Evidence-Based PICO Mapping for EU Joint Clinical Assessment (JCA) Using a Real-Time AI-assisted Living Systematic Literature Review (REAL-SLR): An Advanced Non-Small Cell Lung Cancer (NSCLC) Case Study

Anna Forsythe[1], Neil Hawkins[2], Stacy Grieve[1], Rozee Liu[1], Andrew Briggs[2]

[1]Oncoscope-AI, Miami, FL, USA; [2]University of Glasgow, Oxford, United Kingdom; [3]London School of Hygiene & Tropical Medicine, London, United Kingdom

OBJECTIVES

→ To utilize a **Re**al-Time **AI**-assisted **L**iving SLR (REAL-SLR) approach for evidence-based JCA PICO mapping

CONCLUSIONS

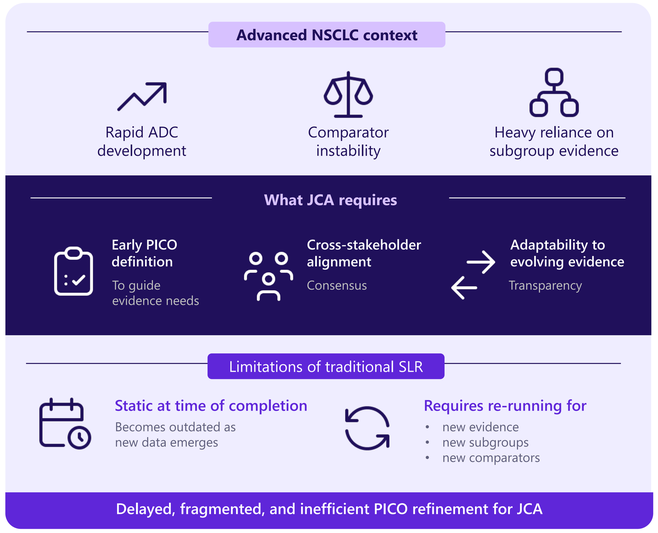
→ REAL-SLR-enabled PICO mapping anchors JCA scoping in the evolving ADC evidence landscape rather than a static SLR

→ Evidence-driven core PICOs based on interventions and sub-populations in published studies improves transparency, reduces rework, and enhances preparedness for JCA in rapidly evolving oncology indications, compared to traditional static and iterative SLR (**Figure 4**)

BACKGROUND

- The EU Joint Clinical Assessment (JCA) requires early, transparent, and evidence-based definition of Population–Intervention–Comparator–Outcome (PICO) frameworks
- In advanced non–small cell lung cancer (NSCLC), the rapid emergence of antibody–drug conjugates (ADCs), evolving comparators, and reliance on subgroup analyses challenge traditional static systematic literature reviews (SLRs) for JCA planning (**Figure 1**)

Figure 1. Challenges in JCA PICO definition using traditional SLR approaches



METHODS

- A PRISMA-compliant REAL-SLR was conducted using protocol-driven searches updated continuously for advanced NSCLC
- Evidence from interventional ADC trials, regulatory sources, clinical guidelines, selected high-quality real-world evidence, and technology assessments was continuously identified, screened, and structured
- For each eligible study, data were extracted on study design, population, intervention, comparator, endpoints, and reported subgroup analyses
- A Real-Time AI-assisted Living SLR (REAL-SLR) (**Figure 2**) was established as a continuously maintained evidence system that
  - Updates evidence through protocol-driven, ongoing searches
  - Structures studies at trial-level (not publication-level)
  - Enables instant re-querying of evidence without re-running the SLR
  - Preserves PRISMA traceability, auditability, and methodological consistency
- This continuously updated evidence-base REAL-SLR was used to define both core and extended JCA PICOs without re-running searches, enabling dynamic refinement

Figure 2. REAL-SLR for JCA PICO mapping

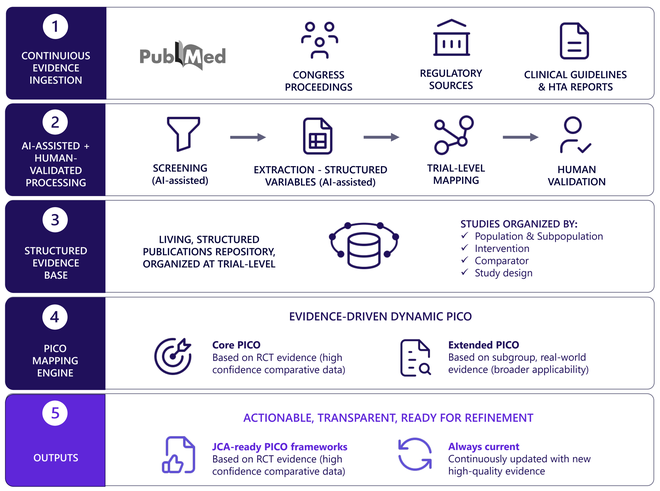
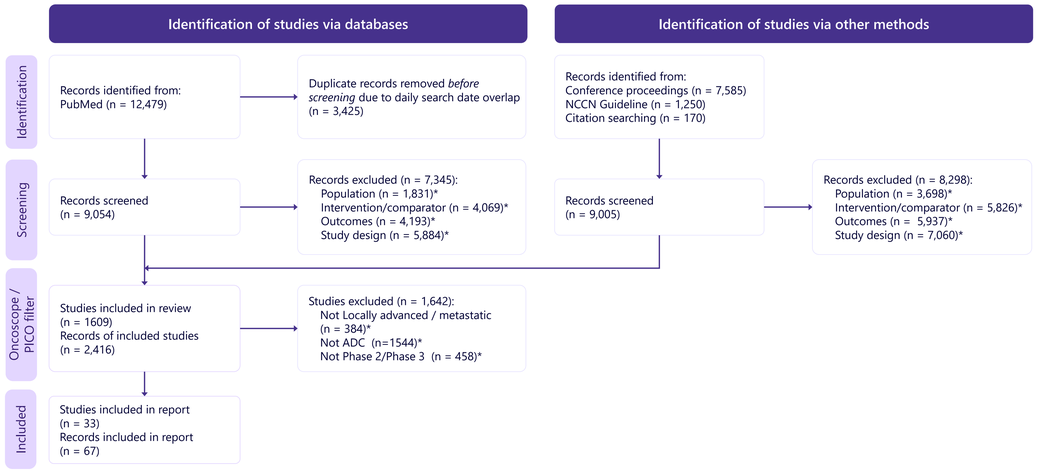


Figure 3. Continuously updated PRISMA (REAL-SLR framework) in NSCLC (updated Apr 16, 2026)



*Reasons for exclusion were not mutually exclusive.

Table 1. Evidence-anchored core PICOs (derived from REAL-SLR)

- Core PICOs were defined based on interventions and comparators evaluated in interventional trials
  → This ensures alignment with HTA expectations for comparative effectiveness

PICO element	Core definition	Evidence anchor from REAL-SLR
Population	Adults with advanced or metastatic NSCLC Histology – any Biomarker – any Line of therapy - any	Derived from published Phase 2 /Phase 3 ADC studies in advanced / metastatic NSCLC
Interventions	5 ADCs evaluated in published RCTs	Datopotamab deruxtecan (TROPION-Lung01) Sacituzumab govitecan (EVOKE-01) Trastuzumab deruxtecan (DESTINY-Lung02) Sacituzumab tirumotecan (OptiTROP-Lung03, OptiTROP-Lung04) Patritumab deruxtecan (HERTHENA-Lung02)
Comparator	SOC Chemo	Docetaxel; Platinum-based chemo; Pemetrexed+platinum-based chemo
Outcomes	OS, PFS, ORR, Grade 3/4 AEs, Treatment discontinuation, QOL	OS, PFS, iPFS, iTTP, DOR, ORR NSCLC-SAQ; EORTC QLQ-C30; EQ-5D 3L Grade 3/4 AEs, Treatment discontinuation; drug-related ILD
Study design	RCTs	6 RCTs included; non-RCTs and pooled analyses excluded from initial PICO mapping

Table 2. Extended PICO mapping for JCA (evidence-based stratification)

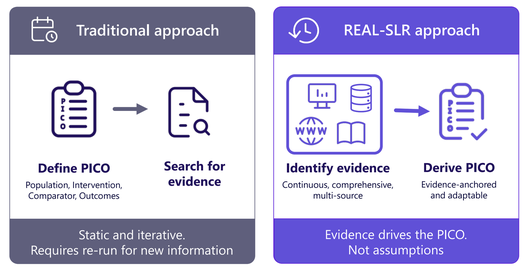
- Extended PICOs reflect biomarker-defined populations, prior treatment exposure, and prognostic characteristics
  → These are critical for JCA subgroup analyses and evidence interpretation across member states

Dimension	Stratification approach	Evidence basis
Molecular stratification	AGA+ populations by specific genomic alteration/ expression; AGA-negative populations by PDL1 TPS	Included AGA+ populations: - ALK rearrangement; - EGFR alteration, Exon 19 deletion, Exon 21 L858R substitution - EGFR Activating mutation (G719X, L861Q, S768I); EGFR Exon 20 insertions - BRAF V600E mutation; - HER2 mutation; HER2-positive IHC3+ - MET Exon 14 skipping mutation; - NTRK 1/2/3 gene fusion; - RET rearrangement; - ROS1 rearrangement; AGA-negative populations: - PDL1 TPS<1%; PDL1 TPS 1-49%; PDL1 TPS≥50%;
Treatment history	Prior therapy exposure (lines and classes)	≥2nd line, prior targeted ≥2nd line, prior ICI; ≥2nd line, prior chemo
Clinical prognostic factors	Key prognostic characteristics shown significance in prior sub-group analyses	Histology: Non-squamous; Squamous Brain metastases: untreated / progression after prior RT

RESULTS

- As of April 16, 2026, the REAL-SLR identified 67 published ADC studies in advanced NSCLC, including 33 Phase 2 or Phase 3 trials (**Figure 3**)
- Six Randomized-controlled trials (RCTs) evaluated 5 distinct ADCs against two comparator strategies: docetaxel and platinum-based chemotherapy (**Table 1**)
- These five interventions and two comparators defined the evidence-anchored core PICOs for JCA planning. Extended PICOs were mapped using available subgroup evidence, including (**Table 2**):
  → biomarker-defined populations (actionable genomic alteration [AGA]–positive tumors stratified by specific AGA expression
  → AGA-negative tumors stratified by PD-L1 tumor proportion score)
  → prior therapy exposure
  → prognostic characteristics (i.e. brain metastases)

Figure 4. Defining PICOs: What changes with REAL-SLR



ABBREVIATIONS

ADC, antibody-drug conjugate; AEs, adverse events; AGA, actionable genomic alteration; ALK, anaplastic lymphoma kinase; DOR, duration of response; EGFR, epidermal growth factor receptor; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ-5D-3L, EuroQol 5-Dimension 3-Level questionnaire; HER2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; iPFS, immune progression-free survival; ILD, interstitial lung disease; NSCLC, non–small cell lung cancer; NTRK, neurotrophic tyrosine receptor kinase; ORR, overall response rate; OS, overall survival; PDL1 TPS, programmed death-ligand 1 tumor proportion score; PFS, progression-free survival; QOL, quality of life; RCTs, randomized controlled trials; RET, rearranged during transfection; ROS1, ROS proto-oncogene 1; RT, radiotherapy; SAQ, symptom assessment questionnaire; SOC, standard of care.

Presented at ISPOR 2026 | May 17-20, 2026 | Philadelphia, PA, USA | Poster Session 1

See more Oncoscope AI publications

ONCOSCOPE AI
REAL-TIME ONCOLOGY LIBRARY