

### Appendix 1: Criteria used to assess rigour of guideline development\*

Systematic search methods used	Details of the strategy used to search for evidence should be provided including search terms used, sources consulted and dates of the literature covered. Sources may include electronic databases (e.g. MEDLINE, EMBASE, CINAHL), databases of systematic reviews (e.g. the Cochrane Library, DARE), handsearching journals, reviewing conference proceedings and other guidelines (e.g. the US National Guideline Clearinghouse, the German Guidelines Clearinghouse). Further point for judgement on completeness of search
Selection criteria clearly described	Criteria for including / excluding evidence identified by the search should be provided. These criteria should be explicitly described and reasons for including and excluding evidence should be clearly stated. For example, guideline authors may decide to only include evidence from randomised clinical trials and to exclude articles not written in English. Further point for judgement on application of criteria
Formulation of recommendations clearly described	There should be a description of the methods used to formulate the recommendations and how final decisions were arrived at. Methods include for example, a voting system, formal consensus techniques (e.g. Delphi, Glaser techniques). Areas of disagreement and methods of resolving them should be specified.
Consider relevant issues for monitoring in recommendations†	The guideline should consider factors relevant to test for monitoring, i.e. variability in measurements/need for repeat testing, rationale presented for interval frequency and PSA threshold, and acknowledge the uncertainties in the natural history of PSA following radical Rx.
Explicit link with supporting evidence	There should be an explicit link between the recommendations and the evidence on which they are based. Each recommendation should be linked with a list of references on which it is based.
Pre-publication external review	A guideline should be reviewed externally before it is published. Reviewers should not have been involved in the development group and should include some experts in the clinical area and some methodological experts. Patients' representatives may also be included. A description of the methodology used to conduct the external review should be presented, which may include a list of the reviewers and their affiliation.
Update procedure described	Guidelines need to reflect current research. There should be a clear statement about the procedure for updating the guideline. For example, a timescale has been given, or a standing panel receives regularly updated literature searches and makes changes as required.

\* This framework is adapted from the 'Rigour of development' section of the original AGREE Instrument: The AGREE Collaboration. The Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument, 2001. London: The AGREE Research Trust (<http://www.agreetrust.org/>).

†Original criterion related to treatment outcomes, i.e. "The guideline should consider health benefits, side effects, and risks of the recommendations. For example, a guideline on the management of breast cancer may include a discussion on the overall effects on various final outcomes. These may include: survival, quality of life, adverse effects, and symptom management or a discussion comparing one treatment option to another. There should be evidence that these issues have been addressed."

**Table of identified guidelines and summary of rigour of development (adapted from AGREE framework (1))**

Body	Brief description	Systematic search methods used	Selection criteria clearly described	Formulation of recommendations clearly described	Consider relevant issues for monitoring in recommendations	Explicit link with supporting evidence	Pre-publication external review	Update procedure described	Total	Comment
AUA 2007 (2)	Localised PCa management guideline	2	3	1	1	1	2	3	13	One database used, search poorly reported; inclusion criteria described but grounds for later exclusion of papers not clear; limited description of recommendation formulation; no basis for interval between measurements; evidence-based recommendations for threshold not possible; NH uncertainty acknowledged in recommendations, variability acknowledged but not in recommendations; no link between recommendations and evidence; External review carried out but not described; update recommended and to include only RCT evidence
AUA 2009 (3)	PSA best practice statement	1	1	2	1	2	2	1	10	No systematic search; inclusion criteria not described; some description of recommendation formulation; No interval between measurements recommended; consensus definition of threshold used; NH uncertainty not acknowledged; variability acknowledged but not in recommendations; some supporting evidence cited; peer review carried out but not described in detail; no mention of update
Aus CN 2002 (4)	Localised PCa management evidence based recommendations	4	1	2	1	2	2	2	14	Comprehensive and systematic search described; inclusion criteria not described; no interval between measurements recommended; states no widely accepted biochemical range applicable; NH uncertainty not acknowledged; variability acknowledged but not in recommendations; some supporting evidence cited; internal review carried out but not described in detail; update recommended but procedure not described
DUA 2007 (5)	PCa management guideline	3	2	3	2	2	2	2	16	Systematic search carried out but not fully described; some description of inclusion criteria; Interval between measurements based on evidence; consensus threshold used for post-RT, no justification for post-RP; NH uncertainty not acknowledged; variability acknowledged but not in recommendations; some link to supporting evidence; external review partly described; update recommended but procedure not described
EAU 2009 (6)	PCa management guideline	2	1	1	1	2	2	1	10	Systematic search carried out but only partly described; no description of inclusion criteria; formulation of recommendations not described; no basis for interval between measurements; consensus thresholds used; NH uncertainty not acknowledged; variability acknowledged but not in recommendations; some link to supporting evidence; external review conducted but not described; no mention of update
NCI PDQ 2008 (7)	PCa treatment evidence based summary for health professionals	1	1	3	3	2	1	2	13	No search described; no description of inclusion criteria; formulation of recommendations not described; No interval between measurements recommended; evidence-based recommendations for threshold post-RT not possible, basis for post-RP threshold given; NH uncertainty acknowledged in recommendations; variability acknowledged but not in recommendations Threshold/variability/uncertainty; some links to supporting evidence; external review not described; limited description of update procedures
NCCN 2009 (8)	PCa management guideline	1	1	1	2	2	1	1	9	No search described; no description of inclusion criteria; no description of formulation of recommendations; some justification given for interval between measurements; consensus threshold used for post-RT, no justification for post-RP; NH uncertainty and

Appendix to: Dinnes J, Hewison J, Altman DG, Deeks JJ. The basis for monitoring strategies in clinical guidelines: a case study of prostate-specific antigen for monitoring in prostate cancer. *CMAJ* 2011. DOI:10.1503/cmaj110600.

Copyright © 2011 Canadian Medical Association or its licensors

										variability not acknowledged; some links to supporting evidence; external review not described; no mention of update
NICE 2008 (9)	PCa diagnosis and treatment guideline	4	3	3	4	3	2	3	<b>22</b>	Systematic search carried out and fully described; inclusion criteria developed for each question but not reported; recommendation formulation described but methods used to deal with disagreement not reported; Attempted to find evidence to justify interval between measurements; relevant discussion regarding choice of thresholds; NH uncertainty and variability acknowledged in recommendations; clear link to supporting evidence; external review no described; update recommended but and procedure described
UK PCWG 1999 (10)	PCa management guideline	3	1	2	2	2	1	1	<b>12</b>	Systematic search carried out and fully described; inclusion criteria developed for each question but not reported; recommendation formulation described but methods used to deal with disagreement not reported; Interval between measurements justified; relevant discussion regarding choice of threshold post-RT only; NH uncertainty not acknowledged, variability acknowledged but not in recommendations; clear link to supporting evidence; external review not described; update recommended but and procedure described

## Studies used to support guideline recommendations

	Study design/aim (extracted from abstract)	Focus of study	Used to support guideline statements on:				
			Frequency	Threshold (RP)	Threshold (RT)	Variability	NH
ASTRO 1997 (11)	Consensus statement providing guidelines for PSA following radiation therapy	ASTRO consensus statement	UK PCWG		UK PCWG, DUA, NCI PDQ		
Cox 1999 (12)	Report of ASTRO consensus panel to develop evidence-based guidelines for (1) prostate re-biopsy after radiation and (2) radiation therapy with rising PSA levels after radical prostatectomy in the management of patients with localized prostatic cancer	ASTRO consensus statement			NCCN		
Roach 2006 (13)	Reports second consensus conference to revise the ASTRO definition of BF	ASTRO consensus statement			NICE, AUA 09, EAU, NCCN, NCI PDQ		
Carroll 2001 (14)	Best practice statement (AUA)	Best practice statement	NICE				
Aus 2006 (15)	Review of high-intensity focused ultrasound (HIFU) and cryosurgery as the primary treatment option in patients with prostate cancer.	Review			EAU		
Bott 2004 (16)	Review of management of recurrence following RP	Review		EAU			
Catton 2003 (17)	Review/comment paper examining follow-up strategies	Review	NICE				
Cookson 2007 (18)	AUA review of the variability in published definitions of biochemical recurrence; recommends a standard definition in patients treated with radical prostatectomy	Review		NICE, AUA 09			AUA 07
Edelman 1997 (19)	Review of available data on follow-up strategies	Review	NICE				
Lee 2005 (20)	Review of PSA kinetics in addition to clinical factors in the selection of patients for salvage local therapy	Review		NCCN			
Nelson 2003 (21)	Review of RP for PCa	Review		DUA		DUA	
Polascik 1999 (22)	Review of PSA	Review		EAU			
Selley 1997 (23)	HTA review of PCa mngmt	Review			Aus CN		
Vicini 2005 (24)	Review of PSA for monitoring pts after radical Rx	Review		NICE			NICE

Appendix to: Dinnes J, Hewison J, Altman DG, Deeks JJ. The basis for monitoring strategies in clinical guidelines: a case study of prostate-specific antigen for monitoring in prostate cancer. *CMAJ* 2011. DOI:10.1503/cmaj110600.

Copyright © 2011 Canadian Medical Association or its licensors

Yao 2003 (25)	Review/comment paper examining follow-up strategies	Review	NICE				
Albertsen 2004 (26)	Retrospective(?) study of 1136 men undergoing surgery or radiation to document patterns of PSA recurrence and quantify extent to which increasing PSA predicts death	NH of pts post-Rx		EAU			
Amling 2001 (27)	Retrospective(?) analysis of 2,782 men who had undergone radical prostatectomy to attempt to determine the best PSA cut point for defining BF	Testing defs of BF		EAU			
Booker 2004 (28)	Study of telephone follow-up led by a specialist nurse for pts undergoing RT	FU acceptability	NICE				
Buyyounouski 2005 (29)	Retrospective(?) review of 688 men who had undergone RT to compare three definitions of biochemical failure (BF) in terms of sensitivity, specificity etc for detecting of clinical progression	Testing defs of BF			DUA		
Cathala 2003 (30)	Feasibility study on 140 patients undergoing RP to determine acceptability of an internet FU service	FU acceptability	NICE				
Cheung 2005 (31)	Retrospective(?) analysis of 101 men who received salvage RT for biochemical failure after RP to compare outcomes for patients who received RT alone and for those who received combined RT and hormonal therapy	Prognosis following salvage Rx		NCCN			
Crook 1997 (32)	Prospective study of 207 to correlate the failure pattern after radiotherapy (RT) with pretreatment PSA and post-RT nadir PSA	NH of pts post-Rx			UK PCWG		
D'Amico 2004 (33)	Retrospective review of 8669 men who had undergone radical Rx to determine whether a short post-Rx PSADT is a suitable surrogate end point for prostate cancer specific mortality	NH of pts w/out-Rx		NICE			
Eastham 2003 (34)	Retrospective analysis of an unscreened population of 972 men over 4 years to determine whether year-to-year fluctuations in PSA levels are due to natural variation, rendering a single PSA test result unreliable.	Measurement variability				EAU	
Frazier 1993 (35)	Analysis of 226 patients who underwent radical perineal prostatectomy to identify whether raised serum PSA infers failure of the procedure	NH of pts post-Rx		NCI PDQ			NCI PDQ
Horwitz 2005 (36)	Determined the sensitivity and specificity of several BF definitions using pooled data on 4,839 patients treated with external beam radiation therapy (RT) alone	Testing defs of BF			AUA 07, AUA 09, NICE		
Klotz 2005 (37)	Reports PSADT in a series of 299 patients undergoing active surveillance for PCa	NH of pts post-Rx	DUA				
Kuban 2006 (38)	Primary study of patients treated with radioisotopic implant as solitary treatment for T1-T2 prostatic adenocarcinoma (n=2,693). Multiple PSA failure definitions were tested for their ability to predict clinical failure.	Testing defs of BF			AUA 07, AUA 09, NICE		NCI PDQ

Leibman 1995 (39)	Retrospective review of 628 patients who underwent RP to determine whether PCA recurrence can occur without an increase in serum PSA	NH of pts post-Rx			EAU		
Nielsen 2008 (40)	Retrospective review of data from 2570 men who had undergone RP to examine the effect of applying the 2005 ASTRO definition of BF (for RT pts) to surgical series.	Testing defns of BF			AUA 09		
Niwakawa 2002 (41)	Study of 221 patients treated with RP to determine the optimal frequency and method of follow-up to minimize medical cost	FU - optimal frequency	DUA				
Oefelein 1995 (42)	Retrospective review of data from 394 men who underwent RP to characterize the incidence of recurrent carcinoma despite undetectable serum PSA levels	NH of pts post-Rx			EAU		
Patel 2005 (43)	Retrospective review of 48 patients who had undergone salvage RT for biochemical relapse after RP to determine whether PSAV is a suitable selection criterion for salvage radiotherapy	Prognosis following salvage Rx		NCCN			
Pickles 2006 (44)	An analysis of a 'prospective' database of 2030 patients who underwent EBRT or brachytherapy to determine the false call rate for PSA relapse according to nine different PSA relapse definitions after a PSA bounce has occurred	Testing defns of BF			NICE		
Pound 1999 (45)	Retrospective review of a large surgical series (n=1997) to examine the natural history of progression to distant metastases in men with raised PSA following surgery	NH of pts post-Rx	DUA, NCCN	NCI PDQ, DUA, NICE, EAU			NCI PDQ, NICE
Ragde 1997 (46)	Study of 126 patients with localised PCA to determine the efficacy of treatment with iodine-125 radionuclides (2 definitions of PSA failure used)	Testing defns of BF		Aus CN			
Ray 2006 (47)	Retrospective(?) review of 4839 patients treated definitively with RT to determine the significance of PSA nadir and time to PSA nadir in predicting biochemical or clinical disease-free survival	NH of pts post-Rx			EAU		
Ritter 1992 (48)	Study of the prognostic value of the PSA in pretreatment evaluation and posttreatment follow-up in 63 patients undergoing RT for localised PCa	NH of pts post-Rx			Aus CN		
Rose 1996 (49)	To identify patients' symptoms following completion of radiotherapy for common cancers by a nurse-managed telephone interview in 111 pts treated with RT.	FU acceptability	NICE				
Sandler 2000 (50)	Retrospective database study of 1844 pts who had undergone RT and had a minimum of 2 post-RT PSAs separated by at least 1 week to determine the significance of biochemical failure i.e. in terms of survival	NH of pts post-Rx			NCI PDQ		NCI PDQ
Sartor 1997 (51)	Primary study of 400 patients treated with radiotherapy to determine whether the rate of PSA rise could differentiate future local versus metastatic failure.	NH of pts post-Rx			UK PCWG		
Stamey 1989 (52)	Study of pre- and post-Rx serum PSA in 102 men who underwent radical prostatectomy to determine usefulness of PSA as a pre-operative marker.	NH of pts post-Rx		NCI PDQ, EAU			
Stephan 2006 (53)	Assessed 5 frequently used commercial assay combinations in sera from 314 patients with prostate cancer (PCa) and 282 men with no evidence of prostate cancer to identify the	Measurement variability				EAU	

Appendix to: Dinnes J, Hewison J, Altman DG, Deeks JJ. The basis for monitoring strategies in clinical guidelines: a case study of prostate-specific antigen for monitoring in prostate cancer. *CMAJ* 2011. DOI:10.1503/cmaj110600.  
Copyright © 2011 Canadian Medical Association or its licensors

	interchangeability of the PSA values						
Stephenson 2004 (54)	Retrospective review of 501 patients who underwent salvage RT following RP to identify those variables indicative of a durable response	Prognosis following salvage Rx		NCCN			
Stephenson 2006 (55)	Tested 10 definitions of BF on 3,125 patients who underwent RP, to identify the one that best explains metastatic progression	Testing defns of BF		AUA 09, EAU, NICE			
Trapasso 1994 (56)	Primary study of patients undergoing radical retropubic prostatectomy (n=601) and followed with serial PSA determinations. Evaluated rate of detectable PSA (greater than 0.4 ng./ml.) as an indicator of cancer progression.	NH of pts post-Rx		EAU	EAU		
Trock 2008 (57)	Retrospective analysis of a cohort of 635 men undergoing RP and who experienced biochemical and/or local recurrence to determine the effect of salvage RT and to identify subgroups for whom salvage treatment is most beneficial	Prognosis following salvage Rx		NCCN			
Ward 2004 (58)	Retrospective cohort study of 211 men with detectable PSA following RP to determine whether PSADT predicts outcomes following salvage radiotherapy	NH of pts post-Rx		NCCN			
Zagars 1997 (59)	Analysis of 841 men with serial PSA determinations who underwent external beam radiation without androgen ablation to determine the kinetics of serum PSA after RT and to evaluate whether such kinetics provide prognostic information.	NH of pts post-Rx			UK PCWG		

Appendix to: Dinnes J, Hewison J, Altman DG, Deeks JJ. The basis for monitoring strategies in clinical guidelines: a case study of prostate-specific antigen for monitoring in prostate cancer. *CMAJ* 2011. DOI:10.1503/cmaj110600.

Copyright © 2011 Canadian Medical Association or its licensors

## References

1. The AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Safety Health Care* 2003; 12: 18-23.
2. American Urological Association. Guideline for the management of clinically localized prostate cancer. 2007 update. Maryland: American Urological Association Education and Research, Inc; 2007.
3. American Urological Association. Prostate-specific antigen best practice statement: 2009 update. Maryland: American Urological Association Education and Research, Inc; 2009.
4. Australian Cancer Network Working Party on Management of Localised Prostate Cancer. Clinical Practice Guidelines: Evidence-based information and recommendations for the management of localised prostate cancer. Canberra, Australia: National Health and Medical Research Council; 2002.
5. Dutch Urological Association. Prostate cancer. Nation-wide guideline version 1.0. Utrecht, Netherlands: Dutch Institute for Healthcare Improvement CBO; 2007.
6. Heidenreich A, Bolla M, Joniau S, van der Kwast TH, Matveev VB, Mason MD, et al. EAU guidelines on prostate cancer. Arnhem, Netherlands: European Association of Urology; 2009.
7. National Cancer Institute. PDQ® Prostate Cancer Treatment. Bethesda, MD: National Cancer Institute. Date last modified 2008. Available at: <http://cancer.gov/cancertopics/pdq/treatment/prostate/HealthProfessional>. Accessed 15-7-0010.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. National Comprehensive Cancer Network Inc; 2009.
9. National Institute for Health and Clinical Excellence. Prostate cancer: diagnosis and treatment. Full guideline. Cardiff: National Collaborating Centre for Cancer; 2008.
10. The Royal College of Radiologists' Clinical Oncology Information Network, British Association of Urological Surgeons. Guidelines on the management of prostate cancer. *Clin Oncol (R Coll Radiol)* 1999; 11: S53-S88.
11. American Society for Therapeutic Radiology and Oncology Consensus Panel. Consensus statement: guidelines for PSA following radiation therapy. *Int J Radiat Oncol Biol Phys* 1997; 37: 1035-1041.
12. Cox JD, Gallagher MJ, Hammond EH et al. Consensus statements on radiation therapy of prostate cancer: guidelines for prostate re-biopsy after radiation and for radiation therapy with rising prostate-specific antigen levels after radical prostatectomy. American Society for Therapeutic Radiology and Oncology Consensus Panel. *J Clin Oncol* 1999; 17: 1155.
13. Roach M, III, Hanks G, Thames H, Jr. et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate



cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. *Int J Radiat Oncol Biol Phys* 2006; 65: 965-974.

14. Carroll P, Coley C, McLeod D et al. Prostate-specific antigen best practice policy--part II: prostate cancer staging and post-treatment follow-up. *Urology* 2001; 57: 225-229.
15. Aus G. Current status of HIFU and cryotherapy in prostate cancer--a review. *Eur Urol* 2006; 50: 927-934.
16. Bott SR. Management of recurrent disease after radical prostatectomy. *Prostate Cancer Prostatic Dis* 2004; 7: 211-216.
17. Catton C, Milosevic M, Warde P et al. Recurrent prostate cancer following external beam radiotherapy: follow-up strategies and management. *Urol Clin North Am* 2003; 30: 751-763.
18. Cookson MS, Aus G, Burnett AL et al. Variation in the definition of biochemical recurrence in patients treated for localized prostate cancer: the American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel report and recommendations for a standard in the reporting of surgical outcomes. *J Urol* 2007; 177: 540-545.
19. Edelman MJ, Meyers FJ, Siegel D. The utility of follow-up testing after curative cancer therapy. A critical review and economic analysis. *J Gen Intern Med* 1997; 12: 318-331.
20. Lee A, D'Amico AV. Utility of prostate-specific antigen kinetics in addition to clinical factors in the selection of patients for salvage local therapy. *J Clin Oncol* 2005; 23: 8192-8197.
21. Nelson JB, Lepor H. Prostate cancer: radical prostatectomy. *Urol Clin North Am* 2003; 30: 703-23, viii.
22. Polascik TJ, Oesterling JE, Partin AW. Prostate specific antigen: a decade of discovery--what we have learned and where we are going. *J Urol* 1999; 162: 293-306.
23. Selley S, Donovan J, Faulkner A et al. Diagnosis, management and screening of early localised prostate cancer. *Health Technology Assessment* 1997; 1(2): 1-96.
24. Vicini FA, Vargas C, Abner A et al. Limitations in the use of serum prostate specific antigen levels to monitor patients after treatment for prostate cancer. *J Urol* 2005; 173: 1456-1462.
25. Yao SL, Dipaola RS, Yao SL et al. An evidence-based approach to prostate cancer follow-up. *Semin Oncol* 2003; 30: 390-400.
26. Albertsen PC, Hanley JA, Penson DF et al. Validation of increasing prostate specific antigen as a predictor of prostate cancer death after treatment of localized prostate cancer with surgery or radiation. *J Urol* 2004; 171: 2221-2225.
27. Amling CL, Bergstralh EJ, Blute ML et al. Defining prostate specific antigen progression after radical prostatectomy: what is the most appropriate cut point? *J Urol* 2001; 165: 1146-1151.
28. Booker J, Eardley A, Cowan R et al. Telephone first post-intervention follow-up for men who have had radical radiotherapy to the prostate: evaluation of a novel service delivery approach. *Eur J Oncol Nurs* 2004; 8: 325-333.

29. Buyyounouski MK, Hanlon AL, Eisenberg DF et al. Defining biochemical failure after radiotherapy with and without androgen deprivation for prostate cancer. *Int J Radiation Oncol Biol Phys* 2005; 63: 1455-1462.
30. Cathala N, Brillat F, Mombet A et al. Patient followup after radical prostatectomy by Internet medical file. *J Urol* 2003; 170: 284-287.
31. Cheung R, Kamat A, de Crevoisier R et al. Outcome of salvage radiotherapy for biochemical failure after radical prostatectomy with or without hormonal therapy. *Int J Rad Oncol Biol Phys* 2005; 63: 134-140.
32. Crook JM, Bahadur YA, Bociek RG et al. Radiotherapy for localized prostate carcinoma. The correlation of pretreatment prostate specific antigen and nadir prostate specific antigen with outcome as assessed by systematic biopsy and serum prostate specific antigen. *Cancer* 1997; 79: 328-336.
33. D'Amico AV, Moul J, Carroll PR et al. Prostate specific antigen doubling time as a surrogate end point for prostate cancer specific mortality following radical prostatectomy or radiation therapy. *J Urol* 2004; 172: S42-S46.
34. Eastham JA, Riedel E, Scardino PT et al. Variation of serum prostate-specific antigen levels: an evaluation of year-to-year fluctuations. *JAMA* 2003; 289: 2695-2700.
35. Frazier HA, Robertson JE, Humphrey PA et al. Is prostate specific antigen of clinical importance in evaluating outcome after radical prostatectomy. *J Urol* 1993; 149: 516-518.
36. Horwitz EM, Thames HD, Kuban DA et al. Definitions of biochemical failure that best predict clinical failure in patients with prostate cancer treated with external beam radiation alone: a multi-institutional pooled analysis. *J Urol* 2005; 173: 797-802.
37. Klotz L. Active surveillance with selective delayed intervention using PSA doubling time for good risk prostate cancer. *Eur Urol* 2005; 47: 16-21.
38. Kuban DA, Levy LB, Potters L et al. Comparison of biochemical failure definitions for permanent prostate brachytherapy. *Int J Radiation Oncol Biol Phys* 2006; 65: 1487-1493.
39. Leibman BD, Dilliogluligil O, Wheeler TM et al. Distant metastasis after radical prostatectomy in patients without an elevated serum prostate specific antigen level. *Cancer* 1995; 76: 2530-2534.
40. Nielsen ME, Makarov DV, Humphreys E et al. Is it possible to compare PSA recurrence-free survival after surgery and radiotherapy using revised ASTRO criterion--"nadir + 2"? *Urology* 2008; 72: 389-393.
41. Niwakawa M, Tobisu K, Fujimoto H et al. Medically and economically appropriate follow-up schedule for prostate cancer patients after radical prostatectomy. *Int J Urol* 2002; 9: 134-140.
42. Oefelein MG, Smith N, Carter M et al. The incidence of prostate cancer progression with undetectable serum prostate specific antigen in a series of 394 radical prostatectomies. *J Urol* 1995; 154: 2128-2131.

43. Patel R, Lepor H, Thiel R et al. Prostate-specific antigen velocity accurately predicts response to salvage radiotherapy in men with biochemical relapse after radical prostatectomy. *Urology* 2005; 65: 942-946.
44. Pickles T, British Columbia Cancer Agency. Prostate-specific antigen (PSA) bounce and other fluctuations: which biochemical relapse definition is least prone to PSA false calls? An analysis of 2030 men treated for prostate cancer with external beam or brachytherapy with or without adjuvant androgen deprivation therapy. *Int J Radiation Oncol Biol Phys* 2006; 64: 1355-1359.
45. Pound CR, Partin AW, Eisenberger MA et al. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA* 1999; 281: 1591-1597.
46. Ragde H, Blasko JC, Grimm PD et al. Interstitial iodine-125 radiation without adjuvant therapy in the treatment of clinically localized prostate carcinoma. *Cancer* 1997; 80: 442-453.
47. Ray ME, Thames HD, Levy LB et al. PSA nadir predicts biochemical and distant failures after external beam radiotherapy for prostate cancer: a multi-institutional analysis. *Int J Radiation Oncol Biol Phys* 2006; 64: 1140-1150.
48. Ritter MA, Messing EM, Shanahan TG et al. Prostate-specific antigen as a predictor of radiotherapy response and patterns of failure in localized prostate cancer. *J Clin Oncol* 1992; 10: 1208-1217.
49. Rose MA, Shrader-Bogen CL, Korlath G et al. Identifying patient symptoms after radiotherapy using a nurse-managed telephone interview. *Oncology Nurs Forum* 1996; 23: 99-102.
50. Sandler HM, Dunn RL, McLaughlin PW et al. Overall survival after prostate-specific-antigen-detected recurrence following conformal radiation therapy. *Int J Radiation Oncol Biol Phys* 2000; 48: 629-633.
51. Sartor CI, Strawderman MH, Lin XH et al. Rate of PSA rise predicts metastatic versus local recurrence after definitive radiotherapy. *Int J Radiation Oncol Biol Phys* 1997; 38: 941-947.
52. Stamey TA, Kabalin JN, McNeal JE et al. Prostate specific antigen in the diagnosis and treatment of adenocarcinoma of the prostate. II. Radical prostatectomy treated patients. *J Urol* 1989; 141: 1076-1083.
53. Stephan C, Klaas M, Muller C et al. Interchangeability of measurements of total and free prostate-specific antigen in serum with 5 frequently used assay combinations: an update. *Clin Chem* 2006; 52: 59-64.
54. Stephenson AJ, Shariat SF, Zelefsky MJ et al. Salvage radiotherapy for recurrent prostate cancer after radical prostatectomy. *JAMA* 2004; 291: 1325-1332.
55. Stephenson AJ, Kattan MW, Eastham JA et al. Defining biochemical recurrence of prostate cancer after radical prostatectomy: a proposal for a standardized definition. *J Clin Oncol* 2006; 24: 3973-3978.

56. Trapasso JG, deKernion JB, Smith RB et al. The incidence and significance of detectable levels of serum prostate specific antigen after radical prostatectomy. *J Urol* 1994; 152: 1821-1825.
57. Trock BJ, Han M, Freedland SJ et al. Prostate cancer-specific survival following salvage radiotherapy vs observation in men with biochemical recurrence after radical prostatectomy. *JAMA* 2008; 299: 2760-2769.
58. Ward JF, Zincke H, Bergstralh EJ et al. Prostate specific antigen doubling time subsequent to radical prostatectomy as a prognosticator of outcome following salvage radiotherapy. *J Urol* 2004; 172: 2244-2248.
59. Zagars GK, Pollack A, Zagars GK et al. Kinetics of serum prostate-specific antigen after external beam radiation for clinically localized prostate cancer. *Radiotherapy and Oncology* 1997; 44: 213-221.