

**S5 Doc: Assessed and discarded items of REMARK checklist – Reasons and definitions**

Item of REMARK checklist	Item evaluated	Reason for discard or Definition based on elements of data extraction sheet*
<b>Introduction</b>		
1. Introduction: study objectives, hypotheses	-	Essentially always mentioned to some extent, especially as some aspects are part of eligibility criteria; in addition, too difficult to assess reliably because it requires background knowledge; this item is not covered by data extraction form
<b>Materials and Methods</b>		
2. Patient characteristics	✓	<b>Definition:</b> C4 Selection: apparently unselected/selected <b>AND</b> C5 Source: yes
3. Patient treatments	-	Too difficult to assess because it requires background knowledge on therapy of patients with different cancer diseases and at different stages
4. Specimen characteristics	-	Too difficult to assess because it requires special expertise about lab measurements; moreover, something is always mentioned
5. Assay methods	-	Too difficult to assess because it requires special expertise about lab measurements; moreover, something is always mentioned
6. Study design: patient selection & time period	✓	<b>Definition:</b> C9 start recruitment: yes <b>AND</b> C10 stop recruitment: yes <b>AND</b> (C11 end of follow up: yes <b>OR</b> C12 median follow up: yes <b>OR</b> J1 completeness of follow up: yes)
7. Clinical endpoints	✓	<b>Definition:</b> (D1 OS: yes <b>AND</b> D3 definition OS: any death/cancer death) <b>OR</b> (D2 DFS: yes <b>AND</b> D4 definition DFS: incl. death/excl. death)
8. Candidate variables	-	Too difficult to assess especially with respect to completeness without background knowledge; some information is always provided
9. Rationale for sample size	✓	<b>Definition:</b> ((G1/H2 OS patients (marker/other): both yes) <b>OR</b> (G3/H4 DFS patients (marker/other): both yes)) <b>AND</b> ((G2/H3 OS events (marker/other): both yes) <b>OR</b> (G4/H5 DFS events (marker/other): both yes)) <b>AND</b> I1 patients: yes <b>AND</b> I2 events: yes
10. All statistical methods	✓	<b>Definition:</b> C5 Model: any stated model (e.g. Cox regression model)
11. Handling of the marker	-	Too difficult to assess because it requires background knowledge; definition of marker positivity is usually provided but often without justification

\* see supplemental document 4 (data extraction sheet) for details (e.g. coding)

**S5 Doc: Assessed and discarded items of REMARK checklist – Reasons and definitions (cont.)**

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<b>Results</b>		
12. Flow of patients	✓	<b>Definition:</b> (E1 patients assessed: yes <b>OR</b> E2 patients excluded: yes) <b>AND</b> E3 analysed patients: yes <b>AND</b> (E4 events OS: yes <b>OR</b> E5 events DFS: yes)
13. Distribution of demographic characteristics	✓	<b>Definition:</b> C6 stage, grade: yes <b>AND</b> C7 age: yes
14. Relationship between marker and standard variables	✓	<b>Definition:</b> J2 relationship to other variables: yes
15. Univariate analyses	✓	<b>Definition:</b> G5 effect estimate of marker: yes <b>AND</b> G6 CI of marker: yes
16. Multivariable analyses	✓	Focus: final model <b>Definition:</b> I4 effect estimate of marker: yes <b>AND</b> I5 effect estimate of other variables: all/some <b>AND</b> I6 CI of marker and other variables: yes
17. Estimated effects with confidence intervals	-	Focus: model including marker <b>AND</b> standard prognostic factors Too difficult to assess without background knowledge regarding standard prognostic factors
18. Further investigations (incl. check of model assumptions)	-	Although at least a check of model assumption can be expected such assessments are rarely reported; other investigations cannot generally be expected from all studies as their necessity depends on specific research setting
<b>Discussion</b>		
19. Results in context of pre-specified hypotheses	-	Too difficult to assess because it requires specific background knowledge; this item is not covered by data extraction form
20. Implications	-	Too difficult to assess because it requires specific background knowledge; this item is not covered by data extraction form

\* see supplemental document 4 (data extraction sheet) for details (e.g. coding)