

# Reported Utilities For Patients With Previously Untreated Advanced/Metastatic Renal Cell Carcinoma - A Systematic Literature Review Update

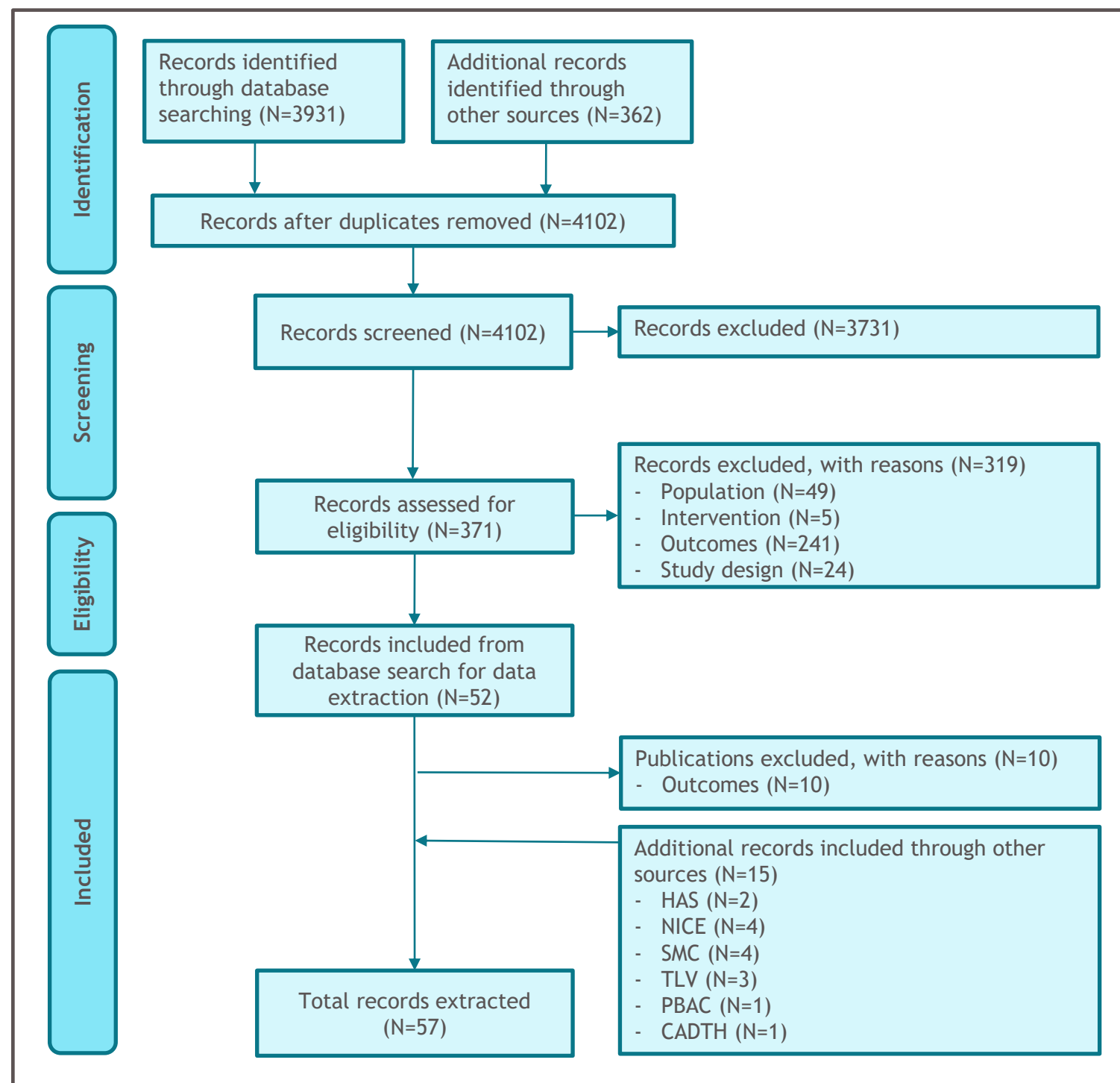
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## Background & Objective

- Kidney cancer, of which renal cell carcinoma (RCC) accounts for approximately 85%, is the 7th most common cancer worldwide in men, and the 10th 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 (NCT03141177), nivolumab + cabozantinib is being compared to 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 all available relevant utility data related to 1L aRCC.

Figure 1. PRISMA diagram



## Methods

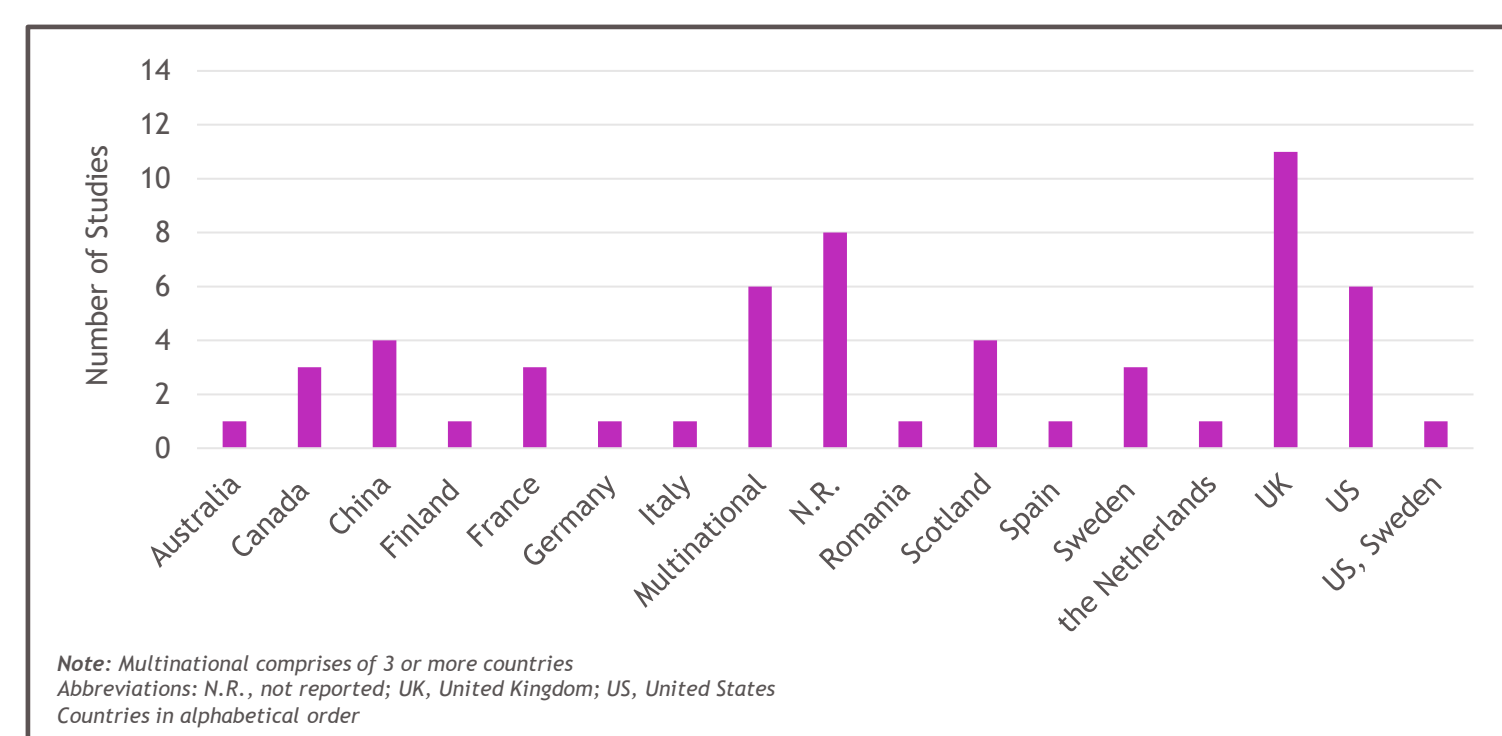
- This review was originally conducted in 2017, with results previously presented.<sup>5</sup> These publications reflect results from the original search and update search conducted early 2020 (as presented in abstract) and July 2020.
- Searches in Embase, MEDLINE, Cochrane library/Centre for Reviews and Dissemination (CRD), health technology assessments (HTA) databases, and National Health Service Economic Evaluation Database were conducted without applying time limits.
- Additionally, clinical 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 hand searched up to July 2020.
- Publications of interest included cost-effectiveness analyses (CEA), clinical trials, observational studies, and HTA assessments.
- Although no formal quality assessment (QA) is required for utility evidence, the included original studies were reviewed for methodological rigor with the use of the NICE approved QA checklists for RCTs and observational studies.

## Results

### Included publications

- The search identified 57 publications<sup>6-62</sup> (Figure 1).
- Most studies were HTA publications (N=21), followed by CEAs (N=17), RCTs (N=8), observational studies (N=6), and additional analyses of RCT data (N=5).
- Publications came most frequently from the UK (Figure 2). One study was conducted in both the US and Sweden.<sup>18</sup>
- Utility evidence was categorized by progression-free (PF) and progressed disease (PD)/post-progression survival health states. Disutility values were also reported for adverse events (AEs) for 1L and 2L treatments from publications.

Figure 2. Number of studies by country



### Health state: progression-free

- Eleven publications reported utility values for the PF health state.<sup>8, 9, 11, 14-17, 19, 39, 49, 50</sup> Interventions varied across publications
- The reported utility values for the PF health state varied from 0.6 to 0.82 depending on intervention and source. The utility value for sunitinib ranged between 0.6325 and 0.8103 (Table 1).

### Health state: progressed disease

- Eleven studies reported a utility value for the PD health state.<sup>6, 8, 9, 11, 14-16, 19, 25, 39, 52</sup> Interventions varied across publications. PD health state utility values were most commonly reported for sunitinib and pazopanib.
- Absolute utility values varied considerably from 0.355 to 0.76 across publications (Table 1).
- Utility values for PD was 0.66 across multiple interventions (avelumab + axitinib, pembrolizumab + axitinib or sunitinib, and sunitinib monotherapy). However, there was overlap in some utility values for PD (e.g., pazopanib and sunitinib both had a utility value of 0.76 in one study<sup>6</sup>).

### Other health states

- Twenty-four publications reported baseline utility values for health states that could not be categorized as PF or PD, such as 1L therapy, intermediate or poor risk, during rest, and with stable disease.<sup>7, 10, 12, 13, 18, 20, 22-27, 39-48, 51, 52</sup>
- The EQ-5D was the most commonly used instrument to derive utility values (N=20).<sup>10, 12, 13, 18, 20, 22-24, 26, 27, 39-41, 43-48, 51, 52</sup>

## Results (continued)

### Disutility values for AEs - 1L

- Seven publications reported (dis)utility values for AEs during 1L treatment.<sup>6, 8-10, 12, 16, 25</sup>
- The types of AE and absolute utility values varied across publications (Table 2).

### Disutility values for AEs - 2L

- Three publications reported (dis)utility values for AEs during 2L treatment (Table 2).<sup>6, 10, 21</sup>
- The disutility values for 2L treatment ranged from -0.075 to -0.0003 across 2 studies.<sup>6, 10</sup> One study reported a value of -0.05 for dyspnea during 2L treatment.<sup>21</sup>

### HTA reports

- Twenty-one HTA publications were identified.<sup>28-38, 53-62</sup>
- Interventions across HTA assessments included sunitinib, nivolumab + ipilimumab, nivolumab, pazopanib, cabozantinib, avelumab + axitinib, and pembrolizumab + axitinib.
- Reported health states varied across publications, and included PF, PD, time before death, disease state (stable), and response (partial/complete).
- Across 16 publications, PF health state utility values ranged from 0.6 to 0.798,<sup>28, 29, 33-38, 53-56, 58, 59, 61, 62;</sup> PD health state values ranged from 0.3545 to 0.798.<sup>28, 29, 33-38, 53-59, 61</sup>
- Four HTAs reported (dis)utility values for AEs during 1L treatment,<sup>28, 29, 34, 36</sup> while only one HTA reported disutility values for AEs for 2L treatment.<sup>31</sup>

Table 1. PF and PD health states from identified publications

Intervention	Specification	Health state	Value
<b>Progression-free health state utility values</b>			
Avelumab + axitinib	-	PF	0.82 <sup>11</sup>
IFN-a or tsemsirrolimus	-	PF	0.6 - 0.78 <sup>14</sup>
Pazopanib	-	PF	0.709 - 0.739 <sup>16, 19, 49, 50</sup>
	Combined treatment	PF	0.7487 <sup>17</sup>
	On-treatment	PF	0.7487 <sup>17</sup>
Pembrolizumab + axitinib or sunitinib	-	PF	N.R. <sup>17</sup>
	-	PF disease	0.73 <sup>9</sup>
Sunitinib	-	PF	0.6832 - 0.73 <sup>11, 16, 19, 49, 50</sup>
	-	PF without AEs	0.795 <sup>16</sup>
	Combined treatment	PF	0.6918 <sup>17</sup>
	On-treatment	PF	0.6325 <sup>17</sup>
	Off-treatment	PF	0.8103 <sup>17</sup>
No distinction by treatment	-	PF	0.6 <sup>15</sup>
	-	PF disease	0.78 <sup>8</sup>
-	-	Patients before progression	0.75 <sup>39</sup>
<b>Progressed disease or post-progression survival health state utility values</b>			
Avelumab + axitinib	-	PD	0.66 <sup>11</sup>
IFN-a	-	Time after progression	0.656 <sup>52</sup>
IFN-a or tsemsirrolimus	-	PD	0.45 - 0.7 <sup>14</sup>
Pazopanib	-	Progression under treatment	0.76 <sup>6</sup>
	-	Post-progression vs. pre-progression survival	0.1580 <sup>16, 19</sup>
Pembrolizumab + axitinib or sunitinib	-	PD	0.66 <sup>9</sup>
Sunitinib	-	PD	0.66 <sup>11</sup>
	-	Progression under treatment	0.76 <sup>6</sup>
	-	Post-progression vs. pre-progression survival	-0.1323 <sup>19</sup>
	-	PD	0.355 - 0.66 <sup>9, 25</sup>
No distinction by treatment	-	PD	0.355 - 0.66 <sup>9, 25</sup>
	-	PS	0.45 <sup>15</sup>
-	-	After progression	0.66 <sup>39</sup>

Note: negative values represent a reported utility decrement, while positive values include the value for the health state  
Abbreviations: AE, adverse event; PD, progressed disease; N.R., not reported; PF, progression-free; PS, progression survival.

Table 2. Published disutility values for adverse events by treatment line

Adverse event	Specification	First-line disutility value	Second-line disutility value
Anemia	Grade 1-2	-0.0114 <sup>6</sup>	-
	Grade 3	0.676 <sup>25</sup>	-
Anorexia	Grade 1-2	-0.0082 <sup>6</sup>	-
	Grade 3-4	-0.0082 <sup>6</sup>	-
Diarrhea	Grade 1-2	-0.0261 to 0.69 <sup>6, 25</sup>	-
	Grade 3+	-0.0261 to 0.534 <sup>6, 25</sup>	-
Dyspnea	Stable disease	-	-0.05 <sup>21</sup>
Fatigue	Fatigue/asthenia grades 1-2	-0.0007 <sup>6</sup>	-
	Fatigue/asthenia grades 3-4	-0.1237 <sup>6</sup>	-
Hypertension	Grade 1-2	0.751 <sup>25</sup>	-
	Grade 3	0.591 <sup>25</sup>	-
Mouth-to-mouth syndrome	Grade 1-2	0.0018 <sup>6</sup>	-
	Grade 3-4	0.0141 <sup>6</sup>	-
Mucositis	Grade 1-2	0.726 <sup>25</sup>	-
	Grade 3	0.526 <sup>25</sup>	-
Nausea / vomiting	Grade 1-2	-0.0151 to 0.635 <sup>6, 25</sup>	-
	Grade 3-4	-0.0532 <sup>6</sup>	-
	Grade 3	0.54 <sup>25</sup>	-
Neutropenia	Grade 1-2	0.0223 <sup>6</sup>	-
	Grade 3-4	0.0223 <sup>6</sup>	-
PPE syndrome	Grade 3	0.469 <sup>25</sup>	-
Proteinuria	Grade 1-2	-0.018 <sup>6</sup>	-
	Grade 3-4	-0.018 <sup>6</sup>	-
Stomatitis	Grade 1-2	-0.0018 <sup>6</sup>	-
	Grade 3-4	-0.0018 <sup>6</sup>	-
Thrombocytopenia	Grade 1-2	-0.0105 <sup>6</sup>	-
	Grade 3-4	-0.024 <sup>6</sup>	-
Not specified	-	-0.1252 to -0.002 <sup>6, 10</sup>	-0.075 to -0.0003 <sup>6, 10</sup>
	Grade 1-2	-0.0947 to 0.014 <sup>8, 9, 16</sup>	-
	Grade 3-5	-0.2044 to 0.157 <sup>8, 9, 16</sup>	-

Note: negative values represent a reported utility decrement, while positive values include the value for the adverse event  
Abbreviations: PPE, palmar-plantar erythrodysesthesia.

## Conclusions

- Treatment-specific utilities are commonly available in the literature, with existing overlap for PF and PD health states in some studies. Utility values for interventions varied widely across interventions, particularly for pazopanib and sunitinib. Further research is needed to determine health values across other 1L aRCC interventions.
- This systematic review only collected utility values. Conclusions about the overall quality of life of RCC patients cannot be made from this study.

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