The utility of clinical registries for guiding clinical practice in upper tract urothelial cancer: a narrative review

Joshua Kealey[1,2]^, Ruth Snider[1,2], Dickon Hayne[3], Ian D. Davis[1,4], Shomik Sengupta[1,2]

[1]Eastern Health Clinical School, Monash University, Melbourne, Australia; [2]Urology Department, Eastern Health, Melbourne, Australia; [3]UWA Medical School, University of Western Australia, Perth, Australia; [4]Oncology Department, Eastern Health, Melbourne, Australia

Contributions: (I) Conception and design: J Kealey, D Hayne, S Sengupta, ID Davis; (II) Administrative support: R Snider; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: J Kealey, R Snider; (V) Data analysis and interpretation: J Kealey, R Snider; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Professor Shomik Sengupta. Level 2, 5 Arnold St., Box Hill, Melbourne, VIC 3128, Australia. Email: shomik.sengupta@monash.edu.

Background and Objective: Upper tract urothelial cancer (UTUC) lacks high-quality evidence to appraise current patterns of presentation, diagnosis, treatment and outcomes as a result of disease rarity and patient heterogeneity. Registries may overcome many of the challenges making clinical trials challenging in UTUC and provide answers to many of the clinical questions that afflict UTUC management. In this narrative review we aim to summarise the design of registries that have contributed to the UTUC literature, discuss their strengths and limitations and the future directions of registries in UTUC.

Methods: Two independent reviewers conducted a search of the OVID MEDLINE database from July 2002–July 2022. Included articles were required to be published in peer reviewed journals and use registry-based methodology to report on UTUC. Search was limited by MeSH and key words and was limited to the English language.

Key Content and Findings: One hundred and forty-four articles were identified and included as reporting on UTUC from a registry-based methodology. Articles utilising registry-based data have substantially increased over the study period with the majority of articles arising from large generalised cancer databases in North America. There has been an increase in UTUC-specific registries in the previous five years that have offered the most granular, complete analysis and these will continue to report in the coming years. The majority of published data assessed epidemiological factors and compared outcomes of treatment modalities with a small proportion of articles focusing on prognostic nomograms and quality of life. Larger cancer registries that contribute the majority of the published analysis are likely subject to significant selection bias when comparing cohorts for treatment analysis and the need for prospective UTUC specific registries is apparent. Future directions include the potential for registry-based randomised controlled trials (RCTs) and clinical quality registries (CQR) that have the ability to change practice and improve care.

Conclusions: The utilisation of registry-based methodology for analysis in UTUC has increased substantially over the last 20 years. In addition to the utilisation of large cancer registries, the creation of UTUC specific registries is likely to contribute the most granular, translatable data in diagnosis and management.

Keywords: Registry; upper tract urothelial carcinoma; transitional cell carcinoma

^ ORCID: 0000-0001-7387-5084.

Introduction

Upper tract urothelial cancer (UTUC) arises from the urothelial lining of the kidney or ureter and accounts for approximately 5–10% of all urothelial cancer (UC) (1). Whilst incidence of UTUC remains low at 1–3 cases/100,000 people/year, it is rising in many nations around the world (2). There are histological similarities between UTUC and bladder UC however the presentation, diagnosis, treatment and outcomes differ significantly. Patients diagnosed with UTUC are likely to be older with more comorbidities and are presenting with more invasive disease (3). This in combination with a low incidence often makes recruitment into clinical trials challenging and costly. For this reason, much of the understanding of UTUC is extrapolated from bladder UC or from systematic reviews that often rely on low-level evidence with many clinical questions remaining unanswered.

Registries are structured data repositories that systematically collect and store health related data (4). Registries collect observational data about a specific exposure, disease, treatment or healthcare resource (5). In general health registries are designed to be broad and have few if any exclusion criteria in order to quickly capture large patient cohorts and relay a real-world experience of patient care. Health related registries come in several different forms with different purposes and requirements.

Disease- or condition-specific registries are the most common form of registry and collect information on patients diagnosed with that disease in a specific setting such as a hospital or outpatient setting (6). These registries provide varied levels of epidemiological, diagnostic, treatment and outcome data. Common examples are cancer registries or rare-disease registries. These are often maintained at a state or national level and many countries around the world maintain comprehensive repositories that can be accessed for clinical research (7).

Drug or medical device registries are designed to monitor the safety and efficacy of medication or devices utilised in healthcare. Their main purpose is to monitor long-term real-world outcomes of medical devices and facilitate recalls where required (8). They are usually maintained by the medical device company, may not be publicly accessible and often collect a very narrow range of data.

Clinical quality registries (CQR) are similar to disease or condition specific registries however collect data to evaluate defined outcomes at predetermined intervals. Outcomes are then benchmarked against set standards, either local or international, and reported in a timely fashion to healthcare providers (9). Commonly assessed predefined outcomes include pre-operative waiting times, surgical margin status and 30-day post-operative complication rates. Whilst observational data analysis and contribution to the literature is provided the extra utility is provided in the ability to identify variations in the process and outcomes of care and adherence to evidence based guidelines. This information can then be reported back to providers and quality improvement processes undertaken with the eventual outcome of improving and standardising patient care. Interest in CQR has increased substantially in recent years as safety and quality of health provision continues to grow as a pillar of healthcare delivery (10).

In this narrative review, we aim to summarise the design of recent and current registries that have contributed to the UTUC literature, discuss their strengths and limitations and the future directions of registries in UTUC in the hope of improving awareness and collaboration with such registries. We present the following article in accordance with the Narrative Review reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-641/rc).

Methods

Two independent reviewers conducted a search of the OVID MEDLINE database from July 2002–July 2022. A third reviewer was utilised only if a there was not consensus regarding articles to be included. The review was conducted between July 2022 and August 2022. Articles included were required to report on UTUC with an observational study design arising from a registry. Single-institutional or multi-institutional retrospective data that did not arise from a registry design was excluded from analysis as it did not meet the definition of a registry. Articles were required to be published in journals and abstracts from meetings were excluded. Where discrepancies on articles to be included arose a third independent reviewer was utilised. Search was limited by MeSH and Key words and was limited to the English language. The search strategy utilised is included in *Table 1*.

Results

A total of 516 articles were identified using the search method outlined, of which 327 were identified for abstract or full text review. Of these articles 144 were included as

Table 1 The search strategy summary

Items	Specification
Date of search	01/07/2022
Databases and other sources searched	OVID and MEDLINE
Search terms used	Free
	Registry
	Database
	Register
	Regist
	Upper Tract Urothelial Carcinoma
	Upper Tract Transitional Cell carcinoma
	UTUC
	Urothelial Cancer
	Upper tract urothelial cancer
	Carcinoma, transitional cell
	Carcinomas, transitional cell
	Cell carcinoma, transitional
	Cell carcinomas, transitional
	Transitional cell carcinoma
	Transitional cell carcinomas
	Cancer, ureteral
	Cancer of ureter
	Cancer of the ureter
	Cancers, ureteral
	Neoplasm, ureteral
	Neoplasms, ureteral
	Neoplasms of ureter
	Ureter cancer
	Ureter, cancer of
	Ureter cancers
	Ureter neoplasm
	Ureter neoplasms
	Ureteral cancer
	Ureteral cancers
	Ureteral neoplasm
	Ureteral neoplasms

Table 1 (*continued*)

Table 1 (*continued*)

Items	Specification
	Kidney neoplasm
	MeSH
	Carcinoma, Transitional Cell
	Ureteral neoplasm
	Kidney neoplasm
	Registries
	Database management systems
Timeframe	1st July, 2002–1st July, 2022
Inclusion and exclusion criteria	Inclusion: registry based observational cohort study, English language, full text available
	Exclusion: single or multicentre once-off data collection that was not in a registry based format. Not published in a medical journal
Selection process	Two independent reviewers separately reviewed all articles, and 3rd reviewer if discrepancy

utilising registry-based data as the basis of the article. The results are grouped and summarised below.

Major North American general registries

Surveillance, epidemiology and end results (SEER) program

The SEER program collects and analyses data from population-based cancer registries that covers approximately 48% of the population in the United States (11). It is facilitated by the National Cancer Institute and routinely collects a wide array of data on numerous tumour types including UTUC. Rather than a single centralised data collection program SEER combines approximately 30 state and regional based cancer registries and allows access to collated data for research purposes. Data available is from 1975 until current and includes demographics, tumour type, tumour stage, initial treatments and some outcome data (12).

The SEER program is the registry with the highest number of published articles on UTUC, with 48 publications to date. Publications utilising the SEER project have increased substantially over the study time period with approximately 75% of publications arising in the last 5 years.

Articles describing incidence, demographics, presentation and diagnosis of UTUC were most common accounting for 23/48 articles, whilst comparison of treatments accounted for 19/48 articles. Since 2020, several articles utilising prognostic scoring systems have also been published using SEER data.

National Cancer Database (NCDB)

The NCDB is a registry of cancer patients treated at institutions accredited by the American Cancer Society and is a joint registry with the American College of Surgeons (13). The NCDB covers approximately 70% of the population of the United States of America and provides in depth demographic data as well as institutional data including institution volume. As data collection only occurs in hospitalised patients rather than population based the generalisability of these results may be more challenging (14). Data was made available to accredited institutions from 2013 and is republished annually.

NCDB was the second most commonly utilised registry in UTUC publications in the study period with 28 published articles. The vast majority of articles were published after 2017 with a steady increase in publications each year. Articles focusing on comparative treatment outcomes were the most common accounting for 18/28 articles, followed by incidence, demographics, presentation and diagnosis 9/28. In comparison to SEER only one article was published utilising the NCDB for a prognostic scoring system.

Other North American registries

The National Surgical Quality Improvement Program (NSQIP) database is the only CQR that was identified to contribute to the UTUC literature. NSQIP provides detailed patient and outcome data for major operations including nephroureterectomy and includes institution and clinician feedback and benchmarking (15). Patient outcomes are tracked up to 30 days and hence publications in UTUC focus on the early post-operative period only (16,17). Follow-up is active and includes screening hospital readmissions, medical records, private surgeons' rooms and direct patient follow-up. Data provided is collected by trained Surgical Clinical Reviewers and analysis is robust and risk-adjusted for patient health and surgical complexity to minimise bias. Over 195 risk-adjusted models are provided to clinicians and institutions and benchmarking occurs via rankings and gives clear indication of an institution's performance and areas of excellence or poor

performance. NSQIP has now expanded outside of North America and has program sites in Australia that are utilising the same registry format to analyse and improve outcomes although data has not been published.

Several other North American registries have utilised claims-based data to publish articles on UTUC although the number of published articles is low (18,19). The majority of these registries include routine data collected for health-related billing practices with analyses for the medical literature a secondary function. Other data from hospital admission registries that are non-specific to cancer or UTUC have also been utilised to assess demographic data of those presenting with UTUC (20).

International general registries

Other large nonspecific cancer registries have been utilised internationally to contribute to the UTUC literature. Scandinavian countries including Denmark (21,22), Norway (2), Iceland (23), and The Netherlands (24) have all contributed to the UTUC literature utilising large cancer and admission based registries. Other European nations have also utilised registry based data to contribute to their understanding of UTUC including Spain (25), Croatia (26), and The United Kingdom via the National Cancer Repository (27). There have also been joint efforts to understand rare cancers such as UTUC in multinational collaborations (28). In the Asia-Pacific region/countries including Japan (29,30), Taiwan (31), and Australia (32) have utilised broad cancer registries and admissions data to publish UTUC articles. Over 80% of articles appraised from these registries focused on local incidence, demographics, presentation and diagnosis of UTUC with the remaining 20% relating to comparative treatment outcomes.

Urology specific registries

The British Association of Urological Surgery (BAUS) registry assesses complications and outcomes up to 30 days post-surgery and has been utilised to assess nephroureterectomy outcomes in the short term (33). It provided a comparatively large patient sample of 863 patients and 119 centres over a 1-year period with detailed analysis of final pathology, operative technique, complications and short-term outcomes after surgery for UTUC. Whilst the BAUS registry is not specific to UTUC it does provide a deeper level of analysis for the operative treatment of UTUC

than non-specific registries. Further research questions of the BAUS registry aim to address outcomes of varying techniques of the managing the distal ureter at nephroureterectomy with at least 2 years of follow-up.

The Retrospective International Database of Invasive/ Advanced Cancer of the Urothelium (RISC) database is a retrospective international multicentre database that collected data on patients with advanced UC including UTUC. Data collection spanned from 2006–2011. There have been several published papers including predictive nomograms and descriptions of chemotherapy utilisation that include patients with UTUC in a broad base of UC patients (34-37).

The Japanese Urological Association Multi-Institutional National Registry was an observational cohort study including 348 institutions that took place in 2005. Data was retrospectively collected for patients diagnosed with UTUC and renal cell cancer; 1,500 UTUC patients were included in the registry which included detailed data regarding operative technique and outcomes in addition to demographic data. Several published articles including comparisons of laparoscopic *vs.* open technique and outcomes and prognostic factors for recurrent disease were published (38-41). There have been no further publications or data collection reported.

UTUC specific registries

Several national, multicentre UTUC registries have been created in the last 20 years in an attempt to understand current practice and outcomes. The French National Collaborative Database of Upper Urinary Tract Urothelial Cancer was a multi-institutional, retrospective cohort study including 20 centres from 1995–2010 that recorded approximately 500 patients who underwent curative intent treatment for UTUC. Published results included comparisons of oncological outcomes of radical segmental ureterectomy *vs.* nephroureterectomy, adjuvant chemotherapy, synchronous bladder tumours during nephroureterectomy and several online nomograms and prognostic tools (42-47). The registry does not appear to have continued after 2010 and no further studies have been published since 2014.

The Taiwan Upper Tract Urothelial Cancer Registry is a multicentre, observational registry that collects and analyses data on patients treated for UTUC. It includes 95 surgeons at 12 centres who retrospectively registered

patients from 1988–2021. In total 3,333 patients underwent nephroureterectomy in the 33-year study period and were included. Published results have included adverse prognostic factors for survival post nephroureterectomy and a comparison of endoscopic treatment vs radical nephroureterectomy for patients with tumours T2 or lower (48-50). The registry remains open and continues to enrol patients with likely further publications.

There has been a recent push to obtain an understanding of UTUC at an international level that will allow comparison and improve applicability of results. The Clinical Research Office of the Endourology Society (CROES)-UTUC registry is the largest and most complete UTUC registry published. The CROES-UTUC registry is an international, multicentre, prospective, observational cohort study with an enrolment period of 5 years (November 2014–November 2019) and a follow-up period of 5 years post inclusion (51). Any patient undergoing a diagnostic or therapeutic procedure for UTUC at participating centres was included. The primary objective is to describe the patterns of presentation, diagnosis, treatment and outcomes of those with UTUC. Further objectives include an assessment of evidence-based guideline adherence, post-operative complications, recurrence rates and mechanisms and comparison of individual treatment outcomes. Data capture is broad and includes demographic data, risk factors, treatments and complications as well as survival data at 1, 3 and 5 years after diagnosis. The registry aimed to recruit 3,000 patients in the 5-year study period.

Enrolment into CROES-UTUC began in 2014 and closed in 2019 with a small pool of published results to date. In total 2,451 patients were enrolled across 125 centres in 37 countries. A single study analysing flexible fibre optic *vs* digital ureteroscopy and enhanced *vs.* unenhanced imaging in the diagnosis and treatment of UTUC has been published with 5-year survival rates to date of writing (52). This study failed to find a significant difference in overall survival or disease-free survival between enhanced and unenhanced imaging techniques. Further analysis of mid and long-term are expected from the CROES-UTUC registry in the near future (51).

The Robotic Surgery for Upper Tract Urothelial Cancer Study (ROBUUST) is an international, multicentre, retrospective cohort study that systematically collects data on patients undergoing minimally invasive (robotic or laparoscopic) surgery for UTUC. The study includes 17 institutions around the world including the United States

502

Kealey et al. Utility of clinical registries in UTUC

Table 2 Origin of published articles including registry type and geographical distribution

Registry type	Publications
Total, n	144
Large generalised cancer or admission based, n/n [%]	117/144 [81]
SEER	48/117 [41]
NCDB	28/117 [24]
Other North American	10/117 [8]
Scandinavian	10/117 [8]
Other European	6/117 [5]
Asia-Pacific	15/117 [13]
Clinical quality, n [%]	1 [1]
Urology specific, n [%]	11 [8]
UTUC specific, n [%]	15 [10]

SEER, Surveillance, Epidemiology and End Results; NCDB, National Cancer Database; UTUC, upper tract urothelial cancer.

Table 3 Focus of the research question for publications utilising registry-based data in UTUC research

Research purpose focus	Number
Epidemiology & diagnosis	43
Incidence	10
Risk factors & presentation	25
Diagnosis	8
Treatment & outcomes	89
Oncological outcomes	32
Survival outcomes	45
Treatment strategies	8
Safety	4
Renal function assessment	1
Cost-assessment	2
Prognostic nomograms	8
Quality of life	1
Total	144

UTUC, upper tract urothelial cancer.

of America, China, Belgium, Italy and Korea and utilises a purpose-built registry for enrolment between February 2006 and March 2020. As of 2021, 877 patients had been enrolled into the registry. Research outputs from the registry have shown a significant intravesical recurrence rate of approximately 25% post-nephroureterectomy with risk factors including previous ureteroscopy, hypertension, positive surgical margin and transurethral bladder cuff resection (53). Results also failed to show a survival benefit from lymph node dissection at time of nephroureterectomy for UTUC (54). Most recently the ROBUUST data was utilised to create a pre-operative nomogram to predict renal insufficiency for cisplatin-based adjuvant therapy post minimally invasive nephroureterectomy (55). Further research outputs are expected in 2023 from the registry that is continuing to enrol.

Discussion

How is registry data utilised in UTUC research?

In total 144 articles were identified as utilising registry-based data to contribute to the understanding of UTUC from a wide variety of study designs and geographical locations (*Table 2*). Individual treatments and their outcomes were the most commonly evaluated aspects of UTUC followed by articles focusing on epidemiology, presentation or diagnosis of UTUC (*Table 3*). Articles relating to risk calculators and prognostic nomograms and quality of life were far less common and accounted for approximately 8% of the published literature.

Registry based publications have increased substantially within the study period with approximately 70% of articles published in the last 5 years of the 20-year study period (*Figure 1*). This increase in publications in the last 5 years is likely related to an increase in registry creation, but also an increase in the understanding of the utility of registries as more outputs are seen in leading publications. Data from registries in some cases have also become more easily accessible to researchers, such as the NCDB which in 2012 allowed access to the registry to involved institutions with the first UTUC publication from this source in 2017. Since that initial publications there have been at least 27 articles published as researchers and clinicians have come to
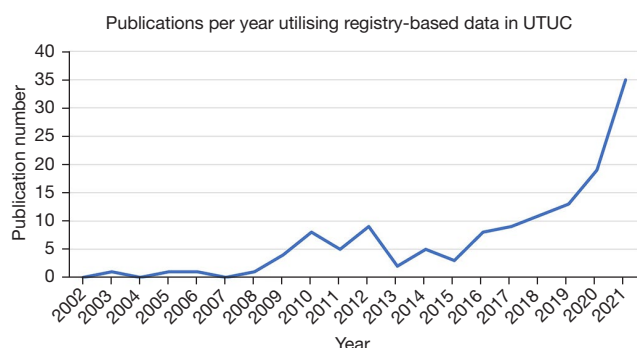
Publications per year utilising registry-based data in UTUC

Figure 1 Number of publications per year utilising registry-based methodology in UTUC. UTUC, upper tract urothelial cancer.

understand the dataset and its potential utility.

Benefits of registry use in UTUC

The most potent strength of registries in UTUC is the sheer volume of patients that are able to be recruited and followed up in a registry-based study format. CROES-UTUC registry has been able to recruit over 2,000 patients in a 5-year period and have excellent follow-up rates to 5 years (52), whilst NCDB publications have been able to analyse up to 8,000 patients in some instances (56). This is in stark contrast to randomised control trials that can often be underpowered and require recruitment over many years and centres to enrol small patient samples. Comparative cost compared to randomised controlled trials (RCTs) is another significant benefit that allows for economical recruitment of such large patient numbers (57). Registry based data collection can occur at a fraction of the cost of running clinical trials, which is especially true in rare malignancies such as UTUC, where multiple sites recruiting only small patient numbers are required to gain a sufficient sample size.

Limitations of registry-based data use

There are several limitations of large databases when analysing UTUC. Registry-based data may be more prone to selection bias due to an inability to randomise patients. This allows for inherent and often unmeasured variables to impact on the various treatments that individual patients receive. Non-specific datasets, such as SEER and NCDB, may be more prone to this given the non-specific nature of the data collected (12). Selection bias can lead to a

comparison of interventions occurring in very different patient cohorts whose differing outcomes may not be solely attributable to the treatment being utilised. Non-participation bias will also be present in these studies as treatment for UTUC is an inclusion criterion in nearly all utilised registries, therefore excluding those that never receive treatment.

The quality of the registry is reliant on the data that is input into the registry. Data quality is nearly impossible to appraise however and occurred in very heterogenous ways depending on the registry in this review (58). In larger, non-specific registers much of this data was either automated or entered by researchers not involved in the care of the patient. In contrast most of the UTUC specific and smaller registries utilised the treating clinician or health team to input data. This may allow for more granular detailed data, but also allows for bias in the data that is collected and analysed. Specifically trained expert data collectors are the gold-standard and occurred in only a small proportion of the included registries. Incomplete data is a common problem no matter the collection method, and inadequate follow-up or documentation may mean that important events and outcomes, such as adverse events, are missed and do not contribute to analysis. Data time points are often dictated by the patient's interactions with the health system, rather than at set intervals as is the case with RCTs, and hence there may be further lack of capture of outcomes of interest.

Protocol publication occurred in only a small pool of the UTUC specific registries. Protocol publication ensures transparency in the research, minimises publication bias and prevents selective reporting of outcomes. Assessment of registry quality is more challenging than RCT critical appraisal and whilst some published assessment tools have been published these have not been validated or widely adopted (59). Publication of the registry protocol and objectives allows for improved peer-review and validity of results and should be part of best-practice in registry creation.

Future directions

CQR have the ability to provide feedback and benchmarking for clinicians, hospitals and organisations and are an increasingly prevalent quality improvement tool (60). Improvement in evidence-based guideline adherence, improved care availability and overall improvement in the quality of care are major benefits of CQR as is a reduction

in the cost of care (10). Such registries have had significant success in other urological malignancies such as prostate cancer and have the ability to cover large cohorts (61). The NSQIP was the only identified example of a CQR in this narrative review and provides detailed clinician feedback up to 30 days post-operatively. There is however a large scope for UTUC specific or large cancer registries to become CQR if they were to feedback to participating centres on a scheduled, routine basis. Disease specific CQR are more resource intensive, however, may attract improved participation given the value of structured reporting and quality improvement processes.

Whilst RCTs remain the gold-standard methodology for treatment comparison, in recent years the registry-based RCT has been utilised to efficiently analyse and follow-up patients in non-urological areas (62). Registry based RCT's embed elements of the RCT, such as randomisation and other data collection into the registry. The registry then collects data as part of routine care. Such data is then utilised as trial data that allows for analysis. This model lends itself particularly well to comparative effectiveness research such as comparison of outcomes of interventions that are potentially equivalent including nephroureterectomy *vs.* endoscopic management of low-risk tumours. Such analysis requires registries that are well planned, executed and maintained, however has the ability to retain the strengths of an RCT while avoiding the high failure rates, significant costs and lack of external validity (63). This may be an especially attractive methodology for a rare cancer such as UTUC with its significant recruiting difficulties.

Conclusions

The utilisation of registry-based data in the UTUC literature has increased exponentially over the 20-year review period. Whilst utilisation of large, generalised cancer registries accounts for the majority of the literature in UTUC there are exciting, large UTUC specific registries that will report in the coming years and are likely to contribute more granular, generalisable data for the diagnosis and treatment of UTUC. The ability to provide feedback and benchmarking to clinicians to improve safety and quality should be a consideration in future registry formation as should registry based RCT's.

Acknowledgments

Footnote

References

1. Ouzzane A, Rouprêt M, Leon P, et al. Epidemiology and risk factors of upper urinary tract tumors: literature review for the yearly scientific report of the French National Association of Urology. Prog Urol 2014;24:966-76.
2. Almås B, Halvorsen OJ, Johannesen TB, et al. Higher than expected and significantly increasing incidence of upper tract urothelial carcinoma. A population based study. World J Urol 2021;39:3385-91.
3. Soualhi A, Rammant E, George G, et al. The incidence and prevalence of upper tract urothelial carcinoma: a systematic review. BMC Urol 2021;21:110.

4. School of Public Health and Preventative Medicine, Monash University. Registry Science Handbook. 2013.

5. Gliklich RE, Dreyer NA, Leavy MB. editors. Registries for Evaluating Patient Outcomes: A User's Guide. Washington, DC, USA: United States Government Printing Office, 2014.

6. Hameed BMZ, S Dhavileswarapu AVL, Naik N, et al. Big Data Analytics in urology: the story so far and the road ahead. Ther Adv Urol 2021;13:1756287221998134.

7. Tyson MD, Barocas DA. Improving quality through clinical registries in urology. Curr Opin Urol 2017;27:375-9.

8. Mauch H, Kaur J, Irwin C, et al. Design, implementation, and management of an international medical device registry. Trials 2021;22:845.

9. Ahern S, Evans SM, Hopper I, et al. Clinical quality registries for clinician-level reporting: strengths and limitations. Med J Aust 2018;208:323.

10. Hoque DME, Kumari V, Hoque M, et al. Impact of clinical registries on quality of patient care and clinical outcomes: A systematic review. PLoS One 2017;12:e0183667.

11. National Cancer Institute. SEER Acknowledgment of Treatment Data Limitations. 2022. Available online: https://seer.cancer.gov/data-software/documentation/seerstat/nov2021/treatment-limitations-nov2021.html#:~:text=Three%20main%20limitations%20affect%20recommended,interpretation%20of%20sequence%20data%20variables

12. Scosyrev E, Messing J, Noyes K, et al. Surveillance Epidemiology and End Results (SEER) program and population-based research in urologic oncology: an overview. Urol Oncol 2012;30:126-32.

13. American College of Surgeons. National Cancer Database. 2022. Available online: https://www.facs.org/quality-programs/cancer-programs/national-cancer-database/

14. Boffa DJ, Rosen JE, Mallin K, et al. Using the National Cancer Database for Outcomes Research: A Review. JAMA Oncol 2017;3:1722-8.

15. American College of Surgeons. National Surgical Quality Improvement Program. 2022. Available online: https://www.facs.org/quality-programs/data-and-registries/acs-nsqip/

16. Hanske J, Sanchez A, Schmid M, et al. A Comparison of 30-Day Perioperative Outcomes in Open Versus Minimally Invasive Nephroureterectomy for Upper Tract Urothelial Carcinoma: Analysis of 896 Patients from the American College of Surgeons-National Surgical Quality Improvement Program Database. J Endourol 2015;29:1052-8.

17. Soodana-Prakash N, Balise R, Nahar B, et al. Perioperative outcomes and complication predictors associated with open and minimally invasive nephroureterectomy. Can J Urol 2018;25:9395-400.

18. Geynisman DM, Broughton E, Hao Y, et al. Real-world treatment patterns and clinical outcomes among patients with advanced urothelial carcinoma in the United States. Urol Oncol 2022;40:195.e1-195.e11.

19. Tinay I, Gelpi-Hammerschmidt F, Leow JJ, et al. Trends in utilisation, perioperative outcomes, and costs of nephroureterectomies in the management of upper tract urothelial carcinoma: a 10-year population-based analysis. BJU Int 2016;117:954-60.

20. Deuker M, Rosiello G, Stolzenbach LF, et al. Sex- and Age-Related Differences in the Distribution of Metastases in Patients With Upper Urinary Tract Urothelial Carcinoma. J Natl Compr Canc Netw 2021;19:534-40.

21. Azawi NH, Næraa SH, Subhi Y, et al. Oncological outcomes of radical nephroureterectomy for upper urinary tract urothelial neoplasia in Denmark. Scand J Urol 2020;54:58-64.

22. Pottegård A, Hallas J, Jensen BL, et al. Long-Term Lithium Use and Risk of Renal and Upper Urinary Tract Cancers. J Am Soc Nephrol 2016;27:249-55.

23. Björnsson O, Jónsson E, Guðmundsson EO, et al. Operative management in patients with upper tract urothelial carcinoma in Iceland: a population-based study. Scand J Urol 2021;55:197-202.

24. van Doeveren T, van der Mark M, van Leeuwen PJ, et al. Rising incidence rates and unaltered survival rates for primary upper urinary tract urothelial carcinoma: a Dutch population-based study from 1993 to 2017. BJU Int 2021;128:343-51.

25. Fernandez Aparicio T, Galan Llopis JA, Cansino Alcaide R, et al. Incidence of upper tract urothelial carcinoma in Spain. Actas Urol Esp (Engl Ed) 2020;44:512-8.

26. Medunjanin D, Sonicki Z, Vena JE, et al. Geographic distribution and risk of upper urothelial carcinomas in Croatia, 2001-2011. BMC Cancer 2019;19:950.

27. Eylert MF, Hounsome L, Verne J, et al. Prognosis is deteriorating for upper tract urothelial cancer: data for England 1985-2010. BJU Int 2013;112:E107-13.

28. Visser O, Adolfsson J, Rossi S, et al. Incidence and survival of rare urogenital cancers in Europe. Eur J Cancer 2012;48:456-64.

29. Nagumo Y, Kawai K, Kojima T, et al. Prognostic impact of non-urothelial carcinoma of the upper urinary tract: Analysis of hospital-based cancer registry data in Japan. Int

J Urol 2021;28:54-60.

30. Shiga M, Nagumo Y, Chihara I, et al. Discrepancy between clinical and pathological T stages in upper urinary tract urothelial carcinoma: Analysis of the Hospital-Based Cancer Registry data in Japan. Int J Urol 2021;28:814-9.

31. Wu J, Chen S, Wu X, et al. Trends of incidence and prognosis of upper tract urothelial carcinoma. Bosn J Basic Med Sci 2021;21:607-19.

32. Woodford R, Ranasinghe W, Aw HC, et al. Trends in incidence and survival for upper tract urothelial cancer (UTUC) in the state of Victoria--Australia. BJU Int 2016;117 Suppl 4:45-9.

33. Connolly SS, Rochester MA; . Nephroureterectomy surgery in the UK in 2012: British Association of Urological Surgeons (BAUS) Registry data. BJU Int 2015;116:780-90.

34. Bamias A, Tzannis K, Harshman LC, et al. Impact of contemporary patterns of chemotherapy utilization on survival in patients with advanced cancer of the urinary tract: a Retrospective International Study of Invasive/Advanced Cancer of the Urothelium (RISC). Ann Oncol 2018;29:361-9.

35. Necchi A, Sonpavde G, Lo Vullo S, et al. Nomogram-based Prediction of Overall Survival in Patients with Metastatic Urothelial Carcinoma Receiving First-line Platinum-based Chemotherapy: Retrospective International Study of Invasive/Advanced Cancer of the Urothelium (RISC). Eur Urol 2017;71:281-9.

36. Bamias A, Tzannis K, Liontos M, et al. Adherence to cisplatin-based regimens prescription in "fit" patients fulfilling platinum eligibility criteria. Impact on outcomes: a retrospective international study of invasive/advanced cancer of the urothelium (RISC) analysis. Ann Oncol 2016;27. doi: 10.1093/annonc/mdw373.27.

37. Bamias A, Tzannis K, Liontos M, et al. Patterns of chemotherapy utilization in metastatic urothelial cancer (mUC): analysis from the retrospective international study of invasive/advanced cancer of the urothelium (RISC) database. Ann Oncol 2016;27. doi: 10.1093/annonc/mdw373.26.

38. Hara T, Fujimoto H, Kondo T, et al. Active heavy cigarette smoking is associated with poor survival in Japanese patients with advanced renal cell carcinoma: sub-analysis of the multi-institutional national database of the Japanese Urological Association. Jpn J Clin Oncol 2017;47:1162-9.

39. Hara T, Fujimoto H, Sakura M, et al. Prognostic factors of recurrent disease in upper urinary tract urothelial cancer after radical nephroureterectomy: Subanalysis of the multi-

institutional national database of the Japanese Urological Association. Int J Urol 2015;22:1013-20.

40. Miyazaki J, Nishiyama H, Fujimoto H, et al. Impact of smoking on the age at diagnosis of upper tract urothelial carcinoma: Subanalysis of the Japanese Urological Association multi-institutional national database. Int J Urol 2015;22:1023-7.

41. Miyazaki J, Nishiyama H, Fujimoto H, et al. Laparoscopic Versus Open Nephroureterectomy in Muscle-Invasive Upper Tract Urothelial Carcinoma: Subanalysis of the Multi-Institutional National Database of the Japanese Urological Association. J Endourol 2016;30:520-5.

42. Ku JH, Moon KC, Jung JH, et al. External validation of an online nomogram in patients undergoing radical nephroureterectomy for upper urinary tract urothelial carcinoma. Br J Cancer 2013;109:1130-6.

43. Pignot G, Colin P, Zerbib M, et al. Influence of previous or synchronous bladder cancer on oncologic outcomes after radical nephroureterectomy for upper urinary tract urothelial carcinoma. Urol Oncol 2014;32:23.e1-8.

44. Colin P, Ouzzane A, Pignot G, et al. Comparison of oncological outcomes after segmental ureterectomy or radical nephroureterectomy in urothelial carcinomas of the upper urinary tract: results from a large French multicentre study. BJU Int 2012;110:1134-41.

45. Audenet F, Colin P, Yates DR, et al. A proportion of hereditary upper urinary tract urothelial carcinomas are misclassified as sporadic according to a multi-institutional database analysis: proposal of patient-specific risk identification tool. BJU Int 2012;110:E583-9.

46. Berod AA, Colin P, Yates DR, et al. The role of American Society of Anesthesiologists scores in predicting urothelial carcinoma of the upper urinary tract outcome after radical nephroureterectomy: results from a national multi-institutional collaborative study. BJU Int 2012;110:E1035-40.

47. Vassilakopoulou M, de la Motte Rouge T, Colin P, et al. Outcomes after adjuvant chemotherapy in the treatment of high-risk urothelial carcinoma of the upper urinary tract (UUT-UC): results from a large multicenter collaborative study. Cancer 2011;117:5500-8.

48. Chen YT, Yu CC, Yeh HC, et al. Endoscopic management versus radical nephroureterectomy for localized upper tract urothelial carcinoma in a high endemic region. Sci Rep 2021;11:4040.

49. Jeldres C, Lughezzani G, Sun M, et al. Segmental ureterectomy can safely be performed in patients with transitional cell carcinoma of the ureter. J Urol

2010;183:1324-9.

50. Chen IA, Chang CH, Huang CP, et al. Factors Predicting Oncological Outcomes of Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma in Taiwan. Front Oncol 2022;11:766576.

51. Baard J, Cormio L, Cavadas V, et al. Contemporary patterns of presentation, diagnostics and management of upper tract urothelial cancer in 101 centres: the Clinical Research Office of the Endourological Society Global upper tract urothelial carcinoma registry. Curr Opin Urol 2021;31:354-62.

52. Soria F, Laguna MP, Roupret M, et al. Flexible fibre optic vs digital ureteroscopy and enhanced vs unenhanced imaging for diagnosis and treatment of upper tract urothelial carcinoma (UTUC): results from the Clinical Research Office of the Endourology Society (CROES)-UTUC registry. BJU Int 2021;128:734-43.

53. Katims AB, Say R, Derweesh I, et al. Risk Factors for Intravesical Recurrence after Minimally Invasive Nephroureterectomy for Upper Tract Urothelial Cancer (ROBUUST Collaboration). J Urol 2021;206:568-76.

54. Hakimi K, Carbonara U, Djaladat H, et al. Outcomes of Lymph Node Dissection in Nephroureterectomy in the Treatment of Upper Tract Urothelial Carcinoma: Analysis of the ROBUUST Registry. J Urol 2022;208:268-76.

55. Wu Z, Chen Q, Djaladat H, et al. A Preoperative Nomogram to Predict Renal Function Insufficiency for Cisplatin-based Adjuvant Chemotherapy Following Minimally Invasive Radical Nephroureterectomy (ROBUUST Collaborative Group). Eur Urol Focus 2022;8:173-81.

56. Almassi N, Gao T, Lee B, et al. Impact of Neoadjuvant Chemotherapy on Pathologic Response in Patients With Upper Tract Urothelial Carcinoma Undergoing Extirpative Surgery. Clin Genitourin Cancer 2018;16:e1237-42.

57. Karanatsios B, Prang KH, Verbunt E, et al. Defining key design elements of registry-based randomised controlled trials: a scoping review. Trials 2020;21:552.

58. Prang KH, Karanatsios B, Verbunt E, et al. Clinical registries data quality attributes to support registry-based randomised controlled trials: A scoping review. Contemp Clin Trials 2022;119:106843.

59. European Network for Health Technology Assessment. Registry Evaluation and Quality Standards Tool (REQueST). 2021. Available online: https://www.eunethta.eu/request-tool-and-its-vision-paper/

60. Australian Commission on Safety and Quality in Health Care. Framework for Australian clinical quality registries. 2014.

61. O'Callaghan M, Papa N, Pase M, et al. Patterns of care for prostate cancer treatment and improving outcomes - are national registries the answer? BJU Int 2021;128 Suppl 1:6-8.

62. Li G, Sajobi TT, Menon BK, et al. Registry-based randomized controlled trials- what are the advantages, challenges, and areas for future research? J Clin Epidemiol 2016;80:16-24.

63. Foroughi S, Wong HL, Gately L, et al. Re-inventing the randomized controlled trial in medical oncology: The registry-based trial. Asia Pac J Clin Oncol 2018;14:365-73.