

(PICO 7) NKR 38: A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI)

Study Name

Osteoporosis Management Program, Decreases Incidence of Hip Fracture in Patients With Prostate Cancer Receiving Androgen Deprivation Therapy

Study ID

Reference(s) to study report(s)

Assessor name / initials / code

Konsensus

Study design (select)
If other, specify

Case-cohort study

Retrospective Cohort study

Specify a target trial specific to the study

The protocol-specified target randomized trial fully applies

No

(if no, define the target trial below)

OR

Participants:

Experimental intervention:

Control intervention:

Patients With Prostate Cancer

Osteoporosis management system / Healty Bones Program HBP

Not in osteoporosis management system /non - Healty Bones Program

Specify the outcome *

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table).

Fractures (Hip fractures)

Specify whether this is a proposed benefit or harm of intervention.

Benefit

Specify the effect of interest

e.g. effect of initiating intervention (as in an intention-to-treat analysis), or effect of initiating and adhering to intervention (as in a per-protocol analysis)

reduce hip fractures

Specify the specific result being assessed

in case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

HR: non-HBP vs HBP 4.19 (95% CI 1.92-9.19)

Preliminary consideration of confounders

a. Within each confounding domain listed in the review protocol, list the relevant variables, if any, measured in this study.

Age, BMI, Earlier fractures, stage of cancer, medical treatments. Further; Race, Diagnosed Osteoporosis, Year of diagnosis with prostate cancer

b. List additional confounding domains, if any, specific to the setting of this particular study. Within each domain, list the relevant variables, if any, measured in this study.

smoking, d-vitamine deficiency, selection bias

c. List additional domains and corresponding measured variables, if any, that the study authors identified as potential confounders that are not included in the above domains.

None

Relationship between confounding domains and potential confounders.

In the table below, “critically important” confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. “Validity” refers to whether the confounding variable or variables fully measure the domain, while “reliability” refers to the precision of the measurement (more measurement error means less reliability).

Confounding domain	Is the domain critically important?*	Measured Variable	Did the authors demonstrate that controlling for this variable was unnecessary?*	Is the domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is adjusting for this variable (alone) expected to move the effect estimate up or down? **
Age	Yes	years	Yes	Yes	No information
BMI	Yes	kg	Yes	Yes	Down
Earlier fractures	Yes	nb	Yes	Yes	Down
Stage of cancer	Yes	stage	Yes	No information	No information
				No information	No information
Medical treatments	Yes	n/N	Yes	Yes	No information
Race	Yes	n/N	Yes	No information	No information
Osteoporosis	Yes	y/n	Yes	No information	No information
Year of diagnosis (prostate cancer)	Yes	years	Yes	No information	No information

Add more rows here if you need to

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistic

** For example, if the crude effect estimate is 1.3, adjustment to 1.6 is up, while adjustment to 0.7 is down. If the effect estimate is 0.7, adjustment to 1.1 is up while adjustment to 0.4 is down.

Preliminary consideration of co-interventions

a. Are the (pre-specified) co-interventions likely to be administered in the context of this study?

NR

b. List additional co-interventions, if any, specific to the setting of this particular study.

NR

Co-interventions

In the table below, “critically important” co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. “Validity” refers to whether the variables fully measure the co-intervention, while “reliability” refers to the precision of the measurement (more measurement error means less reliability).

Co-intervention	Is the co-intervention critically important?*	Did the authors demonstrate that controlling for this co-intervention was unnecessary?	Is the co-intervention measured validly and reliably?	Is presence of this co-intervention likely to favour outcomes in the experimental or the control group
	Yes/No	Yes/No	Yes / No / No information	Select direction
	Yes/No	Yes/No	Yes / No / No information	Select direction

Add more rows here if you need to

Risk of bias assessment (cohort-type studies)

Bias due to confounding	1.1 Is confounding of the effect of intervention unlikely in this study?	Probably Yes	PY
	If Y or PY to 1.1: the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered		Moderate risk
	If N or PN to 1.1:		Y

	<p>1.2. Were participants analysed according to their initial intervention group throughout follow up? If Y or PY to 1.2, answer questions 1.4 to 1.6, which relate to baseline confounding</p> <p>1.3. If N or PN to 1.2: Were intervention discontinuations or switches unlikely to be related to factors that are prognostic for the outcome? If Y or PY to 1.3, answer questions 1.4 to 1.6, which relate to baseline confounding If N or PN to 1.1 and 1.2 and 1.3, answer questions 1.7 and 1.8, which relate to time-varying confounding If Y or PY to 1.2, or Y or PY to 1.3:</p> <p>1.4. Did the authors use an appropriate analysis method that adjusted for all the critically important confounding domains? Probably Yes</p> <p>1.5. If Y or PY to 1.4: Were confounding domains that were adjusted for measured validly and reliably by the variables available in this study? Probably Yes</p> <p>1.6. Did the authors avoid adjusting for post-intervention variables? Not applicable</p> <p>1.7. Did the authors use an appropriate analysis method that adjusted for all the critically important confounding domains and for time-varying confounding? If N or PN to 1.2 and 1.3</p> <p>1.8. If Y or PY to 1.7: Were confounding domains that were adjusted for measured validly and reliably by the variables available in this study?</p> <p>Risk of bias judgement Optional: What is the predicted direction of bias due to confounding?</p>	<p>Yes</p> <p>Probably Yes</p> <p>Probably Yes</p> <p>Not applicable</p> <p>Select judgement Unpredictable</p>	<p>PY</p> <p>PY</p> <p>NA</p> <p>[Support for judgement] The direction is two-sided</p>
Bias in selection of participants into the study	<p>2.1. Was selection into the study unrelated to intervention or unrelated to outcome? Yes</p> <p>2.2. Do start of follow-up and start of intervention coincide for all or most subjects? Yes</p> <p>2.3. If N or PN to 2.1 or 2.2: Were adjustment techniques used that are likely to correct for the presence of selection biases?</p> <p>Risk of bias judgement Optional: What is the predicted direction of bias due to selection of participants into the study?</p>	<p>Yes</p> <p>Yes</p> <p>Select judgement Favours comparator</p>	<p>Y</p> <p>Y</p> <p>[Support for judgement] It goes against the outcome.</p>
Bias in measurement of interventions	<p>3.1. Is intervention status well defined? Yes</p> <p>3.2. Was information on intervention status recorded at the time of intervention? Yes</p> <p>3.3. Was information on intervention status unaffected by knowledge of the outcome or risk of the outcome? Yes</p> <p>Risk of bias judgement Optional: What is the predicted direction of bias due to measurement of outcomes or interventions?</p>	<p>Yes</p> <p>Yes</p> <p>Yes</p> <p>Select judgement Unpredictable</p>	<p>Y</p> <p>Y</p> <p>Y</p> <p>[Support for judgement]</p>
Bias due to departures from intended interventions	<p>4.1. Were the critical co-interventions balanced across intervention groups? Probably Yes</p> <p>4.2. Were numbers of switches to other interventions low? No information</p> <p>4.3. Was implementation failure minor? No information</p> <p>4.4. If N or PN to 4.1, 4.2 or 4.3: Were adjustment techniques used that are likely to correct for these issues?</p> <p>Risk of bias judgement Optional: What is the predicted direction of bias due to departures from the intended interventions?</p>	<p>Probably Yes</p> <p>No information</p> <p>No information</p> <p>Select judgement Unpredictable</p>	<p>PY</p> <p>Not relevant to intervention</p> <p>Not relevant to intervention</p> <p>[Support for judgement] Probably low</p>
Bias due to missing data	<p>5.1. Are outcome data reasonably complete? Probably Yes</p> <p>5.2. Was intervention status reasonably complete for those in whom it was sought? Probably Yes</p> <p>5.3. Are data reasonably complete for other variables in the analysis? Probably Yes</p>	<p>Probably Yes</p> <p>Probably Yes</p> <p>Probably Yes</p>	<p>Fully reported</p>

	5.4 If N or PN to 5.1, 5.2 or 5.3: Are the proportion of participants and reasons for missing data similar across interventions?		
	5.5 If N or PN to 5.1, 5.2 or 5.3: Were appropriate statistical methods used to account for missing data?		
	Risk of bias judgement	Select judgement	[Support for judgement]
	Optional: What is the predicted direction of bias due to missing data?	Unpredictable	Probably low
Bias in measurement of outcomes	6.1 Was the outcome measure objective?	Yes	Clearly described
	6.2 Were outcome assessors unaware of the intervention received by study participants?	Probably No	Not possible to blind
	6.3 Were the methods of outcome assessment comparable across intervention groups?	Yes	
	6.4 Were any systematic errors in measurement of the outcome unrelated to intervention received?	Probably Yes	
	Risk of bias judgement	Select judgement	[Support for judgement]
	Optional: What is the predicted direction of bias due to measurement of outcomes?	Favours experimental	
Bias in selection of the reported result	Is the reported effect estimate unlikely to be selected, on the basis of the results, from...		
	7.1. ... multiple outcome <i>measurements</i> within the outcome domain?	Probably Yes	PY
	7.2. ... multiple <i>analyses</i> of the intervention-outcome relationship?	Probably Yes	
	7.3. ... different <i>subgroups</i> ?	Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Select judgement	[Support for judgement]
	Optional: What is the predicted direction of bias due to selection of the reported result?	Unpredictable	
Overall bias	Risk of bias judgement	Select judgement	[Support for judgement]
	Optional: What is the overall predicted direction of bias for this outcome?	Towards null	Bias tends to go in both directions