First author: Bayley Year: 2001 ID: 107
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]				✓	
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]	✓				
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	4	2	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Bernat Year: 1983 ID: 108
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up			✓		
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics		✓			
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]				✓	
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	3	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Chaichana Year: 2009 ID: 109
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]			✓		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables			✓		
	Loss to follow-up			✓		
	Statement as to the possible effect on the results from missing data			✓		
	Loss to follow-up is not associated with key characteristics			✓		
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]	✓				
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	3	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Fisher Year: 2010 ID: 110
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]			✓		
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]			✓		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results			✓		
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables			✓		
	Loss to follow-up			✓		
	Statement as to the possible effect on the results from missing data			✓		
	Loss to follow-up is not associated with key characteristics			✓		
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors		✓			
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results		✓			
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	0	3	3	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Goldman Year: 1989 ID: 111
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]					✓
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results			✓		
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	1	3	2	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Harrison Year: 1985 ID: 112
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]					✓
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	3	2	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Helweg-Larsen Year: 2000 ID: 113
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]					✓
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	3	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Helweg-Larsen Year: 1995 ID: 114
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]					✓
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results		✓			
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	1	4	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Huddart Year: 1997 ID: 115
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]		✓			
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	3	3	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Husband Year: 2001 ID: 116
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]					✓
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results		✓			
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	3	2	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Klekamp Year: 1998 ID: 117
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up					✓
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]		✓			
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	4	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Kuban Year: 1986 ID: 118
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]			✓		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up					✓
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors		✓			
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]			✓		
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results			✓		
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	2	2	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Levack Year: 2002 ID: 119
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]			✓		
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]				✓	
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results			✓		
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	1	3	1	1	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Loblaw Year: 2005 ID: 62
Reviewer(s): PS/MC – Agreed

Did the review address a clearly focused question?
No – the authors aimed to address a series of questions. (1) What are the clinical symptoms of MSCC? (2) What is the optimal approach for investigating suspected MSCC? (3) Is there a role for systemic corticosteroids in the management of MSCC, and if so, what is the optimal dose? (4) What are the indications for radiotherapy in the management of MSCC? (5) Is there an optimal dose prescription for radiotherapy? (6) What are the treatment options for recurrent MSCC in an area previously irradiated? (7) What are the indications for surgery in the management of MSCC?

Did the authors look for the appropriate sort of papers?
Unclear – all study types were included. Only full publications and abstracts of adult patients with extradural cord compression, but not intramedullary and leptomeningeal cord compression, were included. The authors might have considered limiting inclusion on quality.

Do you think the important, relevant studies were included?
Unclear – however, the authors searched an extensive list of databases. MEDLINE, CANCERLIT, and the Cochrane Library databases were searched to January 2004 using terms: spinal cord compression, nerve compression syndromes, spinal cord neoplasms, clinical trial, meta-analysis and systematic review. Also, abstracts published in the Proceedings of the Annual Meetings of the American Society of Clinical Oncology (up to 2003) and the American Society of Therapeutic Radiology and Oncology (1997 to 2003) were searched for ongoing trials. The Canadian Medical Association Infobase and the National Guidelines Clearinghouse were searched for evidence-based practice guidelines.

Did the review's authors do enough to assess the quality of the included studies?
There was no quality assessment of the included studies. This was a substantial weakness of the review. This resulted in all study designs regardless of quality being included.

If the results of the review have been combined, was it reasonable to do so?
The results of the included studies are not clearly displayed to allow a clear comparison of the different studies and to establish whether it was appropriate to pool the studies and to explain the reasons for any variations in results. Furthermore, the authors have attempted to pool different study designs to address the specific questions highlighted, without undertaking a quality assessment of each study.

What are the overall results of the reviews?
Magnetic resonance imaging is the preferred imaging technique and treatment for patients with MSCC should consider pretreatment ambulatory status, comorbidities, technical surgical factors, the presence of bony compression and spinal instability, potential surgical complications, potential radiotherapy reactions and patient preferences. The authors recognised that in summarising the evidence on the diagnosis and management of MSCC, unfortunately, for many questions raised, the current evidence prevents reliable conclusions from being made.

How precise are the results?
Unclear – the authors are conservative in their interpretation of the studies. However, they have attempted to address too many questions. The authors provide percentages and 95% CIs, with limited discussion of the statistical findings from each study.

Can the results be applied to the local population?
No, because the populations in the included studies were poorly defined and probably different from study to study. The limited discussion of the populations in each included study and the lack of quality assessments make it difficult to draw conclusions as to whether these findings can be applied to the local population.

Were all important outcomes considered?
The authors have made a good attempt at addressing different key questions in this area. However, it is difficult to establish whether other outcomes could have been considered as summary tables outlining the measures used in each study are not provided.

Are the benefits worth the harms and costs?
Although the review discussed issues related to adverse events, there was a lack of consideration of the costs of treatment diagnosis and management of malignant extradural spinal cord compression, and the consequential outcomes of false-positive and false-negative predictions or diagnoses.

First author: Lu **Year: 1998** **ID: 120**
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data		✓			
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	✓				
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]		✓			
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	5	1	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Lu **Year: 2005** **ID: 121**
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data		✓			
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	4	1	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: McCloskey Year: 1993 ID: 122
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up		✓			
	Statement as to the possible effect on the results from missing data			✓		
	Loss to follow-up is not associated with key characteristics		✓			
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	3	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Oka **Year: 2006** **ID: 123**
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]	✓				
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	5	1	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Plunkett Year: 2000 ID: 24
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data			✓		
	Loss to follow-up is not associated with key characteristics		✓			
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)		✓			
	Specified instrument and personnel for measurement of predictive factors		✓			
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]			✓		
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	1	4	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Rose Year: 2009 ID: 88
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]	✓				
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	✓				
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]	✓				
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	5	1	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Roth Year: 2004 ID: 124
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample (i.e. individuals entering the study and their key characteristics [where relevant] and sampling frame are adequately described)		✓			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]				✓	
	Blinding: were estimators of risk factor status and of outcomes blinded?				✓	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?		✓			
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	3	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Sekine Year: 2009 ID: 125
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]				✓	
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	✓				
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]		✓			
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	5	1	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Shah Year: 2003 ID: 126
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	4	1	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Snyder Year: 2005 ID: 127
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]			✓		
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]			✓		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results			✓		
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables				✓	
	Loss to follow-up				✓	
	Statement as to the possible effect on the results from missing data				✓	
	Loss to follow-up is not associated with key characteristics				✓	
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]				✓	
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	1	2	1	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Snyder Year: 2009 ID: 128
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up				✓	
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics		✓			
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]				✓	
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	2	3	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Soerdjbalie-Maikoe Year: 2004 ID: 129
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]			✓		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]	✓				
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	✓				
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]				✓	
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results		✓			
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	3	2	0	1	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Sun Year: 2011 ID: 130
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]		✓			
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results		✓			
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	3	3	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Talcott Year: 1999 ID: 131
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data		✓			
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	✓				
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]		✓			
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	5	1	0	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Taneichi Year: 1997 ID: 89
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]		✓			
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results		✓			
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis		✓			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	3	2	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Venkitaraman Year: 2007 ID: 132
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	4	1	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.

First author: Venkitaraman Year: 2010 ID: 133
Reviewer(s): PS/MC – Agreed

Potential bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA
Study population/ sample selection[a]	Inclusion and exclusion criteria are adequately described [including pretreatment, diagnosis (primary and metastases), start/finish date recruitment]	✓				
	Baseline study sample [i.e. individuals entering the study and their key characteristics (where relevant) and sampling frame are adequately described]	✓				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	✓				
Study attrition	Statement as to exclusions due to missing data:					
	Baseline variables	✓				
	Loss to follow-up	✓				
	Statement as to the possible effect on the results from missing data					✓
	Loss to follow-up is not associated with key characteristics	✓				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described)	✓				
	Specified instrument and personnel for measurement of predictive factors	✓				
	Continuous variables are reported or appropriate (i.e. not data-dependent) cut-off points are used and specified a priori[b]		✓			
	Blinding: were estimators of risk factor status and of outcomes blinded?			✓		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias		✓			
Outcome	Is the outcome clearly defined?	✓				
Confounding measurement and account	Do the authors address potential confounders?[c]			✓		
Analysis	There is sufficient presentation of data to assess the adequacy of the analysis	✓				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	✓				
	TOTAL NUMBER OF TICKS TO THE MAIN QUESTIONS (GREEN BOXES)	4	1	1	0	0

NA, not applicable.

a Is the sampling frame clear (if unclear there is risk of bias), and is the method of sample selection susceptible to bias?

b Cut-off points decided prior to data analysis.

c In particular, if previous treatments were not taken into account in the analyses of potential predictive factors these could confound the validity of other predictive factors that might be identified.