

# INPLASY PROTOCOL

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## Diagnostic value of cell free DNA in thyroid carcinoma: A systematic review and meta-analysis

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**Review Stage at time of this submission:** Preliminary searches.

**Conflicts of interest:**  
None declared.

**Review question / Objective:** In recent years, the incidence of thyroid cancer(TC) is increasing. Cell-free DNA is a new tumor marker for the diagnosis of cancer. The purpose of this meta-analysis is to summarize the published studies and evaluate the value of cfDNA in the diagnosis of thyroid cancer.

**Condition being studied:** In recent years, high levels of circulating cell-free DNA (cf-DNA) have been found to be associated with cancer diagnosis and progression and have shown characteristics of potential candidate as biomarker of cancer response. cfDNA can effectively distinguish thyroid cancer from benign thyroid nodules or healthy patients.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 July 2021 and was last updated on 01 July 2021 (registration number INPLASY202170002).

### INTRODUCTION

**Review question / Objective:** In recent years, the incidence of thyroid cancer(TC) is increasing. Cell-free DNA is a new tumor marker for the diagnosis of cancer. The purpose of this meta-analysis is to summarize the published studies and

evaluate the value of cfDNA in the diagnosis of thyroid cancer.

**Rationale:** cfDNA have the ability to detect thyroid carcinoma.

**Condition being studied:** In recent years, high levels of circulating cell-free DNA (cf-DNA) have been found to be associated



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Benign thyroid nodules, who are confirmed the diagnosis by cfDNA. Participants of any ethnicity, sex, or age will be included.

**Intervention:** cfDNA will be identified as index tests.

**Comparator:** Single-arm studies will also be included if participants, index tests, outcomes meet the inclusion criteria. Comparator tests are not a mandatory indicator.

**Study designs to be included:** Any type of study design such as retrospective studies, prospective studies, case-control studies, if the study had assessed the efficacy of cfDNA in diagnosing TC. Studies that report only sensitivity or specificity will be excluded.

**Eligibility criteria:** Original studies that diagnosed TC by cfDNA and have access to the full text will be included in this systematic review and meta-analysis. Clear reference standards in the original study. True positive (TP), false positive (FP), false negative (FN), and true negative (TN) values for the index tests could be extracted directly or calculated from the original studies. Studies reported in languages other than English, Studies with less than 10 specimens, conference abstracts without full articles, and case reports will be excluded.

**Information sources:** We will search candidate studies that assessing the accuracy of cfDNA for diagnosis of TC through Pubmed, Embase, the Cochrane Library, web of science, CNKI, sinomed, VIP database and WANFANG database. References cited in a review or meta-analysis will also be evaluated to identify additional studies.

**Main outcome(s):** The sensitivity and specificity of the index tests will be considered as the main outcome. Sensitivity is the probability that the index tests will detect positive in an thyroid carcinoma patient. Specificity is the probability that the index tests will detect

negative in a patient with benign thyroid nodules or healthy people.

**Quality assessment / Risk of bias analysis:** Following a revised tool for Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2), two researchers will independently evaluate the study quality. The discrepancy will be handled in the same way as in the data extraction phase. Publication bias assessment is not required by the PRISMA-DTA statement. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) guideline will be used to assess the strength of the body of evidence.

**Strategy of data synthesis:** TP , FP , FN, and TN values for the index tests in each included study will be obtained first, then select STATA software for data analysis,  $I^2 > 50\%$  and  $P < 0.1$  are considered to be heterogeneous. If there is heterogeneity, select the random effect model to merge the effect size, if there is no heterogeneity, select the fixed effect model to merge the effect size.

**Subgroup analysis:** When significant heterogeneity is observed, subgroup, meta-regression and sensitivity analyses will be used to explore sources of heterogeneity. Subgroup and meta-regression analyses will perform on different types of study design; patient selection method; specimen types; target gene; test method; specimen condition; types of control group.

**Sensitivity analysis:** When significant heterogeneity is observed, sensitivity analyses will be used to explore sources of heterogeneity.

**Country(ies) involved:** China.

**Keywords:** Thyroid carcinoma, diagnostic value, cfDNA, meta-analysis.

**Contributions of each author:**

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