

Appendix H: QUADAS2 risk of bias assessment

Study	Random selection or case control	Index test with blinding of gold standard test results	Gold standard test with blinding of index test results	Time interval between index and gold standard	Loss of data from analysis	Overall risk of bias
Antonicelli, 2012 ⁶	Random	yes	Yes	Within 1 day	None reported	Serious risk of bias
Arevalo-Manso, 2016 ⁷	Consecutive	Unclear	unclear	unclear	None reported	Very serious risk of bias
Brito, 2018 ²³	consecutive	yes	unclear	Not simultaneous	None reported	Very serious risk of bias
Brown, 2019 ²⁴	Consecutive	Unclear	No blinding	Simultaneous	5/265 lost due to no index test. Unlikely to be a risk of attrition bias.	Very serious risk of bias
Bumgarner, 2018 ²⁶	Case-control	Yes	Yes	Not simultaneous, but a very short interval between	169 simultaneous 12-lead ECG and KB recordings obtained from study participants, and of these 57 KB recordings were determined as unclassified by the KB algorithm. Of the 57 unclassified KB tracings, 16(28%) were due to baseline artifact and low amplitude of the recording, 12 (21%) were due to a recording of <30 s in duration, 6(10%) were due to a heartrate of	Serious risk of bias

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					<p><50 beats/min, 5 (9%) were due to a heart rate of >100 beats/min, and the remaining 18 (32%) were unclassified due to an unclear reason. However these represent a drawback of the FB and so these should have been designated as negative findings rather than excluded. The authors presented the calculated accuracies using only the interpretable KB values. However they did present the raw data including the missing/unclassified data, which has been used by the systematic reviewer to calculate more pragmatic accuracy values (with designation of missing data as a negative result).</p>	

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Caldwell, 2012 ²⁹	Case-control	partial	partial	Not simultaneous but same session	None reported	Very serious risk of bias
Chen, 2020 ³⁶	Consecutive (later separated to AF/no AF after gold standard but not recruited as such)	Automated so not applicable	Unclear	Unclear but not simultaneous	None reported; a proportion of data reported as 'unclear' but this was catered for in our analysis	Serious risk of bias
Cunha, 2019 ⁴⁹	Consecutive	Unclear	Unclear	Unclear	Unclear	Very serious risk of bias
Desteghe, 2017 ⁵⁸	Consecutive	NA for automated measurements. For manual interpretation readings unclear	Yes, blinded	GS done immediately before IT	Yes – 24/344 lost from analysis because they could not hold device properly. Had they been included a less accurate result may have ensued. But <10% so not a serious risk of bias	Serious risk of bias for automatic readings and very serious for manual readings
Diamantino, 2020 ⁵⁹	Unclear	Automated so not applicable	Yes	Unclear but not simultaneous	None	Serious risk of bias
Doliwa, 2009 ⁶³	consecutive	yes	Yes	Not simultaneous	None reported	Serious risk of bias
Fallet, 2019 ⁷⁶	consecutive	unclear	unclear	Appears to be simultaneous:	None reported	Very serious risk of bias

Study	Random selection or case control	Index test with blinding of gold standard test results	Gold standard test with blinding of index test results	Time interval between index and gold standard	Loss of data from analysis	Overall risk of bias
				'temporally aligned'		
Fan, 2019 ⁷⁷	Unclear but appears to be random	NA as algorithm is automatic	Unclear (only states blinded from baseline characteristics)	simultaneous	4/112 as ECG data unclear – unlikely to pose a significant risk of bias	Serious risk of bias
Gandolfo 2015 ⁷⁹	Unselected consecutive patients admitted with stroke	NA as automated	Yes, cardiologist no knowledge of index test results	<48 hours but usually less than 1 day	None reported	Serious risk of bias
Greg, 2008 ⁸²	Random	NA - automated	No	Simultaneous	None	Very serious risk of bias
Guan, 2020 ⁸⁶	Random	Y	Y	Not simultaneous	Unclear	Serious risk of bias
Haberman, 2015 ⁹⁰	consecutive	unclear	unclear	Not simultaneous	None reported	Very serious risk of bias
Hald, 2017 ⁹¹	Random	The gold standard interpretations were performed 'post-study' so likely that index test interpretations were made prior to any gold standard interpretations. Thus effectively blinded.	Yes, blinded	Simultaneous	No loss of data	No serious risk of bias
Haverkamp, 2019 ⁹⁶	Consecutive	Not applicable as automated	Unclear. Appears possible it was unblinded as the 'reports' of previous 12 lead ECG seems	unclear	Not reported	Very serious risk of bias

Study	Random selection or case control	Index test with blinding of gold standard test results	Gold standard test with blinding of index test results	Time interval between index and gold standard	Loss of data from analysis	Overall risk of bias
			to imply interpretation had already been made. Reports that data were analyses independently by 2 observers, but unclear if this relates to index tests and GS tests.			
Himmelreich, 2019 ¹⁰¹	Consecutive	Yes	Yes	simultaneous	5 missing – 2 for missing 1 lead or 12 lead recordings and 3 for non-overlapping recordings. <10% so not a cause for concern	No serious risk of bias
Hobbs, 2005 ¹⁰⁴	Random	Blinding not stated. Anonymised traces but does not necessarily imply blinding. For automatic measures, NA.	Blinding not stated. Anonymised traces but does not necessarily imply blinding	Simultaneous	Varied between index tests but all involved high attrition at >10%. Possible that the GPs and nurses not returning interpretations were the less accurate participants	Very serious risk of bias
Kaleschke, 2009 ¹¹⁷	Consecutive	Yes – ‘all ECG analyses were blinded to the analysis result of the other ECG modality and to clinical information of the patient’.	Yes- blinded	12 lead ECG ‘immediately’ before index test. Estimated to be a 5-10 second delay	3/508 lost due to technical quality issues (n=2) and insufficient clinical data (n=1). Not a serious risk of attrition bias.	Serious risk of bias

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Kao, 2018 ¹²³	Unclear – possibly case-control	No blinding	No blinding	simultaneous	1 person lost from analysis but due to ineligibility. Therefore no risk of bias	Very serious risk of bias
Karunadas, 2020 ¹²⁶	Unclear	Unclear	Unclear	Simultaneous	None	Serious risk of bias
Kearley, 2014 ¹²⁸	Consecutive	NA as automated for Watch BP and Omron. For cardiologist analysed data for Omron and merlin blinded.	Yes, the cardiologists were blinded to results of index tests and clinical data.	Gold standard done at the end of the same day after the index tests but exact timing unclear	Watch BP: 1 lost; Omron auto analysis: 2 lost Omron ECG trace: 4 lost; Merlin: 20 lost; All <10% so not regarded as significant	Serious risk of bias
Kollias, 2018 ¹³²	Consecutive	NA as fully automated	Unclear (not reported)	simultaneous	None	Serious risk of bias
Koltowski, 2019 ¹³³	consecutive	Unclear – no report of blinding.	Carried out first in all cases but this does not ensure blinding as interpretation could have occurred after index tests. Therefore unclear	Short but not simultaneous	1 lost because of tremors due to Parkinson's disease – no serious risk of attrition bias	Very serious risk of bias
Kristensen, 2016 ¹³⁸	Case control	Yes	Yes	Simultaneous	4 lost due to poor ECG quality. But <10%	No serious risk of bias
Kvist, 2019 ¹⁴⁰	consecutive	Unclear – although index tests done first possible that interpretation could have occurred after gold standard tests completed	Yes	1 hour delay maximum	2 lost due to leaving laboratory before 12 lead ECG completed. <0.2% and so would not affect results	Very serious risk of bias

Study	Random selection or case control	Index test with blinding of gold standard test results	Gold standard test with blinding of index test results	Time interval between index and gold standard	Loss of data from analysis	Overall risk of bias
Lai, 2020 ¹⁴⁴	Consecutive	Unclear	Y	simultaneous	Unclear	Serious risk of bias
Langley, 2012 ¹⁴⁵	Random	Yes – algorithm used	Yes – gold standard assignments of status made in past, long before study inception (and index test evaluation)	simultaneous	None reported - based on pre-existing database	No serious risk of bias
Lewis, 2011 ¹⁵⁰	Random	NA as automated	Yes	Immediately afterwards	None reported	Serious risk of bias
Lin, 2010 ¹⁵³	Case-control. AF and non-AF (defined by gold standard) tested under different conditions and so results cannot be superimposed.	NA as automated	unclear	No - unclear	None reported	Very serious risk of bias
Lown, 2018 ¹⁵⁶	Described as case-control and likely to be as prevalence of AF in study is 57%, way above the expected value	yes	Yes	Not simultaneous but in same session	Zero	Very serious risk of bias
Lyckhage, 2020 ¹⁶⁰	Unclear	Unclear	Unclear	Unclear	None	Very serious risk of bias

Study	Random selection or case control	Index test with blinding of gold standard test results	Gold standard test with blinding of index test results	Time interval between index and gold standard	Loss of data from analysis	Overall risk of bias
Mant, 2007 ¹⁶¹	random	Yes, blinded	Yes, blinded	Simultaneous	3 ECGs lost which is very small compared to total number.	No serious risk of bias
Marazzi, 2012 ¹⁶²	consecutive	NA – fully automated	Cardiologists blinded to index test results	Simultaneous	52 missing. 29 excluded because of willingness to be studied. Other 23 unclear.	Serious risk of bias
McManus, 2013 ¹⁶⁵	Case-control (paired)	Unclear	Unclear	unclear	None reported	Very serious risk of bias
McManus, 2016 ¹⁶⁴	People before and after a cardioversion – thus very much a case-control situation	NA as automated	Unclear	simultaneous	None reported	Serious risk of bias
Mulder, 2012 ¹⁷¹	consecutive	NA as automated	unclear	simultaneous	Not reported	Serious risk of bias
Muller 2009 ¹⁷²	24 with AF and 24 without – thus appears to be case control but described as consecutive	automated	Unclear	Simultaneous	None reported	Very serious risk of bias
Nigolian, 2018 ¹⁷⁷	consecutive	yes	Yes	Not simultaneous	None reported	Serious risk of bias
Osca Asensi, 2020 ¹⁸⁴	Unclear	Unclear	Unclear	Unclear but not simultaneous	Y	Very serious risk of bias
Park, 2015 ¹⁸⁶	Consecutive	Blinded to identity and history of patient but	Blinded to identity and history of patient but	simultaneous	None reported	Very serious risk of bias

Study	Random selection or case control	Index test with blinding of gold standard test results	Gold standard test with blinding of index test results	Time interval between index and gold standard	Loss of data from analysis	Overall risk of bias
		not reported if blinded to GS results	not reported if blinded to IT results			
Poon, 2005 ¹⁹⁵	Random	NA - automated	No	Simultaneous	None	Serious risk of bias
Poulsen, 2017 ¹⁹⁶	consecutive	unclear	unclear	Simultaneous (concurrent)	5 lost – 2 withdrew consent before initiation and 3 had diagnosis changed. So not a threat to validity.	Very serious risk of bias
Proesmans, 2019 ¹⁹⁷	Case-control	NA as automated for PPG device; unclear for 1 lead device	Yes	Probably not	Some data lost due to poor quality, but sensitivity analyses done	Serious risk of bias
Rajakariar, 2020 ²⁰¹	Consecutive	Automated so not applicable	Yes	Index immediately before ECG	None	Serious risk of bias
Renier, 2012 ²⁰⁸	consecutive	yes	Yes	Not simultaneous	67 lost – 40 because of no 12 lead ECG, 12 because heartscan could not be put on chest, 15 refused consent, 3 because of problems with right index position and 7 below 18 years. Only 15 of these relate to outcome, which is <10%.	Serious risk of bias

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Reverberi, 2019 ²⁰⁹	Consecutive	NA as automated	Yes	Not simultaneous	5 missing – due to spontaneous restoration of normal rhythm the day before the CV procedure. <10% so not a cause for concern	Serious risk of bias
Rhys, 2013 ²¹⁰	Random	Yes - done prior to any gold standard interpretation	Not blinded to algorithm result but blinded to GPST2's interpretation	simultaneous	7 excluded – 5 because cardiologists unable to read faxed transmission and 2 because of poor quality ECGs. >10% so potential bias	Very serious risk of bias
Rizos, 2010 ²¹⁴	consecutive	Unclear, but for automatic measures NA.	Unclear	concurrent	none	Very serious risk of bias for manual measures and serious for automatic measures
Ross, 2018 ²¹⁸	consecutive	NA as automated	unclear	concurrent	Significant losses of 21%. 32 due to etiology being pathologic findings, 161 due to incomplete data.	Very serious risk of bias
Roten, 2012 ²¹⁹	consecutive	unclear	unclear	simultaneous	None reported (any transient loss of data included in accuracy analysis)	Very serious risk of bias
Rozen, 2018 ²²⁰	Case-control	NA as automated	yes	Not clear, but probably not simultaneous	Minor losses (n=2) pre-CV due to inappropriate	Serious risk of bias

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					inclusion (n=1), technical issues with CRMA (n=1). 5 missing from post-CV measurements because of normal sinus rhythm at baseline (n=1), contraindication to procedure (n=3), drop-out (n=1). Unlikely to have affected overall results as <10%	
Sabar, 2019 ²²²	Consecutive	Yes	Yes	Not simultaneous	103 missing – due to use for initial refining of algorithm. Not clear if this was part of the pre-hoc design of the study.	Very serious risk of bias
Sejr, 2019 ²³³	Consecutive	yes	Yes	yes	excluded 95 patients, in whom ELR recording was not started correctly, but this is <<10% so not a concern	No serious risk of bias
Slocum, 1992 ²³⁷	Case control	Yes - automated	Unclear	simultaneous	No loss of data	Serious risk of bias
Somerville, 2000 ²⁴⁰	Case control	Unclear	Unclear	Unclear but in same session	86 attended out of 154 invited. However if we can assume 86	Very serious risk of bias

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					were enrolled data loss is zero.	
Stergiou, 2009 ²⁴³	Appears to be case/control	NA as automated	Not reported	Simultaneous	None	Very serious risk of bias
Tieleman, 2014 ²⁵⁸	Random	NA as fully automated	Yes	Short but not simultaneous	None reported	Serious risk of bias
Vaes, 2014 ²⁶⁵	Selective case/control	NA as fully automated	Yes, blinded	Short but not simultaneous	None reported	Very serious risk of bias
Velthuis, 2013 ²⁶⁸	Consecutive	NA as automated	yes	yes	26 people excluded due to detected AF prior to ELR monitoring, 13 excluded as discharged during monitoring or unco-operative and 6 signal quality insufficient. Apart from latter 6, most of these not lost for reasons related to outcome so not a risk of bias	No risk of bias
Vukajlovic, 2010 ²⁷¹	consecutive	yes	Yes	Not simultaneous	none	Serious risk of bias
Wasserlauf, 2019 ²⁷⁵	Consecutive	Unclear	Unclear	simultaneous	None	Very serious risk of bias
Wiesel, 2004 ²⁸¹	NA as automated	Unclear	Unclear	Within 5 minutes	Unclear but 446/464 possible paired readings analysed. The loss of 18 readings probably	Very serious risk of bias

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					does not constitute a risk of attrition bias	
Wiesel, 2009 ²⁸⁰	consecutive	NA as automated	Yes, blinded	Not simultaneous	None reported	Serious risk of bias
Wiesel, 2013 ²⁷⁸	consecutive	Effectively yes, as automated	Yes	ECGs done prior to BP measures so not simultaneous. However short interval of time.	21 lost – 10 withdrew before any readings, 1 did not record any ECG readings, 1 with a pacemaker erroneously registered and 9 did not record logs of AF-BP monitor readings. These relatively high losses may have removed the least compliant from the analysis thus biasing the analysis. However the logistic regression analysis adjusts for this, removing bias.	Serious risk of bias
Wiesel, 2014 ²⁷⁹	consecutive	unclear	Yes	Not simultaneous. ECG done just before index tests but time interval not reported	None	Very serious risk of bias
William, 2018 ²⁸³	Consecutive, but paired analysis in that	yes	yes	Not simultaneous	62 non-interpretable readings, which were not accounted for by	Very serious risk of bias

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	each patient was medically CV or not				paper's own analyses. These could indicate high risk of bias (could be argued that a non-interpretable reading would just prompt a further attempt and so just taking the interpretable readings is probably sensible, but the lack of interpretability may not be random and may be systematic and related to a specific person's waveform)	
Williams, 2015 ²⁸⁴	Case-control but not clear	yes	Yes	simultaneous	4 data points lost due to artefacts in the ECG recordings (or illegible). This does not reflect any issue with the index test and so the exclusion is appropriate and will not cause bias.	Serious risk of bias
Winkler, 2011 ²⁸⁶	consecutive	NA – automated using algorithm	unclear	Not simultaneous	2/60 data points lost due to problems with quality – but unclear if this was in index or gold standard ECG readings.	Very serious risk of bias

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					Nevertheless <10% so not a serious risk of bias	
Yan, 2018 ²⁸⁸	Consecutive	NA as automated	Yes	Not simultaneous but same session	16; presence of pacemaker (n=12), declined to complete all measurements (n=4)	Serious risk of bias
Zwart, 2020 ²⁹⁵	Consecutive	Unclear	Unclear	Unclear	Unclear	Very serious risk of bias