Prospective Longitudinal Health-related Quality of Life Analysis of the Finnish Arm of the PRIAS Active Surveillance Cohort : 11 Years of Follow-up

Lokman, Utku

2022

Lokman , U , Vasarainen , H , Lahdensuo , K , Erickson , A , Muhonen , T , Mirtti , T & Rannikko , A 2022 , ' Prospective Longitudinal Health-related Quality of Life Analysis of the Finnish Arm of the PRIAS Active Surveillance Cohort : 11 Years of Follow-up ' , European Urology Focus , vol. 8 , no. 5 , pp. 1151-1156 . https://doi.org/10.1016/j.euf.2021.06.008

http://hdl.handle.net/10138/353412
https://doi.org/10.1016/j.euf.2021.06.008

EUROPEAN UROLOGY FOCUS 8 (2022) 1151–1156

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus

Prostate Cancer

Prospective Longitudinal Health-related Quality of Life Analysis of the Finnish Arm of the PRIAS Active Surveillance Cohort: 11 Years of Follow-up

Utku Lokman [a,b,c,†,*], *Hanna Vasarainen* [a,b,†], *Kanerva Lahdensuo* [a,b], *Andrew Erickson* [b,d,e], *Timo Muhonen* [f], *Tuomas Mirtti* [b,d], *Antti Rannikko* [a,b]

[a] *Department of Urology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland;* [b] *Research Program in Systems Oncology, Faculty of Medicine, University of Helsinki, Helsinki, Finland;* [c] *Department of Urology, Queen Alexandra Hospital, Portsmouth Hospitals University NHS Trust, Portsmouth, UK;* [d] *Department of Pathology and Medicum, HUS Helsinki University Hospital and University of Helsinki, Helsinki, Finland;* [e] *Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK;* [f] *Department of Oncology, Clinicum, University of Helsinki, Helsinki, Finland*

Article info

Article history:
Accepted June 20, 2021

Associate Editor:
Derya Tilki

Keywords:
Prostate cancer
Active surveillance
Quality-of-life
Treatment change
Discontinuation

Abstract

Background: Living with an untreated cancer may alter quality of life (QoL) in the long term.
Objective: To prospectively study long-term changes in general, mental, and physical QoL in a contemporary active surveillance (AS) patient cohort with low-risk prostate cancer (PCa).
Design, setting, and participants: The study population consisted of patients enrolled in the PRIAS trial in Helsinki University Hospital ($n = 348$). The RAND-36 questionnaire was used to assess general QoL at the start of AS and at 1, 3, 5, 7, 9, and 11 years during follow-up. Patients who had undergone robot-assisted laparoscopic prostatectomy (RALP; $n = 88$) also received the questionnaire after treatment.
Outcome measurements and statistical analysis: Changes over time were analysed using multilevel mixed-effects regression models, and reported as the mean and95% confidence interval. A rule of 0.5 × standard deviation was used to estimate changes of clinical importance.
Results and limitations: Median follow-up until the end of AS or last follow-up was 7.2 (range 0.3–12.7) yr. A decrease was observed in six of eight QoL subdomains at 7 yr. However, all scores were above age-stratified reference values. There was no difference between the group who continued AS throughout the study period and the group who discontinued AS and underwent RALP. More than half of the study cohort discontinued AS ($n = 198$; 57%), 135 men (68%) because of events specified in the protocol and only seven (3.5%) because of anxiety. Metastatic disease developed in six patients (1.7%), and two cases (0.6%) of PCa-related death were recorded among 348 patients in more than 12 yr of overall follow-up. The lack of a randomised control population is a limitation of the study.
Conclusions: Contemporary protocolised AS does not impair general QoL. Men undergoing a treatment change (RALP) did not experience a decrease in QoL before or after their treatment change.
Patient summary: Active surveillance is a safe treatment option for men with low-risk prostate cancer. We show that this follow-up strategy does not cause a decline in patients' general quality of life.

† These authors contributed equally to this work.
* Corresponding author. Department of Urology, Queen Alexandra Hospital, Portsmouth Hospitals University NHS Trust, Southwick Hill Road, Cosham, Portsmouth PO6 3LY, UK. Tel. +44 2392 286000.
E-mail addresses: utku.lokman@nhs.net, utku.lokman@porthosp.nhs.uk (U. Lokman).

https://doi.org/10.1016/j.euf.2021.06.008

1. Introduction

The incidence of prostate cancer (PCa) has increased during recent years, mainly because of the widespread use of prostate-specific antigen (PSA) testing. Although early diagnosis is an important issue in cancer management, it may lead to detection of clinically insignificant cancers, that is, cancers that during one's lifetime are unlikely to become symptomatic, a phenomenon called overdiagnosis. It has been estimated that up to 50% of PCa cases are overdiagnosed [1], with rates being higher in screen-detected series [2].

The purpose of active surveillance (AS) is to delay or avoid treatment-related side effects by reducing unnecessary treatments, which may also reduce treatment-related costs [2]. The European Association of Urology guidelines recommend AS a treatment option for patients with low-risk PCa and selected patients with intermediate-risk PCa [3].

Patients in AS cohorts should by definition be fit for radical treatment. However, the average age of such patients is slightly on the older side and thus they are likely to have comorbidities. In one of the most cited AS cohorts, the Klotz Toronto cohort [4], other-cause mortality exceeded PCa mortality by 18-fold. The same cohort has been followed for more than 15 yr and the results demonstrate that AS is a safe and feasible option for low-risk and some selected intermediate-risk PCa cases. Less than 3% of the patients developed metastatic disease and less than 2% died of PCa [5]. Thus, AS seems to be a safe treatment option for patients with low-risk PCa and is now recommended by most of the guidelines.

However, a cancer left untreated at a still-curable stage may cause stress and anxiety in some patients and ultimately impair their quality of life (QoL). Results concerning anxiety have been variable. Some studies suggest that living with an untreated cancer may lead to an increase in psychological morbidity [2]. Conversely, AS for PCa has been associated with similar or lower psychological morbidity in comparison to the curative treatment option [2]. Recent data obtained from the monitoring arm of the ProtecT trial showed that QoL remained stable for 6 yr of follow-up [6]. However, the monitoring arm in the ProtecT trial represents more of an intermediate phase between watchful waiting (WW) and contemporary AS because it was only based on repeated PSA measurements. Thus, no repeat biopsies or predefined triggers for intervention were used. As a general concept, AS may have a greater impact on QoL than WW, as it includes more diagnostic tests; however this strategy can also reduce stress for patients. To date, there are no data on the longitudinal long-term effects of contemporary AS on QoL.

Here we present data on general QoL in the Helsinki arm of the PRIAS trial with long-term follow-up (median 7.2 yr, range 0.3–12.7 yr), as well as data for patients who discontinued AS and underwent RALP.

2. Patients and methods

The PRIAS study is a prospective AS trial that started in eight countries in 2006, and currently covers 21 countries worldwide. PRIAS comprises 9018 patients in 124 centres as of January 31, 2021. The trial involves a protocolised follow-up strategy for selected men with low-risk PCa; the protocol has been published previously [7].

The ethics committee of Helsinki University Central Hospital approved the PRIAS trial (HUS 276/E6/06).

Patients who had enrolled in the Finnish arm of the PRIAS study ($n = 348$) in Helsinki University Hospital completed the RAND-36 questionnaire at the beginning of surveillance, and in years 1, 3, 5, 7, 9, and 11 during their surveillance. From December 2006 to August 2019, 198 men (57%) had discontinued and 150 (43%) were still on AS. Men who had discontinued AS and had undergone robot-assisted laparoscopic prostatectomy (RALP) also completed the post-treatment questionnaire (median 30.0 mo, range 0.1–55.3 mo after surgery). Of these 198 men, 135 (68%) discontinued AS for protocol-based reasons.

RAND-36 consists of eight domains, including physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and general health. Questionnaire results were converted into scores on a scale of 0–100, with a higher score indicating better health-related QoL [8]. The Finnish version of the RAND-36 has been validated and has a good reproducibility range for the Finnish population (Cronbach α 0.80–0.94). Further details on RAND-36 are provided in the Supplementary material.

Data for continuous variables at baseline are presented as the median and interquartile range (IRQ). Changes and differences between the changes were analysed using multilevel mixed-effects regression models. The observations were considered nested within individuals to account for repeated measurements. Results are presented as means and mean differences between groups with corresponding 95% confidence intervals. SPSS for Windows version 25.0 and Stata version 15.1 (StataCorp, College Station, TX, USA) were used for analyses. Changes greater than 0.5 × standard deviation (0.5 × SD rule) were considered clinically significant [9].

3. Results

At the time of the analysis, 348 patients had entered the trial in Helsinki University Hospital since recruitment started in 2006. Of these, 279 (80%) had returned the RAND-36 questionnaire at baseline and 265 (76%) at least once during follow-up. The median follow-up for the patients who continued AS was 86 (range 4–153) mo. Demographic and clinical data for the study group are summarized in Table 1. Of the 348 men, 150 (43%) were still on AS and 198 (57%) had discontinued. Overall follow-up was 12 yr. The median follow-up until discontinuation for any reason was 21.6 (range 0.3–137.4) mo. A total of 135 men (68%) with a median surveillance time of 18 (range 4–110) mo had changed treatment for protocol-based reasons. Of all the Helsinki PRIAS patients, 13 were lost to follow up, nine of

Table 1 – Descriptive characteristics of the study cohort (Helsinki PRIAS cohort; $n = 348$)

Variable	Result
Mean age, yr (SD)	68 (6.8)
Mean PSA, ng/ml (SD)	5.6 (1.9)
Mean free PSA, ng/ml (SD)	0.8 (0.5)
Mean percentage free PSA, % (SD)	15.1 (7.7)
Mean prostate volume, ml (SD)	43 (15.4)
Mean PSA density, ng/ml/ml (SD)	0.14 (0.04)

SD = standard deviation; PSA = prostate-specific antigen.

whom moved to another city or country; only seven discontinued AS because of anxiety (2.0% of the study cohort) after a median of 6 mo of follow-up. Of the 198 men who discontinued AS, 152 underwent radical treatment. Surgery was the most common treatment (n = 111, 73%). Of those who underwent surgery, 23 men had open RP (21%) and 88 had RALP (79%). Moreover, 41 men in the radical treatment subgroup (27%) had radiotherapy. Of these 41 men, 34 (83%) had external beam RT and seven men (17%) had brachytherapy. For 33 men (9.4% of the entire cohort), other unrelated significant health conditions occurred during AS, so WW was initiated; seven (2.0%) patients died during AS due to unrelated reasons. Six men (1.7%) developed metastatic disease, all diagnosed with grade group 1 PCa, and two (0.6%) died of PCa.

3.1. General QoL

Of the entire cohort of 348 Helsinki PRIAS patients, the RAND-36 questionnaire was returned by 279/348 (80%) at baseline, 254/319 (80%) at 1 yr, 158/199 (80%) at 3 yr, 77/130 (60%) at 5 yr, 62/91 (68%) at 7 yr, 32/47 (68%) at 9 yr, and 12/23 (52%) at 11 yr during AS follow-up, and by 61/88 men (69%) who discontinued AS and underwent RALP (median 30.0 mo, range 0.1–55.3 mo after surgery).

As the number of men remaining at AS follow-up at 9 and 11 yr is limited, we first analysed the data for the first 7 yr. At 7 yr of AS, decreases were observed for six of eight RAND-36 subdomains (Supplementary Table 1); only the decrease in physical functioning could be considered of clinical importance using the 0.5 × SD rule [9]. However, all scores were above age-stratified Finnish reference values (range 47.0–90.3; see Supplementary Table 3 for details) [10]. No changes were observed when the QoL subdomain scores were averaged for the first 7 yr of AS (Supplementary Table 1).

Next, we graphically depicted the RAND-36 subdomain scores for all time points on AS and for men who had discontinued AS and underwent delayed RP; Figure 1 presents the results for general health and Supplementary Figure 1 shows results for all eight RAND-36 domains. All QoL domains remained relatively stable throughout the AS period and we observed no evidence of a difference in QoL subdomains after AS discontinuation and delayed RP.

We then analysed whether men about to discontinue AS and undergo RP had worsening QoL during AS before their treatment change. The number of men on AS beyond 5 yr and discontinuing thereafter is limited, so we analysed the result at 5 yr and then averaged for all time points until 5 yr (Supplementary Table 2). Again, we observed no evidence of a difference.

Finally, we graphically compared men who had remained on AS and men who had discontinued AS and underwent delayed RP; Figure 2 presents the results for general health and Supplementary Figure 2 shows results for all eight RAND-36 domains. As the number of men who discontinued AS and underwent RP beyond 5 yr was limited, we truncated the follow-up at 5 yr. No evidence of a difference was observed.

4. Discussion

Our study, which extended the analysis of QoL in the Helsinki arm of the PRIAS AS cohort up to 11 yr of

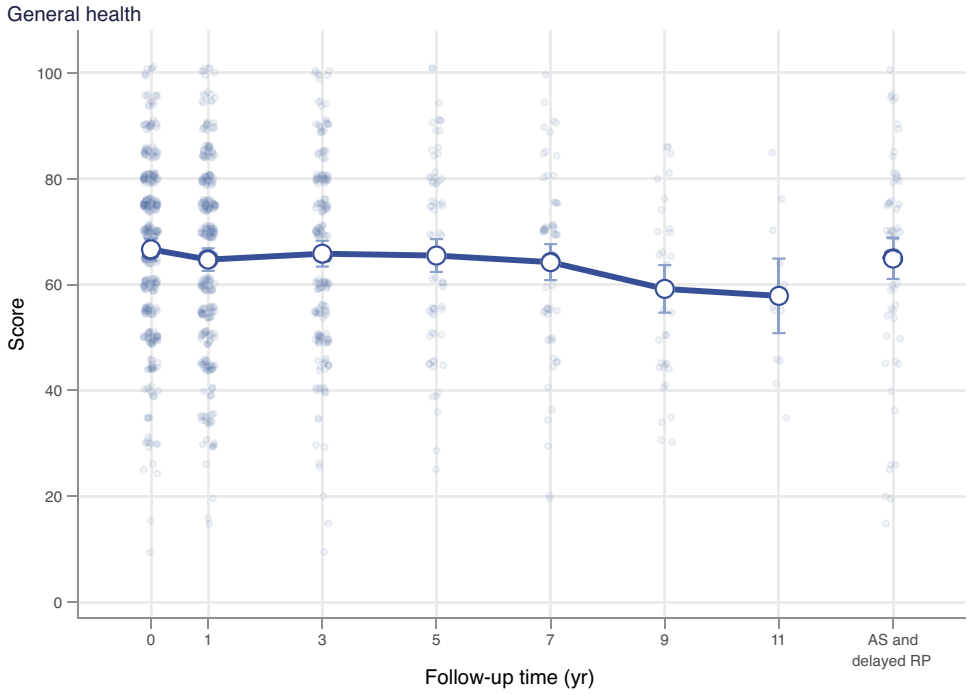

Fig. 1 – RAND-36 results for the general health subdomain for the entire active surveillance (AS) cohort over time analysed using multilevel mixed-effects regression models, and reported as the mean score and 95% confidence interval. Individual scores are represented as background dots. RP = radical prostatectomy. A similar graph for all eight RAND-36 subdomains is provided in Supplementary Figure 1.

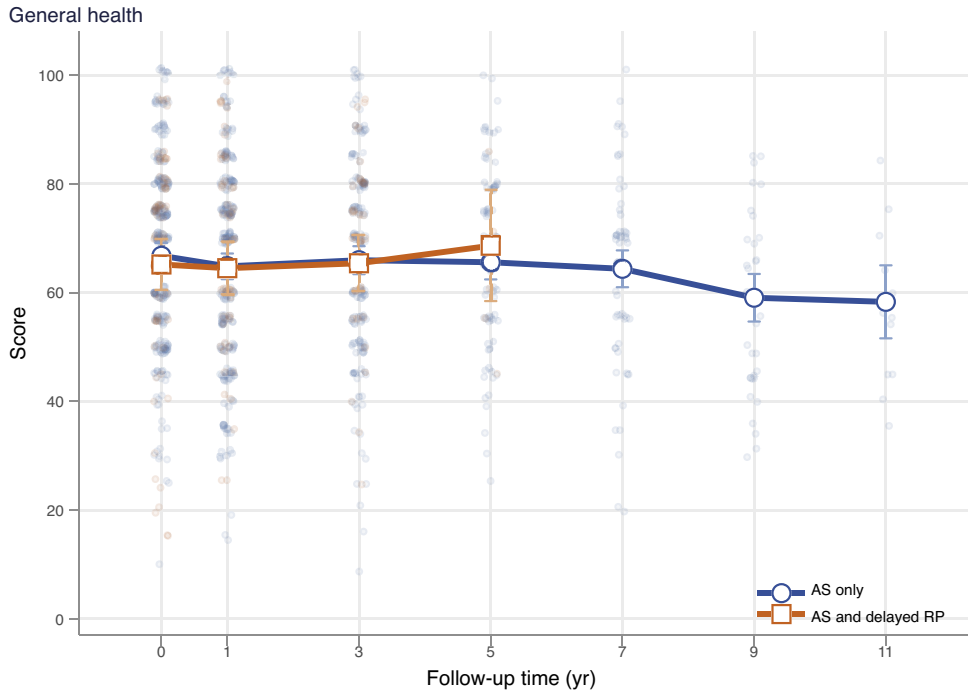

Fig. 2 – Changes in RAND-36 scores for the general health subdomain over time plotted separately for men continuing active surveillance (AS) and men discontinuing AS and undergoing radical prostatectomy (RP) analysed using multilevel mixed-effects regression models and reported as the mean score and 95% confidence interval. As the number of men who discontinued AS and underwent RP beyond 5 yr is limited, we truncated the follow-up at 5 yr. A similar graph for all eight RAND-36 subdomains is provided in Supplementary Figure 2.

surveillance, provides further support for the notion that contemporary AS does not have significant QoL sequelae. Our data indicate that men undergoing a treatment change to RP after a period of AS do not experience a reduction in QoL before or after curative treatment.

The strengths of our study are its prospective and longitudinal design, its use of a validated questionnaire, intermediate- to long-term follow-up, and the low number of patients lost to follow-up (one patient moved abroad). Furthermore, the data support guideline recommendations for contemporary AS, which entails frequent follow-up visits, repeat biopsies, and triggers for intervention. Our results are representative of AS, as they were obtained from the largest AS cohort to date, the PRIAS cohort. The PRIAS cohort comprises more than 9000 patients recruited and followed prospectively worldwide. Clearly, the lack of a randomised control population is a major limitation of our study. In addition, only a general QoL questionnaire (RAND-36) and no disease-specific questionnaires (eg, EPIC-26) or anxiety questionnaires were used in our study. The possible lack of specificity of RAND-36 may hamper the detection of minute changes in, for example, anxiety related to AS [11,12]. Nevertheless, the use of general QoL instruments will still allow future cost-effectiveness analyses and comparisons across different treatment modalities. Importantly, data for the patients who discontinued AS add much value and provide an opportunity to compare the results prospectively during AS and after treatment. The size of the cohort may also be considered a weakness. However, only a few larger contemporary AS cohorts have been published and none of them had prospectively collected longitudinal QoL data such as in the present study.

In contrast to the ProtecT trial, the PRIAS study involves an AS cohort identified using well-defined inclusion criteria, a clear follow-up protocol, and predefined triggers for intervention. Despite the fact that the PRIAS protocol recommends tedious monitoring visits and frequent repeat biopsies, known to be bothersome for patients [8,13], no effect on general QoL was observed. This lack of an apparent effect is in line with a recent analysis with shorter follow-up showing that QoL was comparable between AS patients and patients treated surgically or with RT during 3-yr follow-up. However, erectile function and urinary incontinence were worse in the RP arm [14]. Taken together, these findings are reassuring and emphasise that with respect to general QoL, AS for PCa is safe. Importantly, delayed RP also seems to be safe from a QoL perspective, as men did not experience worsening QoL before or after delayed RP.

Studies on psychological aspects, anxiety, and general QoL during AS are scarce. A rather recent review could only identify ten such studies [15]. One of the main conclusions of the review was that data, especially in the long term, are lacking. The first four papers that reported intermediate- to long-term data concluded that moderate to severe anxiety was an infrequent finding [11,16–18]. In one of the first comparative studies, Thong et al [19] reported comparable QoL scores between retrospectively selected AS and RT cohorts. In another study, short-term QoL was similar

between RP and AS (3-yr follow-up) apart from worse erectile and urinary scores in the RP cohort [20]. In terms of QoL, AS generally seems a better option than RP [21]. Furthermore, in concordance with our results, QoL seems to be stable during AS in various populations globally [15]. Therefore, it appears that although there are no data showing a survival benefit for immediate curative treatment, there is not much to justify RP or RT over AS for low-risk PCa in terms of QoL. Of interest is our finding that when general QoL is compared to baseline, it is not affected by delayed RP. By contrast, worse sexual, urinary, and bowel functions are well-known sequelae of RP and RT, but these changes are not reflected in general QoL. This paradox is in line with data from the ProtecT trial, which found that specific questionnaires demonstrated worsening of urinary, sexual, and bowel functions, but general QoL, measured using the SF-12 instrument, remained stable [6,22].

However, some contradictory findings have been reported. One study claimed that depression and anxiety are more common among AS patients than in the normal population of men of similar age [23] but a systematic review stated that insufficient long-term data exist to draw conclusions [24].

In most of the published AS series, 15–41% of patients had changed treatment within 5 yr of starting surveillance [25], whereas 5–10% of men were actively treated because of anxiety [26]. The updated analysis of anxiety data from the Dutch PRIAS cohort with up to 18 mo of surveillance showed decreasing anxiety [27]. The authors hypothesised that AS patients with anxiety discontinue early on, a statement supported by another study [28], or are more likely to be treated initially rather than put on AS [29]. In our cohort, only seven men discontinued AS because of anxiety and they did so after a median of only 6 mo of AS, which supports the finding of the Dutch study group. In the entire PRIAS study, the number of patients who discontinued AS because of anxiety was 5% after 10 yr of follow-up [30], which is clearly more than the 2% found in our AS cohort. All patients in our cohort who discontinued AS because of anxiety did so very early on, suggesting perhaps a failure in communication between the treating urologist and the patient. Such communication would initially occur in the shared decision-making process when choice of the correct treatment is made. This emphasises the importance of the decision-making process, and is supported by the data from Bellardita et al [11]. Taking together our findings and the current literature, it seems evident that emphasis should be placed on shared decision-making and patient support during the early years of AS, whereas there seems to be less risk of adverse QoL and anxiety during longer follow-up.

5. Conclusions

We showed that contemporary AS does not cause a deterioration in general QoL. The effect of delayed RP on general QoL is also negligible. Future studies should address more specific components of QoL, anxiety, and decision regret during and after AS using validated questionnaires.

Author contributions: Utku Lokman 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: Rannikko, Mirtti, Vasarainen, Lokman.
Acquisition of data: Lokman, Vasarainen, Lahdensuo.
Analysis and interpretation of data: Lokman, Vasarainen, Erickson, Muhonen, Rannikko.
Drafting of the manuscript: Lokman, Vasarainen, Mirtti, Rannikko.
Critical revision of the manuscript for important intellectual content: Rannikko, Mirtti.
Statistical analysis: Lokman, Vasarainen, Rannikko.
Obtaining funding: Rannikko, Mirtti.
Administrative, technical, or material support: Rannikko, Mirtti, Vasarainen.
Supervision: Rannikko, Mirtti.
Other: None.

Financial disclosures: Utku Lokman certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: Research grants for nonprofit academic research were provided by the Finnish Cancer Foundation and the Jane and Aatos Erkko Foundation. The sponsors played no direct role in the study.

Acknowledgments: We thank our prostate cancer nurses. We are grateful to the Finnish Cancer Foundation and the Jane and Aatos Erkko Foundation for research grants. We also thank Markku Peltonen for statistical advice.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euf.2021.06.008.

References

[1] Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context. J Natl Cancer Inst 2009;101:374–83. http://dx.doi.org/10.1093/jnci/djp001.

[2] Rietbergen JB, Hoedemaeker RF, Kruger AE, Kirkels WJ, Schroder FH. The changing pattern of prostate cancer at the time of diagnosis: characteristics of screen detected prostate cancer in a population based screening study. J Urol 1999;161:1192–8.

[3] Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 2017;71:618–29. http://dx.doi.org/10.1016/j.eururo.2016.08.003.

[4] Klotz L, Zhang L, Lam A, Nam R, Mamedov A, Loblaw A. Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. J Clin Oncol 2010;28:126–31. http://dx.doi.org/10.1200/JCO.2009.24.2180.

[5] Klotz L, Vesprini D, Sethukavalan P, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J

Clin Oncol 2015;33:272–7. http://dx.doi.org/10.1200/jco.2014.55.1192.
[6] Donovan JL, Hamdy FC, Lane JA, et al. Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. N Engl J Med 2016;375:1425–37. http://dx.doi.org/10.1056/NEJMoa1606221.
[7] Bul M, Zhu X, Valdagni R, et al. Active surveillance for low-risk prostate cancer worldwide: the PRIAS study. Eur Urol 2013;63:597–603. http://dx.doi.org/10.1016/j.eururo.2012.11.005.
[8] Bokhorst LP, Alberts AR, Rannikko A, et al. Compliance rates with the Prostate Cancer Research International Active Surveillance (PRIAS) protocol and disease reclassification in noncompliers. Eur Urol 2015;68:814–21. http://dx.doi.org/10.1016/j.eururo.2015.06.012.
[9] Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care 2003;41:582–92. http://dx.doi.org/10.1097/01.MLR.0000062554.74615.4C.
[10] Aalto AM, Aro AR, Teperi J. RAND-36 as a measure of health-related quality of life: reliability, construct validity and reference values in the Finnish general population. Helsinki: Stakes; 1999.
[11] Bellardita L, Rancati T, Alvisi MF, et al. Predictors of health-related quality of life and adjustment to prostate cancer during active surveillance. Eur Urol 2013;64:30–6. http://dx.doi.org/10.1016/j.eururo.2013.01.009.
[12] van den Bergh RC, Korfage IJ, Bangma CH. Psychological aspects of active surveillance. Curr Opin Urol 2012;22:237–42. http://dx.doi.org/10.1097/MOU.0b013e328351dcb1.
[13] Kenttamies A, Rannikko A. Magnetic resonance imaging of prostate cancer. Duodecim 2015;131:1233–44.
[14] Barocas DA, Alvarez J, Resnick MJ, et al. Association between radiation therapy, surgery, or observation for localized prostate cancer and patient-reported outcomes after 3 years. JAMA 2017;317:1126–40. http://dx.doi.org/10.1001/jama.2017.1704.
[15] Bellardita L, Valdagni R, van den Bergh R, et al. How does active surveillance for prostate cancer affect quality of life? A systematic review. Eur Urol 2015;67:637–45. http://dx.doi.org/10.1016/j.eururo.2014.10.028.
[16] Punnen S, Cowan JE, Dunn LB, Shumay DM, Carroll PR, Cooperberg MR. A longitudinal study of anxiety, depression and distress as predictors of sexual and urinary quality of life in men with prostate cancer. BJU Int 2013;112:E67–75. http://dx.doi.org/10.1111/bju.12209.
[17] van den Bergh RC, Vasarainen H, van der Poel HG, et al. Short-term outcomes of the prospective multicentre 'Prostate Cancer Research International: Active Surveillance' study. BJU Int 2010;105:956–62. http://dx.doi.org/10.1111/j.1464-410X.2009.08887.x.
[18] Vasarainen H, Lokman U, Ruutu M, Taari K, Rannikko A. Prostate cancer active surveillance and health-related quality of life: results of the Finnish arm of the prospective trial. BJU Int 2012;109:1614–9. http://dx.doi.org/10.1111/j.1464-410X.2011.10677.x.
[19] Thong MS, Mols F, Kil PJ, Korfage IJ, van de Poll-Franse LV. Prostate cancer survivors who would be eligible for active surveillance but were either treated with radiotherapy or managed expectantly: comparisons on long-term quality of life and symptom burden. BJU Int 2010;105:652–8. http://dx.doi.org/10.1111/j.1464-410X.2009.08815.x.
[20] Jeldres C, Cullen J, Hurwitz LM, et al. Prospective quality-of-life outcomes for low-risk prostate cancer: active surveillance versus radical prostatectomy. Cancer 2015;121:2465–73. http://dx.doi.org/10.1002/cncr.29370.
[21] Lardas M, Liew M, van den Bergh RC, et al. Quality of life outcomes after primary treatment for clinically localised prostate cancer: a systematic review. Eur Urol 2017;72:869–85. http://dx.doi.org/10.1016/j.eururo.2017.06.035.
[22] Neal DE, Metcalfe C, Donovan JL, et al. Ten-year mortality, disease progression, and treatment-related side effects in men with localised prostate cancer from the ProtecT randomised controlled trial according to treatment received. Eur Urol 2020;77:320–30. http://dx.doi.org/10.1016/j.eururo.2019.10.030.
[23] Watts S, Leydon G, Eyles C, et al. A quantitative analysis of the prevalence of clinical depression and anxiety in patients with prostate cancer undergoing active surveillance. BMJ Open 2015;5:e006674. http://dx.doi.org/10.1136/bmjopen-2014-006674.
[24] Whiting PF, Moore TH, Jameson CM, et al. Symptomatic and quality-of-life outcomes after treatment for clinically localised prostate cancer: a systematic review. BJU Int 2016;118:193–204. http://dx.doi.org/10.1111/bju.13499.
[25] Selvadurai ED, Singhera M, Thomas K, et al. Medium-term outcomes of active surveillance for localised prostate cancer. Eur Urol 2013;64:981–7. http://dx.doi.org/10.1016/j.eururo.2013.02.020.
[26] Klotz L. Active surveillance, quality of life, and cancer-related anxiety. Eur Urol 2013;64:37–9. http://dx.doi.org/10.1016/j.eururo.2013.01.023.
[27] Venderbos LD, van den Bergh RC, Roobol MJ, et al. A longitudinal study on the impact of active surveillance for prostate cancer on anxiety and distress levels. Psycho-oncology 2015;24:348–54. http://dx.doi.org/10.1002/pon.3657.
[28] Dall'Era MA. Patient and disease factors affecting the choice and adherence to active surveillance. Curr Opin Urol 2015;25:272–6. http://dx.doi.org/10.1097/MOU.0000000000000154.
[29] Latini DM, Hart SL, Knight SJ, et al. The relationship between anxiety and time to treatment for patients with prostate cancer on surveillance. J Urol 2007;178:826–31. http://dx.doi.org/10.1016/j.juro.2007.05.039.
[30] Bokhorst LP, Valdagni R, Rannikko A, et al. A decade of active surveillance in the PRIAS study: an update and evaluation of the criteria used to recommend a switch to active treatment. Eur Urol 2016;70:954–60. http://dx.doi.org/10.1016/j.eururo.2016.06.007.