 (8.7)	419 (10.5)	230 (9.5)	116 (11.4)	1 413 (25.1)
Treatment received after AS, n (%)							*N* = 4 124 (73%)‡
ADT or hormonal therapy	4 (0.3)	18 (0.8)	44 (1.2)	102 (2.5)	105 (4.3)	71 (7.0)	348 (8.4)
Brachytherapy	34 (2.2)	61 (2.5)	105 (2.9)	113 (2.8)	62 (2.6)	10 (1.0)	385 (9.3)
Brachytherapy and ADT	1 (0.1)	2 (0.1)	3 (0.1)	5 (0.1)	1 (0.04)	1 (0.1)	13 (0.3)
EBRT and ADT	2 (0.1)	7 (0.3)	27 (0.8)	62 (1.6)	57 (2.4)	27 (2.7)	182 (4.4)
EBRT and brachytherapy	7 (0.5)	28 (1.2)	51 (1.4)	107 (2.7)	46 (1.9)	12 (1.2)	251 (6.1)
EBRT and brachytherapy and ADT	2 (0.1)	1 (0.04)	8 (0.2)	8 (0.2)	1 (0.04)	0 (0)	20 (0.5)
EBRT alone	17 (1.1)	46 (1.9)	115 (3.2)	148 (3.7)	157 (6.5)	62 (6.1)	545 (13.2)
Focal therapy	4 (0.3)	8 (0.3)	11 (0.3)	13 (0.3)	8 (0.3)	5 (0.5)	54 (1.3)
Radical prostatectomy	293 (18.9)	462 (19.2)	658 (18.4)	555 (13.9)	145 (6.0)	11 (1.1)	2 127 (51.6)
Radical prostatectomy and ADT	0 (0)	0 (0)	3 (0.1)	4 (0.1)	0 (0)	0 (0)	7 (0.2)
Radical prostatectomy, ADT and EBRT	0 (0)	0 (0)	1 (0.03)	0 (0)	0 (0)	0 (0)	1 (0.02)
Radical prostatectomy and EBRT	0 (0)	1 (0.04)	2 (0.1)	0 (0)	1 (0.04)	0 (0)	4 (0.1)
WW	1 (0.1)	7 (0.3)	12 (0.3)	20 (0.6)	31 (1.3)	13 (1.3)	86 (2.1)
Other	16 (1.0)	18 (0.8)	19 (0.5)	23 (0.6)	15 (0.6)	9 (0.9)	101 (2.5)

*ADT, androgen deprivation therapy; AS, active surveillance; EBRT, external beam radiotherapy; IQR, interquartile range; PCa, prostate cancer; WW, watchful waiting. *Database version 'gap3data_2.3', released in June 2017, †Percentage in the last column (All) is based on the total number of patients, the number of patients who discontinued AS, or the number of patients who received treatment after AS, respectively. ‡Proportion refers to the percentage of patients who received treatment after stopping AS.*

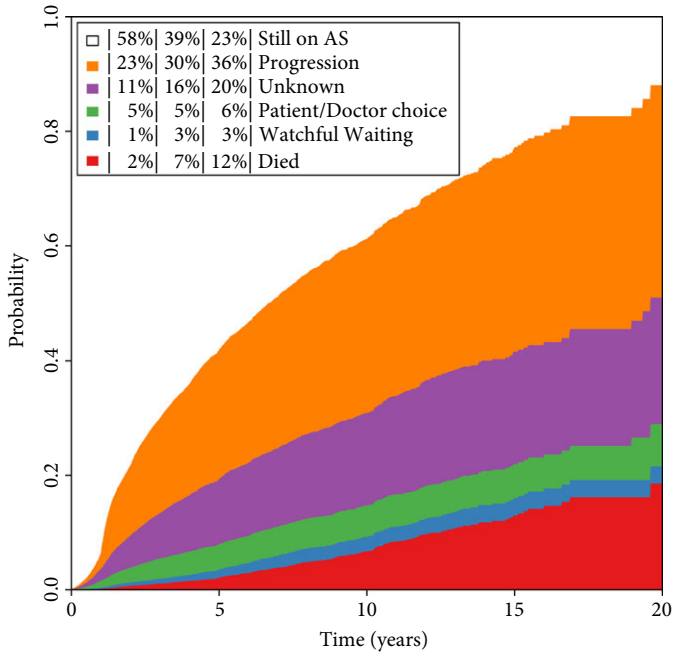
Table 3 Clinical and demographic characteristics and clinical follow-up for all patients who developed metastases during active surveillance and for all patients who developed metastases and died from prostate cancer*.

Characteristics	Distribution of characteristics of patients who developed metastases (*N* = 45)	Distribution of characteristics of patients who developed metastases and died from PCa (*N* = 17)
Median (IQR) age, years	66 (62–72)	66 (64–72)
Charlson comorbidity index, *n* (%)		
0	45 (100)	17 (100)
1	0 (0)	0 (0)
2	0 (0)	0 (0)
≥3	0 (0)	0 (0)
Missing	0 (0)	0 (0)
T stage (at DRE), *n* (%)		
T1	21 (46.7)	6 (35.3)
T2	15 (33.3)	7 (41.2)
T3	2 (4.4)	1 (5.9)
T4	1 (2.2)	1 (5.9)
Unknown	6 (13.3)	2 (11.8)
Gleason grade group, *n* (%)		
<6	3 (6.7)	0 (0)
6	28 (62.2)	10 (58.8)
>6	21 (46.7)	5 (29.4)
Unknown	4 (8.9)	2 (11.8)
PSA ng/mL, *n* (%)		
Median (IQR)	6.9 (4.8–8.7)	7.9 (4.3–12.5)
Missing, *n* (%)	4 (8.9)	1 (5.9)
Prostate volume, cc		
Median (IQR)	44 (31–55)	41 (29–50)
Missing, *n* (%)	23 (51.1)	9 (52.9)
PSA density ng/mL/mL		
Median (IQR)	0.14 (0.10–0.19)	0.14 (0.11–0.19)
Missing, *n* (%)	25 (55.6)	10 (58.8)
Positive cores, *n* (%)		
0	–	–
1	14 (42.4)	5 (29.4)
2	10 (30.3)	4 (23.5)
≥3	9 (27.3)	3 (17.6)
Median (IQR) time to metastasis, years	6.4 (3.5–9.9)	–
Median (IQR) time to death, years	–	10.0 (6.1–12.7)

*IQR, interquartile range; PCa, prostate cancer. *Database version 'gap3data_2.3', released in June 2017.*

A total of 5 625 patients (37%) discontinued AS for the following reasons: 46.2% for protocol-based progression; 3.3% switched to watchful waiting; 9.1% discontinued through patient or clinician choice; 7.0% died; and 25.1% discontinued for unknown reasons. For all patients who discontinued AS, treatment was reported in 73% of the cases (n = 4 124). Treatment after discontinuation was radical prostatectomy in 51.6% of patients, external beam radiotherapy in 13.2% of patients, brachytherapy in 9.3% of patients and primary androgen deprivation/hormonal therapy in 8.4% of patients (Table 2). Figure 1 shows the cumulative incidence curves of reasons for discontinuing AS. The percentage of total area shaded for each colour in the figure can be interpreted, at any

Fig. 1 Discontinuation of active surveillance (AS) over time (n = 14 033). Protocol-based progression indicates clinical and pathological progression, clinical progression, other PSA kinetics, pathological progression, PSA progression (PSA doubling time <3 years), or radiological progression.



time point, as the risk of discontinuing AS for that stated reason.

Of the 15 101 patients, 1 068 patients (7.1%) did not yet have available follow-up data. Among the remaining 14 033 patients, after 5, 10 and 15 years of follow-up, respectively, 58%, 39% and 23% of patients were still on AS, 23%, 30% and 36% discontinued because of protocol-based progression, 5%, 5% and 6% discontinued through patient or clinician choice, 1%, 3% and 3% switched to watchful waiting, 2%, 7% and 12% died (mostly from another cause), and 11%, 16% and 20% discontinued for unknown reasons.

Discussion

In recent years, AS has evolved from an experimental protocol to become a broadly accepted, in fact, preferred, management strategy for men diagnosed with low-risk PCa [15]. Nevertheless, consensus on inclusion criteria, surveillance schedules and intervention thresholds for AS of men with low-risk PCa is currently lacking. With this in mind, the Movember Foundation launched the GAP3 initiative.

Several findings deserve particular attention. GAP3 is the largest effort of its type to integrate patient data from men with PCa on AS. With >15 000 patients, the Movember AS database is the largest centralized PCa AS database to date,

comprising the majority of the world's AS patient data. Large volumes of AS data have been collected routinely for many years by the affiliated centres worldwide; hence, the central data source enables comparisons of determinants for inclusion and follow-up in AS, and subsequent clinical outcomes (e.g. disease progression), between cohorts and countries and it allows us to determine variable patterns over time. Data capture is nearly complete (i.e. available for at least 90% of the centres) for key variables such as: serum PSA levels, Gleason score and clinical stage at time of PCa diagnosis; serum PSA levels, T stage by DRE and biopsy characteristics during follow-up; and reasons for discontinuing AS, treatment choices and cause of death. The database thus has a significant amount of highly informative patient data on AS for low-risk PCa. It can therefore make significant contributions to the development of evidence-based consensus guidelines for AS, and as a result, improve the lives of men diagnosed with low-risk PCa.

There are some limitations that need to be considered when using data from GAP3. The database is 'ambidirectional', meaning that it has both a retrospective and a prospective component. Up until now, the GAP3 database has been purely a retrospective database. As a consequence, there was limited control over data collection, and the data of interest were sometimes incomplete or inconsistently measured. For instance, in 18 cohorts the reason for discontinuation of AS is not available. For future analyses, the individual centres will be requested to supply the missing data (if available). During the course of the GAP3 project, it has become apparent that there is an urgent need to assess the value of MRI with respect to disease monitoring in patients on AS. The current patient series has only limited imaging data from MRI, and currently, almost no data are available for quality of life and genomic testing. However, additional funding has now been secured from the Movember Foundation to sustain the database and to add a prospective element, thereby providing the opportunity to collect evidence on imaging (MRI), molecular (genomics) markers, patient-related outcomes and more.

Metastatic disease or death from PCa are ultimate endpoints by which AS should be evaluated [16]; however, because of the slow-growing nature of low-risk PCa, prospective evaluation of these endpoints requires at least another 10–15 years of follow-up [16]. To date, mainly data from non-mature prospective clinical trials of AS, which have a mean follow-up of <10 years, are available. The GAP3 database currently also has limited follow-up time, but will in future provide the main resource of real-world data on AS management.

In the global database, PCa death and metastasis remain rare events (both <1%). Current analyses therefore make use of surrogate endpoints such as discontinuation of AS and/or changes in PCa treatment. Nevertheless, follow-up is ongoing until at least 2019, so that in the future GAP3 will contain even more valuable data and provide better insight into patient outcomes.

Active surveillance is evolving into a well-accepted management strategy for appropriately selected men. Unless the over-diagnosis of indolent PCa is reduced by alternative diagnostic strategies, AS will continue to play an important role. The GAP3 initiative will make significant contributions to this field of research by offering standard, evidence-based guidelines [3]. Clinicians will be able to use these guidelines more confidently to identify patients who are suitable for AS and also to decide whose PCa has progressed and will, therefore, require treatment. Such guidelines will provide reassurance to patients that they have made the best treatment choice for their type of disease [3]. Longer follow-up, achieved by ongoing commitment of GAP3 participating centres, and the evaluation of, for instance, imaging and new biomarkers, will result in more valuable data and eventually in better patient outcomes.

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Conflict of Interest

None declared.

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Appendix A

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Abbreviations: AS, active surveillance; GAP3, Global Action Plan Prostate Cancer Active Surveillance initiative; IQR, interquartile range; PCa, prostate cancer.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Participating centers and number of patients.
Table S2. Protocol overview: Recommendations for patient selection for each participating center.
Table S3. Protocol overview: Recommendations for follow-up monitoring for each participating center.
Table S4. Characteristics at time of PCa diagnosis for all men included in the GAP3 cohort for each participating center.