Blodprov för tidig diagnostik av Alzheimers sjukdom

Bilaga 1 Tabell 2–10

Tabell 2 Sammanfattning av studier avseende serum- eller plasmanivåer av Aβ som anger sensitivitet och specificitet.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Blasko et al 2008 [6] Österrike	Prospektiv kohortstudie *Studietid* 2000–2005 *Markör* Aβ42 *System* Plasma *Analysmetod* ELISA *Referenstest* Diagnos enligt NINCDS-ADRDA	AD=98 K=389 Åldersmatchade ≥75 år 59,4% kvinnor 40,6% män *Bortfall* 1 505 kontaktades, 606 undersöktes 119 föll bort vid uppföljning efter 2,5 år	Aβ42-koncentrationer skiljde sig inte mellan AD-patienter och kontroller men ökade hos individer som under 2 års tid konverterade från kognitivt friska till AD med 20 pg/mL *Diagnostisk träffsäkerhet frisk→AD* Sens: 54% Spec: 63%	Hög studiekvalitet *Kommentar* Studien täcker in ett kliniskt relevant spektrum av patienter och metod samt reproducer-barhet beskrivs i stor detalj Cut-offnivå datadriven

Aβ42 = *Amyloid β*; **AD** = *Alzheimer's disease (Alzheimers sjukdom)*; **ELISA** = *Enzyme-linked immunosorbent assay*; **K** = *Kontrollgrupp*; **NINCDS-ADRDA** = *National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association*; **Sens** = *Sensitivitet*; **Spec** = *Specificitet*

Tabell 3 Sammanfattning av studier av låg studiekvalitet avseende serum- eller plasmanivåer av Aβ som anger sensitivitet och specificitet.

Författare År, referens	Studiekvalitet	Kommentar
Baranowska-Bik et al 2008 [10]	Låg studiekvalitet	Avsaknad av uppgift om referensstandard

Tabell 4 Sammanfattning av studier avseende serum- eller plasmanivåer av Aβ som inte anger sensitivitet och specificitet.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Tamaoka et al 1996 [19] Japan	Tvärsnittstudie *Studietid* Okänt *Markör* Aβ40 Aβ42 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=28 K=25 Åldersmatchade *Bortfall* Ej angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat	Medelhög studiekvalitet
Matsubara et al 1999 [14] USA	Tvärsnittstudie *Studietid* Okänt *Markör* Aβ40 Aβ42 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=36 K=26 Åldersmatchade *Bortfall* Ej angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 lätt förhöjt, stort överlapp	Medelhög studiekvalitet
Mehta et al 2000 [20] USA	Tvärsnittstudie *Studietid* Ej angivet *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=78 K=61 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 lätt förhöjt vid AD (stort överlapp) Aβ42 oförändrat Aβ42/Aβ40 oförändrade vid AD	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 4 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Mayeux et al 2003 [21] USA	Prospektiv kohortstudie *Studietid* Ej angivet *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=79 K=365 Ej ålders- eller könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 förhöjt, stort överlapp Aβ42 förhöjt, stort överlapp Aβ42/Aβ40 oförändrat	Medelhög studiekvalitet
Fukumoto et al 2003 [22] USA	Tvärsnittstudie *Studietid* Okänt *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=146 K=92 Åldersmatchade *Bortfall* Ej angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40, Aβ42 samt Aβ42/Aβ40 oförändrade vid AD	Medelhög studiekvalitet
Sobow et al 2005 [23] Polen	Tvärsnittstudie *Studietid* 2000–2003 *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=54 K=39 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40, Aβ42 samt Aβ42/Aβ40 oförändrade vid AD	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 4 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Van Oijen et al 2006 [24] Neder-länderna	Prospektiv kohortstudie *Studietid* 1990–2004 *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* Luminex *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Incident AD=289 K=1 394 Ålders- och könsmatchat *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 lätt förhöjt, stort överlapp Aβ42 oförändrat Aβ42/Aβ40 lätt sänkt, stort överlapp	Medelhög studiekvalitet
Graff-Radford et al 2007 [25] USA	Prospektiv kohortstudie *Studietid* 1992–2003 *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Frisk-MCI eller -AD=53 Kognitivt friska=510 *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat Lätt sänkt Aβ42/Aβ40-kvot, stort överlapp	Medelhög studiekvalitet
Fagan et al 2007 [26] USA	Prospektiv kohortstudie *Studietid* Ej angivet *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Mild AD=49 K=90 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat Aβ42/Aβ40 oförändrat	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 4 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Abdullah et al 2007 [27] USA	Tvärsnittstudie *Studietid* Ej angivet *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma och serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=67 K=146 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 lätt förhöjt, stort överlapp Aβ42 oförändrat Aβ42/Aβ40 lätt sänkt, stort överlapp	Medelhög studiekvalitet
Lopez et al 2008 [28] USA	Prospektiv kohortstudie *Studietid* 1998–2003 *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=88 K=117 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat Aβ42/Aβ40 oförändrat	Medelhög studiekvalitet
Schupf et al 2008 [29] USA	Prospektiv kohortstudie *Studietid* 1998–2003 *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Incident AD=104 K=1 021 Köns-, men inte åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 förhöjt Aβ42/Aβ40 oförändrat	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 4 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Lambert et al 2009 [33] Frankrike	Prospektiv kohortstudie *Studietid* 1999–2005 *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Plasma *Analysmetod* Luminex *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=154 K=985 Ålders- och könsmatchat *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat Aβ42/Aβ40 lätt sänkt, stort överlapp	Medelhög studiekvalitet
Luis et al 2009 [34] USA	Tvärsnittsstudie *Studietid* Ej angivet *Markör* Aβ40 Aβ42 Aβ42/Aβ40 *System* Serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=25 K=40 Ålders- och könsmatchat *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat Aβ42/Aβ40 oförändrat	Medelhög studiekvalitet
Le Bastard et al 2009 [35] Belgien	Prospektiv kohortstudie *Studietid* 1999–2005 *Markör* Aβ42 *System* Plasma *Analysmetod* Luminex *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=49 K=29 Köns- men inte åldersmatchat *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ42 oförändrat Ingen korrelation till CSF	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 4 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Hansson et al 2010 [36] Sverige	Prospektiv kohortstudie *Studietid* 1999–2005 *Markör* Aβ40 Aβ42 *System* Plasma *Analysmetod* Luminex *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=48 K=38 Ålders- och könsmatchat *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Aβ40 oförändrat Aβ42 oförändrat Aβ42/Aβ40 oförändrat	Hög studiekvalitet

Aβ40/Aβ42 = *Amyloid β-40/Amyloid β-42*; **AD** = *Alzheimer's disease (Alzheimers sjukdom)*; **ELISA** = *Enzyme-linked immunosorbent assay*; **K** = *Kontrollgrupp*; **NINCDS-ADRDA** = *National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association*; **SELDI** = *Surface-enhanced laser desorption/ionization*; **Sens** = *Sensitivitet*; **Spec** = *Specificitet*

Tabell 5 Sammanfattning av anti-Aβ-studier av låg studiekvalitet som anger sensitivitet och specificitet.

Författare År, referens	Studiekvalitet	Kommentar
Brettschneider et al 2005 [11]	Låg studiekvalitet	Omatchade grupper
Xu et al 2008 [12]	Låg studiekvalitet	Bristande beskrivning av indextestet

Tabell 6 Sammanfattning av studier avseende anti-Aβ som inte anger sensitivitet och specificitet.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Weksler et al 2002 [37] USA	Tvärsnittsstudie *Studietid* Okänt *Markör* Anti-Aβ *System* Serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=39 K=39 Oklart om ålders- och könsmatchade *Bortfall* Ej angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Anti-Aβ titer i serum lägre vid AD	Medelhög studiekvalitet
Mruthinti et al 2004 [38] USA	Tvärsnittsstudie *Studietid* Ej angivet *Markör* Anti-Aβ *System* Plasma *Analysmetod* RIA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=33 K=42 Ej åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Anti-Aβ titer i plasma högre vid AD	Medelhög studiekvalitet
Moir et al 2005 [39] USA	Tvärsnittstudie *Studietid* Ej angivet *Markör* Anti-Aβ *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=59 K=59 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Anti-Aβ titer i plasma lägre vid AD, stort överlapp	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 6 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Jianping et al 2006 [40] Kina	Tvärsnittsstudie *Studietid* 2005–2006 *Markör* Anti-Aβ *System* Serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=20 K=40 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Anti-Aβ titer i serum lägre vid AD	Medelhög studiekvalitet
Song et al 2007 [41] Korea	Tvärsnittsstudie *Studietid* 2003–? *Markör* Anti-Aβ *System* Serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Incident AD=153 K=193 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Anti-Aβ titer i serum lägre vid AD	Medelhög studiekvalitet
Gustaw et al 2008 [42] USA	Tvärsnittsstudie *Studietid* Ej angivet *Markör* Anti-Aβ *System* Serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=54 K=49 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Anti-Aβ titer i serum högre vid AD	Medelhög studiekvalitet

AD = *Alzheimer's disease (Alzheimers sjukdom)*; **ELISA** = *Enzyme-linked immunosorbent assay*; **K** = *Kontrollgrupp*; **NINCDS-ADRDA** = *National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association*; **RIA** = *Radioimmunoassay*; **Sens** = *Sensitivitet*; **Spec** = *Specificitet*

Tabell 7 Sammanfattning av studier avseende tbc-APPkv som inte anger sensitivitet och specificitet.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Di Luca et al 1998 [43] Italien	Tvärsnittsstudie *Studietid* Ej angivet *Markör* APPkv *System* Trombocyter *Analysmetod* Western blot *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=32 K=25 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Tbc-APPkv sänkt	Medelhög studiekvalitet
Borroni et al 2002 [44] Italien	Tvärsnittsstudie *Studietid* Okänt *Markör* APPkv *System* Trombocyter *Analysmetod* Western blot *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=40 K=40 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Tbc-APPkv sänkt	Medelhög studiekvalitet
Sanchez- Gonzalez et al 2006 [45] USA	Tvärsnittsstudie *Studietid* Ej angivet *Markör* APPkv *System* Trombocyter *Analysmetod* Western blot *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=26 K=46 *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Tbc-APPkv sänkt	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 7 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Zainaghi et al 2007 [46] Brasilien	Tvärsnittsstudie *Studietid* Ej angivet *Markör* APPkv *System* Trombocyter *Analysmetod* Western blot *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Mild AD=23 K=29 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* Tbc-APPkv lätt sänkt, stort överlapp	Medelhög studiekvalitet

AD = *Alzheimer's disease (Alzheimers sjukdom)*; **K** = *Kontrollgrupp*; **NINCDS-ADRDA** = *National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association*; **Sens** = *Sensitivitet*; **Spec** = *Specificitet*; **Tbc-APPkv** = *Trombocyt-APP-kvot*

Tabell 8 Sammanfattning av studier avseende serum- eller plasmanivåer av ACT som anger sensitivitet och specificitet.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Lieberman et al 1995 [9] USA	Tvärsnittsstudie *Studietid* Ej angivet *Markör* ACT *System* Serum *Analysmetod* Radial immunodiffusion *Referenstest* Diagnos enligt DSM-IIIR	AD=57 K=67 Ej ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Förhöjd ACT-koncentration vid Alzheimers sjukdom (medel ± SD, 73±22 mg/dL) jämfört med kontroller (48±8,1 mg/dL) En cut-off på 60 mg/dL gav: sens: 82% spec: 74%	Medelhög studiekvalitet *Kommentar* Cut-offnivå datadriven

ACT = *α1-antichymotrypsin*; **AD** = *Alzheimer's disease (Alzheimers sjukdom)*; **DSM-IIIR** = *Diagnostic and Statistical Manual of Mental Disorders-III revised*; **K** = *Kontrollgrupp*; **SD** = *Standardavvikelse*; **Sens** = *Sensitivitet*; **Spec** = *Specificitet*

Tabell 9 Sammanfattning av studier avseende serum- eller plasmanivåer av ACT av låg studiekvalitet som anger sensitivitet och specificitet.

Författare År, referens	Studiekvalitet	Kommentar
Licastro 2000 [13]	Låg studiekvalitet	Avsaknad av uppgift om vilken referensstandard som användes
Matsubara 1999 [14]	Låg studiekvalitet	Påtagligt dåligt matchade grupper

Tabell 10 Sammanfattning av studier avseende serum- eller plasmanivåer av ACT som inte anger sensitivitet och specificitet.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Pirttila et al 1994 [47] USA/Finland	Tvärsnittsstudie *Studietid* Okänt *Markör* ACT *System* Serum *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=40 K=42 Ålders- och könsmatchade *Bortfall* Ej angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT oförändrat	Medelhög studiekvalitet
Licastro et al 2000 [48] Italien	Tvärsnittsstudie *Studietid* Okänt *Markör* ACT *System* Plasma *Analysmetod* Radial immunodiffusion *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=145 K=51 Ålders- men inte könsmatchade *Bortfall* Ej angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT lätt förhöjt, stort överlapp	Medelhög studiekvalitet
McIlroy et al 2000 [49] Irland	Tvärsnittsstudie *Studietid* Ej angivet *Markör* ACT *System* Serum *Analysmetod* Radial immunodiffusion *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=106 K=105 Ålders- och könsmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT lätt förhöjt, stort överlapp	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 10 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
DeKosky et al 2003 [50] USA	Tvärsnittsstudie *Studietid* Okänt *Markör* ACT *System* Plasma *Analysmetod* Radial immunodiffusion *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=359 K=113 Köns- men inte åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT lätt förhöjt, stort överlapp	Medelhög studiekvalitet
Engelhart et al 2004 [15] Holland	Prospektiv kohortstudie *Studietid* 1990–1999 *Markör* ACT *System* Plasma *Analysmetod* Nefelometri *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	Incident AD=140 K=539 Oklart om ålders- och könsmatchat *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT lätt förhöjt, stort överlapp Starkast association till VAD	Medelhög studiekvalitet
Nielsen et al 2007 [51] Sverige	Tvärsnittsstudie *Studietid* 1999–2003 *Markör* ACT *System* Plasma *Analysmetod* Radial immunodiffusion *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=258 K=37 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT lätt förhöjt, stort överlapp	Medelhög studiekvalitet

Tabellen fortsätter på nästa sida

Tabell 10 Fortsättning.

Författare År, referens Land	Studiedesign	Population Bortfall	Resultat	Studiekvalitet Kommentarer
Porcellini et al 2008 [52] Italien	Tvärsnittsstudie *Studietid* Ej angivet *Markör* ACT *System* Plasma *Analysmetod* ELISA *Kontrollmetod* Diagnos enligt NINCDS-ADRDA	AD=195 K=830 Åldersmatchade *Bortfall* Ej tydligt angivet	Sens: Ej angivet Spec: Ej angivet *Förändring vid AD* ACT lätt förhöjt, stort överlapp	Medelhög studiekvalitet

ACT = *α1-antichymotrypsin*; **AD** = *Alzheimer's disease (Alzheimers sjukdom)*; **ELISA** = *Enzyme-linked immunosorbent assay*; **K** = *Kontrollgrupp*; **NINCDS-ADRDA** = *National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association*; **Sens** = *Sensitivitet*; **Spec** = *Specificitet*; **VAD** = *Vascular Alzheimer's disease*

Bilaga 2 Litteratursökning

Litteratursökning har utförts i databaserna PubMed, Cochrane Library och Embase t o m februari 2012. För en mer detaljerad beskrivning av vilka söktermer och begränsningar som använts, se Tabell 11. Förutom sökningar i databaser har referenslistor granskats i relevanta arbeten.

Tabell 11 Sökstrategi.

PubMed 1950–2012 (feb)							
Sökstrategi: diagnostisk tillförlitlighet av biomarkörer i perifert blod för att diagnostisera Alzheimers sjukdom							
Alzheimer disease Alzheimer (TW) Alzheimer's (TW) Alzheimers (TW)	AND	Biological markers Biological marker(s) (TW) Marker(s) (TW) Biomarker(s) (TW) Biochemical marker(s) (TW) Amyloid Amyloid (TW) Amyloid-beta (TW) Amyloidbeta (TW) Beta-amyloid (TW) Abeta (TW) A-beta (TW) A beta (TW) ACT (TW) Alpha 1 antichymotrypsin (TW) Alpha 1 anti chymotrypsin (TW) Alpha1 antichymotrypsin (TW) Alpha1 anti chymotrypsin (TW) App (TW)	AND	Blood Blood (TW) Plasma (TW) Serum (TW)	AND	Diagnosis Diagnosis (TW) Diagnose (TW) Diagnosing (TW) Diagnostic(s) (TW) Predict(ive) (TW) Predictor(s) (TW) Prediction (TW) Predicting (TW) Determine (TW) Determining (TW) Determination (TW) Detect(ing) (TW) Detection (TW)	AND	Clinical trial (PT) Validation studies (PT) Comparative study (PT) Prospective studies Sensitivity and specificity Cohort studies Prospective (TW) Controlled (TW) Control(s) (TW) Comparison (TW) Compare(d) (TW) Comparative (TW) Cross sectional (TW) Sensitivity (TW) Specificity (TW) Validity (TW) Validate (TW) Validation (TW)
Sökstrategi: ekonomiska aspekter av att använda biomarkörer i perifert blod för att diagnostisera Alzheimers sjukdom							
Alzheimer disease Alzheimer (TW) Alzheimer's (TW) Alzheimers (TW)	AND	Biological markers Biological marker(s) (TW) Marker(s) (TW) Biomarker(s) (TW) Biochemical marker(s) (TW) Amyloid Amyloid (TW) Amyloid-beta (TW) Amyloidbeta (TW) Beta-amyloid (TW) Abeta (TW) A-beta (TW) A beta (TW) ACT (TW) Alpha 1 antichymotrypsin (TW) Alpha 1 anti chymotrypsin (TW) Alpha1 antichymotrypsin (TW) Alpha1 anti chymotrypsin (TW) App (TW)	AND	Blood Blood (TW) Plasma (TW) Serum (TW)	AND	Economics Economic(s) (TW) Costs and cost analysis Cost(s) (TW) Cost analysis (TW) Cost benefit analysis Cost benefit (TW) Cost effective(ness) (TW) Cost utility (TW) Willingness to pay (TW)		

Tabellen fortsätter på nästa sida

Tabell 11 Fortsättning.

Cochrane Library t o m 2012 (feb)							
Sökstrategi: diagnostisk tillförlitlighet av biomarkörer i perifert blod för att diagnostisera Alzheimers sjukdom samt ekonomiska aspekter							
Alzheimer disease Alzheimer (ti, ab, kw) Alzheimer's (ti, ab, kw) Alzheimers (ti, ab, kw)	AND	Amyloid beta-Protein Precursor Amyloid (ti, ab, kw) Amyloid-beta (ti, ab, kw) Amyloid beta (ti, ab, kw) Beta-amyloid (ti, ab, kw) Amyloidbeta (ti, ab, kw) Abeta (ti, ab, kw) A-beta (ti, ab, kw) A beta (ti, ab, kw) alpha 1-Antichymotrypsin ACT (ti, ab, kw) Alpha 1 antichymotrypsin (ti, ab, kw) Alpha 1 anti chymotrypsin (ti, ab, kw) Alpha1 antichymotrypsin (ti, ab, kw) Alpha1 anti chymotrypsin (ti, ab, kw) App (ti, ab, kw)	AND	Blood Blood (ti, ab, kw) Plasma (ti, ab, kw) Serum (ti, ab, kw)	AND	Diagnosis Diagnosis (ti, ab, kw) Diagnose (ti, ab, kw) Diagnosing (ti, ab, kw) Diagnostic(s) (ti, ab, kw) Predict(ive) (ti, ab, kw) Predictor(s) (ti, ab, kw) Prediction (ti, ab, kw) Predicting (ti, ab, kw) Determine (ti, ab, kw) Determining (ti, ab, kw) Determination (ti, ab, kw) Detect(ing) (ti, ab, kw) Detection (ti, ab, kw)		
Embase t o m 2012 (feb)							
Sökstrategi: diagnostisk tillförlitlighet av biomarkörer i perifert blod för att diagnostisera Alzheimers sjukdom samt ekonomiska aspekter							
Alzheimer disease/exp	AND	Biological marker/exp	AND	Blood/exp	AND	Clinical trial/exp Validation study/exp Comparative study/exp Sensitivity and specificity/exp Prospective study/exp Cohort analysis/exp Diagnosis/exp Cost/exp Cost (TW) Cost benefit analysis/exp Cost benefit analysis (TW) Economic aspect/exp Economic aspect (TW) Cost effectiveness analysis/exp Cost effectiveness analysis (TW)	AND	[embase]/lim

Söktermerna i PubMed har utgjorts av MeSH-termer (NLM:s kontrollerade nyckelord, Medical Subject Heading) om inget annat anges.
PT = *publication type;* **TW** = *text word*
Söktermerna i Cochrane Library har utgjorts av MeSH-termer (NLM:s kontrollerade nyckelord, Medical Subject Heading) om inget annat anges.
ti = *title;* **ab** = *abstract;* **kw** = *keyword*
Söktermerna i Embase har utgjorts av nyckelord specifika för databasen om inget annat anges.
/**exp** = *explode;* **TW** = *text word;* /**lim** = *limitation*

Bilaga 3 Granskningsmall för diagnostiska studier

Study identification *Including author, title, reference, year of publication*					
Review question no:	Checklist completed by:				
1	Was the spectrum of participants representative of the patients who will receive the test in practice?	Yes	No	Unclear	N/A
2	Were selection criteria clearly described?	Yes	No	Unclear	N/A
3	Was the reference standard likely to classify the target condition correctly?	Yes	No	Unclear	N/A
4	Was the period between performance of the reference standard and the index test short enough to be reasonably sure that the target condition did not change between the two tests?	Yes	No	Unclear	N/A
5	Did the whole sample or a random selection of the sample receive verification using the reference standard?	Yes	No	Unclear	N/A
6	Did participants receive the same reference standard regardless of the index test result?	Yes	No	Unclear	N/A
7	Was the reference standard independent of the index test? (that is, the index test did not form part of the reference standard)	Yes	No	Unclear	N/A
8	Was the execution of the index test described in sufficient detail to permit its replication?	Yes	No	Unclear	N/A
9	Was the execution of the reference standard described in sufficient detail to permit its replication?	Yes	No	Unclear	N/A
10	Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	No	Unclear	N/A
11	Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	No	Unclear	N/A
12	Were the same clinical data available when the test results were interpreted as would be available when the test is used in practice?	Yes	No	Unclear	N/A
13	Were uninterpretable, indeterminate or intermediate test results reported?	Yes	No	Unclear	N/A
14	Were withdrawals from the study explained?	Yes	No	Unclear	N/A
15	Were the number, training, and expertise of the persons executing and reading the index tests and the reference standard described?	Yes	No	Unclear	N/A
16	Were methods for calculating test reproducibility described?	Yes	No	Unclear	N/A
17	Were estimates of diagnostic accuracy and measures of statistical uncertainty (e.g., 95% confidence intervals) reported?	Yes	No	Unclear	N/A
18	Was the conflict of interest stated?	Yes	No	Unclear	N/A

Notes on use of Methodology checklist: studies of diagnostic test accuracy

This checklist is designed for the evaluation of studies assessing the accuracy of specific diagnostic tests. It does **not** address questions of the usefulness of the test in practice, or how the test compares with alternatives. Such questions should be assessed using the checklists for studies on interventions.

The questions in this checklist are aimed at establishing the validity of the study under review – that is, making sure that it has been carried out carefully, and that the conclusions represent an unbiased assessment of the accuracy and reliability of the test being evaluated. Each question covers an aspect of methodology that is thought to make a difference to the reliability of a study.

Checklist items are worded so that a 'yes' response always indicates that the study has been designed and conducted in such a way as to minimise the risk of bias for that item. An 'unclear' response to a question may arise when the answer to an item is not reported, or not reported clearly. 'N/A' should be used when a study of diagnostic test accuracy cannot give an answer of 'yes' no matter how well it has been done.

1. Was the spectrum of participants representative of the patients who will receive the test in practice?

What is meant by this item

Differences between populations in demographic and clinical features may produce measures of diagnostic accuracy that vary considerably; this is known as spectrum bias. Reported estimates of diagnostic test accuracy may have limited clinical applicability (generalisability) if the spectrum of participants tested is not representative of the patients on whom the test will be used in practice. The spectrum of participants takes into account not only the severity of the underlying target condition but also demographic features and the presence of differential diagnoses and/or comorbidities.

How to score this item

Studies should score 'yes' for this item if you believe, based on the information reported, that the spectrum of participants included in the study was representative of those in whom the test will be used in practice. This judgement should be based on both the method for recruitment and the characteristics of those recruited. Studies that recruited a group of healthy controls and a group known to have the target disorder will be coded as 'no' on this item in nearly all circumstances. Reviewers should prespecify what spectrum of participants would be acceptable, taking into account factors such as disease prevalence and severity, age and sex. Clinical input may be required from the Guideline Development Group (GDG). If you think that the population studied does not fit into what you specified as acceptable, the study should be scored as 'no'. If there is insufficient information available to make a judgement, this item should be scored as 'unclear'.

2. Were selection criteria clearly described?

What is meant by this item

This refers to whether studies have reported criteria for entry into the study.

How to score this item

If you think that all relevant information regarding how participants were selected for inclusion in the study has been provided, then this item should be scored as 'yes'. If study selection criteria are not clearly reported, then this item should be scored as 'no'. In situations where selection criteria are partially reported and you feel that you do not have enough information to score this item as 'yes', then it should be scored as 'unclear'.

3. Was the reference standard likely to classify the target condition correctly?

What is meant by this item

The reference standard is the method used to determine the presence or absence of the target condition. Indicators of diagnostic test accuracy are calculated by comparing the results of the index test with the results of the reference standard. Estimates of test performance are based on the assumption that the index test is being compared with a reference standard that is 100% sensitive and specific. If there are any disagreements between the reference standard and the index test, it is assumed that the index test is incorrect. Thus the use of an inappropriate reference standard can bias estimation of the diagnostic accuracy of the index test.

How to score this item

Making a judgement about the accuracy of the reference standard may not be straightforward. You may need to consult a member of the GDG to determine whether a test is an appropriate reference standard. If a combination of tests is used, you may have to consider carefully whether these were appropriate.

If you believe that the reference standard is likely to classify the target condition correctly, then this item should be scored as 'yes'. If you do not think that the reference standard is likely to have classified the target condition correctly, then this item should be scored as 'no'. If there is insufficient information to make a judgement, then it should be scored as 'unclear'.

4. Was the period between performance of the reference standard and the index test short enough to be reasonably sure that the target condition did not change between the two tests?

What is meant by this item

Ideally, the results of the index test and the reference standard are collected on the same participants at the same time. If this is not possible and there is a delay, misclassification may occur because of either spontaneous recovery or progression of the disease. This is known as disease progression bias. The length of the period that may cause such bias will vary between conditions. For example, a delay of a few days is unlikely to be a problem for chronic conditions. However, for infectious diseases a delay of only a few days between performance of the index test and the reference standard may be important. This type of bias may also occur in chronic conditions in which the reference standard involves clinical follow-up of several years.

You will have to make judgements about what is considered 'short enough'. You should think about this before beginning your review, and define what you consider to be short enough for the specific topic area that you are reviewing. You may need clinical input to decide this.

How to score this item

When to score this item as 'yes' is related to the target condition. For conditions that progress rapidly, a delay of a even few days may be important. For such conditions this item should be scored as 'yes' if the delay between the performance of the index test and the reference standard is very short – a matter of hours or days. However, for chronic conditions, disease status is unlikely to change in a week, a month or even longer. For such conditions, longer delays between performance of the index test and reference standard may be scored as 'yes'. If you think that the period between the performance of the index test and the reference standard was sufficiently long that disease status may have changed between the performance of the two tests, then this item should be scored as 'no'. If insufficient information is provided, it should be scored as 'unclear'.

5. Did the whole sample or a random selection of the sample receive verification using the reference standard?

What is meant by this item

Partial verification bias (also known as work-up bias, [primary] selection bias or sequential ordering bias) occurs when not all of the study group receive confirmation of the diagnosis by a reference standard. If the results of the index test influence the decision to perform the reference standard, then biased estimates of test performance may arise. If participants are randomly selected to receive the reference standard, the overall diagnostic performance of the test is, in theory, unchanged. However, in most cases this selection is not random, possibly leading to biased estimates of the overall diagnostic accuracy. Partial verification bias generally only occurs in diagnostic cohort studies in which participants are tested using the index test before the reference standard.

How to score this item

If it is clear from the study that all participants (or a random selection) who received the index test went on to receive verification of their disease status using a reference standard, even if this reference standard was not the same for all participants, then this item should be scored as 'yes'. If some of the participants who received the index test did not receive verification of their true disease state (or the selection was not random), then this item should be scored as 'no'. If this information is not reported, this item should be scored as 'unclear'.

6. Did participants receive the same reference standard regardless of the index test result?

What is meant by this item

Differential verification bias occurs when some of the index test results are verified by a different reference standard. This is a particular problem if these reference standards differ in their definition of the target condition; for example, histopathology of the appendix and natural history for the detection of appendicitis. This usually occurs when participants who test positive on the index test undergo a more accurate, often invasive, reference standard test than those with negative results on the index test. The link (correlation) between a particular (negative) test result and being verified by a less accurate reference standard can lead to biased estimates of test accuracy. Differential verification bias generally only occurs in diagnostic cohort studies in which all participants are tested using the index test before the reference standard is performed.

How to score this item

If it is clear that participants received verification of their true disease status using the same reference standard, then this item should be scored as 'yes'. If some participants received verification using a different reference standard, then this item should be scored as 'no'. If this information is not reported, this item should be scored as 'unclear'.

7. Was the reference standard independent of the index test? (that is, the index test did not form part of the reference standard)

What is meant by this item

When the result of the index test is used in establishing the final diagnosis, incorporation bias may occur. This incorporation will probably increase the amount of agreement between index test results and the outcome of the reference standard, and hence result in overestimation of the various measures of diagnostic accuracy. For example, a study investigating magnetic resonance imaging (MRI) for the diagnosis of multiple sclerosis could have a reference standard composed of clinical follow-up, cerebrospinal fluid analysis and MRI. In this case, the index test forms part of the reference standard. It is important to note that knowledge of the results of the index test does not automatically mean that these results are incorporated in the reference standard. This item will only apply when a composite reference standard is used to verify disease status. In such cases it is essential that a full definition of how disease status is verified and which tests form part of the reference standard is provided.

How to score this item

For studies in which a single reference standard is used, this item will not be relevant and should be scored as 'N/A'. If it is clear that the index test did not form part of the reference standard, then this item should be scored as 'yes'. If it appears that the index test formed part of the reference standard, then this item should be scored as 'no'. If this information is not reported, this item should be scored as 'unclear'.

8 & 9. Was the execution of the index test described in sufficient detail to permit its replication? Was the execution of the reference standard described in sufficient detail to permit its replication?

What is meant by these items

A sufficiently detailed description of the execution of the index test and the reference standard is important for two reasons. Firstly, variation in measures of diagnostic accuracy can sometimes be traced back to differences in the execution of index tests and reference standards. Secondly, a clear and detailed description (or references) is needed to implement a certain test in another setting. If tests are executed in different ways then this would be expected to have an impact on test performance. The extent to which this would be expected to affect results depends on the type of test being investigated.

How to score these items

If the study reports sufficient details to permit replication of the index test and the reference standard, then these items should be scored as 'yes'. In other cases these items should be scored as 'no'. In situations where details of test performance are partially reported and you consider that you do not have enough information to score these items as 'yes', then they should be scored as 'unclear'.

10 & 11. Were the index test results interpreted without knowledge of the results of the reference standard? Were the reference standard results interpreted without knowledge of the results of the index test?

What is meant by these items

This issue is similar to the blinding of the people who assess outcomes in intervention studies. Interpretation of the results of the index test may be influenced by knowledge of the results of the reference standard, and vice versa. This is known as review bias, and may lead to inflated measures of diagnostic test accuracy. The extent to which this can affect test results will be related to the degree of subjectivity in the interpretation of the test result – the more subjective the interpretation, the more likely that the interpreter can be influenced by the results of the index test in interpreting the results of the reference standard, and vice versa. It is therefore important to consider the topic area that you are reviewing and to determine whether interpretation of the results of the index test or the reference standard could be influenced by knowledge of the results of the other test.

How to score these items

If the study clearly states that the test results (index test or reference standard) were interpreted blind to the results of the other test, then these items should be scored as 'yes'. If this does not appear to be the case, then they should be scored as 'no'. If this information is not reported, these items should be scored as 'unclear'. If in the topic area that you are reviewing the index test is always performed first, then interpretation of the results of the index test will usually be done without knowledge of the results of the reference standard. Similarly, if the reference standard is always performed first, then the results will be interpreted without knowledge of the results of the index test. In situations where one form of review bias does not apply, the item should be scored as 'N/A'. If interpretation of test results is entirely objective, then test interpretation is not susceptible to review bias and the item should be scored as 'N/A'. Another situation in which this form of bias may not apply is when test

results are interpreted in an independent laboratory. In such situations it is unlikely that the person interpreting the test results will have knowledge of the results of the other test (either index test or reference standard).

12. Were the same clinical data available when the test results were interpreted as would be available when the test is used in practice?

What is meant by this item

The availability of information on clinical data during the interpretation of test results may affect estimates of test performance. In this context, clinical data are defined broadly to include any information relating to the participant that is obtained by direct observation, such as age, sex and symptoms. The knowledge of such factors can influence the diagnostic test result if the test involves an interpretative component. If clinical data will be available when the test is interpreted in practice, then these should also be available when the test is evaluated. However, if the index test is intended to replace other clinical tests, then clinical data should not be available. Thus, before assessing studies for this item it is important to determine what information will be available when test results are interpreted in practice. You should consult the GDG to identify this information.

How to score this item

If clinical data would normally be available when the test results are interpreted in practice and similar data were available when interpreting the index test results in the study, then this item should be scored as 'yes'. Similarly, if clinical data would not be available in practice and these data were not available when the index test results were interpreted, then this item should be scored as 'yes'. If this is not the case, then this item should be scored as 'no'. If this information is not reported, this item should be scored as 'unclear'. If interpretation of the index test is fully automated, this item may not be relevant and can be scored 'N/A'.

13. Were uninterpretable, indeterminate or intermediate test results reported?

What is meant by this item

A diagnostic test can produce an uninterpretable, indeterminate or intermediate result with varying frequency, depending on the test. These problems are often not reported in studies on diagnostic test accuracy, the uninterpretable results simply being removed from the analysis. This may lead to the biased assessment of the test characteristics. Whether bias will arise depends on the possible correlation between uninterpretable test results and the true disease status. If uninterpretable results occur randomly and are not related to the true disease status of the individual then, in theory, these should not have any effect on test performance. It is important that uninterpretable results are reported so that the impact on test performance can be considered; however, poor quality of reporting means that this is not always the case.

How to score this item

If it is clear that all test results, including uninterpretable, indeterminate or intermediate results, are reported, then this item should be scored as 'yes'. If the authors do not report any uninterpretable, indeterminate or intermediate results, and if the results are reported for all participants who were described as having been entered into the study, then this item should also be scored as 'yes'. If you think that such results occurred but have not been reported, then this item should be scored as 'no'. If it is not clear whether all study results have been reported, then this item should be scored as 'unclear'.

14. Were withdrawals from the study explained?

What is meant by this item

This occurs when participants withdraw from the study before the results of both the index test and the reference standard are known. If participants lost to follow-up differ systematically from those who remain, for whatever reason, then estimates of test performance may be biased. Poor quality of reporting of withdrawals may make the impact on estimates of test performance difficult to determine.

How to score this item

If it is clear what happened to all participants who entered the study, for example if a flow diagram of study participants is reported, then this item should be scored as 'yes'. If the authors do not report any withdrawals and if results are available for all participants who were reported to have been entered into the study, then this item should also be scored as 'yes'. If it appears that some of the participants who entered the study did not complete the study (that is, did not receive both the index test and the reference standard), and these participants were not accounted for, then this item should be scored as 'no'. If it is not clear whether all participants who entered the study were accounted for, then this item should be scored as 'unclear'.

15. Variability in the manipulation, processing, or reading of the index test or reference standard will affect measures of diagnostic accuracy. Many studies have shown reader variability, especially in the field of imaging. The amount of the readers training can help readers to judge whether similar results are attainable in their own settings, with possibly less experienced readers. Professional background, expertise, and prior training to improve

interpretation and to reduce inter-observer variation all affect the quality of reading. Readers are more likely to interpret results from (subjective) tests as abnormal in settings with higher prevalences of the target condition, a tendency known as context bias. The example describes the reference standard in a study of a model that uses results of commonly performed laboratory tests to identify men who are heavy drinkers.

16. The index test and the reference standard are seldom perfect. Their reproducibility varies, and limited reproducibility adversely affects diagnostic accuracy. Observer variability can arise with imaging tests when the reader must summarize visual observations in a statement about the presence of disease. It also arises during classification, when the reader must use the data to place patients into diagnostic categories. Instrument variability concerns the amount of variation that arises during the operation of devices or systems, such as automated laboratory measurements. Other terms for this form of variation include imprecision, analytic methodological variation, or analytical noise (error). Poor reproducibility adversely affects diagnostic accuracy. If possible, authors should evaluate the reproducibility of the test methods used in their study and report their procedure to do so. For quantitative assays, it is useful to report imprecision as the coefficient of variation at two or more specified mean values near clinical decision points as obtained by repeating the test over a specified number of days. Withinrun coefficients of variation are appropriate if all patient samples were analyzed in a single run. In the example, the authors used the kappa statistic to express interobserver variability for conventional angiography and MRA in the detection of renovascular disease.

17. The final aim of a study of diagnostic accuracy is to produce an expression of how well the test results corresponded with the presence or absence of the target condition, as established by the reference standard. The values presented in the report should be taken as estimates. Due to chance variations in the patients submitted to the tests and other factors, the results are likely to differ over replications of the study in the same study population. The reporting of precision will show the reader the range of likely values around an estimate of diagnostic accuracy. Many journals require or strongly encourage the use of confidence intervals as measures of precision. A 95% confidence interval is conventional. Only 50% of the reports of diagnostic evaluations published in 1996 or 1997 in the *British Medical Journal* reported precision for the estimates of diagnostic accuracy.

18. Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

Questions 1–14 originates from QUADAS, 15–17 from STARD and 18 originates from AMSTAR.

References

- **QUADAS:** National Institute for Health and Clinical Excellence. The guidelines manual, Appendix G: Methodology checklist: the QUADAS tool for studies of diagnostic test accuracy. 2009.
- **STARD:** Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. Ann Intern Med 2003;138:W1-12.
- **AMSTAR:** Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 2007;7:10.