**Table S1:** The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Checklist for Diagnostic Test Accuracy.

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **PRISMA-DTA Checklist Item** | **Reported on page #** |
| **TITLE / ABSTRACT** | | |  |
| Title | 1 | Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies. | 1 |
| Abstract | 2 | Abstract: See PRISMA-DTA for abstracts. | 3 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4 |
| Clinical role of index test | D1 | State the scientific and clinical background including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design). | 4 |
| Objectives | 4 | Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s). | 4 |
| **METHODS** | | |  |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address). If available, provide registration information including registration number. | 4 |
| Eligibility criteria | 6 | Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4 |
| Search | 8 | Present full search strategies for all electronic databases and other sources searched including any limits used such that they could be repeated. | 4 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 5 |
| Definitions for data extraction | 11 | Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting). | 5 |
| Risk of bias and applicability | 12 | Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question. | 5, Table S2 |
| Diagnostic accuracy measures | 13 | State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion). | 5 |
| Synthesis of results | 14 | Describe methods of handling data, combining results of studies, and describing variability between studies. This could include but is not limited to a) handling of multiple definitions of target condition, b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards. | 5 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **PRISMA-DTA Checklist Item** | **Reported on page #** |
| Meta-analysis | D2 | Report the statistical methods used for meta-analyses if performed. | 5 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression) if done, indicating which were pre-specified. | 5 |
| **RESULTS** | | |  |
| Study selection | 17 | Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis if applicable) with reasons for exclusions at each stage, ideally with a flow diagram. | 5 |
| Study characteristics | 18 | For each included study, provide citations and present key characteristics including a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources. | 6 |
| Risk of bias and applicability | 19 | Present evaluation of risk of bias and concerns regarding applicability for each study. | 6 |
| Results of individual studies | 20 | For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot. | 6 |
| Synthesis of results | 21 | Describe test accuracy including variability if meta-analysis was done. Include results and confidence intervals. | 6 |
| Additional analysis | 23 | Give results of additional analyses if done (e.g., sensitivity or subgroup analyses, meta-regression, analysis of index test, failure rates, proportion of inconclusive results, adverse events). | 6 |
| **DISCUSSION** | | |  |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence. | 6 |
| Limitations | 25 | Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research). | 7 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test). | 8 |
| **FUNDING** | | |  |
| Funding | 27 | For the systematic review, describe the sources of funding and other support as well as the role of the funders. | 9 |

**Table S2.** Search strategy used in each database.

|  |  |
| --- | --- |
| Our search strategy was based on “Target condition” AND “Index test”. Each search term of “Target condition” or “Index test” was combined with “OR”. Database search was conducted on January 7, 2021. | |
| MEDLINE via Ovid | Search terms |
| A serum anti-glomerular basement membrane antibody | Exp Anti-Glomerular Basement Membrane Disease/  (anti-GBM disease?).ab,ti.  (anti-GBM antibody disease?).ab,ti.  (crescentic glomerulonephritis type I).ab,ti.  (Goodpasture\*).ab,ti.  (pulmonary-renal syndrome?).ab,ti. |
| Anti-glomerular basement membrane disease | (antiglomerular basement membrane antibod\*).ab,ti.  (anti-GBM antibod\*).ab,ti.  (collagen autoantibod\*).ab,ti.  Exp Fluorescent Antibody Technique/  (FEIA).ab,ti.  (fluorescence enzyme immunoassay?).ab,ti.  (fluoroenzymeimmunoassay?).ab,ti.  (radioimmunoassay?).ab,ti.  Exp Enzyme-Linked Immunosorbent Assay/  (ELISA).ab,ti.  (enzyme-linked immunosorbent assay?).ab,ti.  (enzymoimmunoassay?).ab,ti.  (enzyme labeled immunoassay?).ab,ti.  (enzyme coupled immunoassay?).ab,ti.  (enzyme-linked immuno assay?).ab,ti.  Exp Blotting, Western/  (Western blot).ab,ti.  (Immunoblotting).ab,ti.  (dot blot assay?).ab,ti.  Exp Luminescent Measurements/  (CLEIA).ab,ti.  (chemiluminescen\*).ab,ti.  (multiplex immunoassay?).ab,ti. |
| Embase via Embase.com |  |
| Serum anti-glomerular basement membrane antibody | "Goodpasture syndrome"/exp  "anti-GBM disease?":ab,ti  "anti-GBM antibody disease?":ab,ti  "crescentic glomerulonephritis type I":ab,ti  "Goodpasture\*":ab,ti  "pulmonary-renal syndrome?":ab,ti |
| Anti-glomerular basement membrane disease | "antiglomerular basement membrane antibod\*":ab,ti  "anti-GBM antibod\*":ab,ti  "collagen autoantibod\*":ab,ti  "fluorescent antibody technique"/exp  FEIA:ab,ti  "fluorescence enzyme immunoassay?":ab,ti  fluoroenzymeimmunoassay?:ab,ti  radioimmunoassay?:ab,ti  "enzyme linked immunosorbent assay"/exp  ELISA:ab,ti  "enzyme-linked immunosorbent assay?":ab,ti  "enzymoimmunoassay?":ab,ti  "enzyme labeled immunoassay?":ab,ti  "enzyme coupled immunoassay?":ab,ti  "enzyme-linked immuno assay?":ab,ti  "Western blotting"/exp  "Western blot":ab,ti  Immunoblotting:ab,ti  "dot blot assay?":ab,ti  Luminescence/exp  CLEIA:ab,ti  "chemiluminescen\*":ab,ti  "multiplex immunoassay?":ab,ti |
| Central |  |
| Serum anti-glomerular basement membrane antibody | [Anti-Glomerular Basement Membrane Disease] explode all trees  (anti-GBM disease?):ti,ab,kw  (anti-GBM antibody disease?):ti,ab,kw  (Goodpasture syndrome?):ti,ab,kw  (Goodpasture\*):ti,ab,kw |
| Anti-glomerular basement membrane disease | (antiglomerular basement membrane antibod\*):ti,ab,kw  (anti-GBM antibod\*):ti,ab,kw  (collagen autoantibod\*):ti,ab,kw  [Fluorescent Antibody Technique] explode all trees  (FEIA):ti,ab,kw  (fluorescence enzyme immunoassay?):ti,ab,kw  (fluoroenzymeimmunoassay?):ti,ab,kw  (radioimmunoassay?):ti,ab,kw  [Enzyme-Linked Immunosorbent Assay] explode all trees  (ELISA):ti,ab,kw  (enzyme-linked immunosorbent assay?):ti,ab,kw  (enzymoimmunoassay?):ti,ab,kw  (enzyme labeled immunoassay?):ti,ab,kw  (enzyme coupled immunoassay?):ti,ab,kw  (enzyme-linked immuno assay?):ti,ab,tkw  [Blotting, Western] explode all trees  (Western blot):ti,ab,kw  (Immunoblotting):ti,ab,kw  (dot blot assay):ti,ab,kw  [Luminescent Measurements] explode all trees  (CLEIA):ti,ab,kw  (chemiluminescen\*):ti,ab,kw  (multiplex immunoassay?):ti,ab,kw |
| ICTRP |  |
|  | “Anti-GBM disease” OR “Goodpasture” |

**Table S3.** Risk of bias and applicability assessment using the modified Quality Assessment of Diagnostic Accuracy Studies tool.

|  |  |  |
| --- | --- | --- |
| Risk of bias | Signaling questions | Explanations |
| Patient selection | * Was a consecutive or random sample of patients enrolled? * Was a case-control design avoided? * Did the study avoid inappropriate exclusions?a | a: Inappropriate exclusions were defined as excluding patients who could not undergo a renal biopsy. |
| Index test | * Were the index test results interpreted without the knowledge of the results of the reference standard?b * If a threshold was used, was it pre-specified? | b: We assessed the risk of bias based on whether it affected the diagnostic accuracy of the index test. |
| Reference standard | * Is the reference standard likely to correctly classify the target condition?c * Were the reference standard results interpreted without the knowledge of the results of the index test?d * Were the criteria of a reference standard for the target condition pre-specified? | c: Typically, renal biopsy results of anti- GBM disease are focal or diffuse segmental crescentic glomerulonephritis and the presence of linear fluorescence of IgG along the GBM. However, dependency only on pathology could lead to misdiagnosis because linear IgG staining in immunofluorescence stains is not specific to anti-GBM disease. Clinical diagnosis based on clinical presentation and renal biopsy results with immunofluorescence stains can make a diagnosis of anti-GBM disease correctly.  d: We assessed the risk of bias based on whether it affected the diagnostic accuracy of the index test. |
| Flow and timing | * Was there an appropriate interval between index test(s) and reference standard?e * Did all patients receive a reference standard? * Did patients receive the same reference standard? * Were all patients included in the analysis?f | e: Appropriate interval between the index test and reference standard was considered to be less than or equal to 1 year. We decided “1 year” because antibodies become undetectable within an average of 11 months after the treatment of anti-GBM diseases (Lancet. 1986 Jan 4;1(8471):5-8.).  f: We assessed the risk of bias based on whether missing data in the studies affected the diagnostic accuracy of the index test. |
| Applicability |  |  |
| Patient selection | Is there a concern that the included patients do not match the review question? | g: We assessed whether the included patients matched our target population or patients who were suspected of anti-GBM disease. |
| Index test | Is there a concern that the index test, its conduct, or interpretation differ from the review question? | h: We assessed whether the index tests are commercially available. |
| Reference standard | Is there a concern that the target condition as defined by the reference standard does not match the review question? | i: We assessed whether the diagnosis of anti-GBM disease was made based on the biopsy procedures which are available in daily clinical site. |

GBM, glomerular basement membrane

**Figure S1.** Assessment of the risk of bias and applicability for each domain in the included studies.

High risk of bias and high concerns for applicability in the patient selection domain was due to the case control design. Because number of excluded patients in the analysis was not clear in Busch et al, we judged it as high risk of bias in the flow and timing domain.

**Figure S2.** Univariate forest plots of sensitivity and specificity of serum anti-glomerular basement membrane antibodies.

The sensitivity and specificity of serum anti-glomerular basement membrane antibodies were high, and heterogeneity was not large.