Name of first reviewer: *Name of second reviewer:*

Study details	
Study ID (Endnote ref)	
First author surname and year of publication	
Country	
Study design	
Study setting	
Number of centres	
Time period/study duration	
Follow up period	
Funding	
Competing interests	
Answers which part of interest 1. All 2. More than 10% don't get reference standard 3. Concordance only 4. 2 cancers	
Aim of the study	
Description of study format (study design/set up)	
Patient selection	
Inclusion criteria:	
Exclusion criteria:	

Study flow	
Item	
Number of people screened for eligibility	
Number of eligible people	
Number of people included in study	
People excluded from the study, number and reason(s)	
Strategies the study relates to (1-10)	

Baseline characteristics	
Item	
Age mean (SD) Median (range)	
Ethnicity	
Any previous/concurrent cancers? Type No. (%)	
Any information regarding relatives and their history	
Any people included with known lynch syndrome	
Comments	

Testing methods	
Tumour testing	
IHC	
Age at specimens collection	
Method of IHC testing	
List proteins IHC performed on (e.g. MLH1, MSH2, MSH6, PMS2)	
Description of how positive and negative staining has been defined	
Description of quality assurance (name guidance used)	
Test undertaken blind to other tests?	
MSI	
MSI primers used	
Method of MSI testing	
Source for control tissue (e.g. blood/normal endometrium tissue from patient, pooled normal tissue)	
Markers (specify which markers were used, e.g. original Bethesda)	
Description of how MSI-High, MSI-Low and MSI-Stable were defined	

Threshold pre-specified (y/n)	
Test undertaken blind to other tests?	
Data management	
Description of quality assurance (can name guidance used)	
Testing method – MLH1 Promoter hypermethylation	
Method of MLH1 promoter hypermethylation testing	
Test undertaken blind to other tests?	
Description of quality assurance (can name guidance used)	
Germline testing	
Sequencing/next-generation sequencing	
Where DNA obtained from	
Genes analysed	
Method of germline testing (e.g. how DNA extracted, equipment used)	
Test undertaken blind to other tests?	
Description of quality assurance (can name guidance used)	

MLPA	
Where DNA obtained from	
Genes analysed	
Method of germline testing	
Test undertaken blind to other tests?	
Description of quality assurance (can name guidance used)	
Other eligible reference standards (array-based comparative genomic hybridization or long-range PCR, specify which)	
Where DNA obtained from	
Genes analysed	
Method of germline testing	
Test undertaken blind to other tests?	
Description of quality assurance (can name guidance used)	
MLH1 Promoter hypermethylation testing	**As a reference standard test, in non-tumour tissue. Not an official reference standard!**
Where DNA obtained from	
Method of germline testing	

Test undertaken blind to other tests?	
Description of quality assurance (can name guidance used)	

Number receiving index test(s) and reference standard(s)	
Number receiving IHC	
Number excluded from IHC, with reason(s)	
Number receiving MSI	
Number excluded from MSI testing, with reason(s)	
Number receiving MLH1 promoter hypermethylation testing	
Number excluded from MLH1 promoter hypermethylation testing, with reason(s)	
Number receiving sequencing (specify if sequencing/next-generation sequencing)	
Number excluded from sequencing, with reason(s) ***Make a note of the number refusing germline testing**	
Number receiving MLPA	
Number excluded from MLPA, with reason(s)	

Number receiving (specify other applicable reference standard here)	
Number excluded from (other reference standard), with reason(s)	

Outcomes – whole sample/complete testing strategy	
Provide brief description of testing strategy that paper provides results for:	
Outcome	
Lynch diagnoses, n/N (%)	
TP	
TN	
FP	
FN	
Sensitivity, % (95% CI)	
Specificity, % (95% CI)	
PPV, % (95% CI)	
NPV, % (95% CI)	
Likelihood ratios	
Diagnostic odds ratios	
ROC curves	
Test failures, n/N (%)	
Indeterminate results, n/N (%)	
Time from index test given to test result	
Time from test (specify) given to diagnosis	

Concordance between IHC and MSI • n/N (%) agreement/concordance • n/N (%) disagreement/discordance • Kappa (specify type, e.g. unweighted)	
Types/frequencies of Lynch syndrome genetic mutations (MLH1, MSH2, MSH6, PMS2)	
Other Lynch-like variants, n	
Paper definition (e.g. variants of unknown clinical significance, presumed Lynch)	
Characteristics of other Lynch syndrome variants (e.g. family history, IHC results and discordant cases between the two index tests)	
Notes/comments (anything at all, but make a note if paper reports on use of more than one MSI panel)	

Outcomes – whole sample/testing strategy using few than the standard 4 proteins (any combination – repeat table as required)	
(Specify which proteins included in IHC)	
Outcome	
Lynch diagnoses, n/N (%)	
TP	
TN	
FP	
FN	
Sensitivity, % (95% CI)	
Specificity, % (95% CI)	
PPV, % (95% CI)	
NPV, % (95% CI)	
Likelihood ratios	
Diagnostic odds ratios	
ROC curves	
Test failures, n/N (%)	
Indeterminate results, n/N (%)	Indeterminate results, n/N (%)
Time from index test given to test result	
Time from test (specify) given to diagnosis	
Concordance between IHC and MSI • n/N (%) agreement/concordance • n/N (%) disagreement/discordance • Kappa (specify type, e.g. unweighted)	
Characteristics of discordant cases	

Types/frequencies of Lynch syndrome genetic mutations (MLH1, MSH2, MSH6, PMS2)	
Other Lynch-like variants, n	
Paper definition (e.g. variants of unknown clinical significance, presumed Lynch)	
Characteristics of other Lynch syndrome variants (e.g. family history, IHC results and discordant cases between the two index tests)	
Notes/comments	

Outcomes - whole sample/pre-specified subgroups				
Outcome	Age subgroups		Prior LS-cancer subgroup	
	<70	>70	Prior LS cancer	No prior LS cancer
Lynch diagnoses, n/N (%)				
TP				
TN				
FP				
FN				
Sensitivity, % (95% CI)				
Specificity, % (95% CI)				
PPV, % (95% CI)				
NPV, % (95% CI)				

Likelihood ratios				
Diagnostic odds ratios				
ROC curves				
Test failures, n/N (%)				
Indeterminate results, n/N (%)				
Time from index test given to test result				
Time from test (specify) given to diagnosis				
IHC/MSI concordance • n/N (%) agreement/concordance • n/N (%) disagreement/discordance • Kappa (specify type, e.g. unweighted)				
Other Lynch-like variants, n				
Paper definition (e.g. variants of unknown clinical significance, presumed Lynch)				
Characteristics of other Lynch syndrome variants (e.g. family history, IHC results and discordant cases between the two index tests)				
Notes/comments				

Authors' comments & conclusion
Reviewer's comments & conclusion