

# INPLASY PROTOCOL

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

**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** The purpose of this study was to investigate the effect of different states of ground glass opacity and final histological classification on the EGFR

**The diagnostic value of presence of ground glass opacity and final histological classification in distinguishing subtypes of EGFR mutations of stage IA non-small cell lung cancer: a systematic review and meta-analysis**

Qiu, JH<sup>1</sup>; Ma, Z<sup>2</sup>; Li, RY<sup>3</sup>; Liu, BY<sup>4</sup>; Tian, Y<sup>5</sup>; Tian, H<sup>6</sup>.

**Review question / Objective:** The purpose of this study was to investigate the effect of different states of ground glass opacity and final histological classification on the EGFR mutation in non-small lung cancer through included high-quality retrospective studies.

**Condition being studied:** The investigators of this study were experienced thoracic surgeons. Any disagreements that arose during the study were resolved through mutual discussion.

**Eligibility criteria:** Specific selection criteria were as follows: (1) adult patients who underwent EGFR-related genetic testing on their own tumor samples; (2) reported at least one relevant outcome (see below) and had a control group; and (3) were written in English. Some papers were excluded for the following reasons: (1) no outcome of interest, (2) insufficient or missing data for analysis, (3) written in a language other than English, and (4) non-human participants.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 February 2023 and was last updated on 25 June 2023 (registration number INPLASY202320043).

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## METHODS

**Participant or population:** Adult patients who underwent EGFR-related genetic testing on their own tumor samples.

**Intervention:** Presence of ground glass opacity.

**Comparator:** Non-existence of ground glass opacity.

**Study designs to be included:** Retrospective case-control study.

**Eligibility criteria:** Specific selection criteria were as follows: (1) adult patients who underwent EGFR-related genetic testing on their own tumor samples; (2) reported at least one relevant outcome (see below) and had a control group; and (3) were written in English. Some papers were excluded for the following reasons: (1) no outcome of interest, (2) insufficient or missing data for analysis, (3) written in a language other than English, and (4) non-human participants.

**Information sources:** A literature review was conducted in four online databases, Pubmed, EMBASE, Cochrane Library, and Web of Science, and the search time was up to May 15, 2023.

**Main outcome(s):** The primary outcome of interest was the relationship between ground-glass opacity in patients' tumors and their EGFR gene mutation. Other relevant outcomes included demographics (age, gender, smoking history), imaging features (Cavitation, lobulation, spiculation, air bronchogram, pleural traction and vascular convergence), and finally pathologic staging.

**Quality assessment / Risk of bias analysis:** In this systematic review and meta-analysis, the quality of case-control studies was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS). Egger's test was used to detect possible

publication bias, and the presence of significant publication bias was determined if  $P < 0.05$  for Egger's test.

**Strategy of data synthesis:** All statistical analyses were performed with the use of the STATA 16 software package. This systematic review and meta-analysis used the Cochrane Q test and the I<sup>2</sup> statistic to quantify the degree of heterogeneity, with an I<sup>2</sup> greater than 50% considered to be substantial. In our study, random-effects models were used to calculate pooled effect sizes to reduce potential bias.

**Subgroup analysis:** To assess the effect of tumor histological findings on EGFR mutation subtypes, subgroup analysis was performed: the group was divided into invasive adenocarcinoma and minimally invasive adenocarcinoma.

**Sensitivity analysis:** The stability of the pooled estimates was further examined using a sensitivity analysis, in which the effect of each study on the overall estimate could be tested by sequentially omitting individual studies.

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

**Keywords:** EGFR mutation, molecular alteration, lung adenocarcinoma, thoracic CT, ground glass opacity, meta-analysis.

### Contributions of each author:

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