

# Cost-Effectiveness Models and Resource Use/Cost Inputs for Untreated Advanced/Metastatic Renal Cell Carcinoma- A Systematic Literature Review

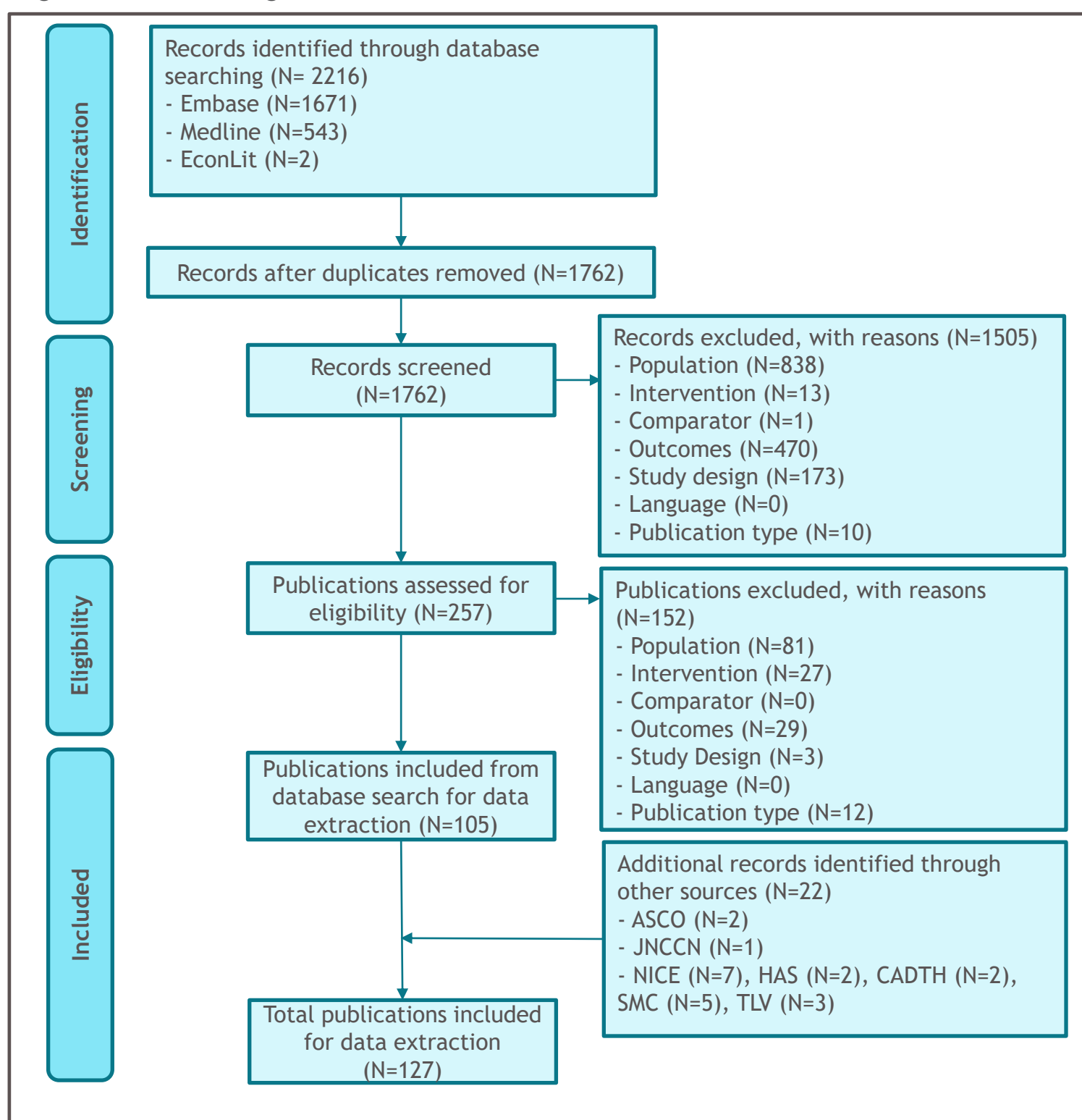
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## Background & Objective

- Kidney cancer, of which renal cell carcinoma (RCC) accounts for approximately 85%, is the 7<sup>th</sup> most common cancer worldwide in men, and the 10<sup>th</sup> most common cancer worldwide in women.<sup>1</sup>
- Nivolumab (Opdivo®) is an immunoglobulin G4 human monoclonal antibody (IgG4 HuMAb) that binds to the programmed cell death-1 (PD-1) receptor, blocking the interaction of PD-1 with its ligands, PD-L1 and PD-L2.<sup>2,3</sup>
- Within the phase 3 randomized controlled trial (RCT) CheckMate 9ER (CM-9ER, NCT03141177), nivolumab + cabozantinib is being compared with sunitinib in first-line (1L) advanced or metastatic renal cell carcinoma (aRCC) patients with a clear-cell component.<sup>4</sup>
- To determine the cost-effectiveness of nivolumab in combination with cabozantinib, a health economic model assessing it as a 1L treatment for aRCC is being developed.
- To support the development of the economic model, this systematic literature review (SLR) was conducted to ascertain and evaluate the availability of health economic evidence (costs, resource use, and economic evaluations), in the global published literature, for patients with previously untreated aRCC.

Figure 1. PRISMA diagram



## Methods

- A search of Embase, MEDLINE, MEDLINE-IN-PROCESS, and EconLit was conducted without applying time limits.
- Additionally, health technology assessments' (HTA) databases and National Health Service Economic Evaluation Database (NHS EED) were searched via Center for Reviews and Dissemination (CRD) databases. Clinical conferences, health economic conferences, and HTA websites (including the National Institute for Health and Care Excellence (NICE), Haute Autorité de santé (HAS), the Canadian Agency for Drugs and Technologies (CADTH), the pan-Canadian Oncology Drug Review (pCODR) the Scottish Medicines Consortium (SMC), and Tandvårds- och läkemedelsförmånsverket (TLV) were also searched without applying time limits.
- Studies were reviewed by two independent reviewers using predefined PICOS selection criteria.
- The population of interest was restricted to patients with previously untreated advanced or metastatic RCC. Given the scope of this SLR, no exclusions were made based on interventions or comparators.
- Publications of interest were restricted to economic evaluations (including cost utility analyses [CUA], costs effectiveness analyses [CEA], budget impact analysis [BIA], and costs minimization analyses [CMA]), and studies reporting healthcare resource use (HCRU) or cost data for aRCC. Clinical trials were excluded.
- Following the data-extraction process, a critical appraisal of the quality of selected CEA studies published as full journal articles was performed (Drummond checklist).<sup>5</sup>

Figure 2. Study design of reported economic evaluation (N=89)

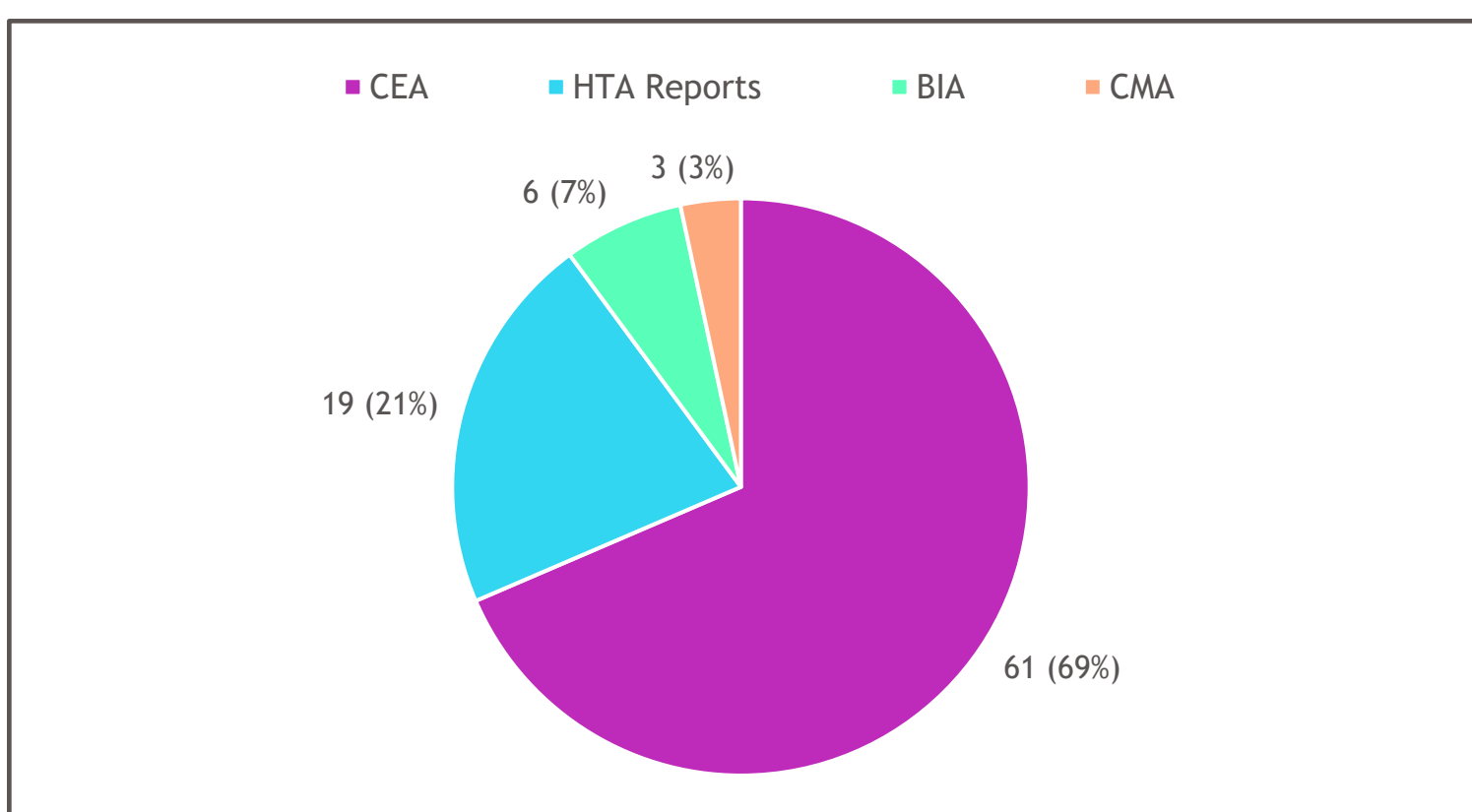
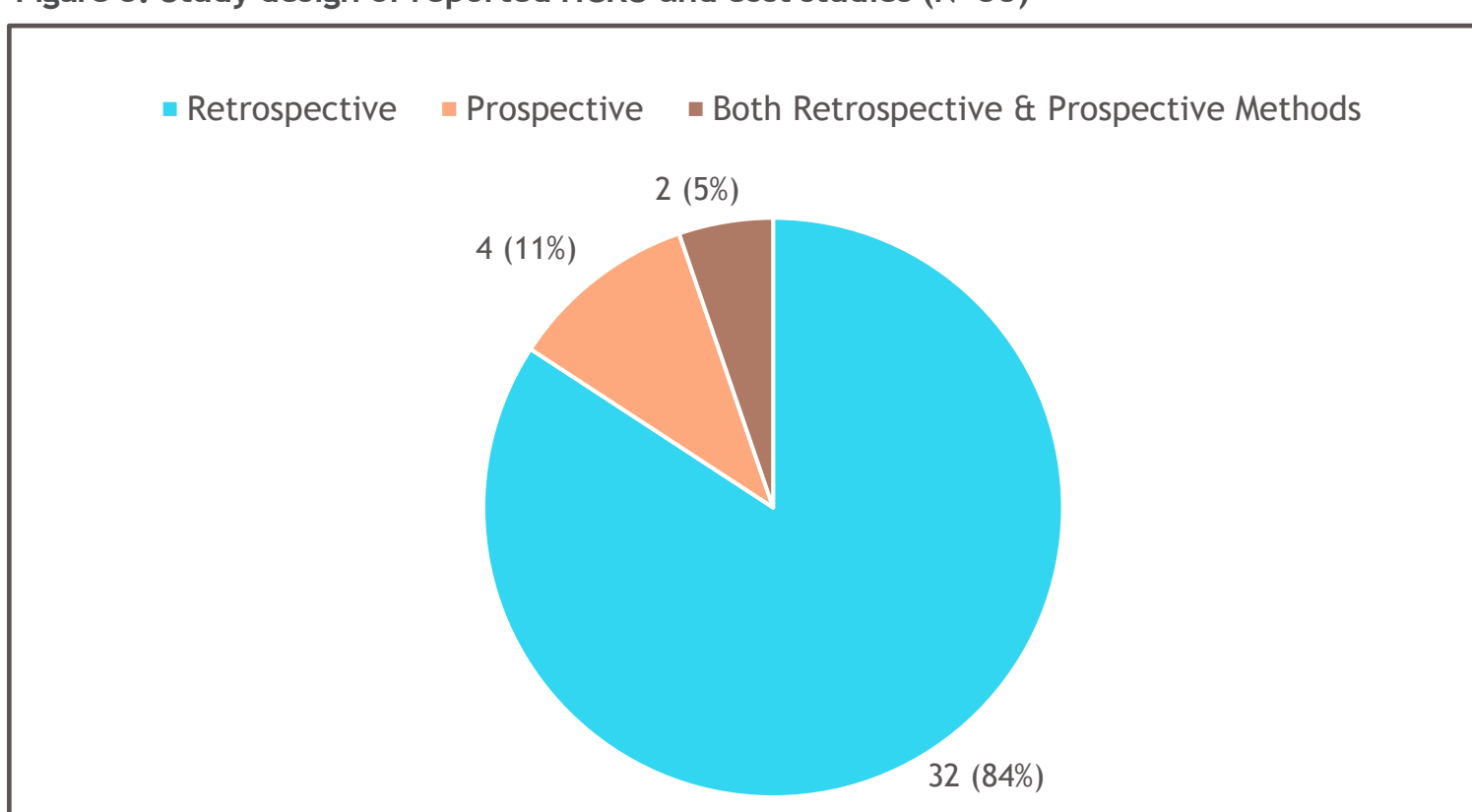


Figure 3. Study design of reported HCRU and cost studies (N=38)



## Results

### Included publications

- The search identified 127 publications (of which 45% were full-text publications) reporting economic evidence (Figure 1).
- These publications and results reflect original searches conducted in August 2019 (as presented in abstract) and an update of the search in July 2020.

### Economic evaluations

- In total, 89 economic evaluations were identified in several countries (Figure 2 & Figure 4).
- The CEAs were conducted by use of different model types.
  - Most models developed by manufacturers were three-state partitioned survival models, whereas models developed by independent researchers were often Markov models.
  - For the US, 2 patient-level, discretely integrated condition event (DICE) simulation models were identified.
- For half of the CEA models (n=31), it was reported that a subsequent line of therapy (second-line) was included in the model.
- Various types of costs were considered depending on the included interventions and health states (Table 1).
- Within the 19 HTA reports, various submission information was identified regarding economic cost-effectiveness models for 1L aRCC.

### HCRU and cost studies

- In total, 38 HCRU and cost studies were identified in several countries (Figure 3 & Figure 4).
- The majority of these studies (n=36) reported resource use and/or costs, while the remaining 2 studies reported only resource use.
- The 38 studies reported on various costs related to 1L aRCC (Table 1).

Figure 4. Study location of identified studies

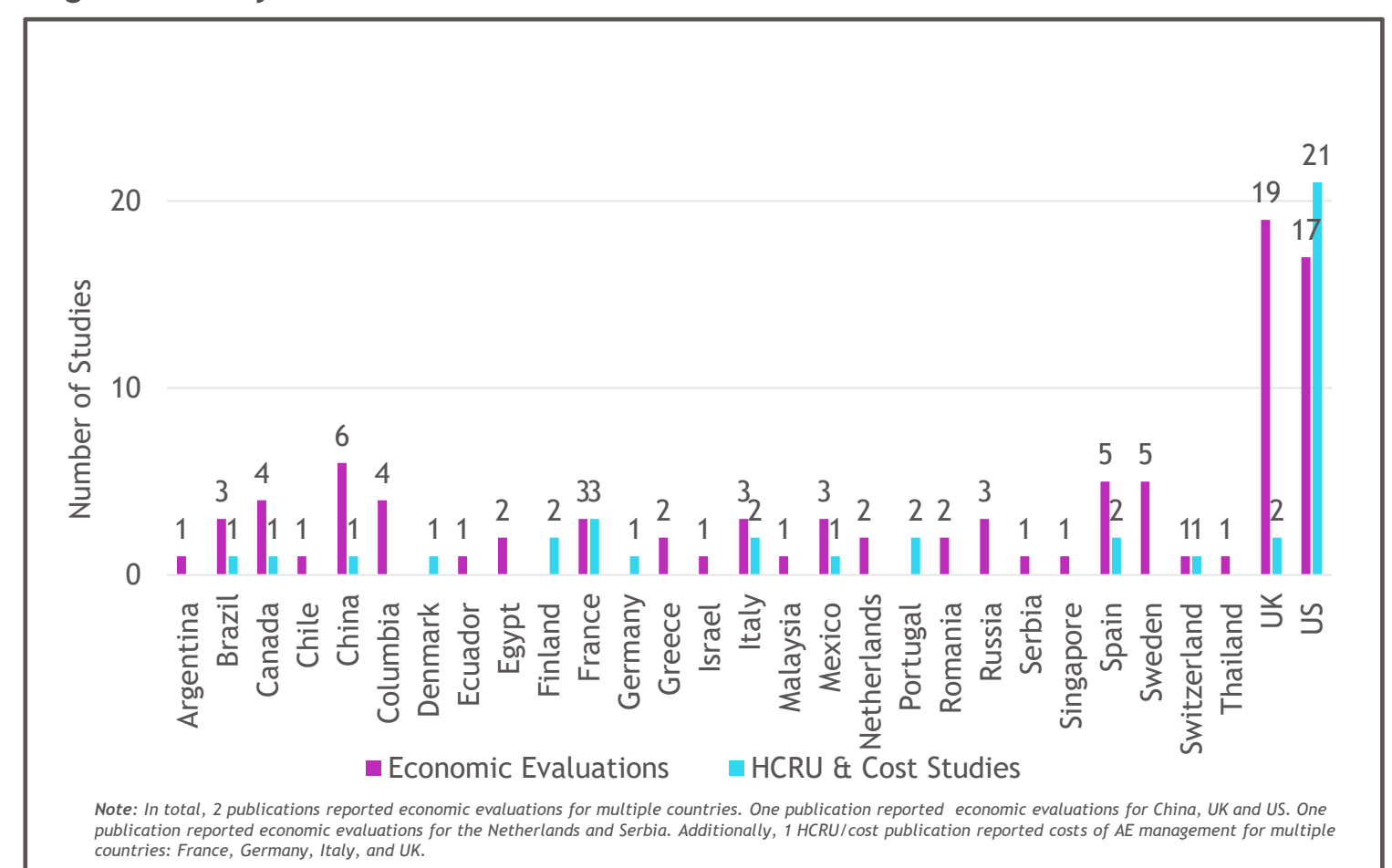


Table 1. Identified economic evidence

	Economic Evaluations (89 studies)	HCRU & Cost Studies (38 studies)
<b>Data Sources</b>	<ul style="list-style-type: none"> <li>Clinical trial data from COMPARZ<sup>6</sup>, CheckMate 214<sup>7</sup>, KEYNOTE-426<sup>8</sup> and JAVELIN Renal 101<sup>9</sup>, except for one Canadian model which was populated with real-life data from the Canadian Kidney Cancer Information System (CKCis) database.</li> </ul>	<ul style="list-style-type: none"> <li>Clinical trial data</li> <li>Cost analysis using a linear decision analytic model</li> <li>Claims databases including Truven Health MarketScan Commercial, US HealthCore Integrated Research Database, LifeLink Health Plan Claims Database, Medicare Supplemental, and Coordination of Benefits (Medicare) databases</li> <li>CKCis</li> <li>National Cancer Registration and Analysis Service</li> </ul>
<b>Cost Considerations</b>	<ul style="list-style-type: none"> <li>Drug acquisition costs</li> <li>Drug administration</li> <li>Adverse event management</li> <li>Disease monitoring</li> <li>Routine care (e.g. scheduled medical office visits)</li> <li>Unscheduled hospitalizations or emergency department visits related to treatment</li> <li>Subsequent therapies</li> <li>Best supportive care</li> <li>Palliative care</li> </ul>	<ul style="list-style-type: none"> <li>Drug acquisition costs</li> <li>Drug administration</li> <li>Adverse event management</li> <li>Disease monitoring</li> <li>Routine care (e.g. scheduled medical office visits)</li> <li>Unscheduled hospitalizations or emergency department visits related to treatment</li> <li>Subsequent therapies</li> <li>Best supportive care</li> <li>Palliative care</li> <li>Productivity loss</li> </ul>

## Conclusions

- Treatment-specific cost-effectiveness data for previously untreated aRCC patients are available in the global literature; however, more granular and local-level evidence of HCRU data in this population is needed to cover interventions and countries more broadly.
- As more than half of the evidence was published in conference abstracts, these studies provided limited information regarding methods and used inputs for analysis. Results from these studies should therefore be interpreted with caution.

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- Allysen Kaminski and Cathelijne Alleman are employees of Pharmerit - an OPEN Health Company and were paid consultants to Bristol Myers Squibb in connection with this study.