National Institute for Health and Care Excellence

FINAL

Prostate cancer: diagnosis and management

[H] Evidence review for follow-up protocols after radical treatment

NICE guideline NG131

Evidence reviews

May 2019

These evidence reviews were developed by the NICE Guideline Updates Team

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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Follow-up strategy after radical treatment for prostate cancer

Review question

What is the most clinically- and cost-effective follow-up protocol for people with prostate cancer who have had radical treatment, with specific regard to duration of follow-up, frequency of follow-up appointments, the type of examination or blood tests, the respective roles of primary and secondary care in follow-up?

Introduction

For people who have had radical treatment, the aim of follow-up is to check whether or not prostate cancer has responded to treatment, identify and help them deal with any adverse events or side effects of treatment and give them a chance to ask any questions they may have. Currently, there is very little guidance addressing the duration of follow-up, frequency of follow-up appointments, the type of examination or blood tests and the roles of primary and secondary care in follow-up.

The aim of this review was to determine the best follow-up for people post radical treatment for prostate cancer.

This review identified studies that fulfilled the conditions specified in Table 1. For full details of the review protocol, see appendix A.

Table 1: PICO table

Population	People with localised prostate cancer who have had radical treatment.
Interventions	Different follow up protocols - for example • supported self-management • shared care • survivorship • remote follow up
Comparator	Usual care Different follow up protocols - for example • supported self-management • shared care • survivorship • remote follow up
Outcomes	• Patient/ carers satisfaction • Quality of life (e.g. Anxiety) • Biochemical Recurrence • Severe adverse events • Other PROMS

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual (2014). Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 and 2018 conflicts of interest policies

Clinical evidence

Included studies

A systematic literature search was conducted for interventional (including randomised control trials) and observational studies without a date limit. The search found 8,058 references. These were screened on title and abstract, with 73 full-text papers ordered as potentially relevant studies. Studies were excluded if they did not include the intervention and control as specified in the protocol. Studies were later excluded at the data extraction stage if they failed to meet any of the other criteria specified in the protocol.

Three systematic reviews were identified but they were all excluded because their included studies did not meet the criteria set out in the protocol.

Four randomised control trials were included in this review.

A second set of searches was conducted at the end of the guideline development process for all updated review questions using the original search strategies, to capture papers published whilst the guideline was being developed. These searches, which included articles up to August 2018, returned 324 references for this review question and these were screened on title and abstract. No additional relevant references were found.

See evidence tables for details – appendix E and full references in appendix I

Excluded studies

Details of the studies excluded at full-text review are given in appendix H along with a reason for their exclusion, and full references are detailed in Appendix I.

Summary of clinical studies included in the evidence review

Short Title	Sample characteristics	Interventions	Controls
Davis (2013) USA	Sample size 94 participants Split between study groups Intervention - 49 participants Control - 45 participants Mean age (SD) 62.0 (7.5) years Duration of follow-up 7 months	Symptom monitoring plus feedback Participants received written and verbal (by telephone) instructions on how to use the technology-assisted monitoring system - participants were instructed to call the automated system 3 business days prior to their next 2 follow-up visits with their physician - the men completed the Prostate Cancer Subscale (PCS) of the Functional Assessment of Cancer Therapy-Prostate (FACT-P), a 12-item subscale that measures problems specific to prostate cancer	Usual care saw their physicians as scheduled but did not use the monitoring system before each follow-up visit and no feedback was provided to physicians
Dieperink (2013) Denmark	Sample size 161 participants Split between study groups Intervention - 79 participants Control - 82 participants Loss to follow-up Intervention - 1 lost to follow up (2 dropped out) Control - 2 lost to follow up - (2 dropped out) Mean age (SD) Intervention - 68.2 (4.8) years Control - 69.0 (5.2) years Duration of follow-up 12 months	Multidisciplinary rehabilitation - one physician visit 4 weeks after radiotherapy - instructed in an individually suited multidisciplinary programme during two nursing counselling sessions and during two additional sessions of counselling by physical therapists aiming the exact need of each individual patient - The patient was recommended to bring his spouse along for all counselling and instructions in order to increase understanding of and compliance with the exercises suggested (detailed follow up protocol provided in the article)	Usual care - one physician visit 4 weeks after radiotherapy - No systematic education

Short Title	Sample characteristics	Interventions	Controls
Emery (2017) Australia	Sample size 84 participants Split between study groups Intervention - 42 participants Control - 42 participants Loss to follow-up no loss to follow up Mean age (SD) Intervention - 67.4 (7.0) years Control - 65.8 (8.2) years Duration of follow-up 12 months	Shared care Shared care model where 2 of the visits were replaced by the GP visits, at 6 and 9 months. An additional GP visit shortly after treatment for prostate cancer intended to re-engage the patient with his GP. In addition to the altered schedule of follow-up - with the following components i. structured systematic communication using a survivorship care plan ii. GP clinical management guidelines and local resources iii. a register and recall system to prompt the participant and his GP about follow up appointments iv. screening for distress using the Distress Thermometer and unmet needs using a prostate cancer-specific problem check list v. patient information resources about prostate cancer and treatment side effect	Usual care clinical care according to the current hospital practice with visits every 3 months to the treating urologists or radiation oncologist team. Visits included a PSA test, review of any treatments, and clinical examination where indicated.
Giesler (2005) USA	Sample size 99 couples Split between study groups Intervention - 48 participants Control - 51 participants Mean age (SD) Intervention - 66.7 (no SD) years Control - 61.1 (no SD) years Duration of follow-up 12 months	Menu-driven computer program Participants met once each month for 6 months with a nurse intervenor (twice in person and 4 times by telephone). first visit- which occurred within 6 weeks after the conclusion of active therapy, the nurse intervenor primarily focused on assessing and managing bowel and urinary function problems After the visit, participants were provided with a videotape to view at home (Living and Loving: Sexuality and the Prostate Cancer Patient) During the second visit, which occurred 1 month later, the nurse used the computer program to evaluate problems related to sexual functioning, cancer worry, dyadic adjustment, depression, and other cancer-related problems. On subsequent encounters, the patient and spouse were asked to discuss issues and concerns that may not have been addressed effectively during the previous sessions and to identify any new problems that may have arisen. Intervention visits were scheduled to occur once every month during the first 6 months after completion of treatment with the first 2 visits in person and the remaining visits over the telephone	Usual care Authors did not provide a description of what was included in the control group

See appendix E for full evidence tables.

Quality assessment of clinical studies included in the evidence review

See appendix G for full GRADE tables.

Economic evidence

Standard health economics filters were applied to the clinical search strategy for this review question. In total, 1,933 references were returned, of which 1,931 could be confidently excluded on screening of titles and abstracts. The remaining two studies were reviewed in full text, and found not to be relevant.

Included studies

None

Excluded studies

Details of studies excluded after consideration at the full-text stage are provided in appendix H

Summary of studies included in the economic evidence review

Economic model

This question was not prioritised for economic modelling.

Evidence statements

See Summary of clinical studies included in the evidence review for description of interventions

Multidisciplinary rehabilitation versus usual care

Very low- to low-quality evidence from 1 RCT reporting data on 161 people who had completed radical treatments for prostate cancer could not differentiate health-related quality of life at 6 months, in those people who received multidisciplinary rehabilitation compared to those who received usual care.

Shared care versus usual care

Very low- to low-quality evidence from 1 RCT reporting data on up to 82 people who had completed radical treatments for prostate cancer could not differentiate health-related quality of life at 12 months, in those people who received shared care compared to those who received usual care.

Menu-driven computer program versus usual care

Very low-quality evidence from 1 RCT reporting data on 99 people who had completed radical treatments for prostate cancer could not differentiate health-related quality of life at 7 months, in those people who received menu-driven computer program compared to those who received usual care.

Technology assisted symptom monitoring versus usual care

Very low-quality evidence from 1 RCT reporting data on 70 people who had completed radical treatments for prostate cancer could not differentiate health-related quality of life at 12 months, in those people who received follow-up care in the form of technology assisted symptom monitoring compared to those who received usual care.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee agreed the critical outcomes were patient reported measures such as health-related quality of life, depression and anxiety. The committee also noted that outcomes relating to duration of follow up, frequency of follow-up appointments and the type of examinations or blood tests were of interest.

The quality of the evidence

The committee agreed that the evidence presented was not applicable to the review question posed. The committee explained that the studies did not address any elements relating to duration of follow-up, frequency of follow-up and the type of examinations or blood tests that need to be carried out and when they need to be carried out.

Benefits and harms

The committee made recommendations based on their expert opinions and reached a consensus. It agreed that since the consensus recommendation reflected current best practice there would be no additional harms associated with the recommendation. Making a recommendation to encourage best practice could improve patient care in some areas and therefore an overall benefit would be accrued.

Cost effectiveness and resource use

There was no cost effectiveness evidence for this review.

Other factors the committee took into account

The committee discussed the different follow-up strategies implemented across different regions of the country and noted that there were several inconsistencies and variations in how different trusts were following up patients after radical prostate cancer treatment. Some of the strategies mentioned included the use of a computer PSA tracker in monitoring PSA levels, recovery packages which included holistic needs assessments 6-8 weeks post treatment and the use of band 4 staff (sometimes referred to as associate practitioners) to follow up patients on health, psychological and functional issues.

The committee extensively discussed a survivorship programme from Southampton (True NTH). The programme is a self-management programme for people who have completed active treatment and have stable PSA. The programme includes workshops and holistic needs assessments to assess health, social and wellbeing needs. Patients are encouraged to peer support. Patients manage their own care using a tailored computer system and monitored remotely by a specialist cancer

team. Each person has a dedicated support worker who they are encouraged to contact about any concerns.

The committee noted that while this programme sounds impressive, it has not been evaluated and its effectiveness is not yet known. It was also concerned about the cost to the NHS of setting up such a programme, especially when the programme may be replicating some of the data systems that are currently in place such as the Somerset Cancer Register. It was also concerned about the coordination of the programme, as well as the staff to carry out the technical monitoring.

The committee also discussed that most follow-up strategies include limited appointment time resulting in little time being spent with a patient and often appear like a checklist.

Appendix A – Review protocols

Review protocol for Follow-up strategies after radical treatment

ID	Field (based on PRISMA-P	Content
I	Review question	What is the most clinically- and cost-effective follow-up protocol for people with prostate cancer who have had radical treatment, with specific regard to: • duration of follow-up • frequency of follow-up appointments • the type of examination or blood tests • the respective roles of primary and secondary care in follow-up?
II	Type of review question	Intervention/Observation
III	Objective of the review	To determine the optimum follow-up for people post radical treatment for prostate cancer *This area was identified as requiring an evidence review during the scoping phase of the update.*
IV	Eligibility criteria – population/disease/condition/issue/domain	People with prostate cancer who have had radical treatment (e.g. surgery, radiotherapy, chemotherapy)
V	Eligibility criteria – intervention(s	Different follow up protocols - for example • supported self-management

		• shared care • survivorship • remote follow up
VI	Eligibility criteria – comparator(s)	Different follow up protocols - for example • supported self-management • shared care • survivorship • remote follow up
VII	Outcomes and prioritisation	• Patient/ carers satisfaction • Quality of life (e.g. Anxiety) • Biochemical Recurrence • Severe adverse events • Other PROMS
VIII	Eligibility criteria – study design	RCT data. If less than 5 RCTs then cohort and before and after studies will be considered.
IX	Other inclusion exclusion criteria	• Non English-language papers • Reviews • Case control studies
X	Proposed sensitivity/sub-group analysis, or meta-regression	• Type of follow up protocol • Duration of follow up • Location (primary or secondary care) • Type of radical treatment (prostatectomy, radiotherapy etc.)

XI	Selection process – duplicate screening/selection/analysis	10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. If meaningful disagreements are found between the different reviewers, a further 10% of the abstracts will be reviewed by two reviewers, with this process continued until agreement is achieved between the two reviewers. From this point, the remaining abstracts will be screened by a single reviewer.
XII	Data management (software)	See appendix B below – section 1.3
XIII	Information sources – databases and dates	See appendix C of relevant chapter. No date limit will be used.
XIV	Identify if an update	This is an update, however no previous question identified from previous guideline. **Recommendations affected:** 1.3.40 Discuss the purpose, duration, frequency and location of follow-up with each man with localised prostate cancer[2], and if he wishes, his partner or carers. **[2008]** 1.3.41 Clearly advise men with prostate cancer about potential longer-term adverse effects of treatment and when and how to report them. **[2008]** 1.3.42 Men with prostate cancer who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care in accordance with protocols agreed by the local urological cancer MDT and the relevant primary care organisation(s). Their PSA should be measured at least once a year. **[2008]**

		1.3.43 Check PSA levels for all men with prostate cancer who are having radical treatment at the earliest 6 weeks following treatment, at least every 6 months for the first 2 years and then at least once a year thereafter. **[2008]** 1.3.44 Do not routinely offer DRE to men with localised prostate cancer while the PSA remains at baseline levels. **[2008]** 1.3.45 After at least 2 years, offer follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications to men with a stable PSA who have had no significant treatment complications, unless they are taking part in a clinical trial that requires formal clinic-based follow-up. Direct access to the urological cancer MDT should be offered and explained. **[2008]**
XV	Author contacts	Guideline updates team, National Institute for Health and Care Excellence (contact adam.okeefe@nice.org.uk)
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
XVII	Search strategy – for one database	For details please see appendix C of relevant chapter
XVIII	Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix E (clinical evidence tables) or H (economic evidence tables).
XIX	Data items – define all variables to be collected	For details please see evidence tables in appendix E (clinical evidence tables) or H (economic evidence tables).
XX	Methods for assessing bias at outcome/study level	See Appendix B below – see section 1.4.1

XXI	Criteria for quantitative synthesis (where suitable)	See Appendix B below
XXII	Methods for analysis – combining studies and exploring (in)consistency	See Appendix B below – see section 1.4.2
XXIII	Meta-bias assessment – publication bias, selective reporting bias	See Appendix B below – see section 1.4.3 and 1.4.5
XXIV	Assessment of confidence in cumulative evidence	See Appendix B below - see section 1.4.3
XXV	Rationale/context – Current management	For details please see the introduction to the evidence review in the main file.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee will develop the guideline update. The committee was convened by the NICE Guideline Updates Team and chaired by Waqaar Shah in line with section 3 of Developing NICE guidelines: the manual. Staff from NICE will undertake systematic literature searches, appraise the evidence, conduct meta-analyses and cost-effectiveness analyses where appropriate, and draft the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
XXVII	Sources of funding/support	The NICE Guideline Updates Team is an internal team within NICE.

XXVII	Name of sponsor	The NICE Guideline Updates Team is an internal team within NICE.
XXIX	Roles of sponsor	The NICE Guideline Updates Team is an internal team within NICE.
XXX	PROSPERO registration number	N/A

Appendix B – Methods

Evidence synthesis and meta-analyses

Where possible, meta-analyses were conducted to combine the results of studies for each outcome/predictor. For mean differences, where change from baseline data were reported in the trials/studies and were accompanied by a measure of spread (for example standard deviation), these were extracted and used in the meta-analysis. Where measures of spread for change from baseline values were not reported, the corresponding values at study end were used and were combined with change from baseline values to produce summary estimates of effect. These/All studies were assessed to ensure that baseline values were balanced across the treatment/comparison groups; if there were significant differences in important confounding variables at baseline these studies were not included in any meta-analysis and were reported separately.

Evidence of effectiveness of interventions

Quality assessment

Individual RCTs and quasi-randomised controlled trials were quality assessed using the Cochrane Risk of Bias Tool. Cohort studies were quality assessed using the CASP cohort study checklist. Each individual study was classified into one of the following three groups:

- Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size.
- Moderate risk of bias – There is a possibility the true effect size for the study is substantially different to the estimated effect size.
- High risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.

Each individual study was also classified into one of three groups for directness, based on if there were concerns about the population, intervention, comparator and/or outcomes in the study and how directly these variables could address the specified review question. Studies were rated as follows:

- Direct – No important deviations from the protocol in population, intervention, comparator and/or outcomes.
- Partially indirect – Important deviations from the protocol in one of the population, intervention, comparator and/or outcomes.
- Indirect – Important deviations from the protocol in at least two of the following areas: population, intervention, comparator and/or outcomes.

Methods for combining intervention evidence

Meta-analyses of interventional data were conducted with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011).

Where different studies presented continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes were all converted to the same scale before meta-analysis was conducted on the mean differences. Where outcomes measured the same underlying

construct but used different instruments/metrics, data were analysed using standardised mean differences (Hedges' g).

A pooled relative risk was calculated for dichotomous outcomes (using the Mantel–Haenszel method). Both relative and absolute risks were presented, with absolute risks calculated by applying the relative risk to the pooled risk in the comparator arm of the meta-analysis.

Fixed- and random-effects models (der Simonian and Laird) were fitted for all syntheses, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models were the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model were clearly not met, even after appropriate pre-specified subgroup analyses were conducted, random-effects results are presented. Fixed-effects models were deemed to be inappropriate if one or both of the following conditions was met:

- Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. This decision was made and recorded before any data analysis was undertaken.
- The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$.

In any meta-analyses where some (but not all) of the data came from studies at high risk of bias, a sensitivity analysis was conducted, excluding those studies from the analysis. Results from both the full and restricted meta-analyses are reported. Similarly, in any meta-analyses where some (but not all) of the data came from indirect studies, a sensitivity analysis was conducted, excluding those studies from the analysis.

Meta-analyses were performed in Cochrane Review Manager v5.3.

Minimal clinically important differences (MIDs)

The Guideline Committee were asked to prospectively specify any outcomes where they felt a consensus MID could be defined from their experience. In particular, any questions looking to evaluate non-inferiority (that one treatment is not meaningfully worse than another) required an MID to be defined to act as a non-inferiority margin. The committee did not identify any specific minimal important difference thresholds relevant to this guideline.

For standardised mean differences where no other MID was available, an MID of 0.2 was used, corresponding to the threshold for a small effect size initially suggested by Cohen et al. (1988). Where a range of MIDs was provided, the middle value of the range was selected; MIDs other than those using the threshold suggested by Cohen et al. (1988) are presented in Table 2. For relative risks where no other MID was available, a default MID interval for dichotomous outcomes of 0.8 to 1.25 was used. The line of no effect was specified by the committee as an MID for hazard ratios.

Table 2: Identified MIDs

Outcome	Recommended MID	Chosen MID*	Source
EPIC Urinary function summary score or urinary incontinence	6 – 9	-7.5, 7.5	Skolarus, TA, Dunn, RL, Sanda MG et al. Minimally Important Difference for the Expanded Prostate Cancer Index Composite Short Form. Urology. 2015; 85 (1): 101-106
EPIC Urinary irritation/obstruction	5-7	-6,6	Skolarus, TA, Dunn, RL, Sanda MG et al. Minimally Important Difference for the Expanded Prostate Cancer Index Composite Short Form. Urology. 2015; 85 (1): 101-106
EPIC Sexual function summary score	10 – 12	-11, 11	Skolarus, TA, Dunn, RL, Sanda MG et al. Minimally Important Difference for the Expanded Prostate Cancer Index Composite Short Form. Urology. 2015; 85 (1): 101-106
EPIC Bowel function summary score	4 - 6	-5, 5	Skolarus, TA, Dunn, RL, Sanda MG et al. Minimally Important Difference for the Expanded Prostate Cancer Index Composite Short Form. Urology. 2015; 85 (1): 101-106
FACT - G Functional Assessment of Cancer Therapy	4	-4,4	Cella D, Eton DT, Lai JS, Peterman AH, Merkel DE, J Pain Symptom Manage. 2002 Dec; 24(6):547-61.Combining anchor and distribution-based methods to derive minimal clinically important differences on the Functional Assessment of Cancer Therapy (FACT) anemia and fatigue scales.
SF-12 Short form-12 – Total score	6.8	-6.8,6.8	Schmitt JS, De Fabio RP. “Reliable Change and Minimum Important Difference (MID) Proportions Facilitated Group Responsiveness Comparisons Using Individual Threshold Criteria” Journal of Clinical Epidemiology. 2004;57:1008–18.
SF-36 Short form-36 – Total score	2-4	-3,3	Swigris JJ, Brown KK, Behr J, du Bois RM, King TE, Raghu G, Wamboldt FS Respir Med. 2010 Feb; 104(2):296-304. The SF-36 and SGRQ: validity and first look at minimum important differences in IPF
Hospital Anxiety and Depression Scale – depression	1.19	-1.2, 1.2	Bernhard, J., Sullivan, M., Hurny, C. et al. 2001. Clinical relevance of single item quality of life indicators in cancer clinical trials. British Journal of Cancer 84(9) 1156-1165
Hospital Anxiety and Depression Scale - anxiety	0.89	-0.89, 0.89	Bernhard, J., Sullivan, M., Hurny, C. et al. 2001. Clinical relevance of single item quality of life indicators in cancer clinical trials. British Journal of Cancer 84(9) 1156-1165
*The mid-point was chosen because the reference article provided a range			

GRADE for pairwise meta-analyses of interventional evidence

GRADE was used to assess the quality of evidence for the selected outcomes as specified in ‘Developing NICE guidelines: the manual (2014)’. Data from RCTs was initially rated as high quality and the quality of the evidence for each outcome was downgraded or not from this initial point. If non-RCT evidence was included for intervention-type systematic reviews then these were initially rated as either moderate quality (quasi-randomised studies) or low quality (cohort studies) and the

quality of the evidence for each outcome was further downgraded or not from this point, based on the criteria given in Table 3

Table 3: Rationale for downgrading quality of evidence for intervention studies

GRADE criteria	Reasons for downgrading quality
Risk of bias	Not serious: If less than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from studies at high risk of bias, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies at high and low risk of bias.
Indirectness	Not serious: If less than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between direct and indirect studies.
Inconsistency	Concerns about inconsistency of effects across studies, occurring when there is unexplained variability in the treatment effect demonstrated across studies (heterogeneity), after appropriate pre-specified subgroup analyses have been conducted. This was assessed using the I^2 statistic. N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study. Not serious: If the I^2 was less than 33.3%, the outcome was not downgraded. Serious: If the I^2 was between 33.3% and 66.7%, the outcome was downgraded one level. Very serious: If the I^2 was greater than 66.7%, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies with the smallest and largest effect sizes.
Imprecision	If an MID other than the line of no effect was defined for the outcome, the outcome was downgraded once if the 95% confidence interval for the effect size crossed one line of the MID, and twice if it crosses both lines of the MID. If the line of no effect was defined as an MID for the outcome, it was downgraded once if the 95% confidence interval for the effect size crossed the line of no effect (i.e. the outcome was not statistically significant), and twice if the sample size of the study was sufficiently small that it is not plausible any realistic effect size could have been detected. Outcomes meeting the criteria for downgrading above were not downgraded if the confidence interval was sufficiently narrow that the upper and lower bounds would correspond to clinically equivalent scenarios.

The quality of evidence for each outcome was upgraded if any of the following three conditions were met:

- Data from non-randomised studies showing an effect size sufficiently large that it cannot be explained by confounding alone.

- Data showing a dose-response gradient.
- Data where all plausible residual confounding is likely to increase our confidence in the effect estimate.

Publication bias
Publication bias was assessed in two ways. First, if evidence of conducted but unpublished studies was identified during the review (e.g. conference abstracts, trial protocols or trial records without accompanying published data), available information on these unpublished studies was reported as part of the review. Secondly, where 10 or more studies were included as part of a single meta-analysis, a funnel plot was produced to graphically assess the potential for publication bias.

Evidence statements
Evidence statements for pairwise intervention data are classified in to one of four categories:

- Situations where the data are only consistent, at a 95% confidence level, with an effect in one direction (i.e. one that is 'statistically significant'), and the magnitude of that effect is most likely to meet or exceed the MID (i.e. the point estimate is not in the zone of equivalence). In such cases, we state that the evidence showed that there is an effect.
- Situations where the data are only consistent, at a 95% confidence level, with an effect in one direction (i.e. one that is 'statistically significant'), but the magnitude of that effect is most likely to be less than the MID (i.e. the point estimate is in the zone of equivalence). In such cases, we state that the evidence could not demonstrate a meaningful difference.
- Situations where the data are consistent, at a 95% confidence level, with an effect in either direction (i.e. one that is not 'statistically significant') but the confidence limits are smaller than the MIDs in both directions. In such cases, we state that the evidence demonstrates that there is no difference.
- In all other cases, we state that the evidence could not differentiate between the comparators.

Health economics
Literature reviews seeking to identify published cost–utility analyses of relevance to the issues under consideration were conducted for all questions. In each case, the search undertaken for the clinical review was modified, retaining population and intervention descriptors, but removing any study-design filter and adding a filter designed to identify relevant health economic analyses. In assessing studies for inclusion, population, intervention and comparator, criteria were always identical to those used in the parallel clinical search; only cost–utility analyses were included. Economic evidence profiles, including critical appraisal according to the Guidelines manual, were completed for included studies.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations (NICE guidelines manual; 2014). This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the committee for a specific topic within the guideline.

There are 2 parts of the appraisal process. The first step is to assess applicability (that is, the relevance of the study to the specific guideline topic and the NICE reference case); evaluations are categorised according to the criteria in Table 4.

Table 4 Applicability criteria

Level	Explanation
Directly applicable	The study meets all applicability criteria, or fails to meet one or more applicability criteria but this is unlikely to change the conclusions about cost effectiveness
Partially applicable	The study fails to meet one or more applicability criteria, and this could change the conclusions about cost effectiveness
Not applicable	The study fails to meet one or more applicability criteria, and this is likely to change the conclusions about cost effectiveness. These studies are excluded from further consideration

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (that is, methodological quality); see categorisation criteria in Table 5.

Table 5 Methodological criteria

Level	Explanation
Minor limitations	Meets all quality criteria, or fails to meet one or more quality criteria but this is unlikely to change the conclusions about cost effectiveness
Potentially serious limitations	Fails to meet one or more quality criteria and this could change the conclusions about cost effectiveness
Very serious limitations	Fails to meet one or more quality criteria and this is highly likely to change the conclusions about cost effectiveness. Such studies should usually be excluded from further consideration

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

Appendix C – Literature search strategies

Medline strategy, searched 30th May 2018 Database: Ovid MEDLINE(R) 1946 to Present with Daily Update
1 exp Prostatic Neoplasms/
2 Prostatic Intraepithelial Neoplasia/
3 (prostat* adj4 (neoplas* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta* or angiosarcoma* or sarcoma* or teratoma* or lymphoma* or blastoma* or microcytic* or carcino* or leiomyosarcoma* or lump*)).tw.
4 PIN.tw.
5 or/1-4
6 exp Prostatic Neoplasms/su
7 exp Prostatectomy/
8 (radical adj4 prostatectom*).tw.
9 (radical adj4 (therap* or treatment*)).tw.
10 or/6-9
11 exp radiotherapy/
12 radiotherap*.tw.
13 (radiat* adj4 (therap* or treatment*)).tw.
14 ((external* or conformal*) adj4 (irradiat* or therap* or treat*)).tw.
15 ((interstitial* or intracavit* or implant* or surface* or internal*) adj4 (irradiat* or radiation*)).tw.
16 curietherap*.tw.
17 (radioisotope* adj4 (irradiat* or therap* or treat*)).tw.
18 ((seed* or permanent*) adj2 implant*).tw.
19 Brachytherapy/
20 brachytherap*.tw.
21 (Hyperfraction* or Hyper-fraction* or Hyper fraction* or Hypofraction* or Hypo-fraction* or Hypo fraction*).tw.
22 ((high* or full* or maximum* or larg* or escalat* or supplement* or low* or minimum* or small*) adj4 (dose* or dosage* or schedule*)).tw.
23 (HDR or LDR).tw.
24 or/11-23
25 10 or 24
26 Follow-Up Studies/ or Aftercare/
27 ((Aftercare or after car* or after-car* or after treat or after-treat*) adj6 prostat*).tw.
28 ((Follow-up* or follow up*) adj6 prostat*).tw.
29 ("follow-up protocol*" or "follow-up strateg*" or "follow-up appointment*" or "follow-up clinic*" or "follow-up car*" or "follow-up review*" or "follow-up regime*" or "follow-up checklist*" or "follow-up procedure*" or "follow-up treat*" or "follow-up therap*" or "follow-up program*" or "follow-up plan*" or "follow-up polic*" or "follow-up approach*" or "follow-up schedule*" or "follow-up scheme*" or "follow-up practice*" or "follow-up system*").tw.
30 ("follow up protocol*" or "follow up strateg*" or "follow up appointment*" or "follow up clinic*" or "follow up car*" or "follow up review*" or "follow up regime*" or "follow up checklist*" or "follow up procedure*" or "follow up treat*" or "follow up therap*" or "follow up program*" or "follow up plan*" or "follow up polic*" or "follow up approach*" or "follow up schedule*" or "follow up scheme*" or "follow up practice*" or "follow up system*").tw.
31 ("repeat* protocol*" or "repeat* strateg*" or "repeat* appointment*" or "repeat* clinic*" or "repeat* car*" or "repeat* review*" or "repeat* regime*" or "repeat* checklist*" or "repeat* procedure*" or "repeat* treat*" or "repeat* program*" or "repeat* plan*" or "repeat* polic*" or "repeat* schedule*" or "repeat* scheme*" or "repeat* system*").tw.
32 ("review* protocol*" or "review* strateg*" or "review* appointment*" or "review* clinic*" or "review* car*" or "review* checklist*" or "review* procedure*" or "review* treat*" or "review* program*" or "review* plan*" or "review* polic*" or "review* approach*" or "review* schedule*" or "review* scheme*" or "review* system*").tw.
33 *Neoplasm Recurrence, Local/
34 Recurrence/ and exp Prostatic Neoplasms/
35 Disease-Free Survival/ and exp Prostatic Neoplasms/
36 Survivorship/ and exp Prostatic Neoplasms/

Medline strategy, searched 30th May 2018 Database: Ovid MEDLINE(R) 1946 to Present with Daily Update
37 ((Overall or free) adj1 surviv*).tw. 38 Survivorship*.tw. 39 ((Disease* or pathological*) adj1 (progress* or surviv* or recurrence*)).tw. 40 (Clinical adj1 (progess* or recurrence*)).tw. 41 metasta* recurrence*.tw. 42 "Biochemical no Evidence of Disease".tw. 43 "Bio-chemical no Evidence of Disease".tw. 44 ((Biochemical* or bio-chemical*) adj1 recurrence*).tw. 45 Patient Discharge/ and exp Prostatic Neoplasms/ 46 (Discharge* and prostat*).tw. 47 Self Care/ and exp Prostatic Neoplasms/ 48 Self-Management/ and exp Prostatic Neoplasms/ 49 ((self* adj1 (care* or manage*)) and prostat*).tw. 50 or/26-49 51 5 and 25 and 50 52 Animals/ not Humans/ 53 51 not 52 54 Comment/ or Letter/ or Editorial/ or Historical article/ or (conference abstract or conference paper or "conference review" or letter or editorial or case report).pt. 55 53 not 54 56 limit 55 to english language

Note: SIGN systematic review, RCT and observational study filters appended to strategy. Date limit applied from 2005 to 2018.

Study design filters

The MEDLINE systematic review, randionmised controlled trials (RCT), diagnostic, and observational studies filters are presented below.
NICE Systematic review 1. Meta-Analysis.pt. 2. Network Meta-Analysis/ 3. Meta-Analysis as Topic/ 4. Review.pt. 5. exp Review Literature as Topic/ 6. (metaanaly$ or metanaly$ or (meta adj3 analy$)).tw. 7. (review$ or overview$).ti. 8. (systematic$ adj5 (review$ or overview$)).tw. 9. ((quantitative$ or qualitative$) adj5 (review$ or overview$)).tw. 10. ((studies or trial$) adj2 (review$ or overview$)).tw. 11. (integrat$ adj3 (research or review$ or literature)).tw. 12. (pool$ adj2 (analy$ or data)).tw. 13. (handsearch$ or (hand adj3 search$)).tw. 14. (manual$ adj3 search$).tw. 15. or/1-14 16. Animals/ not Humans/ 17. 15 not 16
NICE RCT 1. Randomized Controlled Trial.pt. 2. Controlled Clinical Trial.pt. 3. Clinical Trial.pt. 4. exp Clinical Trials as Topic/ 5. Placebos/

The MEDLINE systematic review, randionmised controlled trials (RCT), diagnostic, and observational studies filters are presented below.
6. Random Allocation/ 7. Double-Blind Method/ 8. Single-Blind Method/ 9. Cross-Over Studies/ 10. ((random* or control* or clinical*) adj3 (trial* or stud*)).tw. 11. (random* adj3 allocat*).tw. 12. placebo*.tw. 13. ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw. 14. (crossover* or (cross adj over*)).tw. 15. or/1-14 16. Animals/ not Humans/ 17. 15 not 16
SIGN Systematic review 1. Meta-Analysis as Topic/ 2. meta analy$.tw. 3. metaanaly$.tw. 4. Meta-Analysis/ 5. (systematic adj (review$1 or overview$1)).tw. 6. exp Review Literature as Topic/ 7. or/1-6 8. cochrane.ab. 9. embase.ab. 10. (psychlit or psyclit).ab. 11. (psychinfo or psycinfo).ab. 12. (cinahl or cinhal).ab. 13. science citation index.ab. 14. bids.ab. 15. cancerlit.ab. 16. or/8-15 17. reference list$.ab. 18. bibliograph$.ab. 19. hand-search$.ab. 20. relevant journals.ab. 21. manual search$.ab. 22. or/17-21 23. selection criteria.ab. 24. data extraction.ab. 25. 23 or 24 26. Review/ 27. 25 and 26 28. Comment/ 29. Letter/ 30. Editorial/ 31. animal/ 32. human/ 33. 31 not (31 and 32) 34. or/28-30,33 35. 7 or 16 or 22 or 27 36. 35 not 34

The MEDLINE systematic review, randionmised controlled trials (RCT), diagnostic, and observational studies filters are presented below.

SIGN RCT

1 Randomized Controlled Trials as Topic/
2 randomized controlled trial/
3 Random Allocation/
4 Double Blind Method/
5 Single Blind Method/
6 clinical trial/
7 clinical trial, phase i.pt
8 clinical trial, phase ii.pt
9 clinical trial, phase iii.pt
10 clinical trial, phase iv.pt
11 controlled clinical trial.pt
12 randomized controlled trial.pt
13 multicenter study.pt
14 clinical trial.pt
15 exp Clinical Trials as topic/
16 or/1-15
17 (clinical adj trial$).tw
18 ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw
19 PLACEBOS/
20 placebo$.tw
21 randomly allocated.tw
22 (allocated adj2 random$).tw
23 or/17-22
24 16 or 23
25 case report.tw
26 letter/
27 historical article/
28 or/25-27
29 24 not 28

McMaster Diagnosis studies

1. sensitiv:.mp. OR diagnos:.mp. OR di.fs.

Prostate Diagnosis subheadings (OVID)

1. Prostate/dg or Prostatic Neoplasms/dg

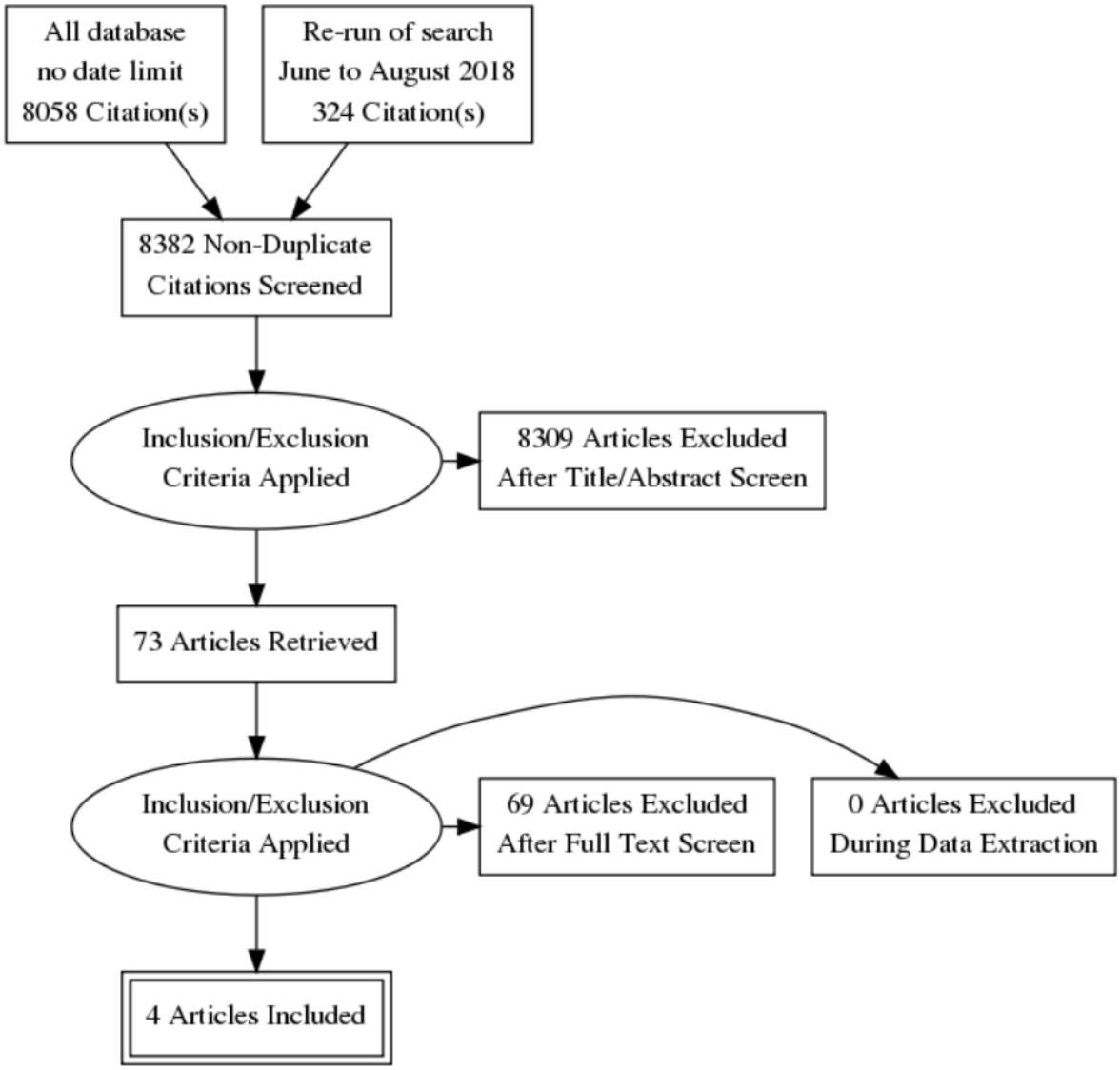
SIGN Observational studies

1 Epidemiologic studies/
2 Exp case control studies/
3 Exp cohort studies/
4 Case control.tw.
5 (cohort adj (study or studies)).tw.
6 Cohort analy$.tw.
7 (Follow up adj (study or studies)).tw.
8 (observational adj (study or studies)).tw.
9 Longitudinal.tw.
10 Retrospective.tw.

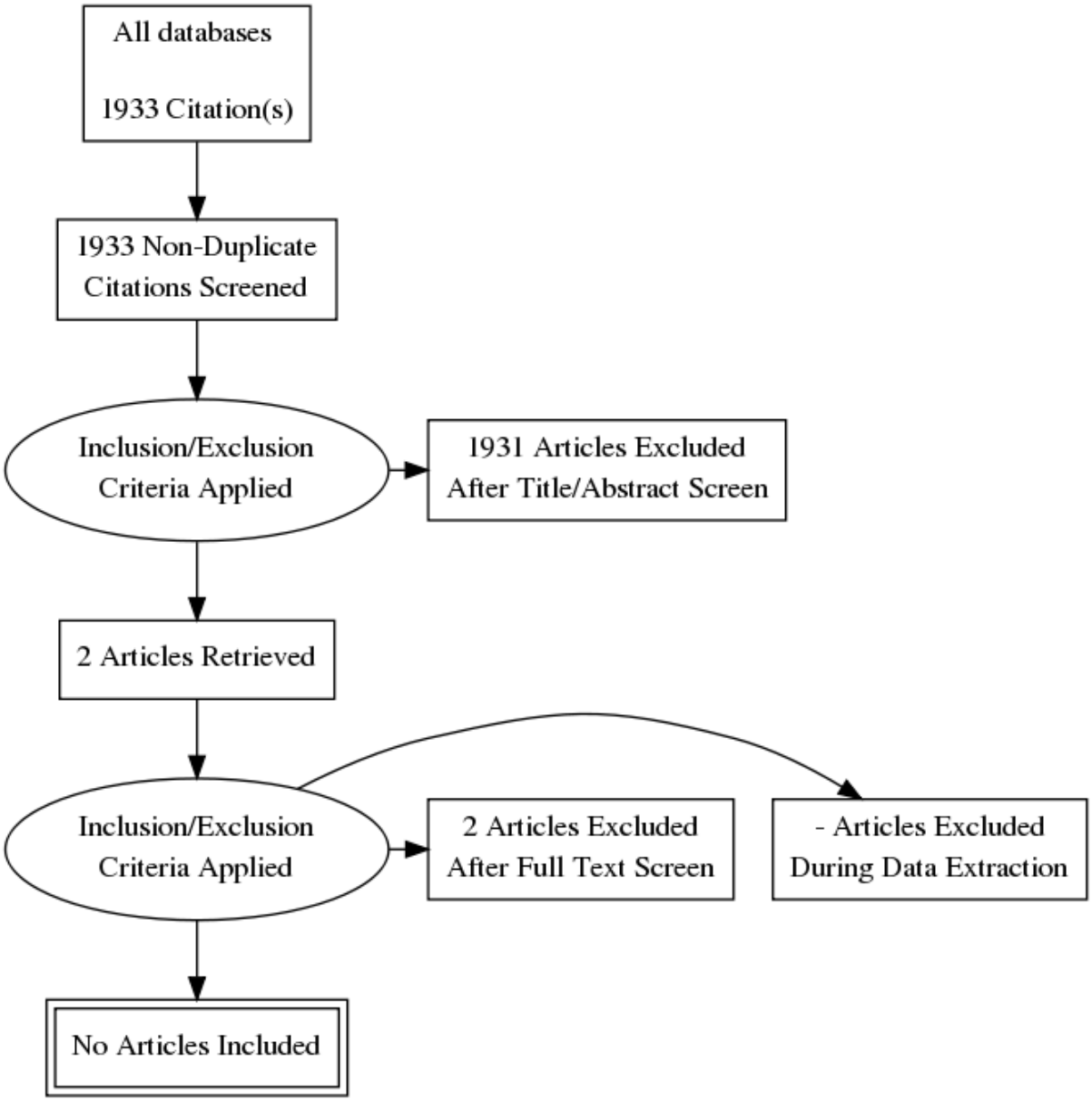
The MEDLINE systematic review, randionmised controlled trials (RCT), diagnostic, and observational studies filters are presented below.
11 Cross sectional.tw. 12 Cross-sectional studies/ 13 or/1-12 *Note: the following terms were removed from this filter for RQ9 searches:* • *exp case control studies/* • *Case control.tw.*

Appendix D – Study selection

Clinical evidence



Economic evidence


All databases
1933 Citation(s)
1933 Non-Duplicate Citations Screened
Inclusion/Exclusion Criteria Applied
1931 Articles Excluded After Title/Abstract Screen
2 Articles Retrieved
Inclusion/Exclusion Criteria Applied
2 Articles Excluded After Full Text Screen
- Articles Excluded During Data Extraction
No Articles Included

Appendix E – Evidence tables

Short Title	Study characteristics	Quality Assessment
Davis (2013)	Study type Randomised controlled trial Study details Study location USA Study setting Hospital/Medical Centre Study dates No details provided Duration of follow-up 7 months Sources of funding National Cancer Institute Inclusion criteria early-stage PCa survivors who were 10-19 months post-treatment scheduled follow-up appointment with a urologist or radiation oncologist ability to read and understand English Access to a telephone the ability to manipulate a telephone keypad to complete the survey Sample characteristics Sample size 94 participants Split between study groups Intervention - 49 participants Control - 45 participants Mean age (SD) 62.0 (7.5) years Interventions Symptom monitoring plus feedback received written and verbal (by telephone) instructions on how to use the technology-assisted monitoring system - participants were instructed to call the automated system 3	Random sequence generation Unclear risk of bias No details provided Allocation concealment Unclear risk of bias No details provided Blinding of participants and personnel Unclear risk of bias No details provided Blinding of outcome assessment Unclear risk of bias No details provided Incomplete outcome data Low risk of bias None identified Selective reporting Low risk of bias None identified Other sources of bias Low risk of bias None identified Overall risk of bias High No randomisation strategy provided

Short Title	Study characteristics	Quality Assessment
	business days prior to their next 2 follow-up visits with their physician - the men completed the Prostate Cancer Subscale (PCS) of the Functional Assessment of Cancer Therapy-Prostate (FACT-P), a 12-item subscale that measures problems specific to prostate cancer Controls Usual care saw their physicians as scheduled but did not use the monitoring system before each follow-up visit and no feedback was provided to physicians Outcome measure(s) General HRQOL Measured by SF-12 Cancer-specific HRQOL Measured by Functional Assessment of Cancer Therapy – General (FACT-G) Prostate cancer–specific HRQOL Measured by The UCLA Prostate Cancer Index (UCLA-PCI) Doctor/patient communication. Measured by Primary Care Assessment Survey (PCAS) Post-visit ratings (PVR) Patients and physicians rated their perceptions about how well symptoms/ HRQOL issues were addressed	Directness Directly applicable
Dieperink (2013)	Study type Randomised controlled trial Study details Study location Denmark Study setting Hospital Study dates 1 February 2010 to 31 January 2012 Sources of funding Odense University Hospital Research Foundation, the University of Southern Denmark, the Danish Cancer Society CIRRO – the Lundbeck Foundation Center for Interventional Research in Radiation Oncology, the Department of Oncology, OUH, the Mette Hede	Random sequence generation Unclear risk of bias "Patients were randomly assigned to the intervention group or usual care (control group) in a ratio of 1 : 1 after the completion of radiotherapy" Allocation concealment Low risk of bias "The randomisations were externally handled by the Department of Clinical Research at Odense University Hospital, Denmark, and the allocation sequence was concealed from the

Short Title	Study characteristics	Quality Assessment
	Nielsen Foundation, the Danish Nurses Organization Research Foundation, and the Propa Vita Foundation. Inclusion criteria men aged 18 years old or over with biopsy-documented adenocarcinoma of the prostate Exclusion criteria former prostatectomy, not able to speak Danish, or included in other protocols Sample characteristics Sample size 161 participants Split between study groups Intervention - 79 participants Control - 82 participants Loss to follow-up intervention - 1 lost to follow up (2 dropped out) control - 2 lost to follow up - (2 dropped out) Mean age (SD) intervention - 68.2 (4.8) years Control - 69.0 (5.2) years Interventions Symptom monitoring plus feedback - one physician visit 4 weeks after radiotherapy - instructed in an individually suited multidisciplinary programme during two nursing counselling sessions and during two additional sessions of counselling by physical therapists aiming the exact need of each individual patient - The patient was recommended to bring his spouse along for all counselling and instructions in order to increase understanding of and compliance with the exercises suggested (detailed follow up protocol provided in the article) Controls Usual care - one physician visit 4 weeks after radiotherapy - No systematic education Outcome measure(s) General HRQOL sf- 12	research team." Blinding of participants and personnel Unclear risk of bias No details provided Blinding of outcome assessment Unclear risk of bias No details provided Incomplete outcome data Low risk of bias None identified Selective reporting Low risk of bias None identified Other sources of bias Low risk of bias None identified Overall risk of bias Moderate No details provided on how the randomisation sequence was generated Directness Directly applicable

Short Title	Study characteristics	Quality Assessment
	Prostate cancer–specific HRQOL measured By EPIC (Expanded Prostate Cancer Index Composite)	
Emery (2017)	Study type Randomised controlled trial Study details Study location Australia Study setting Primary and Secondary care Study dates Between November 2011 and July 2013 Duration of follow-up 12 months Inclusion criteria ability to read and understand English Men who had completed radical treatment for prostate cancer within the previous 8 weeks Had a GP who agreed to participate Exclusion criteria Prostate cancer with high risk features men on androgen deprecation therapy after completion of radiotherapy metastatic disease or treatment with palliative intent severe cognitive or psychiatric disorder Sample characteristics Sample size 84 participants Split between study groups intervention - 42 participants control - 42 participants Loss to follow-up no loss to follow up Mean age (SD)	Random sequence generation Low risk of bias "Randomization was performed using a centralized independent tele-randomization system at the National Health and Medical Research Council (NHMRC) Clinical Trials Centre, stratified by hospital site and treatment type" Allocation concealment Unclear risk of bias It is unclear if the allocation was concealed or to whom it was concealed Blinding of participants and personnel Unclear risk of bias it is unclear - the authors do not mention blinding Blinding of outcome assessment Unclear risk of bias It is unclear - the authors did not mention blinding Incomplete outcome data Low risk of bias none identified Selective reporting Low risk of bias none identified

Short Title	Study characteristics	Quality Assessment
	intervention - 67.4 (7.0) years control - 65.8 (8.2) years Interventions Shared care Shared care model where 2 of the visits were replaced by the GP visits, at 6 and 9 months. An additional GP visit shortly after treatment for prostate cancer intended to re-engage the patient with his GP. In addition to the altered schedule of follow-up - with the following components i. structured systematic communication using a survivorship care plan ii. GP clinical management guidelines and local resources iii. a register and recall system to prompt the participant and his GP about follow up appointments iv. screening for distress using the Distress Thermometer and unmet needs using a prostate cancer-specific problem check list v. patient information resources about prostate cancer and treatment side effect Controls Usual care clinical care according to the current hospital practice with visits every 3 months to the treating urologists or radiation oncologist team. Visits included a PSA test, review of any treatments, and clinical examination where indicated. Outcome measure(s) Prostate cancer–specific HRQOL Measured using EPIC Depression Measured using the Hospital and Anxiety Depression scale Unmet needs Measured using the Cancer Survivors Unmet Needs measure Patient satisfaction measured using the Short-form Patient Satisfaction Questionnaire	Other sources of bias Low risk of bias none identified Overall risk of bias Moderate Due to the lack of clarity on whether or not there was blinding. Critical as all outcomes were patient reported Directness Directly applicable
Giesler (2005)	Study type Randomised controlled trial Cluster randomised controlled trial Study details Study location	Random sequence generation Unclear risk of bias No details provided Allocation concealment Unclear risk of bias

Short Title	Study characteristics	Quality Assessment
	USA Study setting multisite Study dates No details provided Duration of follow-up 4 months, 7 months and 12 months Inclusion criteria men aged 18 years old or over with biopsy-documented adenocarcinoma of the prostate ability to read and understand English received a diagnosis of stage T1a-T2c prostate carcinoma to be scheduled to undergo or to have undergone surgery, external beam radiation, or brachytherapy to have a spouse or relationship partner who also was willing to participate and who enrolled within 2 weeks after the conclusion of therapy Sample characteristics Sample size 99 couples Split between study groups intervention - 48 participants control - 51 participants Mean age (SD) intervention - 66.7 (no SD) years control - 61.1 (no SD) years Interventions Menu-driven computer program met once each month for 6 months with a nurse intervenor (twice in person and 4 times by telephone). first visit- which occurred within 6 weeks after the conclusion of active therapy, the nurse intervenor primarily focused on assessing and managing bowel and urinary function problems After the visit, participants were provided with a videotape to view at home (Living and Loving: Sexuality and the Prostate Cancer Patient) During the second visit, which occurred 1 month later, the nurse used the computer program to evaluate problems related to sexual functioning, cancer worry, dyadic adjustment, depression, and other cancer-related problems. On subsequent encounters, the patient and spouse were asked to discuss issues and concerns that may not have been addressed effectively	No details provided Blinding of participants and personnel Low risk of bias Interviewers were blind to the group assignment of participants. Blinding of outcome assessment Low risk of bias Outcome assessment was blinded because the interviewers were not aware of allocations Incomplete outcome data Low risk of bias None identified Selective reporting Low risk of bias None identified Other sources of bias High risk of bias The authors did not provide details of the standard of care Overall risk of bias High No randomisation strategy was provided, and it is unclear if there was any blinding of participants or personnel Directness Directly applicable

Short Title	Study characteristics	Quality Assessment
	during the previous sessions and to identify any new problems that may have arisen. Intervention visits were scheduled to occur once every month during the first 6 months after completion of treatment with the first 2 visits in person and the remaining visits over the telephone Controls Usual care Authors did not provide a description of what was included in the control group Outcome measure(s) General HRQOL measured by SF- 36 Prostate cancer–specific HRQOL assessed using the Prostate Cancer Quality of Life Instrument (PCQoL), Depression measured by the Centre for Epidemiologic Studies-Depression Scale	

Appendix G – GRADE tables

Multidisciplinary rehabilitation versus usual care – 6 months follow-up

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Disease-specific health related quality of life measured using the Expanded Prostate Cancer Index Composite – 6 months follow up (4 weeks post radiotherapy to 24 weeks post radiotherapy)								
Domain – Urinary irritation MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 6.00 (0.64, 11.6)	Serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – Urinary incontinence MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 2.40 (-2.34, 7.14)	Serious[1]	N/A	Not serious	Serious[3]	Low
Domain – Urinary function MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 5.10 (1.08, 9.12)	Serious[1]	N/A	Not serious	Serious[3]	Low
Domain – Sexual function MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 2.80 (-1.86, 7.46)	Serious[1]	N/A	Not serious	Serious[3]	Low
Domain – Bowel function MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 2.10 (-3.61, 7.81)	Serious[1]	N/A	Not serious	Serious[3]	Low
Domain – Hormonal function MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 4.30 (0.15, 8.45)	Serious[1]	N/A	Not serious	Serious[3]	Low

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
General health related quality of life measured using the Short Form-12 questionnaire 6 months follow up								
Domain- Physical Component Summary MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 3.60 (1.34, 5.86)	Serious[1]	N/A	Not serious	Serious[3]	Low
Domain- Mental Component Summary MD >0 favours multidisciplinary rehabilitation								
1 Study Dieperink (2013)	RCT	161	MD 0 (-2.48, 2.48)	Serious[1]	N/A	Not serious	Serious[3]	Low

1. Moderate risk of bias - no details on how the randomisation sequence was generated – downgraded once
2. 95% confidence interval crosses both ends of a defined MID interval – downgrade twice
3. 95% confidence interval crosses one end of a defined MID interval – downgrade once

Shared care versus usual care – 12 months follow-up

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Disease-specific health related quality of life measured using the Expanded Prostate Cancer Index Composite –								
Domain – Urinary function MD >0 favours shared care								
1 Study Emery (2017)	RCT	81	MD 2.10 (-4.29, 8.49)	Serious[1]	N/A	Not serious	Serious[2]	Low
Domain – Sexual function MD >0 favours shared care								
1 Study Emery (2017)	RCT	79	MD -5.30 (-14.8, 4.20)	Serious[1]	N/A	Not serious	Serious[2]	Low
Domain – Bowel function MD >0 favours shared care								
1 Study Emery (2017)	RCT	82	MD 1.70 (-3.87, 7.27)	Serious[1]	N/A	Not serious	Serious[2]	Low
Domain – Hormonal function MD >0 favours shared care								

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
1 Study Emery (2017)	RCT	82	MD -3.70 (-10.0, 2.60)	Serious[1]	N/A	Not serious	Serious[2]	Low
Anxiety and Depression measures using Hospital Anxiety and Depression Score tool								
Domain - Anxiety MD >0 favours shared care								
1 Study Emery (2017)	RCT	82	MD -0.10 (-1.56, 1.36)	Serious[1]	N/A	Not serious	Very Serious[3]	Very Low
Domain - Anxiety MD >0 favours shared care								
1 Study Emery (2017)	RCT	82	MD -0.10 (-1.64, 1.44)	Serious[1]	N/A	Not serious	Very Serious[3]	Very Low

1. Moderate risk of bias - no details on how the randomisation sequence was generated – downgraded once
2. 95% confidence interval crosses one end of a defined MID interval – downgrade once
3. 95% confidence interval crosses both ends of a defined MID interval – downgrade twice

Menu-driven computer program versus usual care 7 months follow up

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Disease-specific health related quality of life measured using the Prostate Cancer Quality of Life -								
Domain – Urinary function MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD -3.50 (-12.6, 5.56)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Urinary limitation MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD 6.20 (-3.81, 16.2)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Urinary bother MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD -4.00 (-15.0, 7.03)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Sexual function MD >0 favours menu-driven computer program								

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
1 Study Giesler (2005)	RCT	99	MD 10.0 (-0.72, 20.7	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Sexual limitation MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD 9.24 (1.97, 16.51)	Very serious[1]	N/A	Not serious	Not serious	Very low
Domain – Sexual bother MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD 5.91 (-4.99, 16.8)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Bowel function MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD -3.60 (-10.0, 2.84)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Bowel limitation MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD -0.47 (-4.73, 3.79)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Bowel bother MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD 3.80 (-5.89, 13.5)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low
Domain – Cancer worry MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD 11.1 (2.50-19.7)	Very serious[1]	N/A	Not serious	Not serious	Very low
General health related quality of life measured using the SF-36 tool								
Domain – Mental Health Index MD >0 favours menu-driven computer program								
1 Study Giesler (2005)	RCT	99	MD 3.80 (-5.89, 13.5)	Very serious[1]	N/A	Not serious	Very serious[2]	Very low

1. High risk of bias – due to lack of sequence generation and allocation concealment – downgraded twice
2. 95% confidence interval crosses both ends of a defined MID interval – downgrade twice

Technology assisted symptom monitoring versus usual care 12 months follow up

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Disease-specific health related quality of life measured using the UCLA Prostate Cancer Index tool								
Domain – Urinary function MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -0.60 (-7.19, 5.99)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – Sexual function MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -0.20 (-14.4, 13.9)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – Bowel function MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -2.00 (-8.83, 4.83)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Service satisfaction measured using the Primary Care Assessment Survey (PCAS) tool								
Domain – Communication MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD 1.90 (-5.14, 8.94)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – Interpersonal MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -1.20 (-9.41, 7.01)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – overall MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -0.70 (-5.02, 3.62)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
General health related quality of life measured using the FACT-G tool								
Total score MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -1.40 (-6.93, 4.13)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain - Physical well-being MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -0.80 (-2.26, 0.66)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low

No. of studies	Study design	Sample size	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Domain - Social well-being MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -0.50 (-2.29, 1.29)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – Emotional well-being MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD -0.10 (-1.44, 1.24)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low
Domain – Functional well-being MD >0 favours technology assisted symptom monitoring								
1 Study Davis (2013)	RCT	70	MD 0.10 (-2.01, 2.21)	Very serious[1]	N/A	Not serious	Very serious[2]	Very Low

3. High risk of bias – due to lack of sequence generation and allocation concealment – downgraded twice
4. 95% confidence interval crosses both ends of a defined MID interval – downgrade twice

Appendix H – Excluded studies

Clinical studies

Short Title	Title	Reason of Inclusion
Abdollah (2015)	Long-term cancer control outcomes in patients with clinically high-risk prostate cancer treated with robot-assisted radical prostatectomy: results from a multi-institutional study of 1100 patients	Study does not contain any relevant interventions
Abern (2013)	Delayed radical prostatectomy for intermediate-risk prostate cancer is associated with biochemical recurrence: possible implications for active surveillance from the SEARCH database	Study does not contain any relevant interventions
Aghazadeh (2018)	National Comprehensive Cancer Network Favorable Intermediate Risk Prostate Cancer-Is Active Surveillance Appropriate?	Study does not contain any relevant interventions
Ahove (2010)	Which patients with undetectable PSA levels 5 years after radical prostatectomy are still at risk of recurrence?--implications for a risk-adapted follow-up strategy	Study does not contain any relevant interventions
Ball (2006)	Prospective longitudinal comparative study of early health-related quality-of-life outcomes in patients undergoing surgical treatment for localized prostate cancer: A short-term evaluation of five approaches from a single institution	Study does not contain any relevant interventions
Bourke (2015)	Survivorship and Improving Quality of Life in Men with Prostate Cancer	Not a peer-reviewed publication
Buckstein (2013)	Long-term outcomes and toxicity in patients treated with brachytherapy for prostate adenocarcinoma younger than 60 years of age at treatment with minimum 10 years of follow-up	Study does not contain any relevant interventions
Carlsson (2009)	Nationwide population-based study on 30-day mortality after radical prostatectomy in Sweden	Study does not contain any relevant interventions
Chade (2012)	Cancer control and functional outcomes of salvage radical prostatectomy for radiation-recurrent prostate cancer: a systematic review of the literature	Study does not contain any relevant interventions
Chalubinska-Fendler (2015)	Availability and outcomes of radiotherapy in Central Poland during the 2005-2012 period - an observational study	Study does not contain any relevant interventions
Chaplin (2005)	Digital rectal examination is no longer necessary in the routine follow-up of men with undetectable prostate specific antigen after radical prostatectomy: the implications for follow-up	Observational study no comparator group

Short Title	Title	Reason of Inclusion
Chen (2015)	Design of the North Carolina Prostate Cancer Comparative Effectiveness and Survivorship Study (NC ProCESS)	Participants not received treatment
Chen (2017)	Comparisons of health-related quality of life among surgery and radiotherapy for localized prostate cancer: A systematic review and meta-analysis	Study does not contain any relevant interventions
Chung (2013)	Sexual Rehabilitation and Cancer Survivorship: A State of Art Review of Current Literature and Management Strategies in Male Sexual Dysfunction Among Prostate Cancer Survivors	Review article but not a systematic review
Eisemann (2015)	The ProCaSP study: Quality of life outcomes of prostate cancer patients after radiotherapy or radical prostatectomy in a cohort study	Details of the follow up protocol were not detailed
Faithfull (2011)	Self-management after prostate cancer treatment: evaluating the feasibility of providing a cognitive and behavioural programme for lower urinary tract symptoms	Before and after study would be an include
Faithfull (2015)	Self-management for chronic symptoms in the survivorship phase of illness: a randomised controlled trial of a group intervention for radiotherapy side effects versus usual care for men after treatment for prostate cancer	Conference abstract
Fox (2013)	Quality of cancer survivorship care in the military health system (TRICARE)	Observational study without any follow -up strategy as per protocol
Galvão (2014)	A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR	Study does not contain any relevant interventions
Gilbert (2015)	Quality of life and satisfaction among prostate cancer patients followed in a dedicated survivorship clinic	Duplicate reference
Gilbert (2015)	Quality of life and satisfaction among prostate cancer patients followed in a dedicated survivorship clinic	Data not reported in an extractable format Unable to calculate sd values
Goonewardene (2015)	Psychosexual care in prostate cancer survivorship: A systematic review	Systematic review did not identify any randomised control trials
Helgesen (2000)	Follow-up of Prostate Cancer Patients by On-demand Contacts with a Specialist Nurse: A Randomized Study	Data not reported in an extractable format
Hojan (2017)	Inflammation, cardiometabolic markers, and functional changes in men with prostate	Study participants were before

Short Title	Title	Reason of Inclusion
	cancer. A randomized controlled trial of a 12-month exercise program	experiencing radiotherapy
Huang (2010)	Health related quality of life for men treated for localized prostate cancer with long-term followup	Study does not contain any relevant interventions
Hvid (2016)	Effect of a 2-year home-based endurance training intervention on physiological function and PSA doubling time in prostate cancer patients	Study does not contain any of the outcomes of interest
Iremashvili (2012)	Pathologic prostate cancer characteristics in patients eligible for active surveillance: a head-to-head comparison of contemporary protocols	Study does not contain any relevant interventions
Iremashvili (2012)	Clinical and demographic characteristics associated with prostate cancer progression in patients on active surveillance	Study does not contain any relevant interventions
Iremashvili (2013)	Prognostic implications of partial sampling of radical prostatectomy specimens: comparison of 3 methods	Study does not contain any relevant interventions
Kenfield (2011)	Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study	Study does not contain any relevant interventions
King (2012)	The timing of salvage radiotherapy after radical prostatectomy: a systematic review	Study does not contain any of the outcomes of interest
Lavallee (2014)	Survival of men with prostate cancer undergoing radical prostatectomy in Ontario	Study does not contain any relevant interventions
Loblaw (2017)	Follow-up Care for Survivors of Prostate Cancer - Clinical Management: a Program in Evidence-Based Care Systematic Review and Clinical Practice Guideline	Review article but not a systematic review
Lughezzani (2010)	Head-to-head comparison of the three most commonly used preoperative models for prediction of biochemical recurrence after radical prostatectomy	Study does not contain any relevant interventions
Mathieu (2017)	Role of survivin expression in predicting biochemical recurrence after radical prostatectomy: a multi-institutional study	Study does not contain any relevant interventions
May (2007)	Validity of the CAPRA score to predict biochemical recurrence-free survival after radical prostatectomy. Results from a european multicenter survey of 1,296 patients	Study does not contain any relevant interventions
Miller (2005)	Long-term outcomes among localized prostate cancer survivors: health-related quality-of-life changes after radical	Study does not contain any relevant

Short Title	Title	Reason of Inclusion
	prostatectomy, external radiation, and brachytherapy	interventions
Mitchell (2005)	Ability of 2 pretreatment risk assessment methods to predict prostate cancer recurrence after radical prostatectomy: data from CaPSURE	Study does not contain any relevant interventions
Miyake (2015)	Proposed salvage treatment strategy for biochemical failure after radical prostatectomy in patients with prostate cancer: A retrospective study	Study does not contain any relevant interventions
Moreira (2009)	Validation of a nomogram to predict disease progression following salvage radiotherapy after radical prostatectomy: results from the SEARCH database	Study does not contain any relevant interventions Validation study
Moreira (2010)	Definition and preoperative predictors of persistently elevated prostate-specific antigen after radical prostatectomy: results from the Shared Equal Access Regional Cancer Hospital (SEARCH) database	Observational study without any follow -up strategy as per protocol
Moreira (2010)	Postoperative prostate-specific antigen nadir improves accuracy for predicting biochemical recurrence after radical prostatectomy: Results from the Shared Equal Access Regional Cancer Hospital (SEARCH) and Duke Prostate Center databases	Observational study without any follow -up strategy as per protocol
Moreira (2010)	Predictors of secondary treatment following biochemical recurrence after radical prostatectomy: results from the Shared Equal Access Regional Cancer Hospital database	Observational study without any follow -up strategy as per protocol
Morris (2009)	Population-based study of biochemical and survival outcomes after permanent 125I brachytherapy for low- and intermediate-risk prostate cancer	Study does not contain any relevant interventions
Murgic (2017)	Comparison of conventionally fractionated and hypofractionated schedule for postprostatectomy salvage radiotherapy: early results from non-randomized observational study	Conference abstract
Murray (2016)	Prediction model for early biochemical recurrence after radical prostatectomy based on the Cancer of the Prostate Risk Assessment score and the presence of secondary circulating prostate cells	Study does not contain any relevant interventions
Naik (2016)	Posttreatment Prostate-Specific Antigen 6 Months After Radiation With Androgen Deprivation Therapy Predicts for Distant Metastasis-Free Survival and Prostate Cancer-Specific Mortality	Observational study without any follow -up strategy as per protocol
Nam (2012)	Population based study of long-term rates of surgery for urinary incontinence after radical prostatectomy for prostate cancer	Observational study without any follow -up strategy as per protocol

Short Title	Title	Reason of Inclusion
Namiki (2006)	Changes in quality of life in first year after radical prostatectomy by retropubic, laparoscopic, and perineal approach: Multi-institutional longitudinal study in Japan	Observational study without any follow -up strategy as per protocol
Namiki (2006)	Quality of life after brachytherapy or radical prostatectomy for localized prostate cancer: a prospective longitudinal study	Observational study without any follow -up strategy as per protocol
Namiki (2007)	Impact of salvage therapy for biochemical recurrence on health-related quality of life following radical prostatectomy	Study does not contain any relevant interventions
Nicolaisen (2014)	Quality of life and satisfaction with information after radical prostatectomy, radical external beam radiotherapy and postoperative radiotherapy: a long-term follow-up study	Observational study without any follow -up strategy as per protocol
Novara (2012)	Systematic review and meta-analysis of studies reporting oncologic outcome after robot-assisted radical prostatectomy	Systematic review did not identify any randomised control trials
Orom (2018)	Racial or Ethnic and Socioeconomic Disparities in Prostate Cancer Survivors' Prostate-specific Quality of Life	Observational study without any follow -up strategy as per protocol
Paterson (2015)	Exploring prostate cancer survivors' self-management behaviours and examining the mechanism effect that links coping and social support to health-related quality of life, anxiety and depression: a prospective longitudinal study	Study does not contain any relevant interventions
Shangguan (2017)	Management of prostate cancer patients with locally adverse pathologic features after radical prostatectomy: feasibility of active surveillance for cases with Gleason grade 3 + 4 = 7	Study does not contain any relevant interventions
Smaldone (2010)	Eligibility for active surveillance and pathological outcomes for men undergoing radical prostatectomy in a large, community based cohort	Study does not contain any relevant interventions
Stanciu (2015)	A pilot randomised controlled trial of personalised care after treatment for prostate cancer (TOPCAT-P): nurse-led holistic-needs assessment and individualised psychoeducational intervention: study protocol	Study protocol
Venderbos (2017)	Long-term follow-up after active surveillance or curative treatment: quality-of-life outcomes of men with low-risk prostate cancer	Observational study without any follow -up strategy as per protocol Cross sectional study
Vieira (2014)	Prostate cancer follow-up needs: do patients and professionals agree?	Review article but not a systematic review

Short Title	Title	Reason of Inclusion
Watson (2011)	Views of health professionals on the role of primary care in the follow-up of men with prostate cancer	Qualitative research
Watson (2014)	PROSPECTIV - A pilot trial of a nurse-led psychoeducational intervention delivered in primary care to prostate cancer survivors: study protocol for a randomised controlled trial	Study protocol

Economic studies

Short Title	Title	Reason of Inclusion
Barocas (2014)	Economic evaluation of diagnostic localization following biochemical prostate cancer recurrence	It addresses a hypothesised prostate cancer specific functional imaging technology
Emery (2017)	ProCare Trial: a phase II randomized controlled trial of shared care for follow-up of men with prostate cancer	Not a full economic evaluation

Appendix I – References

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Appendix J – Research recommendations

Question	**What is the most clinically- and cost-effective follow-up protocol for people with prostate cancer who have had radical treatment, with specific regard to: duration of follow-up, frequency of follow-up appointments, the type of examination or blood tests, the respective roles of primary and secondary care in follow-up?**
Population	People with localised prostate cancer who have had radical treatment.
Intervention	Different follow up protocols - for example • supported self-management • shared care • survivorship • remote follow up
Comparator	Usual care Different follow up protocols - for example • supported self-management • shared care • survivorship • remote follow up
Outcomes	• Patient/ carers satisfaction • Quality of life (e.g. Anxiety) • Biochemical Recurrence • Severe adverse events • Other PROMS
Study design	Randomised control trials/Prospective cohort study
Potential criterion	**Explanation**
Importance to patients, service users or the population	It is important that people receive a level of follow up that is appropriate and measured. The balance of quality of life and appropriate follow up to monitor for recurrence is key.
Relevance to NICE guidance	X Priority: The committee was unable to make new recommendations because of the paucity of evidence. New research in this area could allow recommendations to be made at future updates.
Current evidence base	The current evidence base for this patient group is small and uninformative.

Equality	No additional equality issues are envisaged relating to this study over and above those applying generally to vulnerable groups of people.
Feasibility	There is a large enough population of people