Treatment decision-making in localised kidney cancer

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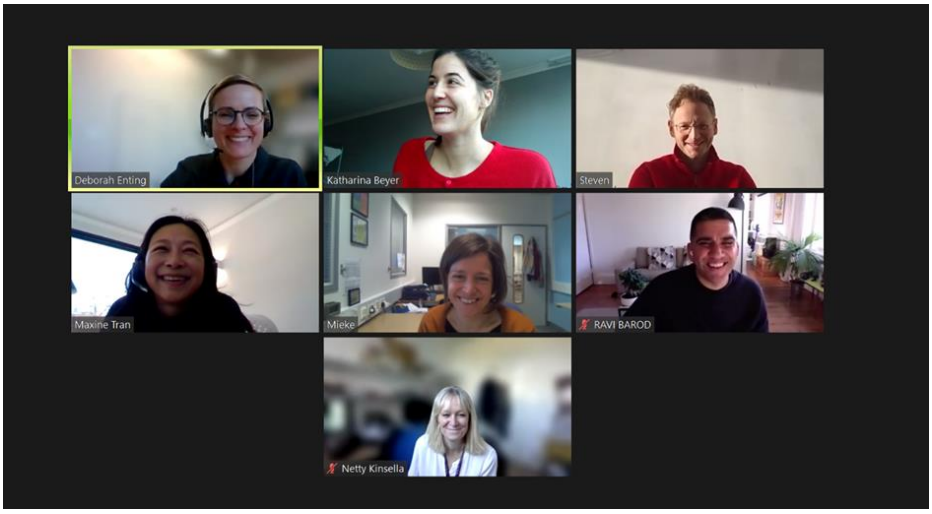

Abstract

Background and aims: Over the past two decades, there has been a significant increase in the number of patients diagnosed with localised kidney cancer. While surgery has been the standard treatment in clinically fit patients, less invasive treatments like ablation and active surveillance are now also available.

This PhD, therefore, aims to understand the multifactorial process of decision-making, providing an understanding of the support patients require in the treatment decision-making process using a six-stage approach.

Methods: This applied thesis uses a mixed methods multi-stage design with an emergent approach. To improve the objectivity and structure of the work, the theoretical framework of Glatzer et al. was used, which comprises three domains of decision-making: disease-specific characteristics, decision-maker specific factors, and contextual factors. As a result, the methodological plan of this PhD contains the following six steps.

1. Systematic literature review to understand the patient experience during treatment-decision making.
2. Mixed methods systematic review to understand barriers and facilitators to treatment decision-making overall.
3. Cross-sectional study to understand whether the experiences of patients during the COVID-19 pandemic impacted any of the data gathered in 1) and 2) (i.e., contextual factor).
4. Systematic review on heterogeneity in outcome definition and reporting to provide a deeper understanding of the diversity of outcomes used in clinical guidelines.
5. Synthesis of step 1-4 to develop a qualitative semi-structured interview guide.
6. Semi-structured interviews and focus groups to pilot the discussion guide and to improve the understanding of decision-maker related factors from a patient perspective and their supportive care needs across Europe.

Results: The first systematic literature review identified the limited evidence looking at patient decision-making as I identified only five studies. Currently most of the literature focuses on decision-making from a Health Care Professional (HCP)'s view. Hence, this work was extended with a mixed methods systematic review which identified further barriers and facilitators to treatment decision-making across the three domains (kidney cancer specific characteristics, decision maker related factors, and contextual factors): prognostic factors, patient demographics, predictive tools, patient-physician interaction, infrastructure, access to the healthcare system, and economic variables.

These two reviews were further enriched with the cross-sectional survey evaluating COVID-19 as a contextual factor. Thirty-six HCPs from the UK responded, and five main themes emerged: diagnostics, treatment, consultations and supportive care, HCP satisfaction, and delivery of future kidney cancer care. The COVID-19 pandemic was found to have a significant impact on the practice and perspective of HCPs working in kidney cancer in the NHS during the first six months of the outbreak.

To explore and understand the language used in kidney cancer diagnostics and the potential impact on decision-making, a systematic review on outcome reporting heterogeneity identified multiple terms used to refer to similar outcomes and variations in definitions of staging.

To enable a deeper insight into the findings from the previous stages, a preliminary semi-structured interview guide was formulated. Finally, to test the developed discussion guide and develop a codebook enabling a robust analysis, three focus groups and four interviews on decision-maker-related factors with patients across Germany, the UK, and the Netherlands were conducted. The most prominent themes discussed were shared decision-making, supportive care, and patient empowerment. Participants also highlighted important facilitators for the decision-making process: access to charities, support groups, peer support, Cancer Nurse Specialist and psycho-oncology support, a shared decision-making environment, and digital and non-digital information tools.

Conclusion: The combined findings of this six-step approach offer insights into the treatment decision-making process in localised kidney cancer. It was found that patients are keen to actively participate in this decision-making process, but factors, such as changes in the way clinicians and patients engage in consultations as a result of the COVID-19 pandemic, make this challenging. Moreover, the emotional toll of the cancer journey and the current heterogeneity of outcome reporting in clinical guidelines require consideration. The findings from this PhD thesis can thus be used to further develop research focused on establishing appropriate shared decision-making tools and supportive care measures.

Table of contents

Acknowledgement **3**

Abstract **5**

List of Publications **13**

List of Tables **14**

List of Figures **15**

List of Abbreviations **17**

Chapter 1: Introduction and Research Objectives **20**

Chapter 2: Background **22**

2.1. The Kidney 22

2.2. Kidney Cancer 23

2.2.1. Epidemiology 23

2.2.2. Kidney Cancer Subtypes and Pathophysiology 24

2.2.2.1. Clear Cell RCC 25

2.2.2.2. Papillary RCC 26

2.2.2.3. Chromophobe RCC 26

2.2.2.4. Benign Renal Tumours 26

2.2.3. Grading 27

2.2.4. Staging 28

2.2.5. Anatomic Classification Systems 29

2.2.6. Risk Factors 29

2.2.7. Screening 31

2.2.8. Modes of Presentation 31

2.3. Management of Localised Kidney Cancer 34

2.4. Current Practice in Localised Kidney Cancer Treatment 36

2.4.1. Treatment Pathway 37

2.4.2. Introducing the Decision-making Process: linking theories with the context of localised kidney cancer 38

2.4.3. Introduction to Shared Decision-making in Localised Kidney Cancer 39

2.5. Summary of Chapter 2 40

Chapter 3: Research Method and Methodological Plan **41**

3.1. Research Method: Applied Research 41

3.2. Mixed Methods Approach 42

3.2.1. Multistage Design 42

3.2.2. Emergent Mixed Methods Approach 43
3.3. Theoretical Framework 43
3.4. Methodological Plan 45
3.4.1. Understanding the Patient Experience in the Treatment Decision-making Process… 46
3.4.2. Barriers and Facilitators to Decision-making 46
3.4.3. Contextual Factors Involved in the Treatment Decision-making Process 47
3.4.4. Kidney Cancer Specific Characteristics Related to the Treatment Decision-making Process 47
3.4.5. Data Synthesis of Stages 1-4 48
3.4.6. Decision Maker Related Factors for the Treatment Decision-making Process . 48
3.5. Summary of Chapter 3 49
Chapter 4. Understanding the Barriers and Facilitators Driving Treatment Decisions in Localised Kidney Cancer 50
4.1. Systematic Review: Factors that influence patients' views on treatment decision-making in stage I kidney cancer: a commentary piece 50
4.1.1. Introduction 50
4.1.2. Methods 51
4.1.3. Results 51
4.1.4. Discussion 54
4.1.4.1. Limitations 54
4.1.5. Conclusion 54
4.2. Mixed Methods Systematic Review: The current evidence for factors that influence treatment decision-making in localised kidney cancer 56
4.2.1. Introduction 56
4.2.2. Methods 57
4.2.3. Results 64
4.2.4. Evidence synthesis 68
4.2.5. Discussion 71
4.2.6. Limitations 76
4.2.7. Conclusion 76
4.3. Summary of Chapter 4 77
Chapter 5. Contextual Factors: Cross-sectional survey to understand the impact of COVID-19 on treatment decision-making in localised kidney cancer 78
5.1. How did the COVID-19 pandemic impact the National Healthcare System in the UK during the first 6 months - a cross-sectional survey 79

5.1.1. Methods....79
5.1.2. Results....80
5.1.3. Discussion....87
5.1.4. Conclusion....89
5.2. Summary of Chapter 5....91
Chapter 6. Kidney Cancer Specific Factors: The heterogeneity in Outcome Definition and Reporting in Localised Kidney cancer....92
6.1. Systematic Review of the Heterogeneity in Outcome Definition and Reporting in Localised Kidney cancer....92
6.1.1. Aims and Objectives....93
6.1.2. Identification of Relevant Studies....93
6.1.3. Evidence Synthesis....96
6.1.4. Discussion....110
6.1.5. Conclusion....112
6.2. Summary of Chapter 6....113
Chapter 7. Data Synthesis to Develop a Semi-structured Interview Guide for Focus Groups and Interviews....114
7.1. Introduction....114
7.2. Identifying the Research Method for Using the Semi-structured Interview Guide....115
7.3. Retrieving and Using Previous Knowledge....116
7.3.1. Critical Evaluation of Existing Knowledge....116
7.3.2. The Need for Additional Empirical Data....118
7.4. Formulating the Preliminary Semi-structured Interview Guide....118
7.5. Pilot Testing of the Interview Guide....120
7.6. Summary of Chapter 7....122
Chapter 8. Decision Maker Related Factors: Focus Groups/ Interviews with Patients....123
8.1. Introduction....123
8.2. Methods....124
8.2.1. Ethics....124
8.2.2. Semi-structure Interview Guide....125
8.2.3. Sampling....125
8.2.4. Participants....125
8.2.5. Sample Size....126
8.2.6. Recruiting Patients....127

8.2.7. Consent 127
8.2.8. Anonymity and Confidentiality 127
8.2.9. Transcription and Translation 128
8.2.10. Data Analysis 128
8.3. Results 129
8.3.1. Participant Demographics and Cancer Characteristics 129
8.3.2. Codebook Development 131
8.3.3. Codebook Testing and Refinement 131
8.3.4. Coding and Identifying Themes 132
8.3.5. Quality Control of the Codebook 133
8.3.6. Qualitative Data Analysis 134
8.4. Discussion 151
8.4.1. Identified Themes that Impacted the Decision-making Process 153
8.4.2. Supportive Care Needs 158
8.5. Summary of Chapter 8 163
Chapter 9: Overall Conclusion and Future Directions 164
9.1. Summary of the Thesis 164
9.2. Future Research Direction 167
Addendum: The Impact of the COVID-19 pandemic on this thesis 170
References 171
Appendix 1: Factors that influence patients' view on treatment decision-making in localised kidney cancer (Poster) 186
Appendix 2: Factors that influence patients' view on treatment decision-making in localised kidney cancer 187
Appendix 3: The Current Evidence For Factors that Influence Treatment Decsion Making in Localized Kidney Cancer: A Mixed Methods Systematic Review 191
Appendix 4: How does COVID-19 impact treatment decision-making for clinicans in localised kidney cancer 204
Appendix 5: A Systematic Review of Heterogeneity in Outcome Definition and Reporting in Localised Renal Cancer 206
Appendix 6: Ethics application KCL 215
Appendix 7: COREQ checklist 216
Appendix 8: Semi-structured Topic guide 218
Appendix 9: Invitation letter patients 221
Appendix 10: Information Sheet for Participants 222
Appendix 11: Consent 227

Endorsement

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The “Exploring the perspectives of patients with localised kidney cancer on their treatment decisions: a qualitative study” abstract presented at the International Kidney Cancer Symposium (2023) won the 3. Merit Award for best abstracts.

List of Publications

Publications Included in Thesis.

Abstracts

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Manuscripts

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5. Beyer, K., Widdershoven, C., Kinsella, N., et al.: A systematic review of heterogeneity in outcome reporting, definition, and measurement in localised kidney cancer. European Urology Open Science, 2022.

Blog post

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List of Tables

Table 1: WHO classification of RCC subtypes 24

Table 2: Fuhrman grade classification 27

Table 3: ISUP/ WHO grading system for ccRCC and pRCC 28

Table 4: TNM stages for renal cell carcinoma 28

Table 5: Most common symptoms 32

Table 6: Keyword search terms 51

Table 7: Summary table- Factors influencing patient decision-making 53

Table 8: Search strategy mixed methods review 57

Table 9: Legend- PREF 58

Table 10: PREF Checklist 59

Table 11: Legend STROBE 60

Table 12: Assessment of the literature using the modified STROBE checklist 61

Table 13: Domains and factors that influence treatment decision-making 66

Table 14: Results of the cross-sectional survey 83

Table 15: Outcomes classified 98

Table 16: Outcomes reported in each included study after classification within the taxonomy suggested by Dodd et al. 102

Table 17: Semi-structured interview guide developed by using the knowledge gained in Stage 1-4 119

Table 18: Codebook example 131

Table 19: Need for action to be implemented in practice 151

Table 20: Supportive care needs 158

List of Figures

Figure 1: Methodological overview 21

Figure 2: Location and anatomy of the kidney 23

Figure 3: Imaging modalities.....33

Figure 4: Illustration of a Kidney Biopsy 33

Figure 5: Illustration of a localised kidney cancer pathway 38

Figure 6: Five-Step Framework for Applied Research 41

Figure 7: Conceptual model of decision-making in oncology.....45

Figure 8: Methodological overview of the thesis 46

Figure 9: Modified Decision-Making Framework 47

Figure 10: Methodology overview- Factors that influence patients' views on treatment decision-making in stage I kidney cancer: a commentary piece 50

Figure 11: PRISMA patient preference SR 52

Figure 12: Methodology overview- 1B Mixed methods systematic review: The current evidence for factors that influence treatment decision-making in localised kidney cancer: a mixed methods systematic review 56

Figure 13: PRISMA Flow chart for mixed methods systematic review on barriers and facilitators to treatment decision making 65

Figure 14: Domains that influence treatment decision-making.....67

Figure 15: Methodology overview: 3. Contextual factors involved in the treatment decision-making process 78

Figure 16: Treatment pathway during the 1st wave of the Covid-19 pandemic up to the point of decision-making.....80

Figure 17: Methodology overview: Kidney Cancer Specific Factors: The heterogeneity in Outcome Definition and Reporting in Localised Kidney cancer 92

Figure 18: Search Strategy 94

Figure 19: PRISMA- SR outcomes 96

Figure 20: applied Dodd et al. taxonomy.....97

Figure 21: Methodology: Data synthesis to develop a semi-structured interview guide for focus groups and interviews 114

Figure 22: The phases of a Semi-structured interview guide developed based on synthesis. 115

Figure 23: Synthesis of Stage 1 & 2 (Step 1-3).....117

Figure 24: Synthesis of Critical existing knowledge based on the systematic reviews (Stage 1 & 2) and the additional empirical data (Stage 3 & 4; step 1-4).....118

Figure 25: Methodological overview: Decision maker related Factors: Focus groups/ interviews with patients 123

Figure 26: Recruitment process via IKCC across the three countries.....127

Figure 27: Modified version of the process of code development used to present the steps applied to develop the codebook.....129

Figure 28: Participation information of the focus groups and interview participants.....131

Figure 29: Focus group themes identified (decision making).....133

Figure 30: Focus group themes identified (supportive care) 133

Figure 31: Methodology overview: Overall conclusion and future directions 164

List of Abbreviations

ABC	Arterial Based Complexity Scoring System
AE	Adverse events
AJCC	American Joint Committee for Cancer Staging and End Result
AML	Angiomyolipoma
AS	Active Surveillance
BAUS	British Association of Urological Surgeons
BHD	Birt-Hogg-Dubé syndrome
CARE	Convalescence and Recovery Evaluation
CARES-SF	Cancer Rehabilitation Evaluation System-Short Form
ccRCC	Clear cell RCC
chRCC	Chromophobe RCC
CKD	Chronic Kidney disease
CNS	Cancer Nurse Specialist
COMET	Core Outcome Measures in Effectiveness Trials
COREQ	COnsolidated criteria for REporting Qualitative research checklist
COS	Core Outcome Sets
COVID-19	Coronavirus pandemic
CSS	Cancer-specific survival
DE	Germany
DISSRM	Delayed Intervention and Surveillance Registry
EAU	European Association of Urology
EMUC	European Multidisciplinary Congress on Urological Cancers
EORTC	European Organisation for Research and Treatment of Cancer

EORTC-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FACT-G	Functional Assessment of Cancer Therapy-General
FT	Focal therapy
GQoL	Global Quality of Life
HADS	Hospital Anxiety and Depression Scale
HCPs	Health care professionals
HR	Hazard ratios
IES	Impact of Events Scale
IKCC	International Kidney Cancer Coalition
ISUP	International Society of Urological Pathology
JBI	Joanna Briggs Institute
KCCURE	Kidney Cancer Association
KCUK	Kidney Cancer UK
MDM	Multidisciplinary team meeting
MDT	Multidisciplinary team
MUIS	Mishel Uncertainty in Illness Scale
NCRA	National Cancer Registration and Analysis
NICE	National Institute for Health and Care Excellence
NHS	National Health Institute
NL	The Netherlands
NSS	Nephron sparring surgery
OC	Oncocytoma
OPN	Open partial nephrectomy
OS	Overall survival

PADUA	Preoperative Aspects and Dimensions Used for an Anatomical
PN	Partial Nephrectomy
pRCC	Papillary RCC
PREFS	Purpose, Respondents, Explanation, Findings, and Significance
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PROs	Patient-reported outcomes
QLQ-C30	Quality-of-Life Core Questionnaire
RAPN	Robotic-assisted laparoscopic partial nephrectomy
RCC-SI FKSI	Functional Assessment of Cancer Therapy-Kidney Symptom Index
RCT	Randomised Control Trial
Renal	Cell Carcinoma-Symptom Index
RN	Radical nephrectomy
RPN	Robotic partial nephrectomy
SEER	Surveillance, Epidemiology, and End Results
SES	Socio Economic Status
SF-12	Short Form 12
SF-36	RAND medical outcome survey Short Form 36
SR	Systematic reviews
STROBE	Strengthening The Reporting of OBservational Studies in Epidemiology
TNM	Tumour, Nodes and Metastases
UICC	Union Internationale Contre le Cancer
UK	The United Kingdom
VHL	Von Hippel Lindau
WHO	World Health Organisation

Chapter 1: Introduction and Research Objectives

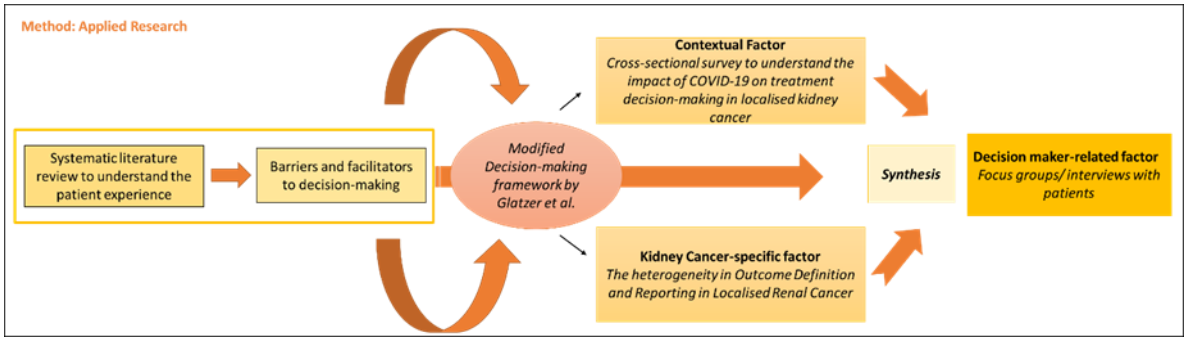
Kidney Cancer is the eighth most common cancer in the UK. In the last two decades, the number of patients diagnosed with small kidney masses has more than doubled, with most of the tumours smaller than 4 cm in size. Despite the small size, 80% of these kidney cancers are malignant (1). Evidence has established that, even if cancerous, these small tumours might not spread or grow, meaning patients may never need invasive treatments (2).

In clinically fit patients, nephron-sparing surgery is the standard treatment for small kidney cancers, however, less invasive treatments such as *ablation* (i.e. radiofrequency ablation and cryoablation) or *active surveillance* (AS) are now available (3). To date, the only Randomised Control Trial (RCT) conducted by the European Organisation for Research and Treatment of Cancer (EORTC) comparing treatment options was heavily underpowered (difficulties in recruitment and ultimately the study was prematurely closed) and heavily criticised (the groups were unequal with higher comorbidities in the partial nephrectomy group) (4).

The available treatments are associated with different risks/ side effects. Surgery treats cancer effectively, but also increases the risk of complications (e.g., bleeding) and treatment-related long-term side effects, such as reduced kidney function (e.g., chronic kidney disease). Ablative techniques come with a higher risk of fostering the persistence of cancer, potentially necessitating secondary treatment, and causing side effects, such as potential kidney injury (5-7). Active surveillance can be seen as a safe option for carefully selected patients with slow growth rates since active surveillance studies report a variance in tumour growth rates from 0.09 cm per year to 0.86 cm per year. However, active surveillance is currently only recommended by international guidelines for patients where the perioperative risks are too high or where an informed choice is made by balancing the risks and benefits of surgery (8). Therefore, utilising shared decision-making is paramount to supporting treatment decision-making given that currently no single management option is superior across all outcomes (8).

Hence, this thesis aims to understand the multifactorial process of decision-making in localised kidney cancer, while also assessing the support patients require in the treatment decision-making process, using a six-stage approach (see Figure 1).

Figure 1: Methodological overview



This thesis sets out the following objectives:

1. To explore the current evidence related to the kidney cancer treatment decision-making process.
2. To provide an understanding of the complex components of decision making in localised kidney cancer.
3. To explore the outcomes, perceptions, views, and experiences related to the process of kidney cancer treatment decision-making.

Chapter 2 provides background information contextualising the thesis by, including an overview of the kidney, kidney cancer, and kidney cancer epidemiology with a specific focus on localised kidney cancer.

Chapter 3 describes the methodology used during this project.

Chapters 4, 5, 6, 7 and **8** are the evidence-gathering chapters. Chapter 4 contains two published systematic reviews, which facilitate an understanding of the current evidence for decision-making in localised kidney cancer, whilst Chapter 5 illustrates changes to the cancer pathway during the COVID-19 pandemic and its impact on kidney cancer. Chapter 6 assesses the heterogeneity of currently collected outcomes to provide the respective evidence base. Chapter 7 presents the data synthesis of Chapters 4-6 to develop a semi-structured interview guide for the focus groups and interviews conducted in Chapter 8.

Chapter 8 presents evidence gathered through focus groups, where the decision-making process of patients is explored, whilst also considering supportive care suggestions to promote a robust discussion.

Finally, **Chapter 9** summarises the five-stages and provides a focus for future research.

Chapter 2: Background

This chapter provides an overview of the biology of the kidney, followed by an introduction to kidney cancer, the different histological subtypes of kidney cancer, and the pathophysiology. The grading and staging of kidney cancer is described, while also explaining the anatomical classification system, finishing with the epidemiology of kidney cancer.

This is followed by a description of localised kidney cancer, which is the focus of this thesis and the treatments offered to patients diagnosed with localised kidney cancer.

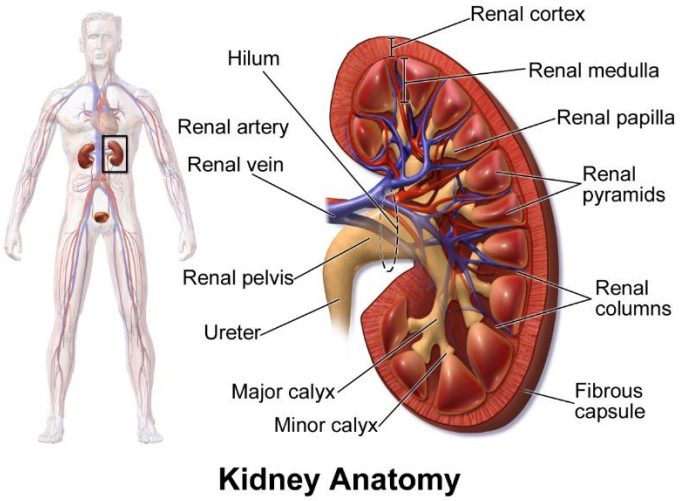
Finally, some key concepts linking treatment decision-making in localised kidney cancer to the concept of shared decision-making are discussed and explained, where necessary.

2.1. The Kidney

In 1662, Lorenzo Bellini was the first person to broadly describe the kidneys in scientific literature (59). The kidneys are two fist-sized bean-shaped organs, which are located near the middle of the back on either side of the spine (see Figure 2) (9). The kidneys act as blood filters and are endocrine organs which remove waste and regulate electrolytes and acid-base homeostasis. They control the body's fluid balance and blood pressure while also regulating bone metabolism and red blood cell production.

Other organs, such as the liver and heart, are closely linked to the function of the kidneys (10). Inside the kidney is a network of tubes known as nephrons, whose predominant function is to filter the blood that passes through the kidney. The 'waste' products (i.e., urea, uric acid, and other metabolic end products) from the nephrons move into the small blood vessels and the ureter. The urine gets collected in the renal pelvis area at the centre of the kidneys and drains down to the ureter and into the bladder (9).

Figure 2: Location and anatomy of the kidney



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2.2. Kidney Cancer

Cancer is understood to be a tumour or mass which is an abnormal growth in the body. *Kidney cancer*, also known as *renal cancer*, is a type of cancer that affects the kidneys. A renal mass is an abnormal growth found in the kidney and can be benign (not cancerous) or malignant (cancerous). Throughout this thesis, the term “kidney cancer” or “kidney masses” will be used when describing renal cancer or renal masses. Masses in the kidney may be solid or cystic. Purely cystic masses are generally benign. Complex cysts have solid elements and ordinarily solid masses tend to be malignant. Kidney cancer comprises a heterogeneous group of cancer subtypes with many molecular and genetic differences which determine different histological subtypes (11).

2.2.1. Epidemiology

2.2.1.1. Incidence

Kidney cancer is the seventh most common cancer in the United Kingdom (UK) and the fourteenth most common cancer worldwide (9, 12). It is the fourteenth most common cancer in women and the seventh most common cancer in men with more than 430,000 new cases worldwide in 2020 (13).

It accounts for around 4.1% of all new cancers, with a median age at diagnosis of 64 years (14). In the UK, kidney cancer incidence rates have increased by almost half (47%) in the last

decade (15). This increase can be mainly explained by the wider application of cross-sectional imaging (forother reasons such as hypertension), which has led to an increase in incidental findings (16, 17). The rates of cT1 kidney masses increased from 40% in 1992 to roughly 70% worldwide in 2015 (18). In the UK, it is estimated that 56% of patients are diagnosed with stage I (T1, N0, MO) or stage II (T2, N0, M0) kidney cancer (51-53).

2.2.1.2. Mortality

Globally, GLOBOCAN reported in 2021 that kidney cancer accounts for 179,368 deaths worldwide and 54,054 deaths (30.1% of global mortality) in Europe. This can be further segmented to 115,600 male deaths and 63,768 female deaths worldwide (1).

The net survival rate for patients diagnosed with Stage I after one year is the highest, with 96% of patients surviving. The lowest one-year net survival rate is reported for patients diagnosed with Stage IV (2013-2017, Data for England). At Stage I and Stage II, one-year net survival rates are similar across genders. For Stage III and IV, the one-year net survival rate is higher for males than females. Five-year net survival rates are similar across all Stages for females and males; ranging from 86% diagnosed at Stage 1 to 12% for patients being diagnosed at Stage 4 (19).

2.2.2. Kidney Cancer Subtypes and Pathophysiology

The most common type of kidney cancer is *renal cell carcinoma (RCC)*. The most frequently occurring histological subtypes of RCC are *clear cell* – 70-75%; *papillary* -10-15% of cases; and *chromophobe* - 5% (16). Rarer kidney cancers include *cystic-solid* (1-4%), *collecting ducts* (1%), *medullary* (1%), *Xp11 translocation* (rare), *mucinous tubular,* and s*pindle cell* (rare), *associated with neuroblastoma* (rare), and *unclassified kidney cancers* (4-6%) (20). Table 1 shows the 2022 WHO classification of RCC subtypes.

Table 1: WHO classification of RCC subtypes

Renal cell tumours	
Clear cell renal tumours	
8310/3	*Clear cell renal cell carcinoma*
8316/1	*Multilocular cystic renal neoplasm of low malignant potential*
Papillary renal tumours	
8260/0	*Papillary adenoma*

Renal cell tumours	
8260/3	*Papillary renal cell carcinoma a*
Oncocytic and chromophobe renal tumours	
8290/0	*Oncocytoma*
8317/3	*Chromophobe cell renal carcinoma*
Other oncocytic tumours of the kidney	
Collecting duct tumours	
8319/3	*Collecting duct carcinoma*
Other renal tumours	
8323/1	*Clear cell papillary renal cell tumour*
8480/3	*Mucinous tubular and spindle cell carcinoma*
8316/3	*Tubulocystic renal cell carcinoma*
8316/3	*Acquired cystic disease-associated renal cell carcinoma*
8311/3	*Eosinophilic solid and cystic renal cell carcinoma*
8312/3	*Renal cell carcinoma, NOS*
Molecularly defined renal carcinomas	
8311/3	*TFE3-rearranged renal cell carcinomas*
8311/3	*TFEB-altered renal cell carcinomas*
8311/3	*ELOC (formerly TCEB1)-mutated renal cell carcinoma*
8311/3	*Fumarate hydratase–deficient renal cell carcinoma*
8311/3	*Hereditary leiomyomatosis and renal cell carcinoma*
Syndrome–associated renal cell carcinoma	
8311/3	*Succinate dehydrogenase–deficient renal cell carcinoma*
8311/3	*ALK-rearranged renal cell carcinomas*
8510/3	*Medullary carcinoma, NOS*
8510/3	*SMARCB1-deficient medullary-like renal cell carcinoma*
8510/3	*SMARCB1-deficient undifferentiated renal cell carcinoma, NOS*
8510/3	*SMARCB1-deficient dedifferentiated renal cell carcinomas*

2.2.2.1. Clear Cell RCC

Clear cell RCC (ccRCC) accounts for 75% of all malignant cases (21, 22). The discovery of the Von Hippel Lindau (VHL) gene by Linehan et al. in 1993 provided a clear foundation for our current understanding of ccRCC biology. The VHL gene is located in the chromosome 3p25 and the main pathway of the ccRCC is through the double-hit deletion of the VHL gene. The VHL gene can be found in 85% of ccRCCs (23). Other mutations in genes frequently associated with ccRCC are PBRM1, SETD2, JARID1C, and BAP1. Characteristics of ccRCC are

defined as cells with clear cytoplasm and nested clusters surrounded by dense endothelial networks (24).

2.2.2.2. Papillary RCC

Papillary RCC (pRCC) is the second most common kidney cancer subtype. It accounts for 10-15% of cases (20, 22). It is a heterogeneous subtype of kidney cancer and can be easily distinguished due to its unique papillae in the tumour (21).

2.2.2.3. Chromophobe RCC

Chromophobe RCC (chRCC) is the third most common kidney cancer subtype and has been demonstrated to have a unique pattern of whole chromosome losses in which one copy of the chromosomes 1, 2, 6, 10, 13, and 17 is lost. This occurs in 86% of chRCC with additional losses of the chromosomes 3, 5, 8, 9, 11, and 18 as well as the chromosome arm 21 in 12-58% of chRCC (21). It originates from the renal collecting duct cells and overall accounts for 5-10% of kidney cancer cases (20, 22).

2.2.2.4. Benign Renal Tumours

Benign renal tumours account for 20% of all small renal masses (<4 cm) with Oncocytoma (OC) and Angiomyolipoma (AML) being the most common of these. The 2016 WHO classification lists 14 subtypes of benign renal neoplasms (25).

2.2.2.4.1. Oncocytoma

First described by Klein and Valensi in 1976 (26), Oncocytomas (OC) accounts for 3-7% of all renal masses (27). These benign tumours originate from the cortical collecting ducts and have a high prevalence in men. In 10% of cases, OC are present in both kidneys, which requires further investigation to understand if there is a link to hereditary RCC (i.e., Birt-Hogg-Dubé (BHD) syndrome). Yearly tumour growth is estimated to be 0.14 cm with lesions >4 cm having an even higher growth rate (8, 28, 29). Currently, it is difficult to differentiate between OC and RCC in imaging, which is reflected in the European Association of Urology (EAU) guidelines (8).

2.2.2.4.2. Angiomyolipoma

Angiomyolipoma (AML) is a benign tumour composed of blood vessels, muscle cells, and fat cells in varying proportions. It can be diagnosed using cross-sectional imaging due to the fat

cellular content which is pathognomonic for this tumour (8). AML is four times more common in females and 90% of patients are asymptomatic when diagnosed.

2.2.3. Grading

The *tumour grade* describes how aggressive the cancer cells are in a tumour. Grading systems have been recognised as prognostic factors for a century. The concept that tumours show differences in their histology and how the degree of differentiation in the tumour predicts the behaviours and outcomes of cancer were first described by Albert Compton Broders at the Mayo Clinic in 1920. The first study which applied grading to kidney cancer was conducted by Hand and Broders in 1932 (30, 31).

Accurate grading of kidney cancer is considered one of the most important prognostic factors, however, several different grading systems have been used. The four-tier Fuhrmann classification is the most commonly applied grading system and has been updated eight times (30, 31). Fuhrman et al. proposed the grading system in 1982 based on the simultaneous assessment of the size and shared prominence of a mass (Table 2). However, over the last decade, the Fuhrman grading system has been increasingly criticised. For example, it is not possible to differentiate according to RCC type, as all but one of the studies that the Fuhrman grading system is built on, did not differentiate between subtypes (30, 32). It has also been highlighted that the grading system lacks interobserver reproducibility and has a "questionable" prognostic significance (30). This has pushed the International Society of Urological Pathology (ISUP) to develop the new WHO/ ISUP grading systems. This grading system is superior to the Fuhrman grading system as it, in addition to its varying applicability (i.e., nucleolar grading), has also been updated to account for the newer kidney cancer subtypes (Table 3) (30).

Table 2: Fuhrman grade classification

Grade	Nuclear diameter	Nuclear shape	Nucleoli
1	1 ~10 µm	Round uniform	Absent inconspicuous
2	2 ~15 µm	Irregularities in outline	Visible at x400
3	3 ~20 µm	Obvious irregular outline	Prominent at x400
4	4 >20µm	Bizarre, often multilobed	Heavy chromatin clumps

Table 3: ISUP/ WHO grading system for ccRCC and pRCC

Grade	Description
1	Nucleoli absent or inconspicuous and basophilic at x400 magnification
2	Nucleoli conspicuous and eosinophilic at x400 magnification, and visible but not prominent at x100 magnification
3	Nucleoli conspicuous and eosinophilic at x100 magnification
4	Extreme nuclear pleomorphism and/ or multinucleate giant cells and/ or rhabdoid and/ or sarcomatous differentiation

2.2.4. Staging

Kidney cancers are staged by tumour size, anatomical location, and spread to determine the most effective treatment options for the patient. In 1978, the Union Internationale Contre le Cancer (UICC) and the American Joint Committee for Cancer Staging and End Result Reporting (AJCC) introduced the Tumour, Nodes and Metastases (TNM) Score, which is the most used classification for RCC's. This staging system was further modified in 1987, 1997, 2002, 2010, 2012, 2016, and 2017 (33). '*T*' indicates the size of the primary tumour, '*N*' describes the tumour spread to regional lymph nodes, and '*M*' indicates metastases (33) (see Table 4).

Table 4: TNM stages for renal cell carcinoma

Stage 1 (*T1; N0; M0*)	TX	Primary tumour cannot be assessed
	T0	No evidence of a primary tumour
	T1a	Tumour ≤ 4 cm, limited to the kidney
	T1b	Tumour > 4 cm and ≤ 7 cm in greatest dimension, limited to the kidney
Stage 2 (*T2; N0; M0*)	T2a	Tumour > 7 cm and ≤ 10 cm in greatest dimension, limited to the kidney
	T2b	Tumour > 10 cm in greatest dimension, limited to the kidney
Stage 3 (*Any T; N0, N1; M0*)	T3a	Tumour extends into the renal vein or its segmental branches, or invades the pelvicalyceal system, or invades perirenal and/or renal sinus fat but not beyond Gerota's fascia
	T3b	Tumour extends into the vena cava below the diaphragm
	T3c	Tumour extends into the vena cava above the diaphragm or invades the wall of the vena cava
Stage 4 (Any T; any N; M0, M1)	T4	Tumour invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

2.2.5. Anatomic Classification Systems

There are many different objective anatomic classification systems which aim to support efforts to standardise the description of kidney cancers such as the Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification system, the R.E.N.A.L. nephrometry score, the C-index, the Arterial Based Complexity (ABC) Scoring System, and the Zonal NePhRO scoring system (34-36). They include variables such as tumour size, exophytic/ endophytic properties, proximity to the collecting system and renal sinus, and anterior/ posterior or lower/ upper pole location. The classifications are predominantly used to predict treatment outcomes (i.e., nephron sparing surgery and ablation (a needle-based treatment that destroys cancerous tissue using extreme cold (i.e., cryotherapy) and extreme heat (radiofrequency)) (8). There has been extensive debate over the years about which classification systems are the most useful and reliable. Due to the heterogeneity of the data, it is currently impossible to prove the superiority of one anatomic classification system over another (18).

2.2.6. Risk Factors

Similar to most cancers, there is no one cause for kidney cancer. The risk factors for kidney cancer overlap with many other cancers (37) and are split into *modifiable risk factors*, which are behaviours and exposures that raise or lower a person's risk, and *non-modifiable (or unmodifiable) risk factors*, which cannot be controlled.

2.2.6.1. Unmodifiable Risk Factors

Age: Kidney cancer incidence has a strong association with age. While it is rare in children and young adults, rates start to increase after the age of 40 (38). In fact, according to the National Cancer Registration and Analysis (NCRA) service, one-third of the new cases are in the 75+ age group (9, 39).

Gender: Incidence rates are lower for females than for males. Kidney cancer has a 2:1 male/ female incidence ratio. This can be explained by socio-cultural and health-related behaviours (e.g., smoking, obesity, and hypertension) (40). In the UK, 1 in 61 females and 1 in 34 males will be diagnosed with kidney cancer during their lifetime (9). The difference in rates between men and women increases with age, with the highest gaps being reported for patients aged 90+ years (9).

Genetics: Around 17% of kidney cancers have a link to hereditary susceptibility, which is connected to ethnicity, pathological subtypes, and clinical stages. Genetic diseases such as Birt-Hogg-Dubé syndrome, tuberous sclerosis, hereditary clear cell, von Hippel-Lindau disease, and hereditary papillary renal carcinoma (HPRC) also contribute to a higher incidence of kidney cancer (38).

2.2.6.2. Modifiable Risk Factors

Obesity: Obesity is a well-established risk factor for kidney cancer. Twenty per cent of cases of kidney cancer are thought to be associated with a high BMI (41). This may be linked to raised insulin, oestrogens, growth factor levels, changing cholesterol, and the impact on the immune system (41).

Smoking: Thirteen percent of cases in the UK are linked to smoking (9, 38). There is a 39% higher risk of smokers developing kidney cancer compared to non-smokers (41). This risk is 50-76% higher for heavy smokers as compared to moderate smokers defined as less than twenty cigarettes per day or more less than 50 years of exposure (9). Therefore, it is important to highlight that this risk is dose-dependent, with the risk sharply increasing in accordance with cigarette consumption (41).

Alcohol: Evidence indicates that alcohol consumption is a preventable risk factor linked to cancers such as the oral cavity, pharynx, oesophagus, liver, and larynx. However, in kidney cancer, evidence has shown that mild alcohol consumption (41), i.e. consuming a bit more than one alcoholic beverage per day (i.e. 15g of alcohol consumed) decreases the risk of kidney cancer (42).

Hypertension: A recent meta-analysis shows that ten out of eighteen studies demonstrate an association between hypertension severity and developing kidney cancer (43). There is a 10% and 22% increased risk for every 10-mmHg increase in systolic and diastolic blood pressure, respectively (41). This may vary between genders. A history of hypertension increases the risk of developing kidney cancer by 67% (44).

Chronic Kidney Disease: Chronic Kidney disease (CKD) has also been suggested as a risk factor for kidney cancer. Evidence describes that the kidney cancer risk is higher for people with end-stage kidney disease who are receiving dialysis (45). However, this might also be linked to increased medical surveillance for patients with an end-stage kidney disease (46).

Medication: Taking medication such as ibuprofen, naproxen, phenacetin, and celecoxib over a long period of time also increases the risk (38). A meta-analysis showed that kidney cancer risk is 32% higher in paracetamol users than in never/ rare users (47).

Diabetes: Diabetes also poses a risk of developing kidney cancer. The increased risk of diabetic patients might be associated with the underlying mechanisms of insulin resistance, hyperinsulinemia, proinflammatory status, and increased oxidative stress (43). A meta-analysis showed that Type I diabetics had a 37% increased risk of kidney cancer (48), as compared to people without diabetes. Concerning Type 2 diabetes, this risk may be higher in insulin users compared to non-insulin users and is not associated with metformin or pioglitazone use (49).

2.2.7. Screening

Even though early diagnosis and screening have been identified as a research priority for kidney cancer (50), currently there is not much evidence identifying the optimal screening modality and target population. To enable successful screening programmes which consider the identified risk factors, more research is needed. This includes an assessment of whether screening can be translated into improved survival benefits, as well as potential harms such as the linked distress on the emotional and psychosocial well-being of screening programmes (e.g., potential false positive, false negative and overdiagnosis). The development and validation of risk prediction models as well as urinary biomarker research present a promising opportunity in the future to limit the currently described harms (51).

2.2.8. Modes of Presentation

Diagnosing patients with kidney cancer can be challenging as kidney cancer often presents itself incidentally. For instance, the increased use of abdominal imaging resulted in an increased number of incidentally detected kidney cancers in recent decades (52).

2.8.1. Symptoms

Around 60% of kidney cancer patients across all stages will present without any symptoms or symptoms unrelated to their kidney cancer (52). For smaller tumours less than 4 cm (small renal masses), this number increases up to 66% (53). Usually, the incidental findings are identified on imaging (52).

Typical symptoms of kidney cancer include blood in the urine (haematuria), lower back pain, and flank pain. Less common symptoms are abnormal red blood cell counts and hypertension. Rarer symptoms include weight loss, fatigue, a persistent high temperature, and relentless heavy sweating (especially at night) (Table 5: Most common symptoms) (54). However, typically, early-stage kidney cancer is asymptomatic and incidental, with the triad of symptoms only presenting in 4-17% of patients (55).

Table 5: Most common symptoms

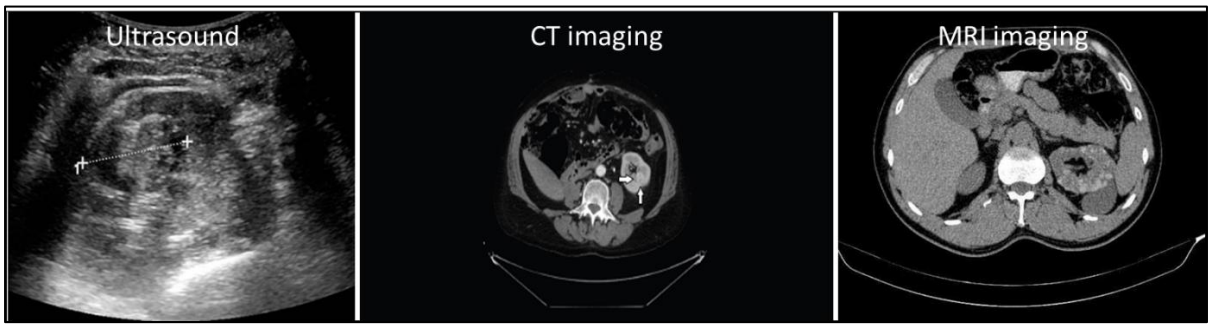
Type of symptom	**Occurrence**
Acute or chronic flank pain	*Common*
Anaemia	*Common*
Hypertension	*Common*
Cachexia, weight loss	*Common*
Gross haematuria	*Less common*
Palpable abdominal mas	*Less common*
Pyrexia	*Less common*
Stauffer's syndrome	*Less common*
Hypercalcaemia	*Less common*
Varicocele	*Rare*
Polycythaemia	*Rare*

2.8.2. Diagnosis of Kidney Cancer: Imaging

The baseline diagnosis of kidney cancer is usually based on imaging (see Figure 3). The most common imaging diagnosis is ultrasound, as it helps to identify patients where a renal mass is suspected. Through the use of ultrasound, it is possible to differentiate between cysts and solid tumours. Complex cysts and solid lesions require additional examination using contrast-enhanced CT or MRI as this will enable an accurate assessment of tumour size, presence or absence of macroscopic fat, tumour characterization as solid or cystic, and tumour enhancement to be presented (56). The main strength of imaging is the non-invasive nature, the availability of CT and MRI infrastructure, and the ability to visualise critical landmarks for T-staging, detect lymph nodes, venous invasion, and distant metastasis (57).

However, it is not possible to provide confident diagnoses of absolute malignancy of the lesion solely using CT or MRI imaging, and therefore tumour biopsy remains the most informative method of detection.

Figure 3: Imaging modalities



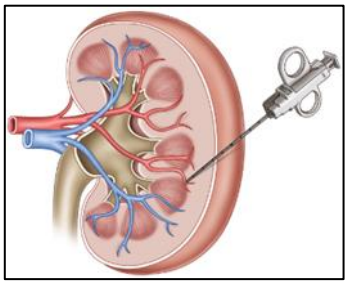
Source: Creative Commons Licenses 2

2.8.3. Detection of Kidney Cancer: Biopsy

The emerging role of biopsy has been debated in recent years. When performing a biopsy, a sample of tissue is taken from the tumour by a urologist (11) (Figure 4: Biopsy). Using biopsies for decision-making was uncommon in the past due to concerns about accuracy and safety. The standard treatment option for solid kidney masses used to be surgery. Yet, the new emerging management options such as the increased use of AS settings have pushed the scientific community to investigate kidney cancer biopsies further.

Current evidence highlights that a renal biopsy has low associated morbidity. Complication rates such as bleeding, arteriovenous fistula, and infection occurred in 0.3-5.3% of cases (58). The main fear around seeding through the biopsy tract is no longer a risk when using modern biopsy techniques (55). However, even though research places expanding importance on kidney cancer biopsies, it remains greatly underused (59).

Figure 4: Illustration of a Kidney Biopsy



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2.3. Management of Localised Kidney Cancer

This thesis examines localised kidney cancer and will thus solely focus on describing treatment options in the localised setting (Stage I, Stage II, see above: Staging 2.2.3).

2.3.1. Radical Nephrectomy and Nephron-sparing surgery/ Partial Nephrectomy

First carried out by Gustav Simon of Heidelberg in 1869 (60, 61), Radical Nephrectomy (RN) describes the classical approach to removing the kidney perirenal fat tissue, adrenal gland, and regional lymph nodes. Radical nephrectomy is usually performed in patients with large and complex tumours or in patients with multiple small kidney tumours (62).

Nephron sparing surgery (NSS), or Partial Nephrectomy (PN) aims to completely remove the tumour while preserving as much of the healthy kidney as possible. The first partial nephrectomy was performed by Vincent Czerny in 1887; this approach went through several experimental stages to better understand the procedure (63). However, faith in partial nephrectomy as a curative treatment option remained low in the urological community until the late 90s when Herr et al. (64) and Fergany et al. (65) published their observational studies on long-term survival outcomes with a low rate of local recurrence and the clear benefit of preserving renal function (64, 65). These studies formed the evidence base of today's kidney cancer surgical practice (63-65).

At present, NSS is the recommended approach when the aim is to surgically treat cT1 lesions. The feasibility of NSS must be considered i.e., technically possible and oncologically safe (3). However, limited evidence is available and the only RCT conducted in this area suggests comparable oncological outcomes for PN versus RN, with PN preserving renal function. The cut off for NSS was 5 cm and only patients with normal contralateral kidneys were included. The trial was heavily underpowered (i.e., sample size was not reached) and prematurely closed (4).

It was not until 2017 that a Cochrane review meta-analysis of RN vs. PN was undertaken, showing that PN was associated with a reduced time to death compared to RN (8, 66).

A current 'hot' topic concerns the use of robotic-assisted laparoscopic partial nephrectomy (RAPN) versus open partial nephrectomy (OPN) (3). Currently, there is no published RCT data available answering the question of which type of surgery is superior. However, retrospective studies suggest a decreased morbidity in the RAPN group with fewer

complications, transfusions, and shorter hospital stays. However, this was linked to the case volume of the hospital. The published studies, therefore, suggest that where technically feasible, RAPN is most commonly used and OPN is mainly reserved for more complex tumours (67).

2.3.2. Ablative Therapies

To preserve renal function, ablative therapies such as cryoablation and radiofrequency ablation are recommended where available. Ablative therapies use cell-destroying properties of extreme temperatures i.e. hot or cold, which cause apoptosis in cancer cells (55). Ablation can be considered in patients with small renal masses (<4 cm) or in those patients who are unfit for surgery, those with a genetic predisposition (e.g., VHL) or if the patient has bilateral tumours or a solitary kidney, to preserve renal function in the remaining portion of the kidney (5).

Percutaneous cryoablation is the most commonly used ablative technique for RCC. In 1995, Uchida et al., reported the first use of percutaneous cryoablation in a canine model using a nitrogen-based system (68, 69). Argon-based cryotherapy was studied by Torre in 1975 and has been implemented in practice since the 1990s to treat solid organ tumours.

Cryoablation describes the effect of high-pressure gas that travels through a pinhole valve into a region of lower pressure. The cooling effect stems from the gases used, i.e., nitrogen and argon, expanding and cooling to temperatures as low as -185 degrees. Through this cooling process, tissue destruction is achieved through direct cell and vascular injury. This ultimately leads to the formation of intra and extracellular ice crystals, which directly kill the tissue (70).

Another ablative technique is Radiofrequency Ablation (RFA). This uses frictional heat, which induces thermal damage at temperatures of 50-120 °C. This results in ionic oscillation (tissue heating).

There are no RCTs comparing ablation (Cryoablation or RFA) with PN (5). However, two observational studies show a higher local recurrent rate after thermal ablation compared with PN, and one identified similar results for PN and percutaneous ablation, however, due to the quality of the studies, it is difficult to draw definite conclusions (5-7).

2.3.3. Active Surveillance

When considering the most appropriate management option for localised kidney cancer, clinicians and patients must consider any patient-specific co-morbidities, as well as the potential impact on quality of life as a result of treatment. International guidelines suggest that Active Surveillance (AS) should be presented as a management option when the risk/ benefit analysis for treatment is equivocal, the patient prefers AS and/ or when the risk of treatment outweighs the oncological benefits (5).

Decision-making factors favouring AS management should take into consideration: patient preference, age, life expectancy <5 years, multiple and/ or high-risk comorbidities, excessive perioperative risk, frailty (poor functional status), patient preference for AS, marginal renal function, tumour size <3 cm, tumour growth <5 mm/ year, non-infiltrative, low complexity, and favourable histology. This is based on the evidence gathered in the last decade on small renal masses (cT1a) and presented by Mir et al. in a systematic review. 28 AS studies were reviewed and confirmed low rates of metastatic progression (1%-6%) and kidney cancer-specific survival (0%-18%) (71). In 2009, the Delayed Intervention and Surveillance Registry (DISSRM) was opened to report outcomes of patients on an AS protocol vs. primary intervention. It is currently one of the largest observational studies, with over four hundred patients on an AS protocol. The authors state that they established that AS is a reasonable and safe primary management strategy for select patients with small renal masses (cT1a) (72). In 2018, McIntosh et al. presented results of their prospective real-world evidence study where they followed 457 patients on AS from 2000-2016. They identified that AS with or without delayed intervention at more than five years is a reasonable and safe option. However, as there is currently no agreed standard, a follow up pathway for AS in localised kidney cancer including follow up is yet to be determined.

2.4. Current Practice in Localised Kidney Cancer Treatment

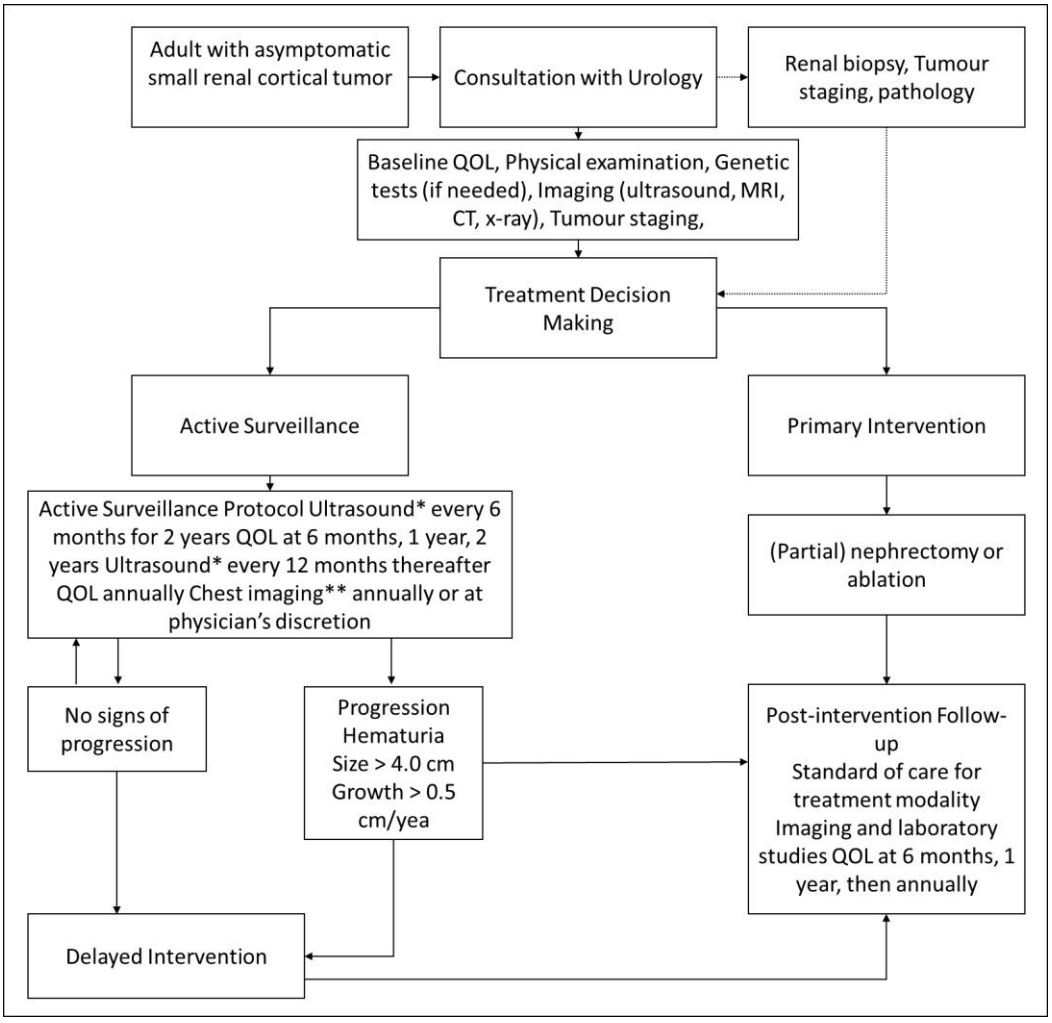
The increase in incidentally found small kidney masses (cT1a) and the increasing evidence that surgically induced CKD can impact morbidity, has shifted the opinion of leading stakeholders in the field to advocate for more conservative approaches (nephron sparing surgery, AS and ablation) (55). The evidence shows that there has been an uptake in PN rather than treating patients with RN across the UK and the US, however, ablation and AS

seem very underutilised. Between 2013-2016, the National Cancer Registration and Analysis Service in the UK identified that 68% of patients with Stage I kidney cancer received surgery (PN or RN). Tran et al. reported by looking at the British Association of Urological Surgeons Nephrectomy Audit that in 2012, 39.7% of patients were treated with PN; this increased to 44.9% in 2016. In 2013, in Australia, 62% of patients received PN (73). In the United States, a study looking at the National Cancer Database showed that between 2004 and 2015, out of 75,691 patients, 57% were managed with PN and 8% of cT1a renal masses with AS (74). According to the US based Surveillance, Epidemiology, and End Results (SEER) data base, 19.4% of 10,218 patients with cT1a renal masses were managed with AS between 2002 to 2011 (75). This shows that surgery remains the mainstay of treatment for Stage I kidney tumours and PN uptake has increased in the last decade. However, this cannot be seen across other more conservative management options, which suggests a current bias in decision-making or the presentation of treatment options by HCPs (76). To reduce bias linked to decision-making, healthcare concepts like shared decision-making have been introduced across cancer care to enable patients and clinicians to ensure improved patient-centred care.

2.4.1. Treatment Pathway

A treatment/ care pathway is a tool to guide the patient journey (77). Often international, national, regional, or local guidelines propose care pathways which aim to guide healthcare professionals on which treatment should be given based on clinical diagnostic assessments. In localised kidney cancer, Figure 5 shows an example of a care pathway.

Figure 5: Illustration of a localised kidney cancer pathway



2.4.2. Introducing the Decision-making Process: linking theories with the context of localised kidney cancer

The evidence presented suggests that the described treatment options vary with respect to potential complications, side effects and intensity of follow-up, and between countries. The successful delivery of information to patients articulating these very different options is therefore a complex task and there have been many attempts at designing tools that facilitate this process.

The decision-making process involves selecting a choice from several alternatives to achieve a desired outcome. This includes thinking under conditions of uncertainty. The decision-making process can be broken down into three key elements (78):

1) It involves multiple options.
2) It is a dynamic process with several sub-processes (going back and forth based on the information).
3) The decision-maker actively engages in the decision-making process to attain the desired outcome (78).

2.4.3. Introduction to Shared Decision-making in Localised Kidney Cancer

Across cancer care, international guidelines on treatment decision-making recognise the importance of involving patients (78, 79). For example, the American Urological Association and the UK NICE guidelines further highlight that these treatment decisions are 'preference sensitive' and recommend implementing shared decision-making (80, 81). Shared decision-making involves choosing tests and treatments based on evidence and the patient's preferences, values, and beliefs.

In 2015, Stiggelbout et al. (78) defined shared decision-making in four steps:

1) The patient is informed by the professional about the treatment decision and the patient's opinion is important.
2) The options are explained (reasons against or in favour of an option).
3) There is a discussion about the patient's preference with the professional.
4) There is a discussion about the patient's decisional role.

Shared decision-making allows healthcare professionals and patients to discuss and share information to enable patients to understand the harms, benefits, and possible outcomes of the different treatment options. It empowers patients to understand their care pathway and to choose the treatment which is right for them. It helps patients to choose the degree to which they want to actively engage in their treatment decision or not take an active role in their decision-making process (82).

The process of shared decision-making is important in facilitating the presentation of options to patients and it is the clinician who has the role of initiating shared decision-making by tailoring the communication strategy toward the patient (80). There are specific cases where shared decision-making is not recommended, for example when dealing with immediate life-threatening decisions or a potential threat to public safety (83).

Nevertheless, in the case of localised kidney cancer where multiple (reasonable) options are available and there seems to be decision-making bias, it is important to understand how to engage in shared decision-making.

2.5. Summary of Chapter 2

This chapter explores the challenges involved in determining an adequate recommended treatment option for patients with Stage 1 localised kidney cancer based on oncological outcomes. Providing additional contextual information on the clinical background of kidney cancer underlines the complexities involved in making an informed decision solely based on oncological outcomes.

Furthermore, this chapter addresses a common significant concern in the current medical practice: the potential for bias in decision-making. Despite comparable oncological outcomes, more than half of Stage 1 kidney cancer patients undergo surgery rather than opting for less invasive treatments. This observation raises important questions about the factors influencing treatment decisions. By emphasizing these issues, this chapter calls attention to the importance of addressing the gaps in understanding the multifactorial factors of the decision-making processes in localised kidney cancer.

Chapter 3: Research Method and Methodological Plan

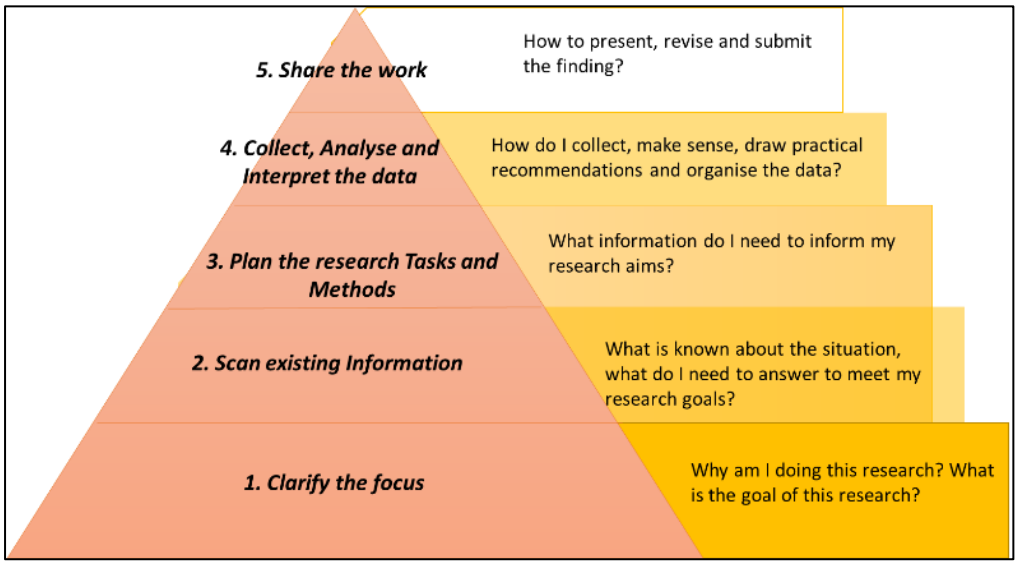
The goal of this chapter is to provide a comprehensive explanation of the research methodology used in this thesis, including the theoretical foundation and the specific methods employed. Moreover, this will provide insights into the *validity* (i.e., how accurately the methods measure what they were intended to measure) and *reliability* (i.e., how consistently the methods measure the concept) of the methods and findings presented in subsequent chapters.

3.1. Research Method: Applied Research

Applied research is the type of research which seeks to solve practical problems or improve the human condition in a real-world setting. It is most relevant in this setting as it facilitates an understanding of the 'real-life' problem of decision-making, unlike basic research, which aims to provide a fundamental understanding of a natural phenomenon (84). Applied research can comprise a wide range of methods and often involves collaboration between different healthcare disciplines working across a range of specialities (84).

A helpful tool to design an applied methods approach is to follow Baimyraeva's five-step framework as shown in Figure 6.

Figure 6: Five-Step Framework for Applied Research



Source: modified framework from Baimyraeva

3.2. Mixed Methods Approach

One approach which is increasingly used in applied research is the mixed method approach, which focuses on collecting and analysing 'mixed' forms of data such as qualitative (e.g., focus groups and interviews) and quantitative data (e.g., epidemiology, binary surveys, observational data).

Johnson et al. defined mixed methods approaches in 2007 as:

> *"… the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the purposes of breadth and depth of understanding and corroboration" (85).*

The concept of mixed methods research was developed by Campbell and Fisk in 1959, in their study "convergent and discriminant validation by the multi-trait-multimethod matrix", which aimed to investigate the validity of psychological traits (i.e., traits refer to enduring, stable characteristics or qualities that define an individual's behaviour, emotions, and thoughts) (86).

Campbell and Fiske argued that psychological traits should be measured by multiple methods to ensure their validity and thus proposed the use of a 'multi-trait-multimethod matrix'. This matrix enables the study of the relationships between traits and methods, including the correlations between them (86).

Mixed methods research has gained in popularity, due to the key advantage of this approach to explore one research question from multiple angles (91-93).

3.2.1. Multistage Design

This thesis adopts a mixed methods multistage design within an emergent approach (87). A multistage approach uses multiple projects to address a single research question and has been found to be effective in especially addressing complex research questions. Multi-stage designs are widely used in health sciences research (87). This offered the opportunity to understand a multifactorial process with different decision-making factors (87).

3.2.2. Emergent Mixed Methods Approach

The emergent mixed methods approach requires the researcher to act on issues that develop throughout the research process. The flexibility and adaptability of an emergent design ensures that the study remains relevant and meaningful in the context of the current environment (87). Whilst this method guides the methodological approach, the use of a theoretical framework improves both the objectivity and the structure of a study focused on decision-making (88). Therefore, this thesis employs a framework to comprehensively examine the various factors that shape decision-making through both qualitative and quantitative data sources.

3.3. Theoretical Framework

A theoretical framework is a conceptual structure that guides the design and interpretation of a study. It provides a systematic and organised way of understanding the research problem and the relationships between the variables being studied. The framework can be based on existing theories or models in the field or can be developed and/ or modified specifically for the study.

This project employed Glatzer et al's framework to establish a clear understanding of the problem and the relationships between this multifactorial decision-making process (89). This leads to more robust and meaningful results while ensuring reliability and validity.

The framework of Glatzer et al. is based on a managerial decision-making framework (first described by Papadakis et al. (90) and later revised by Elbanna et al. (91)) to capture a broad range of factors which influence decision-making in the context of oncology (89). Since the framework was developed particularly for oncology patients, it remains the most useful framework to guide oncology-based decision-making projects. It is centred around the following three 'domains of influence' (89) (see also Figure 7):

A) Disease-specific criteria

The disease-specific criteria describe factors involved in clinical decision-making. These include both clinical criteria such as stage, grade, and location of kidney cancer, and non-clinical factors e.g., age. However, prioritising a treatment based on disease-specific factors can be challenging, given the complexity of individual patient cases (e.g., several co-

morbidities). Therefore, the decision-maker related characteristics need to also be considered.

B) Decision-maker related characteristics

Decision-maker related characteristics greatly influence the decision-making process and involve a variety of individuals, including patients, HCPs, family members, and/ or carers with different roles and responsibilities (89).

Patient related criteria

Patient related criteria emphasises the factors which drive patients during decision-making. Patients provide important information about their health status, symptoms, and personal preferences, and may be very active in the decision-making process by seeking and exchanging information and discussing treatment options (89, 92).

Physician related criteria

Physician related criteria highlights the key factors that influence HCPs' decision-making process. Making a good decision is closely linked to the HCPs' familiarity with the current evidence, their ability to interpret it, and their willingness and access to resources to apply it effectively in clinical practice. Ideally, decision-making should be based on high-level medical evidence and strong guideline recommendations, but this is not always the case (89). Personal preferences can also play a role, as highlighted for example, by Fowler et al., who reported that urologists tend to favour surgery, whereas oncologists prefer radiation (89).

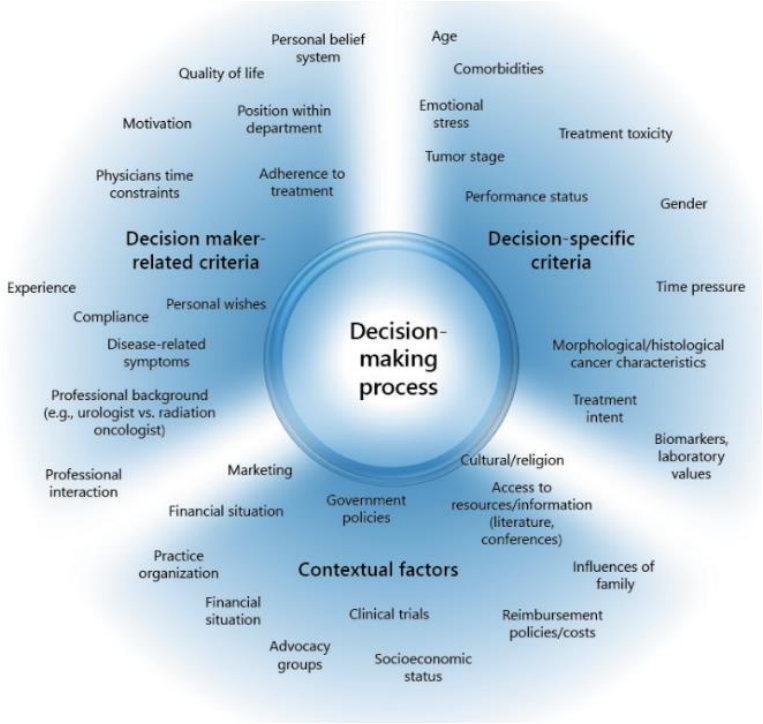
Patient Physician interaction

Patient Physician interaction refers to the relationship between a patient and the HCP. Ideally, the interaction results in the best possible healthcare outcomes for the patient. However, when the decision is difficult due to e.g., comorbidities, or more than one suitable treatment option, finding a solution that meets both parties' needs, and expectations requires open communication and collaboration. Optimisation of patient-physician interactions facilitates the development of the most suitable treatment plan (89).

C) Contextual Factors

Contextual factors are external social and cultural elements, such as organisational structures, environmental conditions, government policies, and healthcare systems or settings (89). These factors are usually not influenced by the other two domains but in turn heavily influence both domains.

Figure 7: Conceptual model of decision-making in oncology

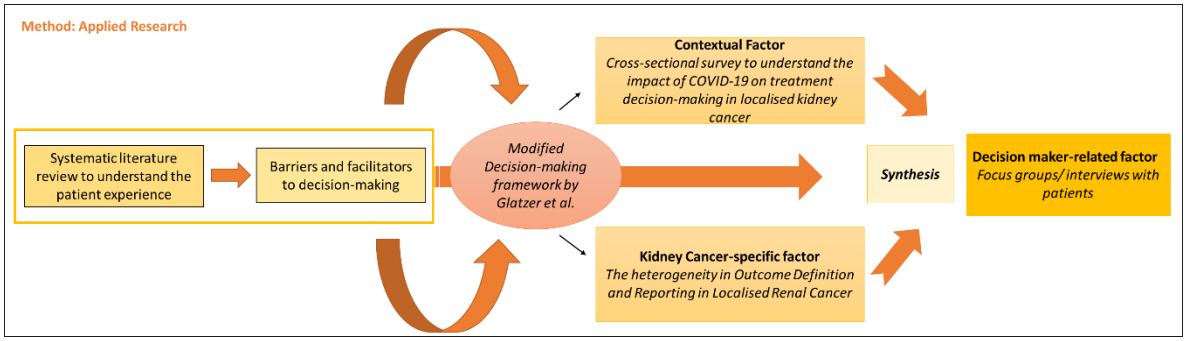


Source: Glatzer et al.- approval received by the author to use the graphic

3.4. Methodological Plan

The second part of this chapter outlines the six steps of the methodological plan applied in this project - a multi-stage emergent mixed methods approach (Figure 8). Methodological details for each step are provided in their relevant chapters further in this thesis.

Figure 8: Methodological overview of the thesis



3.4.1. Understanding the Patient Experience in the Treatment Decision-making Process

A systematic review was conducted to gather evidence on the treatment decision-making process from the patient's perspective in Stage I and II kidney cancer. This was published in Translational Andrology and Urology in 2021 with the title "A Systematic review: Factors that influence patients views on treatment decision-making in Stage I kidney cancer: a commentary piece" (93). Methodological details of this systematic review are further outlined in Chapter 4.

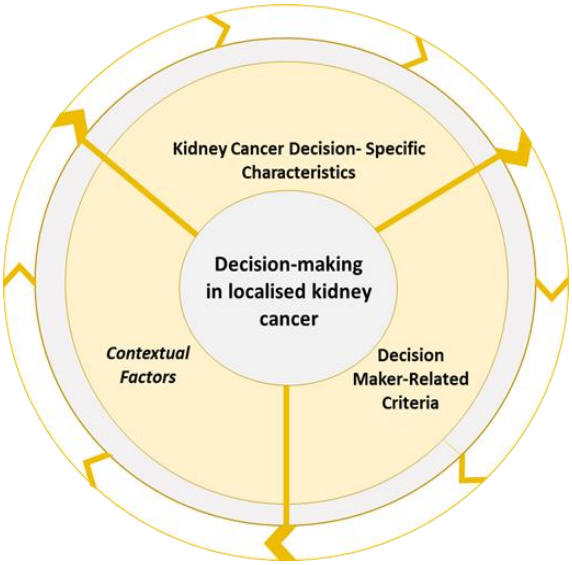
3.4.2. Barriers and Facilitators to Decision-making

Due to the limited evidence presenting the patient's perspective or voice, this thesis additionally includes all factors which influence the decision-making process of the patients and HCPs.

To structure the systematic review, the decision-making framework by Glatzer et al. (89) was employed. As outlined above, this framework helps to categorise the different factors under three overarching domains: (1) kidney cancer decision specific characteristics; (2) decision maker-related criteria; and (3) contextual factors.

During the identification of the barriers and facilitators to treatment decision-making, the decision-making framework was adapted to fit the context of localised kidney cancer. This mixed methods systematic review, entitled "The current evidence for factors that influence treatment decision-making in localised kidney cancer: a mixed methods systematic review", was published in the Journal of Urology (2021) (94). Methodological details of this systematic review are further outlined in Chapter 4.

Figure 9: Modified Decision-Making Framework



This modified version of Glatzer et al's framework guided the next stages of the thesis.

3.4.3. Contextual Factors Involved in the Treatment Decision-making Process

A cross-sectional, descriptive study was designed to understand whether the experiences of patients during the COVID-19 pandemic impacted and changed any of the data gathered in Stage 1. The study offers a snapshot analysis of the situation of the healthcare system during COVID-19. This was published in BJUI Compass (2021): "Cross-sectional survey to understand the impact of COVID-19 on treatment decision-making in localised kidney cancer" (95). Further details of this survey are outlined in Chapter 5.

3.4.4. Kidney Cancer Specific Characteristics Related to the Treatment Decision-making Process

This systematic review on the heterogeneity in outcome definition and reporting aimed to provide a deeper understanding of the diversity of outcomes through the use of a systematic review methodology. This review specifically adhered to the principles outlined by the COMET initiative; a leading expert organization dedicated to the standardisation of outcome reporting (96). In addition, the study was reported in compliance with the COS-STAR reporting guidelines, ensuring the highest level of transparency and rigor in the methodology (97). This work was published in European Urology Open Science in 2022: "Systematic review on the heterogeneity in outcome definition and reporting" (98) and further methodological details are covered in Chapter 6.

3.4.5. Data Synthesis of Stages 1-4

Using the information gathered from Stages 1, 2, 3 and 4, a semi-structured interview guide (99) was then developed based on the following three steps: (1) identifying the research method; (2) retrieving and using previous knowledge; and (3) formulating the preliminary semi-structured interview guide. This guide was reviewed and approved by the steering group committee overseeing this thesis. Details of this data synthesis process are described in Chapter 7.

3.4.6. Decision Maker Related Factors for the Treatment Decision-making Process

To test the discussion guide, focus groups and interviews were held with patients diagnosed with localised kidney cancer in Germany, the UK, and the Netherlands. As part of this qualitative work, a codebook for analysis was developed (100). The codebook was applied to the data to identify themes that shed light on the decision-making process and provide recommendations for supportive care suggestions. This work has been chosen to be presented at the International Kidney Cancer Symposium (April 2023): “Exploring the perspectives of patients with localised kidney cancer on their treatment decisions: a qualitative study.”

3.5. Summary of Chapter 3

The methodology employed in chapter sheds light on the decision-making challenges involved in treating localised kidney cancer.

By adopting an applied research approach, this thesis focuses on solving practical problems and improving the human condition in a real-world setting. This ensures that the research is relevant to the actual decision-making process encountered by patients and HCPs. The use of a mixed methods approach further enhances the comprehensiveness of the study by collecting and analysing qualitative and quantitative data, allowing for all-encompassing understanding of the research question. The multistage design within the emergent mixed methods approach acknowledges the complexity of decision-making and allows for the exploration of various factors influencing the process. By adapting and using Glatzer et al.'s framework, this thesis establishes a theoretical foundation guiding the design and interpretation of the research. It is the only framework developed for the decision-making process in oncology.

While the methodology employed in this thesis effectively addresses the decision-making challenges in localised kidney cancer, it should be noted that alternative methods exist, but were ultimately deemed less appropriate for this study.

For instance, relying solely on quantitative results may limit the depth of understanding that can be achieved regarding the decision-making process. A focus on observational studies could provide real-world insights (101), but pure quantitative data may not adequately capture the subjective experiences and perspectives of patients and HCPs. Decision-making in localised kidney cancer involves complex factors that extend beyond objective observations.

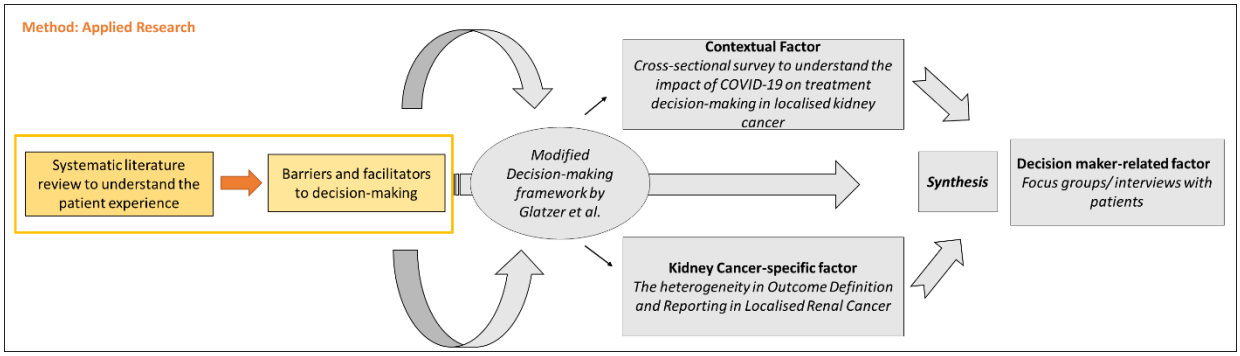
Ultimately, the methodological approach employed in this thesis serves as a critical tool to obtain a comprehensive understanding of the treatment decision-making process in localised kidney cancer.

Chapter 4. Understanding the Barriers and Facilitators Driving Treatment Decisions in Localised Kidney Cancer

This chapter forms the evidence base for this thesis. The first part of the chapter presents an in-depth review of existing literature on patient decision-making. In the second part of this chapter, the search strategy is expanded to further investigate the barriers and facilitators that can affect the decision-making process.

Overall, this chapter illustrates a thorough examination of the literature on decision-making and provides valuable insights into the complexities of the decision-making process.

Figure 10: Methodology overview- Factors that influence patients' views on treatment decision-making in stage I kidney cancer: a commentary piece



4.1. Systematic Review: Factors that influence patients' views on treatment decision-making in stage I kidney cancer: a commentary piece

The findings of the following study were presented as an abstract at the European Multidisciplinary Congress on Urological Cancers (EMUC) in 2019 (see Appendix 1). It was subsequently published in 2019 as a commentary piece in Translational Andrology and Urology Journal (Appendix 2) (93).

4.1.1. Introduction

As explored in Chapter 2, the treatment options for localised kidney cancer are surgery, ablation, and active surveillance (5). Current guidelines highlight the importance of considering objective metrics including oncological outcomes, potential harms or side effects, and overall survival. However, currently, there are no strong recommendations on the best option based on diagnostic and prognostic indicators (8). Therefore, shared

decision-making becomes increasingly important to enable clinicians to recommend an appropriate management plan.

4.1.2. Methods

A systematic review of the evidence guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (102) guidelines was conducted. A computerised literature search of databases (PubMed, Cochrane) was performed to identify full text and abstracts published between January 2004 (WHO classification on renal tumours in adults was updated in 2004) to September 2020. Table 6 shows the keyword search terms used to conduct the examination. Studies were selected and included on the basis of whether: (1) they explored patient views (> 18) on treatment decision-making for localised kidney cancer; and/or (2) they were of sufficient methodological quality (quality was assessed).

Studies were excluded if: (1) they only presented treatment decision-making targeting the view of HCPs; (2) participants were younger than 18; or (3) the patient population was not diagnosed with localised kidney cancer.

Table 6: Keyword search terms

Customise: Date, species, Language
((kidney) OR (renal))
AND
((cancer) OR (malignant) OR (carcinoma) OR (malignancy) OR (tumour) OR (tumor) OR (neoplasm) OR (neoplastic) OR (neoplasia) OR (RCC))
AND
((treatment) OR (intervention) OR (therapy) OR (surgery) OR (chemotherapy) OR (nephrectomy) OR (radiotherapy) OR (“active surveillance”) OR (ablation) OR (ablative) OR (cryotherapy) OR (RFA))
AND
((“patient preference”) OR (“patient choice”) OR (“patient view”) OR (“patient decision”) OR (“patient opinion”) OR (“patient perspective”) OR (“patient perception”) OR (“patient attitude”) OR (“patient motive”) OR (“patient motivation”) OR (“patient beli*”))

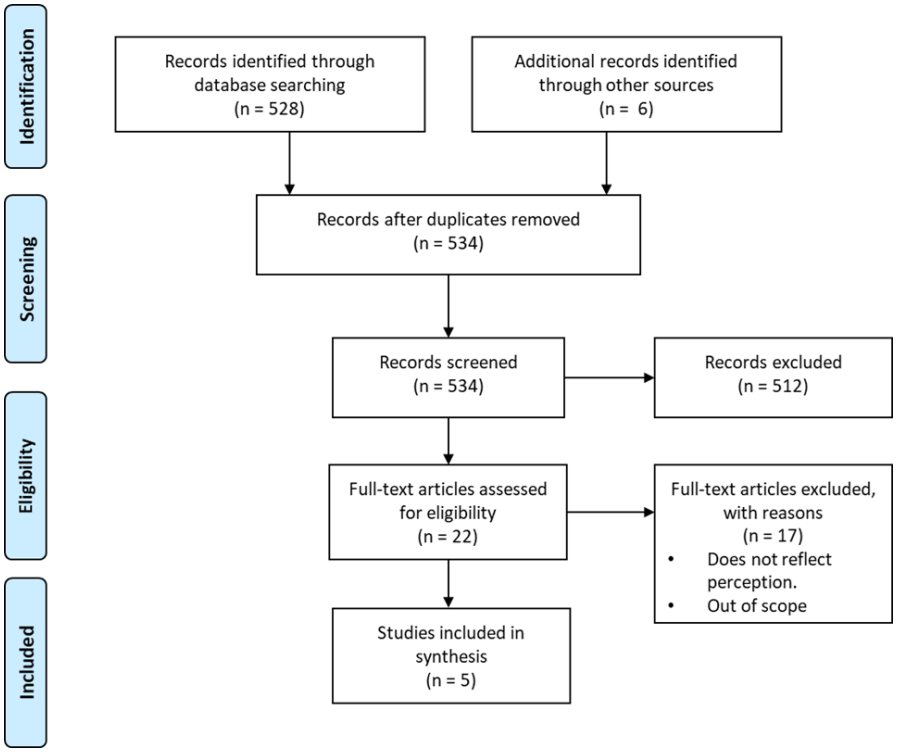
4.1.3. Results

534 studies were identified, of which 528 studies were identified through PubMed and six studies were added using the CENTRAL data base “other sources”, which focuses on Cochrane Systematic reviews. (see Figure 11 for details). Ultimately, five studies were

identified as relevant following full-text screening. The studies were reviewed by two authors (NK and KB).

Data was extracted following a Bayesian approach. Employing a Bayesian approach allows researchers to leverage the strengths of both qualitative and quantitative data, resulting in more exhaustive research results. Applying the Bayesian approach in mixed methods studies aims to support in the development of thematic descriptions. This further allows for a final meta-aggregation of individual syntheses, where quantitative data and qualitative data is combined and translated into qualitative form (103, 104). For each study reviewed, information on treatment decision-making factors identified by patients were extracted. These findings were then cross-checked by a second reviewer (NK).

Figure 11: PRISMA patient preference SR



Five out of twenty-two studies were included in the final synthesis. From the five included studies, the first study evaluates an interdisciplinary service for renal malignancies in Germany (105), whereas the second assesses a patients' or caregivers' perception of information provided in kidney cancer treatment in Canada (106). The third study used a survey to measure decisional quality in patients diagnosed with localised kidney cancer (80).

The fourth and fifth study developed a patient decision aid for surgical treatment and active surveillance in localised kidney cancer (107, 108).

A summary of the factors identified to influence patient decision-making in these studies is shown in Table 7. Key themes emerged around 'Patient-related criteria' and 'Patient-physician interaction.' Two factors were identified for the patient-related criteria: *decisional quality* (e.g., the emotional impact of decision-making or knowledge of kidney cancer) and *patient's perception* (e.g., anxiety, concerns about cancer) (80, 105-107). Factors contributing to the patient-physician interaction centred around patient involvement in decision-making, perceived shared decision-making, and the negative influence of paternalistic care (80, 105, 106).

Table 7: Summary table- Factors influencing patient decision-making

Decision maker criteria	Factors	Supportive care suggestions	Why is this important in clinical practice	Ref
Patient-related criteria'	Patient decisional quality: (= Education level; age; patient satisfaction with care; knowledge of kidney cancer; decisional conflict; emotional impact of decision-making;) Patient's risk perception: (= Fear of recurrence; fatigue; anxiety; concerns about cancer; depression; aches; decreased interest in previously enjoyed activities; decreased interest in previously enjoyed events; decreased interest in previously enjoyed events; reluctance to start new relationships)	Introduce clinical decision aids to increase patient involvement and knowledge about their disease.	Will reduce decisional conflict between the patient and shared decision-making. However, it does not replace counselling.	(80, 107, 108)
		Providing patients/ caregivers with an electronic or written document to act as a reminder/ resource	Will ensure that physicians do not omit or 'gloss over' prominent issues and patient can look up information provided in a less stressful environment.	(106)
		Educational videos and online modules before the appointment	Will prepare patients for consultation.	(80)
Patient-physician interaction	Patient involvement in decision-making: (= Interaction with different specialities; perceived shared decision-making; paternalistic care, (clear) information provided by the doctor; psychological support)	Interdisciplinary counselling service	Will enable the patient to receive a complete picture.	(105)
		Provide more information about their cancer, long-term follow-up, and potential complications.	Setting the scene for decision-making and setting patient expectations	(106)

		Shared decision-making modelling	Consider the role of reimbursement models (US) and private consultations. Increases adherence to clinical management guidelines	(80)

4.1.4. Discussion

The included studies introduce various approaches and gaps at different entry points on how to support patients in their decision-making process and to deter from paternalistic decision-making models. Shirk (2018) and Moretto (2014) concluded that patients lack knowledge even after counselling (80, 106). They are heavily influenced by paternalistic care (80). To improve guidance and enable the patient to actively participate in their care, Huber et al. introduced interdisciplinary counselling in which the patient is encouraged to attend the tumour board (i.e., Multi-Disciplinary Team meeting) (105). This led to a significant shift in treatment decision-making, with documented change in treatment decisions alongside improved satisfaction with care (105). McAlpine et al. developed two patient decision aids for patients with kidney cancer, which aim to improve decisional quality by asking the patient questions to guide the decision (107, 108).

4.1.4.1. Limitations

This mixed methods systematic review captures a wide range of both QN and QL literature. However, due to the aim of identifying articles representing the patient perspective, they (1) explored patient views (> 18) on treatment decision-making for localised kidney cancer; or (2) were of sufficient methodological quality (quality was assessed). For the purpose of this thesis, it was only possible to include five studies, which does not necessarily offer a fully wide-ranging perspective. Hence additional research was performed in the subsequent chapter to dive deeper into the decision-making process from a multifactorial perspective.

4.1.5. Conclusion

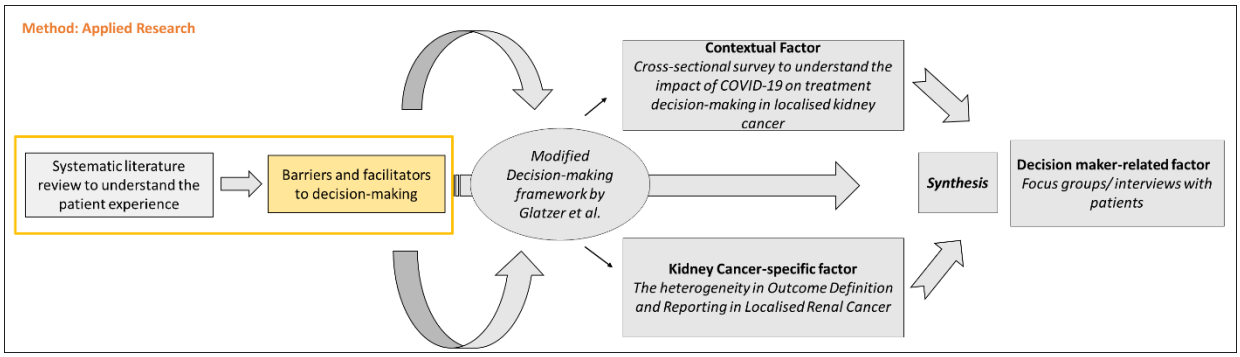
To capture the complexity of decision-making, there is a need to understand the factors that influence patient decision-making. An understanding of these factors is required to reduce the current paternalistic decision-making models of care to one that empowers patients to

take an equally active part in the decision-making process. A limitation of this review is that only a few studies currently have assessed factors affecting patient decision-making in kidney cancer. In contrast, a large proportion of literature is dedicated to exploring factors facilitating HCP's treatment decision-making. Hence, the next section of this chapter focuses on combining both perceptions.

4.2. Mixed Methods Systematic Review: The current evidence for factors that influence treatment decision-making in localised kidney cancer

As the initial systematic review yielded only five studies, a significant gap was identified in the current literature regarding patient perspective and the current environment of treatment decision-making in localised kidney cancer. To address this, the search criteria and inclusion criteria of the first systematic review were broadened and the topic of treatment decision-making in localised kidney cancer was approached as a multifactorial and multifaceted process. This approach was guided by the framework developed by Glatzer et al. (89), which as described earlier, outlines a comprehensive framework for describing decision-making in oncology.

Figure 12: Methodology overview- 1B Mixed methods systematic review: The current evidence for factors that influence treatment decision-making in localised kidney cancer: a mixed methods systematic review



This systematic review has been published in the Journal of Urology in 2022. Cristiane Decat Bergerot and Ulka Vaishampayan examined the review and the Journal of Urology published commentaries of both authors (94). After receiving an invitation to reply to the commentaries, the opportunity presented itself to provide a feature article to highlight the main findings (see Appendix 3) (94).

4.2.1. Introduction

To enable robust treatment discussions and as a result of identifying extensive gaps in the literature, there is a need to determine and understand the barriers and facilitators to treatment decision-making as a multifactorial process. This provides a basis for future research themes to study interventions aimed at facilitating and supporting patients and HCPs during this decision-making process.

Therefore, the purpose of this thesis is to systematically evaluate the literature for factors influencing treatment selection as a management strategy for localised kidney cancer.

4.2.2. Methods

This mixed methods systematic review followed the Joanna Briggs Manual (JBI) on mixed methods systematic reviews (109) and was guided by the PRISMA guidelines (110).

4.2.2.1. Search strategy

Studies published between January 1, 2004, and April 23, 2020, were identified through a systematic search of electronic databases (PubMed and Cochrane Library). The search strategy focused on the use of keyword search terms to identify studies focusing on factors that influence treatment decision-making in localised kidney cancer; kidney OR renal AND cancer AND treatment OR intervention OR decision-making OR barriers OR facilitators (Table 8).

Table 8: Search strategy mixed methods review

PubMed:
((kidney) OR (renal))
AND
((cancer) OR (malignant) OR (carcinoma) OR (malignancy) OR (tumour) OR (tumour) OR (neoplasm) OR (neoplastic) OR (neoplasia) OR (RCC))
AND
((treatment) OR (intervention) OR (therapy) OR (surgery) OR (chemotherapy) OR (nephrectomy) OR (radiotherapy) OR (“active surveillance”) OR (ablation) OR (ablative) OR (cryotherapy) OR (RFA))
AND
(“facilitators*” OR “barriers*” OR “treatment choice” OR “treatment selection” OR ((treatment OR therapy) OR “Therapeutics”) AND *decision-making* OR (“Treatment allocation”))
Customise: date, species, language - 1st of January 2004 and, Humans, English
Cochrane Library
'Kidney cancer' and using customised publication date restrictions (01/01/2004-31/07/2019)

4.2.2.2. Study eligibility and selection criteria

The inclusion criteria recommendations of the JBI Manual for systematic mixed methods reviews were followed (109). Studies were included in which the participants were adults (≥ 18 years of age) diagnosed with localised kidney cancer (T1, T2, T3 N0M0) (8) and excluded if they were conducted before 2004 based on the updated WHO classification on kidney tumours in adults. Therein, the categorisation of kidney tumours was expanded, which

consequently impacted treatment options and decision-making (111). Studies were selected on the basis that: (i) they explored views on treatment decision-making; (ii) they were of sufficient methodological quality; and (ii) their findings could be translated into suggestions for supportive care.

QL studies with less than 20 participants (112), or without a specific statement on thematic data saturation as well as QN studies with less than 100 participants, were excluded.

4.2.2.3. Data Quality

The included QL and QN studies focusing on patients' preferences were evaluated for quality using the Purpose, Respondents, Explanation, Findings and Significance (PREFS) quality checklist, which focuses on five areas: 1) purpose; 2) respondent; 3) explanation; 4) findings; 5) significance (113) (see Table 9).

Table 9: Legend- PREF

P	Purpose whether preference assessment was a core and clearly defined objective of the study
R	Respondence an assessment of the risk of selection bias that might be present if respondents differ from non-respondents
E	Explanation whether the methods are explained in sufficient detail and clarity to enable the replication of a study
F	Findings assessing the potential biases arising from excluding data from the findings
S	Significance whether key results were reported stochastically and with tests of significance
x	reported
-	Not reported

The quality score was calculated by adding one point for each 'yes' answer on the PREFS checklist, with a maximum potential score of 5. From this, the mean PREFS quality score was calculated (see Table 10).

Table 10: PREF Checklist

Authors	Type of Study	Categorisation	Score	Purpose	Respondence	Explanation	Findings	Significance
Alam R, et al. (2019)	QN	HRQoL	5	x	x	x	x	x
Barwari, K et al. (2012)	QL	Survey	5	x	x	x	x	x
Bhindi B, et al. (2018)	QN	Comparison of treatments	2	-	-	-	x	x
Dash A, et al. (2006)	QN	Comparison of treatments	5	x	x	x	x	x
Desai MM, et al. (2005)	QN	Comparison of treatments	3	x	-	x	-	x
Golan S, et al. (2018)	QL	Survey	4	x	x	x	x	-
Gong, E. M, et al. (2008)	QN	Comparison of treatments	3	x	x	x	-	-
Gratzke C, et al. (2009)	QN	HRQoL	4	x	x	x	-	x
Guillotreau J, et al. (2012)	QN	Comparison of treatments	3	x	-	x	-	x
Huber J, et al. (2015)	QL	Interview and focus group	4	x	-	x	x	x
Kwon T, et al. (2015)	QN	Preference	5	x	x	x	x	x
Larcher A, et al. (2017)	QN	Comparison of treatments	5	x	x	x	x	x
Marszalek M, et al. (2009)	QN	Comparison of treatments	4	x	x	x	-	x
Medina-Polo J, et al. (2011)	QN	Comparison of treatments	3	x	-	x	-	x
Moretto, et al. (2014)	QL	Survey	4	x	x	x	-	x
Naya Y, et al. (2015)	QN	Comparison of treatments	4	-	x	x	x	x
Shirk JD, et al. (2018)	QL	Survey	5	x	x	x	x	x

Papers that included cohorts or registries were assessed for strength of evidence. A modified version of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (114) was used (see Table 11). The following items were assessed: clear explanation of all outcomes, exposures and potential confounders, data source, bias, statistical methodology, descriptive data, and characteristics of individuals given. In each of the eleven categories, one point was assigned to each positive response, giving a possible total score of 11 (see Table 12).

Table 11: Legend STROBE

x	reported
-	not reported

Table 12: Assessment of the literature using the modified STROBE checklist

Author and year	Study design	Score	Number of participants, variables			Bias			Statistical methodology		Descriptive data		
			Outcome	Exposure	Confounder	Documented	Addressed	Full description	Missing data	Sensitivity analysis	Demographic	Clinical	Social
Ambani, et al. (2016).	QN	8	x	x	-	x	x	-	x	x	x	x	-
Audenet et al. (2014)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Bjurlin MA, et al. (2017)	QN	11	x	x	x	x	x	x	x	x	x	x	x
Chang X, et al. (2015)	QN	8	x	x	-	x	x	x	x	-	x	x	-
Corradi R, et al. (2017)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Ghanie A, et al. (2018)	QN	6	x	x	-	x	-	x	-	-	x	x	-
Haramis G, et al. (2012)	QN	6	x	x	-	x	-	x	-	-	x	x	-
Kim C.S, et al. (2014)	QN	7	x	x	x	x	-	x	-	-	x	x	-
Klatte T, et al. (2011)	QN	6	x	x	-	x	x	-	-	-	x	x	-

Author and year	Study design	Score	Number of participants, variables			Bias			Statistical methodology		Descriptive data		
			Outcome	Exposure	Confounder	Documented	Addressed	Full description	Missing data	Sensitivity analysis	Demographic	Clinical	Social
Kowalczyk KJ, et al. (2012)	QN	7	x	x	x	x	-	-	-	x	x	x	-
Maturen KE, et al. (2007)	QN	7	x	x	-	x	x	-	x	-	x	x	-
McIntosh AG et al., (2018)	QN	9	x	x	-	x	x	-	x	x	x	x	x
O'Malley RL, et al. (2013)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Parker PA, et al. (2013)	QN	8	x	x	-	x	x	x	-	-	x	x	x
Peyton CC, et al. (2017)	QN	7	x	x	x	x	-	x	-	-	x	x	-
Pierorazio, P. M, et al. (2015)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Shin SJ, et al. (2015)	QN	6	x	x	-	x	x	-	-	-	x	x	-
Tan HJ, et al. (2012)	QN	8	x	x	x	x	-	x	-	-	x	x	x

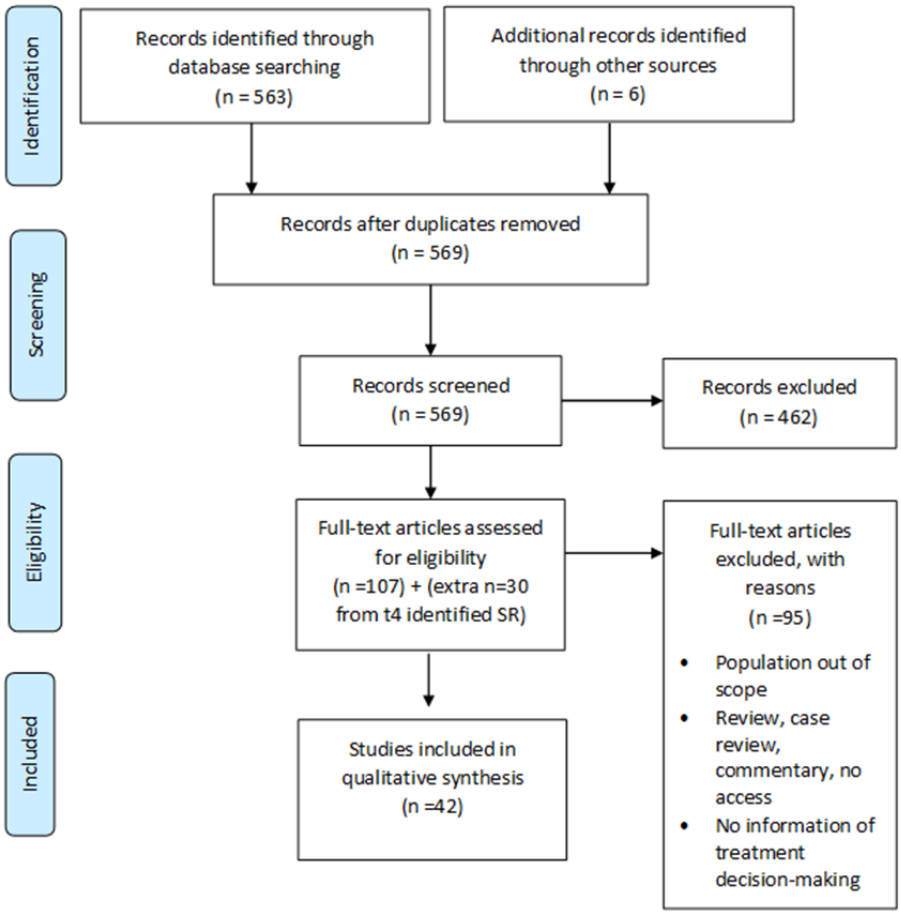
Author and year	Study design	Score	Number of participants, variables			Bias			Statistical methodology		Descriptive data		
			Outcome	Exposure	Confounder	Documented	Addressed	Full description	Missing data	Sensitivity analysis	Demographic	Clinical	Social
Tanagho YS, et al. (2013)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Tomaszewski, J. J, et al. (2014)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Woldu SL, et al. (2014)	QN	6	x	x	-	x	-	-	x	-	x	x	-
Yang C, et al. (2019)	QN	6	x	x	-	x	-	-	-	-	x	x	-
Yasuda Y, et al. (2013)	QN	4	x	x	-	-	-	-	-	-	x	x	-
Zhou, H.-J, et al. (2017)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Zondervan PJ, et al. (2016)	QN	6	x	x	-	x	-	-	-	-	x	x	-

All QN studies included outcome, exposure, descriptive and clinical data and only one study did not report potential bias. However, there was a prominent level of variability found in relation to confounder variables, assessment of bias, missing data, sensitivity analyses, and the characteristics of individuals given social data.

4.2.3. Results

553 unique citations were identified, of which 447 were excluded as review articles, commentaries, or narratives. The full-text screening was carried out on 106 articles. Four of these papers were systematic reviews (SRs), resulting in an additional thirty papers for review. Seventy-nine studies were eventually excluded, resulting in forty-two articles included for synthesis (see Figure 13). Seventeen were QL and QN studies, focusing on patient's preferences, whilst twenty-five were cohort studies. Given the heterogeneous study designs, no statistical comparisons were made.

Figure 13: PRISMA Flow chart for mixed methods systematic review on barriers and facilitators to treatment decision making



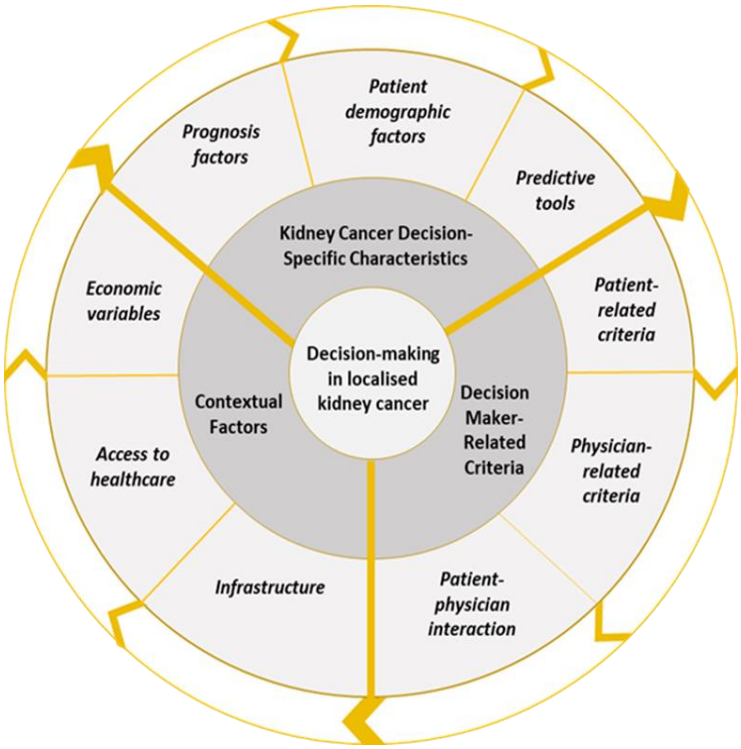
For this mixed method analysis, a meta-aggregation of data was presented using a Bayesian approach, whereby all data was codified into themes. This approach generates summative statements of the evidence to equally inform the topic in a mutually compatible format (Table 13). While the identified papers explore other outcomes, the purpose of this mixed methods systematic review was to capture information on decision-making.

Table 13: Domains and factors that influence treatment decision-making

Domain	Factor	Details	References
Kidney Cancer Specific Characteristics	Prognosis factors Anatomical, histological, clinical, and molecular factors influence decision-making	Pathologic tumour size; tumour stage/ TNM/ anatomic classification; location of tumour/ accessibility. Grade/ Fuhrman nuclear grade/growth rate; growth pattern histology; pathological diagnosis/ data/ stage/ outcome; tumour volume; benign vs malignant; indolent vs aggressive; type of tumour/ RCC subtypes; nephrometry radius; exophytic vs endophytic; anterior/posterior; complexity score/anatomic complexity; multifocal disease/ number of lesion; mass composition; tumour side; state of disease; pain level; single kidney; solidary kidney; kidney function (eGFR)/ preoperative kidney function/ kidney function values; ASA score	(105, 115-134)
	Demographic characteristics	Age; Charlson score CCI/ comorbidities; BMI; gender; race; marital status; Socio Economic Status (SES); education, smoking history; family history of RCC; prior RCC diagnosis/ kidney medical history; employment status; education	(105, 115-119, 121, 124, 126, 128-133, 135-149)
	Predictive tools	Scoring systems: NePhRO scores, C-index; The Predictive Tool to Determine Renal Function Benefit of Nephron Sparing Surgery Compared to Radical Nephrectomy online calculator; R.E.N.A.L.-nephrometry score; The PADUA classification. Diagnostic tools: Imaging (MRI)/ CT Diagnostic accuracy of CT or MRI; Biopsy (Biopsy, CT diagnosis, Biopsy technique & Biopsy Result; Biopsy sensitivity; Biopsy specificity; Biopsy technique; Probability of nondiagnostic biopsy; Probability of biopsy track seeding with malignant cells; clinical behaviour by abdominal imaging)	(115, 116, 118, 120, 123, 125, 129, 135, 150)
Decision Maker-related criteria	Patient related criteria	socioeconomic status; level of education; having an academic degree; history of cancer; history of invasive procedures and history of procedural complications; personal or family history of cancer; anxiety associated with missing a cancer; concern about potential biopsy complications was the primary reason to decline RMB among surveillance patients; reluctance to undergo biopsy; concern about potential biopsy complications; patient preference; QoL	(116, 125, 132, 138)
	Physician related criteria	Surgeons' preference/ surgical modality was chosen at the discretion of the surgeon; surgeon's experience level confidence in the management option	(118, 119, 122, 125, 127, 137, 138, 151)
	Patient physician interaction	Patient physician interaction; clinical decision aids; interdisciplinary discussion	(80, 105-107, 116, 120, 125, 133, 135, 146, 152)
Contextual factors	Economic variables	Insurance; Income by zip code, cost of procedure	(135, 146, 148)
	Access to healthcare	Geographic region; Urban vs Rural; Travel distance; Medicare A or B; shared decision-making in included reimbursement models	(80, 118)
	Health care organisation	Facility type; facility location; shared decision-making; infrastructure available	(80, 116, 119, 135, 151)

The themes identified, were presented using a modified version of Glatzer et al.'s framework 'Decision-making Criteria in Oncology' (Figure 14) (89). These three domains were used and modified to present the factors identified in the literature as barriers or facilitators of treatment decision-making.

Figure 14: Domains that influence treatment decision-making



Source: Modified Glatzer et al.

All abstracts and full texts were screened independently by two reviewers (KB, NK). One researcher extracted the data, after which it was reviewed by a second. Any disagreements arising were resolved through consultation with a third clinical researcher (MVH). The following data was collected: author, year of publication, type of study, patient population and aim of the study, as well as all factors that were identified as influencing decision-making.

4.2.3.1. Study design of included studies

Of the 36 QN studies, twenty-four studies were conducted in the United States of America, six in Europe, two in China, two in Japan, and two in South Korea. The number of study participants was <500 in 24 studies, <1000 in 4 studies and >1000 in 8 studies. Only 10 studies collected data across multiple institutions. Of those, three studies used the SEER

database, two the DISSRM registry, one the national cancer registry, and four studies collaborated with other institutions to collect data and collate results. The single institution studies used their own hospital registry to assess the data collected. Three studies reported HRQoL and two of those are using validated questionnaires/ tools.

Of the included six qualitative studies, three were solely surveys, one a mixed method survey, one study performed a survey and interviews, and one conducted interview and a focus group.

4.2.3.2. Quality scores

The PREFS quality scores ranged from 2 to 5 and the mean PREFs score of the included papers was 4 (SD 0.88). The assessed paper was further categorised using categories suggested by Joy, et al. (113): Four papers fall under the category contingent evaluation (i.e. survey) with the mean score for this category being 4.5 (SD 0.45); Ten papers stated preference or choices of treatment with the mean score of 3.7 (SD 0.96); one paper fell under the category qualitative (i.e., interviews, focus groups) with the score 4. Two studies used a validated HRQoL tool and scored a mean quality score of 4.3 (SD 0.46) (see Table 10).

The mean quality score of papers assessed with the STROBE checklist (114) was 6.44 (SD 1.5), with scores ranging from 4 to 11 (see Table 12).

4.2.4. Evidence synthesis

Within the three domains identified by Glatzer et al., numerous barriers or facilitators to treatment decision-making in kidney cancer were identified and summarised below and in Figure 11.

4.2.4.1. Kidney cancer specific characteristics

Kidney cancer specific characteristics were divided into three domains: prognostic factors, patient demographic factors, and predictive tools.

4.2.4.1.1. Prognostic factors

Facilitators: Fifty percent of included papers highlighted prognostic factors such as anatomical, histological, clinical, and molecular factors. These papers highlighted tumour size at diagnosis as a facilitator to treatment decision-making (105, 115-134), with larger tumours being more likely to be of malignant potential (115, 117).

4.2.4.1.2. Patient demographic factors

Facilitators and Barriers: Seventy-one per cent of papers found that age, comorbidities, BMI and gender influenced treatment decision-making as either a barrier and/ or facilitator based on how they were presented in the paper (105, 115-119, 121, 124, 126, 128-133, 135-149). Of those, five papers highlighted that younger patients were identified as more likely to undergo PN or NSS (including, LPN, or RPN) (126, 131, 136, 145, 148), whereas those undergoing ablation or AS were older with more comorbidities (118, 126, 131, 136, 137, 145-148).

Barriers: Three papers identified race and gender as important barriers to take into consideration (116, 117, 142). O'Malley et al. highlighted in their research that women had a superior comorbidity profile, which would make them better candidates for PN (116). In addition, three studies showed that women were more likely to have benign disease (116, 117, 142), while men were diagnosed with a more aggressive histology, larger tumours, higher grade (117). Despite this, women were found to be more likely to receive RN, with Black women having the highest rate in the presented study (116).

4.2.4.1.3. Predictive tools

Facilitators: Eleven papers described predictive tools to support decision-making (115, 116, 118, 120, 123, 125, 129, 135, 137, 146, 150). The RENAL nephrectomy score was used to help overcome selection bias (133), assist surgeons in preoperative decision-making (150) and correlate with tumour histology and grade (137, 146). Similarly, the PADUA score was reported to support the process of decision-making by identifying the tumour complexity. Four papers highlighted that biopsy results significantly influenced treatment decision-making in most patients (118, 129, 135, 146).

Maturen et al. reported that in their sample, 61% of the biopsies performed resulted in alteration in management and substantive change of treatment (129). Bjurlin et al. noted that, while controlling for demographic and disease characteristics and comorbidity, 61% of patients were more likely to be managed non-surgically of those who received a diagnostic biopsy (118).

4.2.4.2. Decision-maker- related criteria

Decision-maker related criteria were divided into patient related criteria, physician related criteria and patient physician interaction.

4.2.4.2.1. Patient related criteria

Facilitators or barriers: Four papers suggested education status, socioeconomic status (SES), family history of cancer as facilitators or barriers to patients' treatment decision-making (116, 125, 132, 138). One study reported that having an academic degree might be a facilitator in treatment decision-making (125).

Barriers: Cancer anxiety, related to personal as well as family history or the fear of missing a tumour, was reported as a strong barrier to active surveillance in the context of repeating biopsies (125, 132).

4.2.4.2.2. Physician-related criteria

Facilitators: Clinical experience, preference, confidence in management option and evidence-based recommendations were factors identified in the literature as influencing HCPs' treatment decisions (119, 122, 127, 137, 138, 151). Clinical experience of the surgeon was suggested as a factor to facilitate treatment decisions (119). Shin et al. reported that surgeons with more experience are more likely to choose partial nephrectomy, even for complex cases (119).

Barriers: Bjurlin et al. reported that 30% of patients who saw a urologist first were less likely to have a diagnostic biopsy than those who first saw a non-urologist physician (118). The confidence in the management option of HCPs was also reported as a barrier. Golan et al. reported that 40% of their participating urologists completely opposed a kidney mass biopsy (125). 50% of urologists in a study by Barwari et al. indicated that small kidney masses were the least important reason to perform a biopsy and 73% of the urologists very rarely or never recommended kidney mass biopsy for treatment decision-making (151).

4.2.4.2.3. Patient physician interaction

Facilitators: Eight articles reported the importance of shared decision-making as a facilitator (80, 105, 107, 120, 135, 146, 150, 152). Two papers introduced a clinical decision aid to empower the patient to take a definitive decision and to reduce decisional conflict (80, 107).

A Canadian survey highlighted the need to provide additional electronic or written documents to empower the patient to have a meaningful discussion (106).

4.2.4.3. Contextual factors

I divided contextual factors into economic variables, access to health care, and the health care organisation such as type of practice.

4.2.4.3.1. Economic variables

Barriers: Cost of procedure was identified as a barrier or facilitator for treatment decision-making in localised kidney cancer by two studies based in the US (146, 148). ORN and OPN have been reported to be costlier than less invasive treatments. Active surveillance and ablation have been presented as least costly. Understanding the chances of progression could lower costs (146).

4.2.4.3.2. Access to health care

Facilitators: One's geographic region was identified by Bjurlin et al. as a facilitator to getting biopsied (118). Being insured under a certain system contributes to access to health care as either a facilitator or a barrier (148).

4.2.4.3.3. Health care organisation

Facilitators and barriers: Five studies described practice patterns of institutions and type of practice (80, 116, 119, 135, 151) as potential factors influencing treatment decisions. One study identified a significant difference between 'never perform a biopsy' amid HCPs practising in a University hospital compared to other types of practices (151). A similar observation was identified by two studies that reported greater nephron sparing surgery usage in centres of excellence or tertiary centres of excellence (116, 119). Ensuring that a system of shared decision-making is in place can also be interpreted as a facilitator for decision-making in localised kidney cancer (80).

4.2.5. Discussion

This review has identified a multitude of barriers and facilitators to treatment decision-making in kidney cancer, spanning all domains of Glatzer et al.'s 'Decision-making Criteria in Oncology' framework (89). The literature reviewed has shown that the ability of kidney cancer patients to reach decisions about their treatment is affected by kidney cancer

specific criteria, decision maker-related criteria and contextual factors which are consistent themes within the framework.

4.2.5.1. Kidney cancer-specific factors

4.2.5.1.1. Prognostic factors

Prognostic factors were found to be facilitators to decision-making in kidney cancer in this review (105, 115-134). This aligns with the findings reported in Campi et al.'s SR, where it was identified that most decisions were based on tumour-related factors and renal mass growth was the most influential trigger (153). This is consistent with our findings, where prognostic factors are identified as facilitators to clinical decision-making.

4.2.5.1.2. Demographic factors

Some studies included in this review found that age, comorbidities and BMI may have influenced treatment decision-making (105, 115-119, 121, 124, 126, 128-133, 135-149). Patient age has long been highlighted as the most controversial patient demographic factor to base decision-making on across cancer care (154). A scoping review by Tranvag et al. highlighted that it is important to accept the relevance of patient age in a clinical setting, however discussion with the patient should be transparent (154). Puts et al. further suggested that individual geriatric assessments in a multidisciplinary diagnostic environment should include psychological, social and functional capacity instead of using age as a proxy on which to base clinical decision-making (155).

This review also found that patients' gender and ethnicity can have an indirect influence on treatment decision-making in kidney cancer (116, 117, 142). Being black and/ or female has been found to be associated with higher use of RN (116), despite the fact that this ethnic group is at higher risk of chronic kidney disease progressing to end-stage renal disease (156). In support of this finding, Mancini et al. found that gender influences treatment option selection and identified that men were more likely to receive AS or NSS treatments (157). This further supports the findings of our review that potential indirect barriers are linked to demographic factors including race and gender and due to the current observational design of the studies. It would be recommendable for future studies to further investigate how demographic factors like age and gender influence choice.

4.2.5.1.3. Predictive tools

This literature review suggests that predictive tools facilitate decision-making. The PADUA or RENAL score can act as a facilitator to decision-making to support HCPs when quantifying tumour complexity (118, 129, 135, 137, 146, 150). Alvim et al. who compared the predictive accuracy of Nephrometry Scores to assess PN complexity, did not suggest a preference for a single nephrectomy scoring tool (158), which is also reflected in the results of our review.

It was further identified that performing a biopsy is a facilitator to treatment decision-making. Across cancer care, biopsies have long been used to contextualise a cancer diagnosis in regard to type, grade and potential treatment options (159). A recent study by Finelli et al. confirmed the importance of biopsies in respect to progression rates amongst kidney cancer subgroups (160), which ultimately may enable clinicians to present patients with options to avoid overtreatment and treatment complications (160, 161).

4.2.5.2. Decision maker-related criteria

4.2.5.2.1. Patient-related criteria

It was found that education status, SES, a family history of cancer, and cancer anxiety can be barriers to treatment decision-making in kidney cancer (116, 125, 132, 138). Consistent with this review, Campi et al. identified patient preference as a trigger to treatment decision-making in the context of AS. However, they concluded there was a clear lack of evidence exploring the process of patient preference in detail (153). Our review identified cancer anxiety as a strong barrier (125, 132). Numata et al. showed in their research on early-stage malignant brain tumour that patients experiencing anxiety during treatment decision-making are often driven by the fear of uncertainty of prognosis and their future QoL (162).

Results from the studies reviewed indicate that most patients appear to prefer to be involved in their decision-making. However, Laviana et al. found that in most tumour groups, patients do not receive sufficient information to educate themselves on their treatment options (163). They recommended that structured decision aids aimed at guiding and supporting the patient through this process, ultimately reduced anxiety (163) and improved concordance between the patient and clinician (164, 165). Given that anxiety has been identified as a barrier in our review, implementing such decision aids will support the decision-making process. The International Kidney Cancer Coalition (IKCC) has hence

developed and validated a decision-making tool, which can be used to support or share treatment decision-making (107).

4.2.5.2.2. Clinician-related criteria

Clinician confidence in particular management options and the provision of evidence-based recommendations have been suggested as facilitators to treatment decision-making in the studies included in our review (118, 119, 122, 125, 127, 137, 138, 151). It should be noted that clinician bias was highlighted as an influencing factor. Across cancer care, this has been identified in a literature review as 'default' bias, which referred to HCPs presenting a default option relating to the preference of the treating physician (166). In the UK, the implementation of a multidisciplinary team meeting (MDM), where all new patients are discussed by the team of treating cancer clinicians, was suggested to reduce clinician bias in the treatment recommendation process (167). The literature for breast and prostate cancer has shown that MDM discussions also improve guideline adherence (168). Stewart et al. reported that over a period of six years, active surveillance in prostate cancer increased by 80% as a result of MDM discussion prior to patient consultation (169).

4.2.5.2.3. Patient-physician interaction

Patient-physician interaction factors in decision-making were identified, with studies suggesting that shared decision-making is a facilitator in kidney cancer, and that clinical decision aids providing information to patients can also be useful (80, 105-107, 116, 120, 125, 133, 135, 146, 152). There is a clear link between shared decision-making, patient-related criteria, physician related criteria and patient-physician interaction. Bomhof-Roordink et al. emphasised choice awareness as a pivotal concept of shared decision-making. Their review also highlighted that the individual making the final decision is of less importance in a shared decision-making environment, since all stakeholders should be equally educated and mutually agree on the decision (170). In addition, it was suggested in one study that the provision of additional electronic or written documents to the patient can empower the patient to discuss treatments with their physician in a meaningful way (106).

4.2.5.3. Contextual factors

4.2.5.3.1. Economic variables

Economic variables were identified as an important facilitator or barrier to treatment decision-making (135, 146, 148). However, this is highly dependent on the health care system's financial approach, as there are variations at national and local level. The studies identified looked at the US health care system, where disparities in costs of different treatments have been suggested to affect treatment decision-making. Chun-Ru Chien et al. indicated that costs appeared to rise with aggressiveness of the local treatment in the US (171). Nevertheless, there is significant inequality in access to healthcare and insurance in the US (172), which introduces an additional systemic factor that may affect treatment decision-making, which may not apply to other countries.

4.2.5.3.2. Access to healthcare

This SR highlights that limited access to healthcare could potentially affect the decision-making ability (80, 118). This includes regional geographic variation in the offering of kidney cancer diagnosis, treatments, and services.

The relationship between cancer survival and hospital districts was reviewed by Seppä et al., who identified substantial variation across geographical locations in Finland and concluded that the differences were explained by the availability of cancer services and treatment (173). This phenomenon has also been described in other urological cancers (114). Kinsella et al. highlighted the differences in uptake of active surveillance for prostate cancer ranged from 27-80%, further suggesting that this variability is linked to the availability of the technology to deliver surveillance imaging and treatment protocols (114).

Thorstenson et al. recommended that national cancer registries such as the National Swedish Kidney Cancer Register could help to facilitate benchmarking of contextual factors related to health care access across geographical regions (174). Again, this is reflective of research carried out in prostate cancer where population-based registries have been used to benchmark the uptake of treatments across regions and countries to facilitate the distribution of healthcare services (175).

4.2.5.3.3. Healthcare organisation

Treatment decisions in kidney cancer can vary by healthcare centre, for example regarding the use of biopsy or surgical techniques (80, 116, 119, 135, 151). As part of Tran et al.'s observational study, the positive association between type of surgery and complication rate with hospital volume was evaluated in the UK. They found a positive association between hospital volume and the proportion of T1 tumours that were treated with PN rather than RN. They also identified that the complication rate decreased with rising hospital volume. (176).

4.2.6. Limitations

This mixed methods systematic review captures a wide range of both QN and QL literature. Furthermore, the application of a recently published quality assessment tool, specifically developed to assess papers focusing on barriers and facilitators, further strengthens our results (113). However, the included studies were heterogeneous and single centre based, reflecting the current research portfolio in this field. The majority of the QN studies were of an observational nature and the decision-making was retrospectively analysed. Most of the real-world evidence studies reported selection bias, however, we mitigated this by assessing the strength of the studies using the PREFs and STROBE checklists. Nevertheless, additional qualitative research should be performed to ensure the HCP's and patient's voice is captured.

4.2.7. Conclusion

When HCPs and patients decide on the most suitable treatment, they are confronted with multiple factors which influence the process. The clear recommendation from this SR is to consider the multitude of barriers and facilitators to treatment decision-making.

4.3. Summary of Chapter 4

Chapter 4 has revealed that there is limited research available to fully understand the process of treatment decision-making in patients with localised kidney cancer. As a result, the scope of the initially planned systematic review was expanded to gain a more comprehensive understanding of the multifactorial nature of this process.

The findings from this extended mixed methods systematic review have informed the modification of the decision-making framework proposed by Glatzer et al. to better capture the different factors that influence treatment decision-making in the context of localised kidney cancer. Moreover, this chapter provides an overview of the current evidence published. By identifying and examining the various factors that can impact this process, it has the potential to inform the development of more effective supportive care strategies for patients and their families.

This builds the evidence basis for the next research stages, where the impact of contextual factors on treatment decision-making is shown using a snap-shot cross sectional survey of the first six months of COVID-19.

Chapter 5. Contextual Factors: Cross-sectional survey to understand the impact of COVID-19 on treatment decision-making in localised kidney cancer

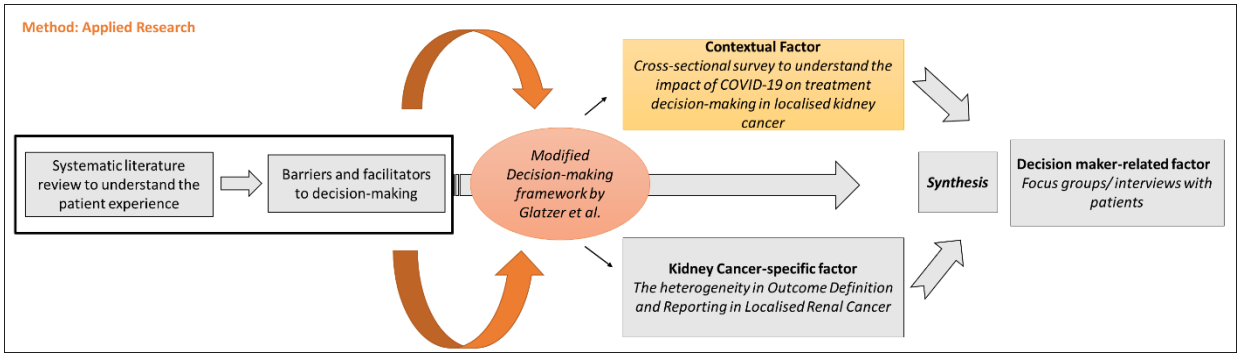
This chapter explores the impact of a key contextual factor, the coronavirus (COVID-19) pandemic, on treatment decision-making in localised kidney cancer (Figure 15).

In early 2020, while this comprehensive systematic review to understand the evidence linked to treatment decision-making in localised kidney cancer was being conducted, the COVID-19 pandemic (a respiratory disease caused by SARS-CoV-2) hit the world and life changed overnight. During times of national/ international crises, necessary influence is exerted by both governmental bodies and medical organisations to ensure medical treatments are risk stratified, balancing risk of mortality due to disease with risk of mortality due to virus (177). Personally, I felt it was therefore important to understand whether the complex multifactorial process of treatment decision-making had been further complicated/ compromised through this unforeseeable contextual factor.

To achieve this, I designed a cross-sectional survey to get a snapshot of the impact of COVID-19 on the healthcare of the NHS within the first 6 months of the pandemic (March-September 2020).

The subsequent manuscript was published as a commentary piece in BJUJ Compass (Appendix 4) (95).

Figure 15: Methodology overview: 3. Contextual factors involved in the treatment decision-making process



5.1. How did the COVID-19 pandemic impact the National Healthcare System in the UK during the first 6 months - a cross-sectional survey

As highlighted above, the COVID-19 pandemic complicated the process of decision-making. Official guidance in the UK and the EU called for non-urgent cancer care to be rationed, delayed and/ or adapted (178) to mitigate the risk of death if COVID-19 was contracted during treatment. In line with this guidance, the British Association of Urological Surgeons (BAUS) recommended that patients diagnosed with localised kidney cancer should be offered a period of surveillance rather than curative treatment (179).

The impact of the COVID-19 pandemic medical guidance on patients was described by kidney patient associations in the US and UK (Kidney Cancer Research Alliance (KCCURE) and Kidney Cancer UK (KCUK), respectively) in small snapshot surveys which explored patient experience, anxiety, and the management thereof (180, 181). They found that anxiety was high in respect to the implications of COVID-19 for cancer treatment and follow-up.

5.1.1. Methods

Building on these initial observations, a cross-sectional, descriptive, web-based survey amongst HCPs (EU and UK) working in centres delivering localised kidney cancer treatments was conducted. This allows for an improved insight into the barriers or hurdles as well as possible opportunities and facilitating factors to supporting patients in their treatment decisions during the COVID-19 pandemic.

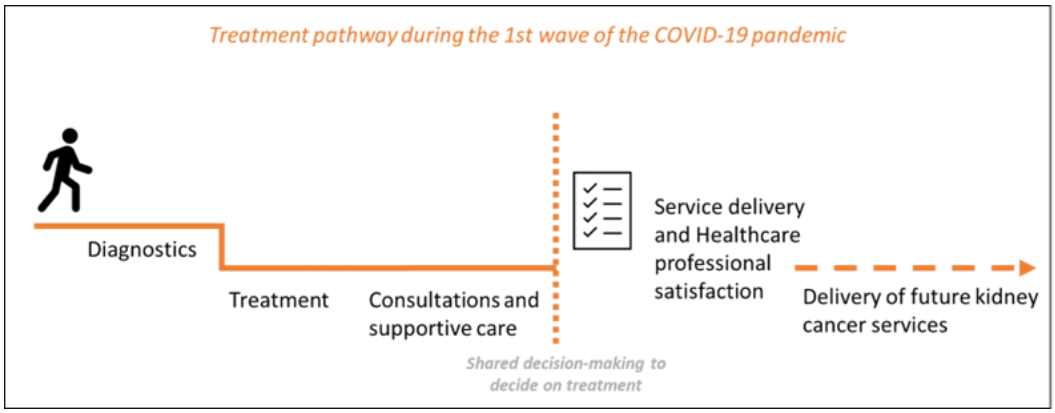
The survey design was informed by multiple sources of information. Firstly, Chapter 4 of the thesis draws upon existing knowledge gained from a rapid scoping review of the literature on COVID-19 and its impact on clinical practice. This literature review provides valuable insights into the facilitators and barriers of decision-making during the pandemic. Additionally, recommendations and guidelines issued by medical societies were also considered when designing the survey questions.

Moreover, the survey design benefitted from the expertise and experiences of the steering group committee, particularly RB and NK. As both members of the committee had first-hand experience with the changes in clinical practice resulting from the pandemic, their insights and knowledge were instrumental in ensuring the survey captured relevant aspects of decision-making in this context.

To define the overall topics of the survey, the treatment pathway (during the 1st COVID-19 wave) up to the point of decision making was reviewed (Figure 16). Using this knowledge, the questions focused on capturing the specific environment and changes experienced by health care professionals treating kidney cancer patients during COVID-19. To capture the moral distress, a validated tool, i.e., the Moral Distress-Scale was used to assess the extent to which individuals perceive conflicts between their ethical values and the actions they are required to take within their roles. The survey was specifically designed to provide a snapshot.
Due to the circumstances at that time, obtaining ethics approval to recruit participants through hospitals was not possible. Additionally, considering the already demanding workload of doctors, the conscious decision was made not to impose any additional burdens on them. As a result, we sought ethics approval through the KCL ethics board and opted to recruit participants through Twitter. The survey was approved as a Minimal Risk Study by the ethics board of KCL.

To analyse the results of the survey, the data was cleaned to check for missing values, outliers, or inconsistencies. I counted the frequency of each response. To evaluate whether there was a statistical associations between doctors and nurses, the Chi-Square test was used. I did not have access to a statistical software (due to the COVID-19 pandemic), and hence calculated the results by hand.

Figure 16: Treatment pathway during the 1st wave of the Covid-19 pandemic up to the point of decision-making



5.1.2. Results

The survey was distributed via Twitter on May 16, 2020 and was open for responses for one month. Overall, 58 respondents (36 from the UK and 22 from outside of the UK) completed the survey, of which 43% were UK doctors, 19% were UK nurses and 38% non-UK doctors. The predefined five main themes from the survey were used to structure the results and

discussion section: (1) diagnostics, (2) treatment, (3) consultations and supportive care, (4) HCP satisfaction, and (5) delivery of future kidney cancer care. Due to disparities in the healthcare guidelines followed by each country, the focus of the report was on the UK. The results of the survey are summarised in detail in Table 14 and explained below.

Theme 1: Diagnostics

Disruption to the diagnostic pathway in the UK was highlighted by 75% of survey respondents, compared to only 27% of non-UK respondents ($p < 0.00$). UK respondents reported several aspects of disruption, including reduced access to imaging (69%), as well as a reduction or lack of access to kidney biopsy (78%) and diagnostic consultations conducted via phone (83%) or video call (25%). Additionally, discussion of newly diagnosed kidney cancer patients in Multidisciplinary Team (MDM) meetings posed an additional challenge. During the COVID-19 pandemic, MDM meetings shifted to virtual platforms overnight. When asked about the preference for virtual events, 55% of UK nurses favoured a return to face-to-face meetings, while only 28% of UK doctors shared the same view.

Theme 2: Treatment

A significant proportion of clinicians who responded to the survey expressed that any treatment delay was deemed unacceptable. Among UK respondents, 58% reported that deferring treatment for 0-12 months for T1a disease, deferring treatment for 3-6 months in T1b disease (53% of respondents) or delaying a treatment for 0-6 months for T2 lesions (83% of respondents) would have an adverse effect on oncological outcomes. Dissatisfaction with the available treatment options during the COVID-19 pandemic was also evident, with none of the UK nurses and only 28% of UK doctors who responded to the survey expressing satisfaction with the treatment options provided to patients.

Theme 3: Consultations and Supportive Care

Telephone and video consultations were widely implemented across the UK in line with the British Association of Urological Surgeons (BAUS) guidance. Our survey identified that the majority of treatment consultations in the UK were conducted via telephone during the COVID-19 pandemic (86% for treatment consultation), compared to video consultations (22%). However, it remains unclear whether healthcare professionals (HCPs) would have felt more satisfied and able to provide supportive care through telemedicine consultations.

Notably, 55% of nurses and 24% of doctors in the UK expressed their opposition to continuing these changes in their clinical practice.

Theme 4: Service Delivery and Healthcare Professional Satisfaction

Respondents reported the UK's deferred treatment plan, which involved the inability to offer surgery or ablation, as a contributor to HCP dissatisfaction. Only 36% of UK respondents were able to perform partial nephrectomies, and a mere 8% were able to perform ablations. Additionally, 47% of UK respondents confirmed an increase in the number of patients contacting their service during the COVID-19 pandemic, while a significant proportion of healthcare professionals (56% of the medical team and 81% of the nursing team) were redeployed. Overall, 47% of UK nurses and doctors expressed satisfaction or high satisfaction with the service they provided during the peak of the pandemic.

Theme 5: Delivery of Future Kidney Cancer Care

A majority of UK respondents (78%) agreed that there is a need for additional resources in various areas, including imaging capacity (78%), theatre capacity (100%), inpatient capacity (78%), outpatient capacity (69%), and workforce resources (58%). Regarding the workforce, the respondents indicated a need for additional support, such as theatre teams (78%), Clinical Nurse Specialists (CNSs) (56%), surgeons (53%), radiologists (47%), administrators/coordinators (39%), and oncologists (33%).

Both doctors and nurses reported a high level of moral distress, with 67% of respondents indicating feeling either "distressed" or experiencing the "worst possible distress." This finding should be given serious consideration by policy makers and hospital executives in their future decision-making.

Table 14: Results of the cross-sectional survey

Theme 1. Diagnostics					
	UK (n=36)		Non-UK (n=22)		
Questions	Frequency	Percentage	Frequency	Percentage	p-value
Q13. Our diagnostic pathway has changed since the start of the COVID-19 pandemic.	27	(75)	6	(27.3)	< .0001
Q10. There has been an increase in enquiries from patients diagnosed with localised kidney cancer (due to delayed-treatment) since the start of the COVID-19 pandemic.					0.291
Strongly disagree - Disagree	8	(22.3)	9	(40,5)	
Neutral	10	(27.8)	8	(36.4)	
Agree - Strongly agree	17	(47.2)	5	(22.7)	
Q9. My patients have access to Cancer Nurse Specialists (CNS) support since the start of the COVID-19 pandemic.					0.024
Q9.1. Normal access	19	(52.8)	8	(36.4)	
Q9.2. Reduced access	16	(44.4)	8	(36.4)	
Focus on UK (n=36)					
			Frequency		Percentage
Q14. What has your imaging capacity been like during the COVID-19 pandemic?					
There is reduced access to imaging			25		(69)
There has been no change			11		(31)
Q15. What has your kidney biopsy capacity been like during the COVID-19 pandemic?					
There is a no access to kidney biopsy			9		(25)
There is reduced access to kidney biopsy			19		(53)
There has been no change			2		(5.6)
We do not carry out kidney biopsy as part of the diagnostic process			5		(13.9)
Missing			1		(2.8)
Q22. I would like to maintain the changes I have made to my clinical in practice with respect to virtual MDTs.					
Nurses (n=11)			Nurses/ Doctors p = 0.446		
Strongly disagree - Disagree			6		(54.6)
Neutral			4		(36.4)
Agree - Strongly agree			1		(9.1)
Doctors (n=25)					
Strongly disagree - Disagree			7		(28)
Neutral			8		(32)
Agree - Strongly agree			10		(40)
Theme 2. Treatment					

Q19. I believe that deferring treatment of T1a kidney lesions during the COVID-19 pandemic will lead to harm if it lasts...		
6-12 months	12	(33.3)
12 months	21	(58.3)
I do not believe deferring treatment of T1a kidney lesions during COVID-19 will lead to harm	3	(8.3)
Q20. I believe that deferring treatment of T1b kidney lesions during the COVID-19 pandemic will lead to harm if it lasts...		
0-3 months	2	(5.6)
3-6 months	19	(52.8)
6-12 months	12	(33.3)
12 months	3	(8.3)
Q21. I believe that deferring treatment of T2 kidney lesions during the COVID-19 pandemic will lead to harm if it lasts...		
0-6 months	30	(83.3)
6-12 months	6	(16.7)
Q12. I am satisfied with the treatment options I can offer patients with localised kidney cancer since the start of the COVID-19 pandemic.		
Very Dissatisfied - Dissatisfied	17	(47.3)
Neutral	12	(33.3)
Satisfied - Very satisfied	7	(19.4)
UK Nurses (n=11)	Nurses / Doctors p = 0.216	
Very dissatisfied - Dissatisfied	6	(54.6)
Neutral	5	(45.5)
UK Doctors (n=25)		
Very Dissatisfied - Dissatisfied	11	(44)
Neutral	7	(28)
Satisfied - Very satisfied	7	(28)
Theme 3. Consultations and supportive care		
Q16. How are your new diagnosis consultations delivered?		
Q16.1. New diagnosis consultations are delivered by phone call	30	(83.3)
Q16.2. New diagnosis consultations are delivered by video call	9	(25)
Q16.3. New diagnosis consultations are delivered by face to face	17	(47.2)
Q16.4. We have deferred patients for diagnostics	2	(5.6)
Q17. How are your treatment consultations delivered?		
Q17.1. Consultations are delivered by phone call	31	(86.1)
Q17.2. Consultations are delivered by video call	8	(22.2)
Q17.3. Consultations are delivered by face to face	22	(61.1)
Q17.5. We send our patients to the cancer centre for treatment consultations	1	(2.8)

Q23. I would like to maintain the changes I have made to my clinical practice with respect to virtual consultations after the COVID-19 pandemic.					
Nurses (n=11)			Nurses/ Doctors p = 0.403		
Strongly disagree - Disagree			6	(54.6)	
Neutral			3	(27.3)	
Agree - Strongly agree			2	(18.2)	
Doctors (n=25)					
Strongly disagree - Disagree			6	(24)	
Neutral			4	(16)	
Agree - Strongly agree			14	(56)	
Theme 4. Service delivery and Healthcare professional satisfaction					
Q4. Our services offer the following treatment options to patients with localised kidney cancer (pre-COVID-19)					
Q4.1. Active Surveillance			36	(100)	
Q4.2. Ablation			31	(86.1)	
Q4.3. Partial nephrectomy			32	(88.9)	
Q4.4. Radical nephrectomy			34	(94.4)	
Q11. We were able to offer the following treatment for patients with localised kidney cancer during the COVID-19 pandemic.					
Q11.1. Active Surveillance			31	(86.1)	
Q11.2. Ablation			3	(8.3)	
Q11.3. Partial nephrectomy			13	(36.1)	
Q11.4. Radical nephrectomy			28	(77.8)	
Q11.5. Deferred treatment			27	(75)	
Q27. I am satisfied with the service I have provided to my patients during the COVID-19 pandemic.					
Very Dissatisfied - Dissatisfied			8	(22.2)	
Neutral			11	(30.6)	
Satisfied - Very satisfied			17	(47.2)	
	UK (n=36)		Non-UK (n=22)		
	Frequency	Percentage	Frequency	Percentage	p-value
Q5. The medical team has been redeployed during COVID-19.	20	(55.6)	5	(22.7)	0.014
Q6. The nursing team has been redeployed during COVID-19.	29	(80.6)	11	(50)	0.015
Theme 5. Delivery of future kidney cancer services					
Q25. Assuming there are no further disruptions to service we will need the following additional resources to support and treat the backlog of patients awaiting treatment in the next 6 months (tick as many as necessary).					
Q25.1. Imaging capacity			28	(77.8)	
Q25.2. Theatre capacity			36	(100)	

Q25.3. Outpatient capacity	25	(69.4)
Q25.4. Inpatient capacity	28	(77.8)
Q25.5. Workforce resources	21	(58.3)
Q26. Assuming there are no further disruptions to service we will need the following additional workforce to support and treat the backlog of patients awaiting treatment in the next 6 months (tick as many as necessary).		
Q26.1. CNS's	20	(55.6)
Q26.2. Surgeons	19	(52.8)
Q26.3. Oncologists	12	(33.3)
Q26.4. Theatre teams	28	(77.8)
Q26.5. Radiologists	17	(47.2)
Q26.6. Administrators/ Co-ordinators	14	(38.9)
Q26.7. We do not need more workforce	6	(16.7)
Q28. Moral distress occurs when you believe you know the ethically correct thing to do, but something or someone restricts your ability to pursue the right course of action.		
0-3 (low)	12	(33.3)
4-6 (medium)	18	(50)
7-10 (high)	6	(16.7)

5.1.3. Discussion

In the context of **diagnostics**, Oderda et al. noted that the delays observed during the pandemic severely impacted patients through the lengthening of both diagnostic and treatment waiting lists. They emphasised the need for healthcare authorities to develop strategies to catch up with diagnostics (182). This was confirmed in our survey as 75% of survey respondents highlighted disruption to the diagnostic pathway in the UK, compared to only 27% for non-UK respondents ($p< 0.00$). UK respondents reported that disruption to the UK diagnostic pathway included a reduced access to imaging (69%), a reduction or no access to kidney biopsy (78%) and delivering diagnostic consultations via phone (83%) or video call (25%). Moreover, discussion of patients newly diagnosed with kidney cancer in the MDM posed another problem. The MDMs are both a forum for discussion, knowledge transfer, and learning between the different professional stakeholders. During COVID-19, MDM meetings were moved to virtual platforms overnight. When asked whether these should remain as virtual events, 55% of nurses in the UK felt that these should revert to a face-to-face meeting, compared to only 28% of UK doctors. The opportunity to connect with the wider team is a unique experience with virtual MDTs possibly leading to a loss of professional understanding and social interaction amongst the team (183). This is of particular relevance to nurse specialists who rely on the relationships they built within the MDT to expedite results and decision-making for patients of concern (71, 184).

With respect to **treatment**, a large proportion of clinicians who responded to the survey felt that any delay was unacceptable, despite consistent evidence in the literature suggesting that patients with localised kidney cancer can safely defer radical treatment (where required) (185, 186). In addition, the EAU Guidelines Office Rapid Response Group (GORRG) on COVID-19 recommended postponement of surgery by 6 months where progression is unlikely (187). Fifty-eight percent of UK respondents reported that deferring treatment for 0-12 months for T1a disease or deferring treatment for 3-6 months in T1b disease (53% of respondents) or a delay of 0-6 month for T2 lesions (83% of respondents) would adversely affect the oncological outcomes. These results reflect the wording of such documents (EAU GORRG), which specifically highlighted the dilemma of selecting the most appropriate candidates who would benefit from a surgical intervention and the challenge of treatment decision-making and follow-up for >4 cm renal masses (187). This might also in part explain

the elevated level of dissatisfaction regarding available treatment options during COVID-19, where none of the UK nurses and only 28% of UK doctors who responded to the survey, were satisfied with the treatment options available to patients.

For **consultations and supportive care**, the main patient focus for HCPs during COVID-19 was to prevent unnecessary risk of exposure. To this end, telephone and video consultations were implemented across the UK in line with BAUS guidance (185). Boehm et al. assessed the willingness of patients to engage with telemedicine (video consultations) and their results suggested that 54% were willing to undertake telemedicine consultations (188). However, this survey identified that the majority of treatment consultations in the UK were carried out via telephone during COVID-19 (86% for treatment consultation) in comparison to video consultation (22%). Therefore, it is unclear whether HCPs would have felt more satisfied and able to provide supportive care using telemedicine consultations. Porpiglia et al. suggested that telemedicine should be continued and embraced as a long- awaited change to practice (189), however, our survey indicates that 55% of nurses and 24% of doctors in the UK would not be in favour of continuing these changes in their clinical practice. This could, in part, be due to the specific clinical work performed e.g., diagnostic consultations or supportive care, where telemedicine may miss the human context such as the affection and emotions which are very difficult to reproduce virtually (189).

The UK's deferred treatment plan (e.g., inability to offer surgery or ablation) was reported by the respondents as a contributor to **HCP dissatisfaction**. Only 36% of UK respondents were able to perform partial nephrectomies and only 8% were able to perform ablations. As reported by KCCURE's and KCUK's snapshot surveys, patients reported experiencing a high level of anxiety during the first six months of the COVID-19 period. Therefore, it is not surprising that 47% of UK respondents confirmed an increase in the number of patients contacting their service during COVID-19 (181, 190). This, combined with widespread re-deployment of healthcare professionals (56% of the medical team and 81% of the nursing team) may explain why only 47% of UK nurses and doctors felt 'satisfied' or 'very satisfied' with the service they provided during the peak of the pandemic. With a demonstrable increase in cancer patient anxiety during COVID-19 (180, 181), consideration should hence be given to the merits of staff redeployment versus patient safety if a second wave pandemic was realised.

For the **delivery of future kidney cancer care**, 78% of UK respondents agreed that there is a need for additional imaging capacity (78%), additional theatre capacity (100%), additional inpatient capacity (78%), additional outpatient capacity (69%), and additional workforce resources (58%). In terms of workforce, the respondents indicated there is a need for additional support, such as theatre teams (78%), CNS's (56%), surgeons (53%), radiologists (47%), administrators/ coordinators (39%), and oncologists (33%). Oderda et al. reported that the waiting time for patients accessing uro-oncology services will triple by the end of June (182). Responding to the additional needs in resources and personnel will be challenging, but necessary (182). This includes a stratified approach to patient assessment in relation to anxiety and depression, as a result of the increased waiting times. Moreover, both doctors and nurses reported a high level of moral distress; 67% of respondents felt either "distressed" or "worst possible distress". This should be taken seriously by policy makers and hospital executives going forward.

5.1.4.1. Limitations

It is important to acknowledge that this recruitment strategy via twitter may have introduced some bias in our respondent population, as it primarily targeted doctors who are active on Twitter. This approach has overlooked the perspectives of doctors who do not use Twitter as a professional platform. Nonetheless, given the urgency of this work, I believed that this method was the most feasible to capture a snapshot of decision-making practices within localised kidney cancer during that critical period.

While the recruitment approach through Twitter may have limited the generalisability of our findings, it provided valuable insights into the perspectives of doctors who actively engage in online discussions and are likely to be more vocal in sharing their experiences. Future studies should aim to incorporate more diverse recruitment strategies to ensure a broader representation of healthcare professionals' perspectives.

5.1.4. Conclusion

This survey has shown high levels of dissatisfaction among HCPs regarding the standard of care delivered during the first 6 months of the COVID-19 pandemic in the UK. This suggests a need to re-visit the guidelines. It is important to ensure the diagnostic pathway is not disrupted, ensure the option to use video consultations is available, prevent the medical team and particularly CNSs to be redeployed, and all available treatment options such as the

ability to perform surgery in COVID-19 cold sites (NHS hospitals which perform “cold” (elective treatments) vs “hot” (acute and urgent) care) is assured.

5.2. Summary of Chapter 5

Chapter 5 has highlighted the significance of the COVID-19 pandemic on clinical practice and perspectives of HCPs working in the NHS in the UK. It revealed that the pandemic affected decision-making in the healthcare system and that HCPs expressed high levels of dissatisfaction with the standard of care being delivered. The survey results emphasised the need to revisit guidelines for care delivery, which was done prior to the second wave of the pandemic (August 2020 to February 2021) (95).

Davis J., the (at the time) chief editor of BJUI Compass, cited this project as an example of how research can inform policy making by utilising innovative research methods such as Twitter to generate snapshot survey data (191). The policy impact (i.e., tailored risk- based approach to treatment delivery) of COVID-19 on treatment decision-making is particularly important in the context of this thesis, as it has affected patients across the entire treatment decision-making pathway and influenced the options presented to localised kidney cancer patients (192, 193).

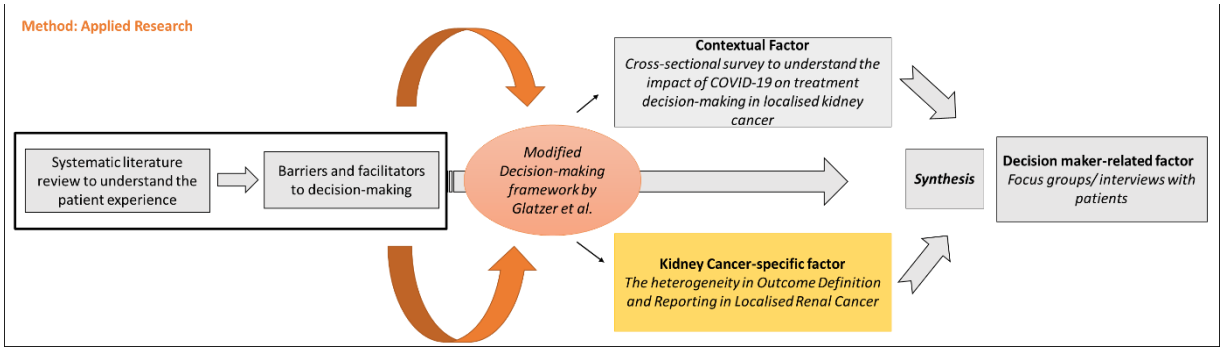
Chapter 6. Kidney Cancer Specific Factors: The heterogeneity in Outcome Definition and Reporting in Localised Kidney cancer

This chapter presents the kidney cancer-specific factors of the thesis (Figure 16) and aims to systematically review the outcomes reported in localised kidney cancer trials and observational studies, as well as how they were defined and measured.

Without a clear understanding as to which outcomes are being reported on in the literature and how they are being defined, it is currently difficult to make relevant comparisons between studies and identify meaningful treatment effects. This can lead to confusion and contributes to uncertainty when trying to make evidence-based decisions about treatment options for patients with localised kidney cancer (194, 195).

This work was published in European Urology Open Science in November 2022 (see Appendix 5) (98). It was also presented at the Kidney Cancer Association Symposium in 2022, where it received the second merit award for best poster presentation.

Figure 17: Methodology overview: Kidney Cancer Specific Factors: The heterogeneity in Outcome Definition and Reporting in Localised Kidney cancer



6.1. Systematic Review of the Heterogeneity in Outcome Definition and Reporting in Localised Kidney cancer

Across many clinical areas including urology, patient-reported outcomes, and clinical outcomes are reported inconsistently with variability in definition and measurement; for instance, in the localised setting of prostate cancer and bladder cancer (96, 196, 197). This makes it difficult to compare and synthesise outcomes and improve guidelines to better direct/support patients and clinicians during treatment decision-making, ultimately

improving results in clinical practice (194, 195). A core outcome set (COS) is a standardised set of prioritised outcomes and is proposed by current research as a solution to decrease heterogeneity in collecting, reporting, and analysing outcomes. COS' in urology are needed because the inconsistencies and variability do not only cause frustration but can also potentially lead to problematic conclusions (196). This issue is also relevant for localised kidney cancer, ultimately resulting in barriers to the multifactorial process of decision-making (198).

This systematic review constitutes the initial stage in the development of a COS for localised renal cancer with the intention to identify a minimum set of outcomes, which are potentially important to health care professionals and patients.

6.1.1. Aims and Objectives

This project aimed to systematically review which outcomes were reported in localised kidney cancer effectiveness trials and observational studies, and how they were defined and measured.

This systematic review followed the guidelines of the Core Outcome Measures in Effectiveness Trials (COMET) initiative, an international expert body which established guidelines on how to develop methodologically robust Core Outcome Sets (COS) (96). The study was reported in accordance with the PRISMA statement and the COS-STAR reporting guidelines, which are relevant to this stage of COS development (97). A project steering committee (SM, MVH, PZ, AB, LM, SD, RB, NK) supported the development from a methodological and clinical aspect. The study protocol was published and registered on PROSPERO (ID: CRD42020198605).

6.1.2. Identification of Relevant Studies

Medline, EMBASE, Cochrane CENTRAL and Cochrane Database of Systematic Reviews (via Ovid) were searched from inception to June 2020. An information scientist was consulted to support in designing the search strategy (see Figure 17). To balance the feasibility and precision of the search, a two-step approach was used. Firstly, all published systematic reviews related to RCC and intervention trials were identified without limiting the search to localised kidney cancer. This was followed by a screening of their 'included studies' lists as a

pragmatic way to identify primary studies potentially meeting the inclusion criteria. Secondly, a search and screening of all localised RCC interventional studies from 2015 was conducted without limiting study designs. This included randomised control trials (RCTs), cohort studies, and case-control studies that reported eligible interventions for localised kidney cancer. It excluded case studies due to their low Oxford Centre for Evidence-Based Medicine: Levels of Evidence (i.e., level of evidence of 4 or lower 15) and unlikeliness to change clinical practice. It also excluded conference abstracts.

Figure 18: Search Strategy

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <June 2022>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to July 20, 2022>, Embase <1974 to 2022 July 25>, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:
1. exp *Kidney Neoplasms/ or exp *Carcinoma, Renal Cell/ ; 2. ((renal or kidney) adj3 (carcinoma* or cancer* or malignan* or tumor* or tumour* or neoplas* or adenocarcinoma* or mass*)).tw,kw.; 3. (((tumor* or tumour*) adj grawitz) or hypernephroma* or hypernephroid carcinoma*).tw,kw. ; 4. or/1-3; 5. general surgery/ or Surgical Procedures, Operative/; 6. (ablat* or laser* or cryotherap* or cryosurger* or cryoablat*).tw.; 7. exp Ablation Techniques/; 8. (high-intensity focused ultrasound or HIFU or cyberknife or cyber knife or vascular-targeted photodynamic or Vascular Targeted Phototherapy).tw,kw.; 9. Nephrectomy/; 10. Nephrectom*.tw,kw.; 11. (delayed or postpone* or post-pone* or deferred or deferring or temporize* or prolong* or (chanage* adj2 date) or put off or hold back or suspended or timing or active* surveillance or active* monitoring).tw,kw.; 12. ((watchful adj3 waiting) or (watch adj3 wait)).tw,kw.; 13. Watchful Waiting/; 14. (electroporation or electropermeabilization or electrotransfer* or padeliporfin or Tookad).tw,kw.; 15. (nephron* adj (sparing or spared*)).tw,kw.; 16. (surgery or surgeris or surgical or operations or operated or procedure*).tw.; 17. ((focal* or focus* or partial) adj2 (intervention* or treat* or therap* or manage* or strateg*)).tw,kw.; 18. (thermal or brachytherap* or radiation or radiotherap* or redio-therap* or irradiat* or radiation* or photoablation* or external beam).tw.; 19. exp Radiotherapy/; 20. or/5-19; 21. 4 and 20; 22. local*.tw,kw.; 23. ((T1* or T 1* or T2* or T 2* or cT1* or c T1* or c T2* or cT2* or T3* or T 3* or T4* or T 4* or cT3* or c T3* or c T4* or cT4* or N0* or N0M0 or M0 or cN0*) adj2 (TNM or stage or cancer or carcinoma)).tw,kw.; 24. ((TNM or stage) adj2 (1* or 2* or 3* or 4* or I or II or III or IV)).tw,kw.; 25. or/22-24; 26. 21 and 25; 27. (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or adolescen* or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.); 28. (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non-human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1 or basic research or cell lines or in vitro or animal model or canine).tw.) not (humans/ or human/ or (men or women or patients or subjects or participants).tw.); 29. case report/ or case reports/ or (case report or a case).ti.; 30. (note or editorial or letter or Comment or news).pt.; 31. note/ or editorial/ or letter/ or Comment/ or news/; 32. conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.; 33. or/27-32; 34. 26 not 33; 35. limit 34 to yr="2015 -current"; 36. remove duplicates from 35; 37. meta-analysis as topic/; 38. Meta-Analysis/; 39.(Systematic review* or meta-analysis).tw,pt.; 40. Meta analysis/ or "systematic review"/; 41. (Medline or Pubmed or Embase or Cochrane or literature search or literature review or National Library of Medicine Database*).tw.; 42. cochrane database of systematic reviews.jn.; 43. (pooled analysis or pooled data).tw.; 44. or/37-43; 45. 21 and 44; 46. randomized controlled trial.pt.; 47. controlled clinical trial.pt.; 48. random*.mp.; 49. placebo*.tw.; 50. drug therapy.fs.; 51. trial.ab.; 52. groups.ab.; 53. (double-blind* or blind* or RCT or RCTs).tw.; 54. or/46-53; 55. 45 and 54; 56. remove duplicates from 55; 57. 56 not 32 ; 58. 36 or 57; 59. remove duplicates from 58

6.1.2.1. Participants

Adults (male and female) with suspected localised kidney cancer, Stage I and Stage II were included.

Those with treatment of renal metastasis or other tumours were excluded.

6.1.2.2. Intervention and Comparator

Studies reporting on any treatment for localised kidney cancer were retained, including but not limited to active surveillance, radical nephrectomy (all modes and approaches), partial nephrectomy (all modes and approaches), cryoablation, radio frequency ablation, microwave ablation, irreversible electroporation, watchful waiting, high-intensity focused ultrasound, or radiotherapy.

6.1.2.3. Eligibility of the Studies

All abstracts and full texts were screened independently by at least two reviewers (CW, KB). Any disagreements were arbitrated by a third review author (SM).

Data were extracted from the included studies independently by two researchers (CW, KB) and checked for accuracy by another reviewer (SM). Data was extracted on study design, author details, year and journal of publication, intervention(s) under investigation, each effectiveness outcome reported, whether the outcome was defined or not, the definition used, the indicators and/ or tool(s) used to operationalise or measure the outcome, the time point or period of outcome measurement, and how the outcome was reported.

6.1.2.4. Data Analysis and Synthesis

The extracted outcome names were coded and categorised according to the outcome reporting taxonomy developed by Dodd et al. (199), which has been suggested by COMET to classify outcomes and group domains (i.e., categories) accordingly.

6.1.2.5. Assessment of Risk of Bias

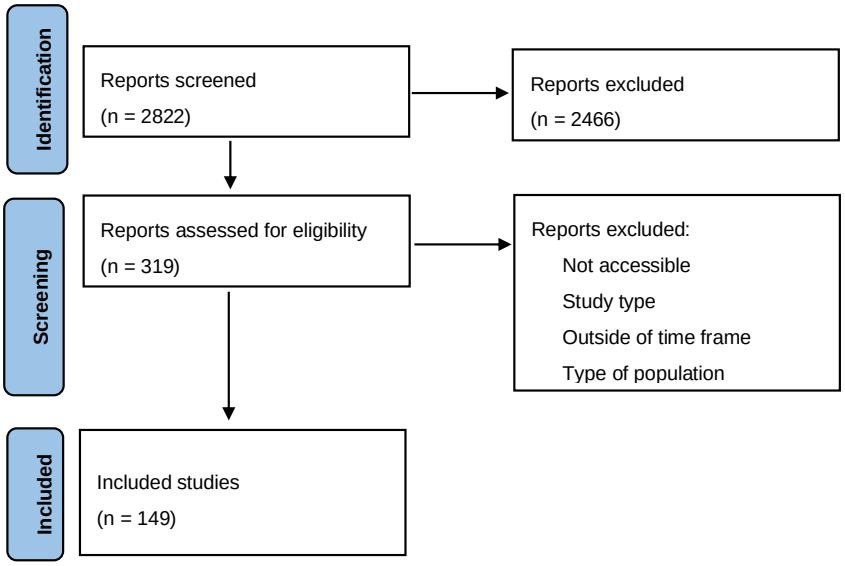
A risk of bias assessment was not conducted as no estimation of effect size of treatments was conducted and solely the qualitative information containing terminology was extracted.

6.1.3. Evidence Synthesis

6.1.3.1. Characteristics of the Included Studies

The initial search included 2,785 abstracts. Of these, 319 full text articles were assessed, of which 149 were included (see Figure 18). Out of the 149 included studies, 97% were observational studies and 5 (3%) studies were RCTs.

Figure 19: PRISMA- SR outcomes



6.1.3.2. Heterogeneity in Outcome Reporting, Detection, and Definitions

A suitable outcome taxonomy for health research must differentiate between high level outcome domain classifications and comprehensively classify all outcomes, whilst also proposing a standardised terminology. Therefore, the outcomes of the included studies were reported on and organised according to the taxonomy developed by Dodd et al. (199) and recommended by the COMET initiative. Taxonomies help to structure general health research vocabularies to reduce inconsistencies and ambiguities in how current studies describe and define outcomes. The Dodd et al. taxonomy has been proposed to increase the reuse value of outcome data (see Figure 19). The taxonomy entails thirty-eight outcome domains within five core areas: death, adverse events, life impact, physiological/ clinical, and resource use (199). The core outcomes are further subclassified as shown in Figure 19.

Figure 20: applied Dodd et al. taxonomy

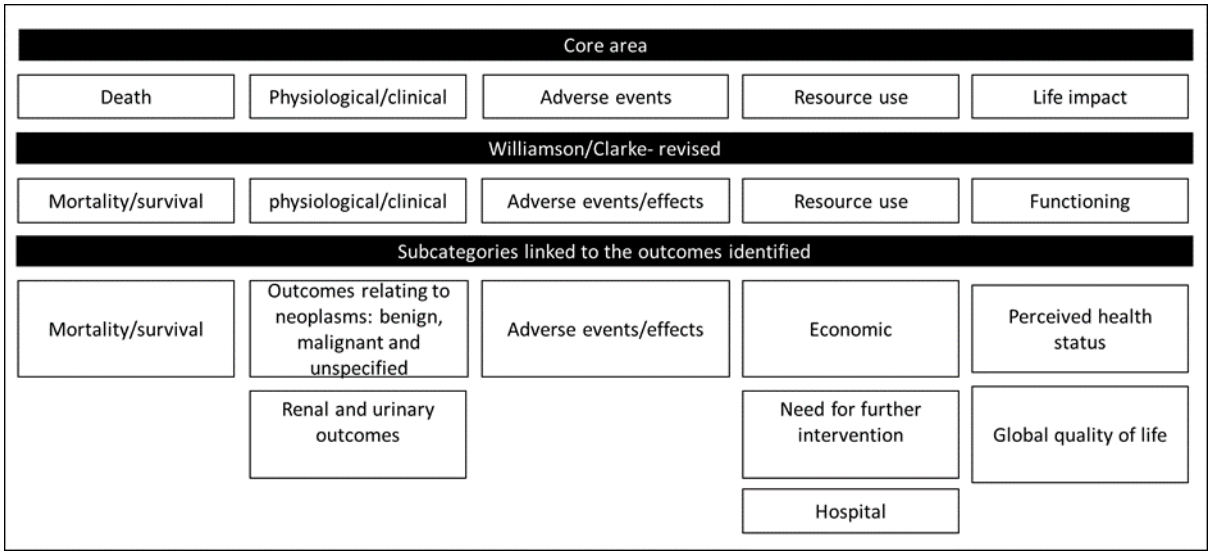


Table 15 shows the outcomes reported by the studies per domain and highlights the heterogeneity of outcomes identified. synonyms and redundant terms have been merged. The next section explains heterogeneity of the terminology in further detail. Table 16 shows which outcomes were reported in the included studies.

Table 15: Outcomes classified

Death	**Adverse events/ effects**	**Physiological or clinical**	**Resource use**	**Life impact**
Mortality/ survival	Adverse events/ effects	Physiological/ clinical	Resource use	Functioning
Mortality/ survival *Overall Survival (OS)* • OS rate • Cumulative survival • Stage related OS • Mean OS • Survival probability 1-yr *Deaths* • Deaths • Death from any cause *Mortality* • Other cause mortality • Mortality events • Overall mortality • Total mortality • X-day mortality *Cancer specific survival* • Renal cell carcinoma–specific survival *Death of kidney cancer* • Number of patients diseased at last follow up • Death of kidney cancer • RCC death • Death from RCC • Death due to cancer *Cancer-specific mortality* • Cancer-specific mortality • Death from non-RCC, other cause mortality OCM	Adverse events *Complications* • Surgical complications • Intraoperative complications • Conversion to nephrectomy • Short-term complications • Conversions • Grade I and Grade II complications • Highest complication grade • Overall complications • 30-days post-operative complications *Bleeding* • Bleeding severity • Units of blood transfused during hospitalization • Estimated bleeding • Bleeding related complications • Haemoglobin post-operative *Perioperative* *Surgical margins* • Surgical margins • Negative margins • Positive surgical margins *Outcomes linked to surgery* • Operation time • Warm ischemia time • Inter-abdominal pressure • Surgical time	Renal and injury outcomes *New Chronic kidney disease CKD* • CKD probability *Stage CKD* • CKD-stage • Upgrade to CKD III-V • CKD upstage • no CKD upstaging • postoperative CKD stage • Postoperative new onset of stage III or IV CKD • Final CKD stage • Patients with acquired stage 3–5 CKD at follow-up, compared to preoperative *Time to CKD* • Decline in CKD stage • Progression to CKD • CKD Upstaged Free Survival • De novo CKD stage 3 • Survival without CKD upstaging • Time to diagnosis of chronic kidney disease (CKD) *Outcomes linked to the procedure* • Mean ablation time • Laser excision time • Median procedure time • Renal outcomes • Urinary function • Oncological outcomes • Collecting system entry	Economic *Cost* • Healthcare expenditure • Medical cost • Total cost • Imaging (linked to costs) • *Medications?*	Perceived health status • Perceived health • Pain • Adverse health outcomes

	• Drainage time • Procedure time • Pneumoperitoneum time • Suture time • WIT ≤25 min • Conversions • Open conversion • Average clamping time • Hb postop • Postoperative drainage time • intra-abdominal pressure • Adverse health outcomes • Clamp less rate *Blood loss* • Mean estimated blood loss • Estimated blood loss • Changes in estimated blood loss • Units of blood transfused during surgery • Transfusion requirement • Transfusion rate • Intraoperative transfusion • Intraoperative ES transfusion • Received transfusions • Perioperative allogenic blood transfusion • % Blood transfusion • blood urea nitrogen (BUN) after 1d and 1m *Trifecta*/ *Pentafecta* • Trifecta • Trifecta rate • Pentafecta reached • Highest complication grade	• Haemostatic agent *eGFR* • Mean eGFR change • Median eGFR preservation • Median % eGFR change • Change in GFR • eGFR preservation (%) • Latest eGFR preservation • DELTA Gfr Change • Last eGFR • eGFR 1-year post-operation • % Change eGFR • eGFR decrease • Postoperative 1-year eGFR % change from baseline to follow-up eGFR *Serum creatinine* • Preoperative creatinine • Creatinine level • Serum creatinine • Difference of serum creatinine levels between pre- and post-operation • Postoperative creatinine level • Postoperative creatinine • Latest creatinine level • % Change in creatinine • Variation of creatinine • DELTA creatinine *RFS* RFS+ time		

	• Low-grade complication			
	Adverse events/ effects or Resource use/ Hospital • Dialysis free probability • No. requiring dialysis • Temporary dialysis • Permanent dialysis	Outcomes relating to neoplasms: benign, malignant, and unspecified (including cysts and polyps) *Metastasis* • Distant metastasis free survival • Distant metastasis • Extrarenal metastasis *Follow-up* • Follow-up • Long-term outcomes • Median postoperative follow up time • Average length follow-up • Median follow up time *Progression free survival (PFS)* • PFS • Systemic PFS • Clinical progression-free survival (CPFS) *Progression* • Local tumour progression • Disease progression *Recurrence* • Local recurrence • Disease free survival (DFS) • Recurrence rate • Recurrence-free survival • Recurrence result *Recurrence linked to time* • Time to local recurrence • Events of local recurrence • Delayed recurrence • Time to recurrence • Local recurrence rate	Need for further intervention • Re-admission	Global quality of life • Health Related Quality of Life

		• Local recurrence free survival • Recurrence (local or metastatic) • Local ipsilateral recurrence • Disease Free Survival		
			Hospital • Length of stay • Postoperative hospitalization time • Hospitalization time • Hospital stays • Average hospital stays • Duration of hospitalization • Duration of postoperative hospital stay • Median hospital stays • Surgical Supplies and devices • Operating room	

Table 16: Outcomes reported in each included study after classification within the taxonomy suggested by Dodd et al.

Author	Design *	Country	OS	Cancer Specific Survival	AE	Adverse events/ effects or Resource use/ Hospital	Renal and injury outcomes	Outcomes relating to neoplasms	Economic	Hospital	Need for further intervention	Perceived Health Impact	Global QoL
Patel S.H.	OS	US	x				x	x					
Li G.	OS	China			x		x			x			
Wang Y.	OS	China			x		x			x			x
Morkos J.	OS	US	x	x		x	x	x					
Alshyarba M.H.M.	OS	Saudi Arabia	x		x								
Wu X.	OS	China			x		x			x			
Packiam V.T.	OS	US			x		x			x			
Yang G.	OS	Not stated	x		x					x			
Rembeyo G.	OS	France	x	x	x		x	x					
Uhlig A.	OS	US	x										
Yu J.	OS	China	x	x	x		x	x					
Kartal I.	OS	Turkey	x		x		x	x					
Jalbani I.K.	OS	Pakistan			x		x			x			
Seon D.Y.	OS	South Korea	x	x	x		x	x					
Choi C.I.	OS	South Korea			x		x			x			
Tan W.S.	OS	US, Puerto Rico	x										
Grant S.R.	OS	US	x										
Chen Y.	RCT	China			x		x			x			
Liu Y.-H.	OS	China			x		x			x			

Sandbergen L.	OS	The Netherlands			x								x
Shapiro D.D.	OS	US		x	x		x	x					
De Cobelli F.	OS	Italy			x		x						
Nayan M	OS	Canada	x	x			x	x					
Jin D	OS	China			x		x			x			
Mourao TC	OS	US, Spain	x	x	x		x			x			
Anglickis M.	OS	Lithuania			x		x	x		x		x	
Marchioni M.	OS	US	x	x									
Li G.	OS	China		x									
Liao X.	OS	US	x	x									
Simone G.	OS	Italy	x	x	x		x	x					
Shao I.-H.	OS	Taiwan			x			x		x			
Antonelli A.	RCT	Italy			x		x			x			
Kitley W.	OS	US	x										
Zhou N.	OS	China			x		x						
Andrews J.R.	OS	US		x				x					
Zhou W.	OS	US		x			x	x					
Fraisse G.	OS	France	x		x			x				x	
Hu M.	OS	China			x								
Abu-Ghanem Y.	OS	Israel	x	x			x	x					
Kavaric P	OS	Montenegro			x		x			x			
Ziegelmueller BK	OS	Germany	x				x	x					
Talenfeld A.D.	OS	US	x	x	x								

Bhindi B.	OS	US	x	x	x		x	x					
Larcher A.	OS	The Netherlands, Italy	x		x		x	x		x			
Xing M.	OS	US	x	x								x	
Ristau B.T.	OS	US, Puerto Rico	x										
Zhao X.	OS	China			x		x	x		x			
Gershman B.	OS	US	x	x			x	x					
Benoit M.	OS	France			x		x	x		x			
Paulucci D.J.	OS	US			x		x	x		x			
Abdel Raheem A.	OS	South Korea		x	x		x	x		x			
Lourenco P.	OS	Canada	x		x		x	x		x			
Hasegawa T.	OS	Japan					x	x			x		
Streja E.	OS	US		x			x						
Borghesi M..	OS	Globally			x		x			x			
Uhlig J.	OS	US	x							x	x		
Ye J.	OS	China			x			x		x			
Park B.K.	OS	Not stated											
Venkatramani V.	OS	US	x							x			
Uhlig A.	OS	US		x									
Zhang M.	OS	US	x	x									
Lee H.	OS	South Korea	x	x	x			x					
Chong J.T.	OS	US			x			x			x		
Chang Y.-H.	OS	Taiwan			x				x	x			

Yang C.	OS	China			x			x		x			
Veys R.	OS	Belgium	x	x	x		x	x					
Banapour P.	OS	US			x		x			x			
Cai Y.	OS	China	x	x			x						
Lanchon C	OS	France			x		x			x			
Venkatramani V,	OS	US	x								x		
Karalli A,	RCT	Sweden										x	
Dong W..	OS	Not stated					x						
Wang D.C.	OS	US	x										
Tang D.H.	OS	US	x	x									
Yin H.	OS	China	x					x					
Shah P.H.	OS	US					x						
Annino F.	OS	Italy			x			x					
Xiaobing W..	OS	China	x					x					
Shum C.F.	OS	US	x					x		x	x		
Luo Y.	OS	US	x	x									
Lee H.	OS	South Korea	x	x	x			x					
Caputo P.A.	OS	US	x	x	x		x						
Lu Q.	OS	China			x		x			x			
Maric P.	OS	Serbia			x								
Matei D.V.	OS	Italy			x	x	x	x		x			
Paulucci D.J.	OS	US			x		x						
Rassweiler J.J.	OS	Germany			x								
Larcher A.	OS	US	x		x			x	x	x	x		
Lenis A.T.	OS	US	x		x								

Wang L.	OS	US			x					x			
Peng D.	OS	China		x	x		x	x		x			
Malkoc E.	OS	US			x			x		x	x		
Long J.-A.	OS	France	x	x	x	x	x	x		x			
Yoo S.	OS	South Korea					x						
Redondo C	OS	Spain			x					x			
Carrion DM	OS	Spain			x		x						
Shah, P.H.	OS	US			x		x						
Moskowitz, D	OS	US	x										
Huang, J.	RCT	China			x		x			x			
Larcher, A	OS	US		x									
Jang, H.A.	OS	South Korea	x	x	x		x	x					
Forbes, C.M.	OS	Canada	x		x		x	x					
Kara O.	OS	Not stated			x		x	x		x			
Takagi T.	OS	Not stated			x		x	x		x			
Oh J.J.	OS	Not stated			x								
Andrade H.S.	OS	Not stated			x	x			x	x			
Dong, W	OS	Not stated	x		x		x	x		x			
Trudeau, T.	OS	US	x		x								
T Ct Lai	OS	China	x	x	x					x			
T-Y Liu	OS	China	x		x		x			x			
Pantelidou, M.	OS	UK			x		x	x		x			

Taiyang Liu	OS	China	x		x		x	x					
Larcher A.	OS	US			x		x						
Hossein R.G.	OS	Iran			x		x						
Komatsuda, A	OS	Japan			x		x						
Janicic, A.	OS	Serbia	x	x									
Lyon, T.D.	OS	US			x					x			
Satkunasivam R.	OS	US	x		x	x	x			x			
Thompson, R.H.	OS	US	x				x	x					
Tabayoyong, W.	OS	US						x					
Alanee, S	OS	US		x									
Zargar, H	OS	US			x		x	x					
Mano, R.	OS	US	x		x		x	x		x			
Chang, X.	OS	China	x	x	x		x	x		x			
Serni, S.	OS	Italy	x	x	x		x	x					
Chung, J.S.	OS	Korea	x	x			x						
Yu, J.	OS	Not stated	x		x								
Weinberg A.C.	OS	US			x				x	x			
Park Y.H.	RCT	South Korea			x					x		x	x
Balasar M.	OS	Turkey			x		x						
O'Malley R.L.	OS	US	x	x			x						
Kim J.H.	OS	South Korea			x		x						
Chang, X.	OS	China	x		x								

Cooper, C.J.	OS	US			x		x						
Alam, R.	OS	US	x	x			x						
Çömez, k	OS	Turkey			x		x			x			
Kopp	OS	US			x		x	x		x			
Danzig	OS	US			x		x						
Hussein	OS	Egypt					x						
Simsek	OS	Turkey			x		x			x			
Fossati, N	OS	Italy		x	x					x			
Ji, C	OS	Italy or China	x	x	x	x	x	x		x			
Mason, R.J.	OS	US					x						
Chehab, M.	OS	Not stated			x								
An, J.Y.	OS	US			x					x			
Rosen, D.C.	OS	US			x		x						
Ramirez, D.	OS	US			x		x						
Malkoc, E.	OS	Turkey			x		x				x		

** Observational study, Randomised Control Trial; Abbreviations used for graphical reasons.: OS – Overall Survival; AE- Adverse Events; US – United States of America; UK- The United Kingdom*

6.1.3.3. Death (Domain: Mortality/ Survival)

The next section explains the heterogeneity of the terminology and the measurement in more detail. Death was reported 103 times. These outcomes were categorised as per the Dodd et al. classification mortality/survival into 'overall survival' and 'cancer specific survival.' 'Overall survival' (OS) was measured in sixty-five studies (44%) (see Table 16). Cancer-specific survival (CSS) was reported in 43 (29%) (see Table 16) of the included studies, as: cancer-specific survival, death from kidney cancer, and cancer-specific mortality.

Definitions of OS and CSS differed across studies (see Table 15). The heterogeneity of the definitions was linked to timepoints. For instance, some studies started measurement at diagnosis whereas others used treatment date as their starting point. The time endpoint also differed, with studies reporting either a rate at a defined time (e.g., 10 years) or hazard ratios based on survival analyses.

6.1.3.4. Adverse Events (Domain: Adverse Events/ Effects)

'Adverse events' (AE) was the most commonly reported outcome (n= 101 (68%), however, many different types of adverse events were reported, sometimes as n/N (number of participants) or percent experiencing the outcome, other times subsumed in a classification system linked to severity or consequences (e.g., Clavien-Dindo). Examples of events that play a role in assessing adverse events include bleeding, operation time, warm ischemia time, inter-abdominal pressure, surgical time, drainage time, serum creatinine, blood loss, trifecta/ pentafecta, and dialysis; these are linked to the complexity of surgery. Many studies have reported several adverse events within one study, but how the events were reported varied across studies (e.g., surgical complications were measured as intraoperative complications, conversion to nephrectomy or short-term complications).

'Adverse events/ effects or Resource use: Hospital' are outcomes that fit into the domain 'adverse events' and 'resource use: Hospital,' which were reported in six studies (4%). Outcomes are reported and measured inconsistently, and examples are Dialysis free probability, the number requiring dialysis, Temporary dialysis, and Permanent dialysis (see Table 15).

6.1.3.5. Life impact/ Functioning (Domain: Perceived health status; Global quality of life)

Only eight studies (5%) reported outcomes reflecting life impact. Five studies (3%) reported outcomes classified as perceived health status, and three studies (2%) reported on Global Quality of Life (GQoL). One study used the short form- 36 (SF-36) and the other used the Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index - 15 Item Version (FKSI-15) PROM (see Table 16).

6.1.3.6. Physiological or clinical (Domain: Physiological or clinical)

Physiological or clinical outcomes were sub-classified as 'renal and injury outcomes' (e.g., New Chronic kidney disease CKD, Stage CKD, Time to CKD). These were defined very heterogeneously and reported in 87 (58%) of the studies and 'outcomes relating to neoplasms' (linked to cancer follow-up and progression reported in 55 (37%) of the studies) according to the Dodd et al. taxonomy (199) (see details in Table 15 and Table 16).

6.1.3.7. Resource use (Domain: Economic, Need for further intervention, Hospital)

'Resource use' consisted of the sub-categories of economic resource (e.g., Healthcare expenditure; reported in 4 studies (3%) as mean or median costs), need for further intervention (e.g., re-admission; reported in eight studies (5%) e.g., measured in binary yes/no categories or medians), and hospital (e.g., length of hospital stays; reported in 58 (39%) studies as mean or median days of the length of hospital stay).

6.1.4. Discussion

To the best of our knowledge, this is the first systematic literature review that describes outcome reporting heterogeneity in localised kidney cancer literature. This builds the framework to develop a COS for localised kidney cancer which aims to reduce outcome reporting, definition, and measurement heterogeneity.

Our systematic review highlights the persistent problem of outcome reporting heterogeneity in localised kidney cancer studies. Multiple terms are used to refer to conceptually similar outcomes, and there is variation in the outcome definitions used. This is problematic when summarising the evidence base to inform decision-making for treatment effectiveness because it is not advisable to synthesise data with different outcome definitions within a meta-analysis. Such practices can produce meaningless summary

statistics. Therefore, cumbersome and often less informative narrative synthesis must be undertaken instead. Furthermore, this work highlights the variety in data reporting and measuring. For instance, if dichotomous outcomes like overall or cancer survival are reported using different methods (e.g., some reporting adjusted hazard ratios (HR) some unadjusted, others a rate at median follow-up, and others at specified time points such as one year or five years, etc.), then such data cannot be easily or reliably synthesised in meta-analysis. When these problems all occur at once, it is not only difficult to interpret the body of evidence but the clinical practice guideline panels also encounter challenges creating recommendations and applying certainty of evidence attachments such as those proposed by the GRADE working group (200).

Worryingly, solely very few patient-reported outcomes (PROs) were identified, which might be related to the fact that there are only a limited number of specific tools available to capture quality of life for kidney cancer. Rossi et al. identified in their systematic review three generic PROMs (RAND medical outcome survey Short Form 36 (SF-36) and Short Form 12 (SF-12), EuroQol (EQ-5D), and Convalescence and Recovery Evaluation (CARE)) and eight cancer specific PROMs (Cancer Rehabilitation Evaluation System-Short Form (CARES-SF), European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) C30, Functional Assessment of Cancer Therapy-General (FACT-G), Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI), Renal Cell Carcinoma-Symptom Index (RCC-SI), Instruments to assess psychological wellbeing Impact of Events Scale (IES), Hospital Anxiety and Depression Scale (HADS), and Mishel Uncertainty in Illness Scale (MUIS)), which are currently being used in kidney cancer. However, out of the eight cancer specific PROM instruments used, only two are kidney cancer specific albeit not stage specific (FKSI, RCC-SI) (201).

Karlsson and Rosenblad et al. assessed the psychometric properties of the most commonly used PROM in kidney cancer, the Functional assessment of cancer therapy—Kidney Symptom Index (FKSI-19; capturing both physical and emotional disease-related symptoms, function/well-being, and treatment side effects) among renal cell carcinoma patients and reported it to be barely fit for this purpose (202). Furthermore, Bergerot et al. (203) conducted a patient survey that identified many questions of the FKI-19 as irrelevant from a patient perspective and therefore stressed the need to incorporate patients in the

development of PRO tools, in order to determine areas of importance each. As such, the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life group is currently developing a renal cell cancer module specifically to be used in combination with their Quality-of-Life Core Questionnaire (QLQ-C30), to address this unmet need.

6.1.4.1. Limitations

Some studies reporting patient-reported outcomes and/or quality of life may have unintentionally been excluded because the search was not specifically geared towards looking for primary qualitative studies of patient experiences of kidney cancer treatment. However, the list of outcomes presented here will be supplemented with outcomes identified in the primary interview study with patients who have been treated for kidney cancer, as well as further review work.

6.1.5. Conclusion

This review indicates that clinical research for localised kidney cancer is impeded by heterogeneity in outcome selection, definitions, and reporting, which once again indicates the difficulty in using disease specific criteria factors to solely guide treatment decision-making.

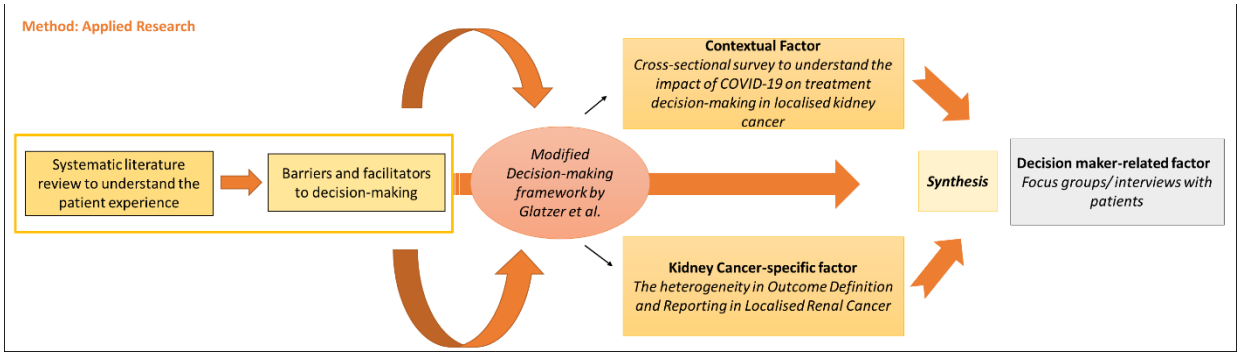
6.2. Summary of Chapter 6

This systematic literature review describes outcome reporting heterogeneity in localised kidney cancer literature by presenting the different terms used in the literature and collating them within a standardised outcome classification taxonomy. The review highlights the ongoing problem of outcome reporting heterogeneity in localised kidney cancer studies, with a multitude of terms used to refer to similar outcomes and the variation in these definitions, making it difficult to interpret the evidence and create clinical practice recommendations. In addition, there is a lack of PROs in localised kidney cancer studies, due to a limited number of specific tools available to capture quality of life in this population. This review could help create an infrastructure to improve standardised data collection by reducing data heterogeneity and support future research and clinical practice recommendations. This in turn, helps to support the development of quality improvement and value-based care guidelines (204), which are essential for healthcare providers to make unbiased decisions.

Chapter 7. Data Synthesis to Develop a Semi-structured Interview Guide for Focus Groups and Interviews

This chapter synthesises the previously conducted research to inform the development of a semi-structured interview guide to aid in understanding treatment decision-making from a patient's perspective (see Figure 20) (Chapter 8).

Figure 21: Methodology: Data synthesis to develop a semi-structured interview guide for focus groups and interviews



7.1. Introduction

Creating a thorough semi-structured interview guide can improve the reliability of qualitative research in multiple ways. Following the guidelines established by Lincoln and Guba (1985) (and modified by Kallio et al.), four stages of the interview guide development process contribute to the trustworthiness of a study, as shown in Figure 21 (99, 205).

Trustworthiness, as defined by Lincoln and Guba, is linked to the concept of credibility, confirmability, and dependability, and should be taken into consideration for rigorous data collection.

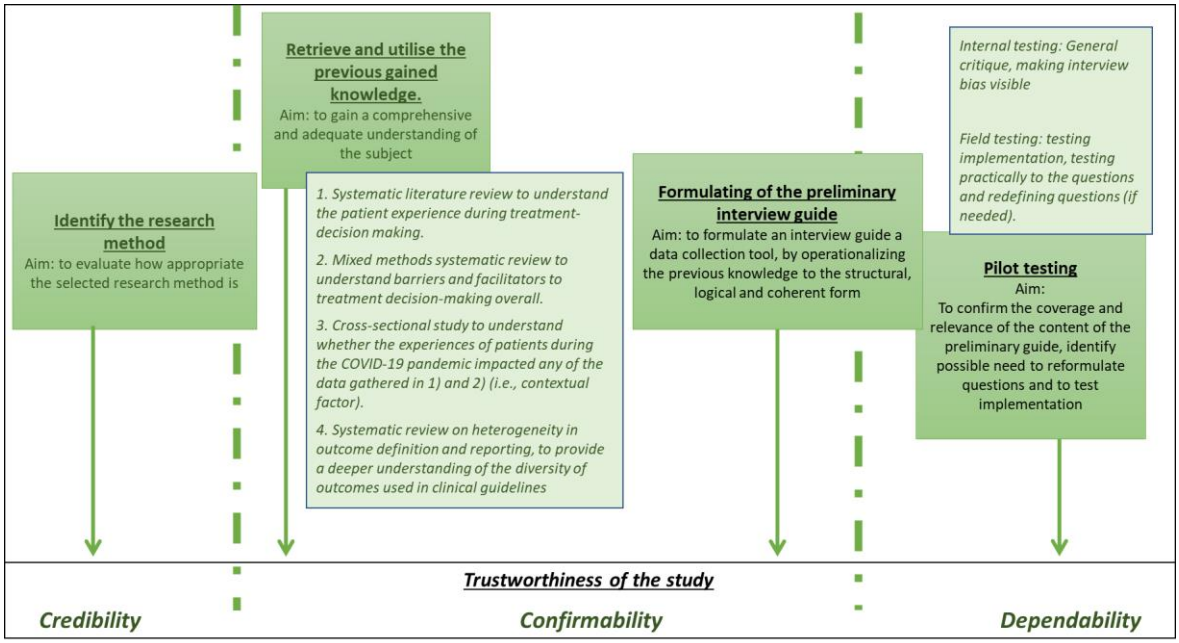
Credibility is concerned with accurately capturing the phenomena being studied (99, 205), which is linked to the chosen research method most suitable for this research.

Confirmability of the study refers to the researcher's objectivity (99, 205). The researcher's subjective role can be minimized by using literature-based and previous empirical knowledge that was systematically collected. Furthermore, feedback from pilot testing contributes to the impartial development of an interview guide (99).

Finally, *dependability* pertains to the ability to reproduce the study under the same conditions (99, 205). Hence, pilot testing the interview guide in the last phase of the development process of this thesis is linked to examining the dependability of the study and making the data collection tool available to other researchers (99).

The next section describes the four methodological steps used to establish the interview guide by ensuring the trustworthiness of the study, following the 'phases of a semi-structured interview guide developed based on synthesis' (99) described in Figure 21.

Figure 22: The phases of a Semi-structured interview guide developed based on synthesis.



Source: Kallio et al (modified)

7.2. Identifying the Research Method for Using the Semi-structured Interview Guide

Focus groups and interviews were used to conduct the qualitative part of this project. Focus groups have been widely used to explore the perspectives and experiences of patients in a healthcare setting (206). A focus group is a small, carefully selected group of individuals who participate in a guided discussion about a particular topic. The goal of a focus group is to gather insights and opinions on the respective topic from this carefully selected group of people. Participants are encouraged to spontaneously comment, compare views, disagree, or share views concerning their decisions (204), which is the main reason why focus groups were chosen as the preferred method to conduct the research. Hence, for the purpose of

this thesis, focus groups are considered as an efficient way to gain insights into a wide spectrum of views about a specific topic (99).

7.3. Retrieving and Using Previous Knowledge

The second development phase involved retrieving and utilizing the knowledge gained in Stages 1-4, which as suggested by Kallio et al. provides a thorough understanding of the subject (99). This required a critical evaluation of existing knowledge (Stages 1 and 2) and the need for additional empirical data (Stages 3 and 4).

7.3.1. Critical Evaluation of Existing Knowledge

The two systematic reviews provided a framework for the interview and were crucial in understanding the treatment decision-making process, thus forming the foundation for the interview guide (99). Figure 22 illustrates the factors identified in both systematic reviews, including: prognosis factors, demographic characteristics, predictive tools, patient related criteria, physician related criteria, patient's risk perception, patient physician interaction, patient involvement, patient decisional quality, economic variables, access to healthcare, and health care organisation. These build the evidence base for the semi-structured interview guide.

Figure 23: Synthesis of Stage 1 & 2 (Step 1-3)

1. Systematic literature review to understand the patient experience

Patient-related criteria'	Patient decisional quality: Education level; patient satisfaction with care; knowledge of kidney cancer; decisional conflict; emotional impact of decision-making; emotional impact of decision-making) Patient's risk perception: Fear of recurrence; fatigue; anxiety; concerns about cancer; depression; aches; decreased interest in previously enjoyed activities; decreased interest in previously enjoyed events; decreased interest in previously enjoyed events; reluctance to start new relationships)

Patient-physician interaction	Patient involvement in decision-making: Interaction with different specialities; perceived shared decision-making; paternalistic care, (clear) information provided by the doctor; psychological support)

Supportive care suggestions	Why is this important in clinical practice
Introduce clinical decision aids to increase patient involvement and knowledge about their disease.	Will reduce decisional conflict between the patient and shared decision-making. However, it does not replace counselling.
Providing patients/caregivers with an electronic or written document to act as a reminder/resource	Will ensure that physicians do not omit or 'gloss over' prominent issues and patient can look up information provided in a less stressful environment.
Educational videos and online modules before the appointment	Will prepare patients for consultation.
Interdisciplinary counselling service	Will enable the patient to receive a complete picture.
Provide more information about their cancer, long-term follow-up and potential complications.	Setting the scene for decision-making and setting patient expectations
Shared decision-making modelling	Consider the role of reimbursement models (US) and private consultations. Increases adherence to clinical management guidelines

2. Barriers and facilitators to decision-making

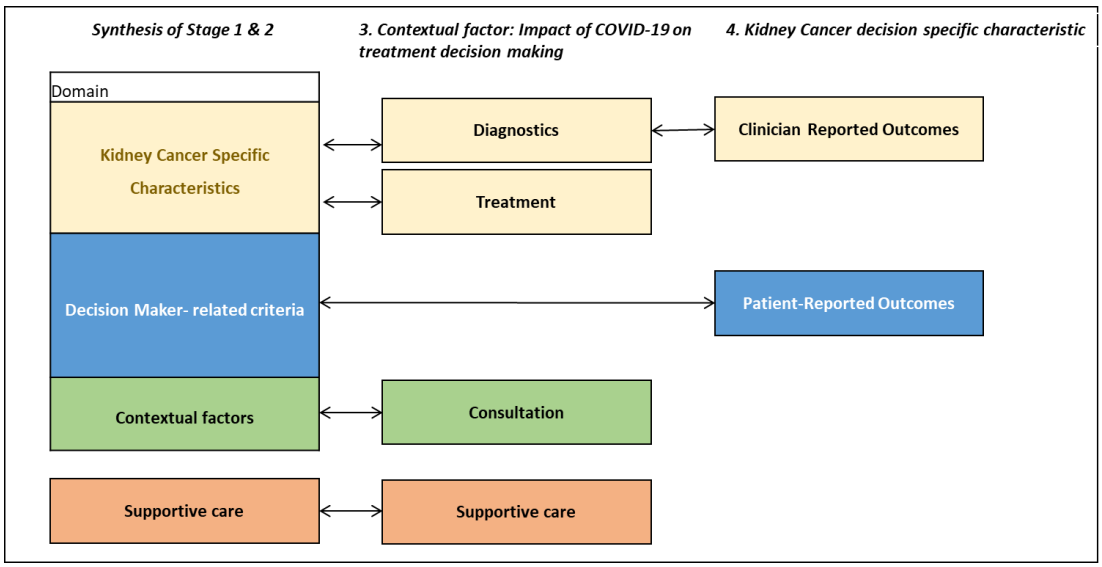
Domain	Factor	Details
Kidney Cancer Specific Characteristics	Prognosis factors Anatomical, histological, clinical, and molecular factors influence decision-making	Pathologic tumor size; tumour stage/ TNM / anatomic classification; location of tumour/ accessibility. Grade/ Fuhrman nuclear grade/ growth rate; growth pattern. histology; pathological diagnosis/ data/ stage/outcome; tumour volume; benign vs malignant; indolent vs aggressive; type of tumour/ RCC subtypes; nephrometry radius; exophytic vs endophytic; anterior/posterior; complexity score/ anatomic complexity; multifocal disease/ number of lesion; mass composition; tumour side; state of disease; pain level; single kidney; solidary kidney; kidney function (eGFR)/ preoperative kidney function/ kidney function values; ASA score
	Demographic characteristics	Age; Charlson score CCI/ comorbidities; BMI; gender; race; marital status; SES; education, smoking history; family history of RCC; prior RCC diagnosis/ kidney medical history; employment status; education
	Predictive tools	Scoring systems: NePhRO scores, C-index; The Predictive Tool to Determine Renal Function Benefit of Nephron Sparing Surgery Compared to Radical Nephrectomy online calculator; R.E.N.A.L.-nephrometry score; The PADUA classification. Diagnostic tools: Imaging (MRI)/ CT Diagnostic accuracy of CT or MRI; Biopsy (Biopsy, CT diagnosis, Biopsy technique & Biopsy Result; Biopsy sensitivity; Biopsy specificity; Biopsy technique; Probability of nondiagnostic biopsy; Probability of biopsy track seeding with malignant cells; clinical behaviour by abdominal imaging)
Decision Maker- related criteria	Patient related criteria	socioeconomic status; level of education; having an academic degree; history of cancer; history of invasive procedures and history of procedural complications; personal or family history of cancer; anxiety associated with missing a cancer; concern about potential biopsy complications was the primary reason to decline RMB among surveillance patients; reluctance to undergo biopsy; concern about potential biopsy complications; patient preference; QoL
	Physician related criteria	Surgeons' preference/surgical modality was chosen at the discretion of the surgeon; surgeon's experience level confidence in the management option
	Patient physician interaction	Patient physician interaction; clinical decision aids; interdisciplinary discussion
Contextual factors	Economic variables	Insurance; Income by zip code, cost of procedure
	Access to healthcare	Geographic region; Urban vs Rural; Travel distance; Medicare A or B; shared decision-making in included reimbursement models
	Health care organisation	Facility type; facility location; shared decision-making; infrastructure available

7.3.2. The Need for Additional Empirical Data

These two reviews were further enriched through the cross-sectional survey evaluating COVID-19 as a contextual factor. The aim was to understand whether the experiences of patients during the COVID-19 pandemic impacted and changed any of the data gathered in Stage 1 and 2. The survey offered a snapshot analysis and identified the following five themes: diagnostics, treatment, consultations and supportive care, HCP satisfaction, and delivery of future kidney cancer care. The COVID-19 pandemic was found to have a significant impact on the practice and perspective of HCPs working in kidney cancer in the NHS during the first six months of the outbreak.

To explore and understand the language used in kidney cancer diagnostics and the potential impact on decision-making, the systematic review on outcome reporting heterogeneity identified multiple terms used to refer to similar outcomes and variations in definitions. Figure 32 describes the links between the new data gathered and the existing knowledge.

Figure 24: Synthesis of Critical existing knowledge based on the systematic reviews (Stage 1 & 2) and the additional empirical data (Stage 3 & 4; step 1-4)



7.4. Formulating the Preliminary Semi-structured Interview Guide

The preliminary semi-structured interview guide to collect data was developed in the third phase of the development process, using the synthesis of data gathered during Stages 1-4. An interview guide is a list of questions designed to direct a conversation towards a specific research topic. The semi-structured format of the guide allows for flexibility, enabling easy

movement between questions and dialogue during the focus groups. The questions were developed to cover the different factors identified in Stages 1-4 and structured by reflecting the modified three domains of decision-making. An overview of the questions and respective semi-structured interview is provided in Table 17.

Table 17: Semi-structured interview guide developed by using the knowledge gained in Stage 1-4

Introduction – Ask the patient to introduce themself. Kidney Cancer Specific Characteristics
How long ago was your diagnosis?
How did you get diagnosed?
How much time was there between when you first experienced symptoms and visiting your GP?
How much time was there between your visit to your GP and your referral to hospital?
Kidney Cancer Specific Characteristics
Prognosis factors, Demographic characteristics, Predictive tools
Thinking back to your consultation where you were given your diagnosis, can you tell me what you were told about your cancer, how you felt and how you were supported through that consultation?
Was the consultation face to face, Telephone, Video? Did you think this medium was appropriate?
What tests/investigation did you receive to enable you and your physician to make the decision on treatment?
Do you have any other health conditions that impacted on your treatment decision?
Did your age influence your choice of treatment?
Did any other factors influence your treatment decision?
Decision Maker- related criteria
Patient related criteria
What helped you decide on the treatment you had for your kidney cancer?
Do you feel your personal treatment preference was acknowledged by the cancer team?
(How) did your family influence your treatment decision?
Were there other influences outside of the healthcare system that helped you come to a treatment decision e.g., church, contact with a charity, friends?
How did your native language i.e., when English is not the native language had an impact?
If your native language is not English, were you offered information in another language? Was this helpful?
Physician related criteria
Did you have enough opportunities/time to talk with your cancer team about what treatments are available?
Were you encouraged to ask questions?

Has your physician explained to you the aims of the treatment (for example to treat cancer) in a way you understood?
Did you have a dedicated CNS to support you through treatment decision-making? Were they hard/easy to contact?
Patient physician interaction
How easy is it for you to discuss your cancer and the treatment with your cancer team?
Did your cancer team make it easy for you to talk openly about issues that concern you?
How easy is it to contact your doctor to discuss any concerns?
Contextual factors
Economic variables
Did financial concerns have any impact of your treatment decision (e.g., the need to work, look after children)?
Access to healthcare
Did your access to the treatment (e.g., travel time/mode of travel to the hospital) have an impact on your treatment decision?
Healthcare organisation
Would telephone/virtual clinics have been helpful?
Can you think of other ways the hospital could have supported you to take a treatment decision? (i.e., additional reading/video material? Support group if not already attended)
Evidence basis
Were you offered other material to support your treatment decision-making e.g., video, DVD, support group access, virtual educational seminar?
End task: Supportive care recommendations
Do you feel anything was missing (or left out) in the decision-making process?
If you could change one thing about your treatment decision-making pathway, what would it be?
Did anything about the decision-making process does not meet your expectations?
How can we improve the support for decision-making for patients?
If you were speaking to someone considering treatment for this same condition and you had to give them advice, what would you say?

7.5. Pilot Testing of the Interview Guide

Kallio et al suggest 'internal testing' as a first step to pilot the semi-structured interview guide. The term 'internal testing' refers to the process of assessing the initial interview guide in conjunction with the research team investigators (99). MVH and NK as well as the TOUR Patient and Public Involvement Coordinator reviewed the semi-structured interview guide with the aim to identify and address ambiguities and leading questions, as well as detecting potential interviewer biases.

After the internal testing, the interview guide was finalised for ‘field testing’ which is described in the next chapter.

7.6. Summary of Chapter 7

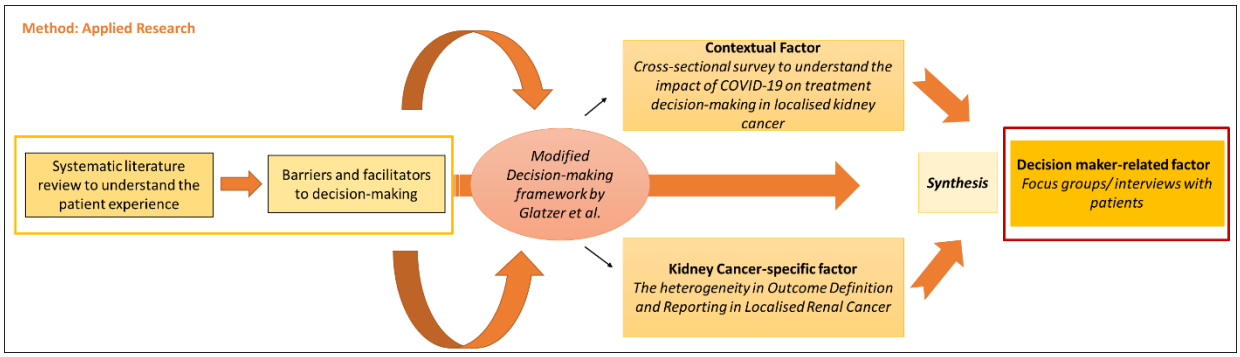
Chapter 7 focused on the development of a semi-structured interview guide to understand how patients make treatment decisions based on Stages 1-4 of the thesis. The development process of the guide focused on enhancing the reliability of the pilot focus groups and interviews, using the methodology of Kallio et al. The methodology aims to ensure the study's trustworthiness. The chapter outlines the various stages involved in the guide's creation, such as selecting the research method, gathering, and applying previous knowledge, and crafting the preliminary semi-structured interview guide.

Chapter 8. Decision Maker Related Factors: Focus Groups/ Interviews with Patients

This chapter describes the qualitative work undertaken to gain further context and an in-depth understanding of the factors that influence patients during the treatment decision-making process (Figure 24). Due to the paucity of qualitative work aimed at understanding the factors that influence patients during treatment decision-making and their supportive care needs, as well as a multifactorial process of decision-making that has the potential to require a different approach, the initial steps in this thesis include the validation of the semi-structured interview guide and development of a thematic coding system.

This work will be presented at the International Kidney Cancer Symposium (April 2023): "Exploring the perspectives of patients with localised kidney cancer on their treatment decisions: a qualitative study".

Figure 25: Methodological overview: Decision maker related Factors: Focus groups/ interviews with patients



8.1. Introduction

As described in Chapter 3 of this thesis, there is a notable gap in understanding the factors that influence treatment decision making from a patient perspective. According to Campi et al., patient preference is a crucial trigger for deciding on a treatment (i.e., AS), highlighting the need for further studies to investigate this aspect (153).

A review by Chandrasekar et al. reported results similar to those presented in Chapter 3 (mixed methods systematic review) in terms of the kidney cancer specific factors that influence treatment decision-making. Decision maker related factors and particularly patient preferences for treatments were not highlighted by Chandrasekar et al., which

potentially indicates how little patients are currently being involved in the treatment decision process in localised kidney cancer. These findings emphasise the need to understand how decision-making is experienced by the patient and further explore the value of shared decision-making in this context through a series of focus groups and interviews (208).

8.2. Methods

A semi-structured interview guide was developed to perform focus groups and interviews as described in Chapter 7.

A homogeneous group was chosen for the focus group, meaning participants had similar experiences i.e., patients were diagnosed with localised kidney cancer. Focus group discussions are typically moderated by an experienced researcher (205). The researcher guides the conversation and ensures that all participants have an opportunity to share their thoughts and ideas. I attended two courses on qualitative research methods to gain experience on how to best facilitate the focus groups (facilitated by KCL and the EAU). The focus groups each ran for about two hours.

In addition, participants who were not able to attend the focus groups or preferred a one-to-one conversation, were given the option of a one-to-one interview. This allowed everybody interested in participating to do so.

The research was conducted across three countries by two researchers (KB and LV) to provide a European view: the UK, the Netherlands, and Germany. Participants were recruited via *Kidney Cancer UK* (KCUK), the *International Kidney Cancer Coalition (IKCC)* (The NL), and *Das Lebenshaus* (Germany) using a selective sampling approach.

To avoid language bias, the focus groups/interviews were conducted by research guides in their respective native languages.

The COnsolidated criteria for REporting Qualitative research (COREQ) checklist was used as a provide a framework of good conduct for the study (see Appendix 7) (209).

8.2.1. Ethics

Ethics approval was sought and granted from KCL to recruit via the IKCC and their respective national patient associations: *Kidney Cancer UK* and *Das Lebenshaus* in Germany. IKCC

supported the recruitment in the NL as this is the headquarter of their office (see Appendix 6).

8.2.2. Semi-structure Interview Guide

As described in Chapter 7, a semi-structured interview guide was developed based on the previous four research stages (see Appendix 8).

8.2.3. Sampling

In qualitative research, the sample size and selection of participants have a profound effect on the quality of the research. A 'selective sampling' technique, non-randomised sampling was used, which was defined by Schatzman and Strauss in 1973 as: selecting people according to the aims of the research (210).

Selective sampling is a useful technique when a limited number of participants is available, and the researcher wants to choose a group that is representative of the population being studied. This method allows researchers to focus on specific subgroups within the population, gathering more detailed and in-depth data.

In the context of this study, participants who had received a diagnosis of localised kidney cancer were invited. Rather than setting a specific quota for the number of patients per country or treatment, the goal was to examine the decision-making process itself, with a focus on the treatment options presented and the patient's active involvement in the decision-making process. This allowed for a specific focus on patients, who have been diagnosed with localised kidney cancer. By utilising selective sampling in this way, it was possible to gain a deeper understanding of how patients make decisions about their treatment options in this context.

8.2.4. Participants

Based on the selective sampling method, participants (adults >18) were invited based on their diagnosis of kidney cancer and their willingness to participate in the focus groups and interviews.

8.2.4.1. Recruitment across three countries

The focus groups were conducted across three countries (Germany, the NL and the UK). Including participants from three different countries, helped to capture a broader range of

cultural perspectives and experiences, and helped to enhance the research validity. This enabled me to identify themes which might be important in one country but deemed less so in the other. Moreover, different country perspectives also provide the potential to find a solution to a problem which has been addressed in one of the countries. The diversity of the cultural backgrounds of the participants provided me with a comprehensive understanding of treatment decision-making.

Furthermore, the diversity of the three different healthcare systems also helped to understand underlying contextual factors. All three health care systems differ in how treatments are reimbursed, resulting in differing access to health care but also supportive care services (e.g., patients in Germany are able to use rehabilitation services after their treatment to help them to recover in an outpatient setting).

8.2.5. Sample Size

Theoretical saturation has been a frequently discussed topic in the literature. It started with Glaser and Strauss in their book 'The discovery of grounded theory' and has been defined in various ways by researchers to justify where 'no new information' emerges in the data being collected (211). However, this statement has been seen as problematic, as different criteria exist for data saturation, and because there is no clear consensus on what constitutes a sufficient sample size or level of data saturation for qualitative research. Therefore, the decision was made to follow Low et al.'s approach of 'pragmatic saturation' (211) where data saturation can be reached when the following questions are answered/resolved:

- Does your conceptual model provide a comprehensive and robust explanation of the phenomenon under investigation, addressing both how and why questions? Does it account for deviant cases that may not fit the expected pattern? Is it consistent with prior research in the relevant literature?
- Has your conceptual model been informed by a thorough review of the relevant literature?
- Does the analysis focus on concepts rather than individuals, groups, or cases?

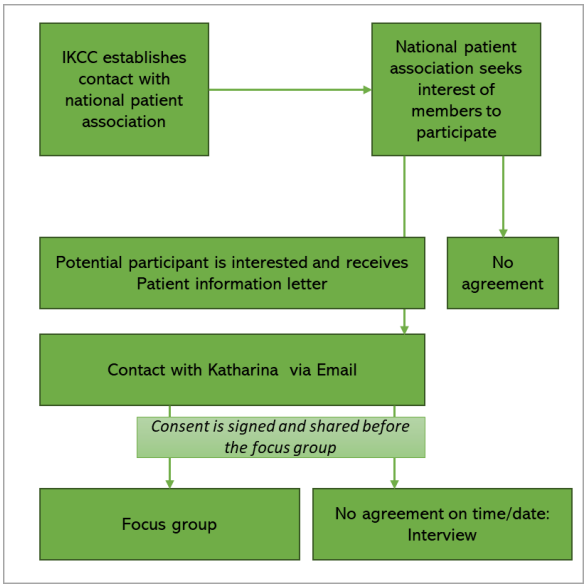
- Does your conceptual model generate categories or general concepts that are applicable beyond the specific context of your study, by being situated within the broader social context (211).

8.2.6. Recruiting Patients

Figure 25 shows the recruitment process based on the different recruitment strategies, which as described above was led by the IKCC. Patients were recruited via the IKCC, who reached out to the three respective national patient associations to understand who was interested in participating in the focus groups and interviews.

Participants were free to withdraw at any point of the project, without having to give a reason.

Figure 26: Recruitment process via IKCC across the three countries



8.2.7. Consent

A patient information letter was distributed to all interested participants (Appendix 9, 10). A GDPR approved consent form (developed by KCL) was then shared with confirmed participants at least two days before the scheduled focus group (see Appendix 11).

8.2.8. Anonymity and Confidentiality

Microsoft Teams was used to conduct and record the online focus groups and one-on-one interviews. KCL supports the use of Microsoft Teams for health research due to the end-to-end encryption, multi-factor authentication, and data protection policies compliance

(GDPR). Audio recordings were not transferred between sites or shared. The data was saved on a local folder on a KCL-one drive. No one other than the core research team members (LV and KB) had access to confidential data (contact details were only shared within the core research group). Confidentiality of all study participants was maintained throughout the process. Participants were allocated a study number upon recruitment, which was used to identify participant data by the core team.

Any quotes used in the results were therefore anonymous. All files were anonymised using participant ID numbers before any transfer occurred. The data has been archived, in line with GDPR policy, until the thesis has been completed.

8.2.9. Transcription and Translation

The English and German focus groups/interviews were transcribed using the Microsoft Teams application, which provides automatic transcription while the focus group/ interview is running. The Dutch focus groups/interviews were transcribed using clear voice (the KCL supported transcription service) since the Microsoft Teams application currently does not support transcription in Dutch.

8.2.10. Data Analysis

To develop a rigorous and replicable analysis, a codebook was developed (100, 212). A codebook is a tool used in thematic analysis to organise and keep track of the codes assigned to data during the coding process (100). The goal of the codebook is to provide a clear and organised approach to managing codes, so that codes can consistently and accurately be applied to the data during the analysis phase. Figure 26 shows a modified version of the process of code development as described by Roberts et al. (100).

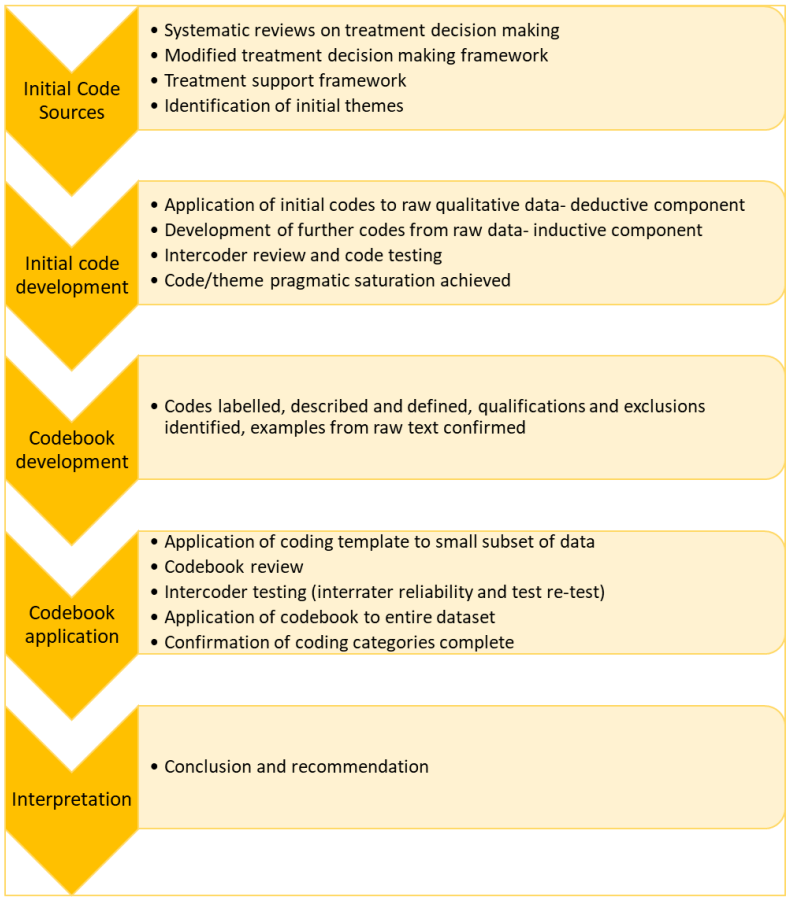
To analyse the data, thematic analysis was used. This type of analysis aims to identify patterns, whereby themes/codes can be developed, while also enabling iterative reasoning (i.e., repeating a sequence of steps, each time refining and improving), where both deductive and inductive approaches are employed (100, 212).

Deductive analysis refers to an analytical approach where the researcher applies a general theory to specific raw data in an attempt to test this theory. Conversely, inductive analysis helps to identify new themes or overarching theories based on single data points. Applying

the two approaches at various moments allows for a deepened understanding of patterns inside and outside of the predictive codes.

Roberts et al. defines this as a 'critical realism ontological approach' i.e., the deductive approach provides an initial structure to develop the codebook, while the inductive approach helps to allow to identify new themes which come up from the semi-structured research design (100).

Figure 27: Modified version of the process of code development used to present the steps applied to develop the codebook



8.3. Results

8.3.1. Participant Demographics and Cancer Characteristics

Three focus groups across three countries (DE, NL, and UK) and four interviews across two countries (UK/NL) were conducted between June to October 2022. Due to the absence of participants in the scheduled focus groups in the UK, we adapted our approach by conducting individual interviews with the one person who did attend. To optimize our time and

resources, we also rescheduled with one additional participant from the original focus group. In the Netherlands, considering the preferences of the participants and aiming to create a comfortable environment, we conducted individual interviews instead of focus groups for the two participants. This approach ensured that both participants felt at ease and allowed for a more personalised and meaningful interaction during the interviews.

Fifteen patients (6/9 female/male) and one carer (female) participated (see Figure 27). Due to the recruitment process, detailed clinical information (e.g., age, detailed cancer characteristics) was not available.

The focus group in the NL were with patients that had a genetic mutation i.e., VHL. LV conducted the focus group while I was present to support the discussion, as needed.
VHL patients and normal kidney cancer patients may have different experiences due to the underlying conditions and factors specific to each group such as: VHL patients develop various tumours, including kidney cancer. 'Other' kidney cancer patients, on the other hand, do not have this genetic syndrome and may have acquired kidney cancer due to other. This fundamental difference in disease etiology can impact the overall disease progression, prognosis, and treatment options available.
The VHL syndrome is typically hereditary and can be present from birth. VHL patients may experience the onset of kidney cancer at a younger age compared to other kidney cancer patients. Due to the known increased risk of developing tumours, VHL patients often undergo regular screening and surveillance for early detection of kidney cancer. 'Other' kidney cancer patients may not have undergone routine screenings specifically targeting kidney cancer unless they had other risk factors or symptoms that led to their diagnosis. This impacts the experience and knowledge of VHL patients, given their years of experience, they have more time to process the diagnosis and inform themselves about treatment options. Moreover, the treatment considerations differ since VHL patients may require tailored treatment plans based on their unique genetic profile, however, this may also enable them to increase their health literacy on kidney cancer treatment as they may be faced with multiple decisions compared to kidney cancer patients, who typically receive standard treatment options and are often faced for the first time with a cancer diagnosis (213).

The duration of the focus groups exceeded that of the interviews, with the focus groups typically lasting between 1.5 to 2 hours, while the interviews ranged from 45 to 60 minutes.

The focus groups and interviews were transcribed verbatim and translated by a native speaker.

Figure 28: Participation information of the focus groups and interview participants

	Germany		UK		The NL	
	Female	***Male***	***Female***	***Male***	***Female***	***Male***
Focus groups	3	2	1	2	1	3
Interviews	0	0	2	0	0	2

8.3.2. Codebook Development

Codes were developed using the Glatzer et al's decision-making framework (89) and employing an inductive approach. The review process of data gathered during the first focus group (German) involved a process of highlighting 'code-able' text (i.e., passages of text that are linked by a common theme) to help structure the data. This formed the first draft of the codebook.

8.3.3. Codebook Testing and Refinement

The draft codebook was then applied to two further datasets gathered in two additional focus groups (NL and UK) to evaluate whether the same codes applied or whether new codes emerged (see Table 18)

Table 18: Codebook example

Glatzer et al. decision-making framework		**New codes emerging**	**Description**	***Examples***
Decision maker related criteria	Patient-related criteria	The importance of patient empowerment in treatment decisions	This theme highlights how personal preferences and individual circumstances influence the treatment decision-making process. The quotes express preferences for certain treatment options, and their healthcare teams took these preferences into account when deciding on a suitable option.	*"Then the urologist (…) discussed this extensively with me and my wife, also because of the consequences. I have a slightly lower kidney function than normal, which was then, at that time forty-two and then the urologist in the hospital thought it would be good to investigate whether a kidney-saving operation is possible. Because it was a big risk if there is only one kidney left, that at some point my kidney function will be insufficient and well then you come close to the dialysis option and a transplant." (NL)*

8.3.4. Coding and Identifying Themes

The transcripts of the three focus groups and four interviews were then coded based on the structure of the codebook using QSR's NVivo version 12 to allow a systematic coding approach, where raw text was matched to the codes. NVivo is a qualitative data analysis computer software package produced by QSR International, used in qualitative research to structure and code qualitative data.

In order to better understand the connections between themes, a process of "displaying data" was employed. The graphics below (Figure 28, 29) demonstrate how visualisation was employed to contextualise the relationship between themes and subthemes with coloured bubbles/squares representing the strength of the themes based on the number of participants that discussed the theme during the focus group.

Figure 29: Focus group themes identified (decision making)

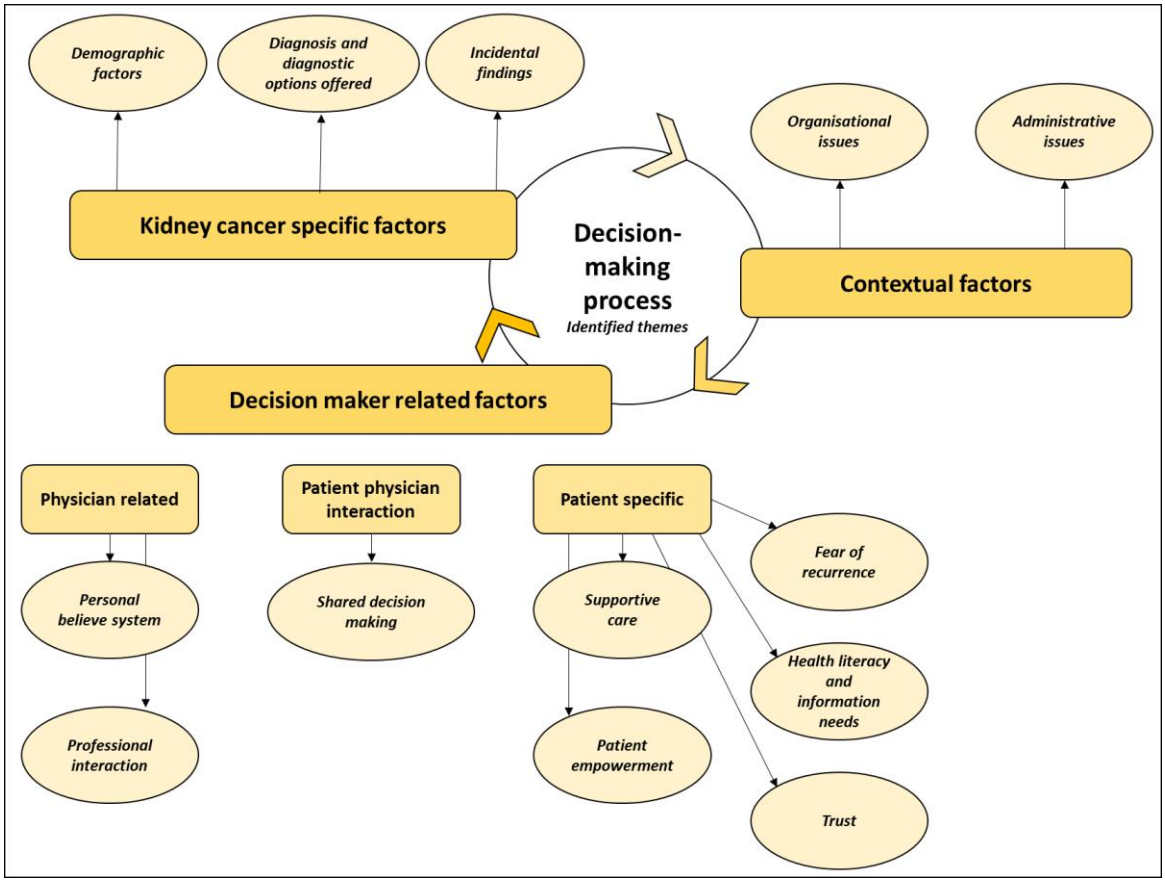
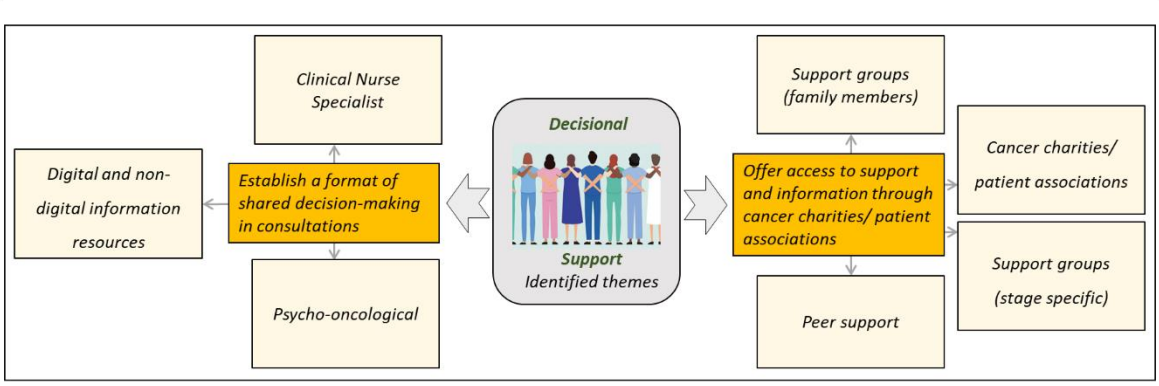


Figure 30: Focus group themes identified (supportive care)



8.3.5. Quality Control of the Codebook

The final step to ensure rigorous data analysis was to include a measure of quality assurance or control, such as: “consistent judgement across various viewers”. To test this, the reviewers (first reviewer KB and second reviewer LV) used a nominal comparison, a qualitative research method that involves cross checking data by comparing themes and codes.

In a first step, the codebook was reviewed. In a second step, the overall analysis (including quotes) was compared and highlighted by a reviewer if they felt that content was missing based on the interviews performed. This was then discussed to determine whether another code or specific quote should be added.

8.3.6. Qualitative Data Analysis

The qualitative data analysis of the patient experience was split into two parts:

1. Themes impacting the decision-making process; and
2. Supportive care needs to improve decision-making

8.3.6.1. Identified Themes that Impacted the Decision-making Process

The focus groups and interviews revealed twelve themes across three decision-making framework domains (kidney cancer specific characteristics, decision maker related factors, and contextual factors). During the analysis 1-2 quotes per identified theme/subtheme were selected to illustrate the theme (214).

8.3.6.1.1. Kidney cancer specific characteristics

Across the domain kidney cancer specific characteristics, participants highlighted two themes: Diagnostic options offered to enable treatment decision-making and Specific patient characteristics influencing treatment decision-making

- Diagnostic options offered to enable treatment decision-making

The review of the focus group data found that participants diagnosed with kidney cancer as a result of other investigations, were affected in their treatment decision-making process. Overwhelming feelings were expressed by one participant, as shown below, highlighting that they felt rushed and under pressure to accept the treatment option presented to them without fully understanding the involved risks.

"Yes, so I did not have any symptoms at all. As I said, I only had a routine prostate examination. I have an enlarged prostate and the urologist also took the opportunity to examine my kidneys with an ultrasound and found it. At first, I did not accept that there was a tumour (…) And then it actually went very quickly. A few days later I had a CT scan, and a week later I was scheduled for surgery. It was on Friday, and I went under the knife on

Monday. I was under pressure to meet the deadline, and when I look back on it now, I am not sure whether this time pressure was so necessary. I did not ask for a second opinion; I just accepted it as it was." (Participant from Germany, Focus group)

As identified during the mixed methods systematic review, **diagnostic options, particularly in the setting of small renal mass biopsies,** can help patients in their treatment decision-making when the imaging tests are not clear enough to permit surgery. The use of biopsies seems to vary between countries as this was expressed by the German participants in the focus groups/interviews.

"I don't think biopsies are done very often in Germany. We rarely hear in the patient association that a biopsy was done, they always operate directly." (Participant from Germany, Focus group)

It also seems to vary between hospitals, as a participant from the UK who chose AS as their preferred treatment option highlighted:

"He (the consultant) wanted to do a biopsy, whereas the other two (consultants) had said definitely don't do a biopsy. I agreed to the biopsy." (Participant from the UK, Interview)

- Specific patient characteristics influencing treatment decision-making

As previously identified in the systematic review (Stage 1B) **demographic factors "age" and "comorbidities"** can influence the treatment decision-making process.

"I am 74 years old. And because I am also a vascular patient, I don't feel that I will live to be a hundred years old, so to speak. That was also a reason, my life expectancy. Yes, maybe I will live to be 90. But statistically, a vascular patient has a somewhat worse prognosis compared to those without vascular problems. So, taking that into account, I just thought, and that 10%, let's take the gamble. And thus, opted for that cryoablation. Plus, it's just way too dangerous with my arteries. If it doesn't work out with my arteries, then I may die during the operation." (Participant from the NL, Interview)

VHL patients experience a different treatment journey to other patients, with the uncertainty of their **genetic disorder and age** shaping their approach to choosing the right treatment.

“I think since I was twenty-four, that’s about 17-18 years ago now, I had my first kidney surgery. And since then, several smaller tumours were removed and over the years, because you have VHL disease, you are scanned every year. And the size of the tumours is monitored. And yes, there were a number of times that the tumours became too big, so they had to intervene to prevent metastases. Since the last operation, they intervened, three times now (surgery, followed by ablation two time).” (Participant from the NL, (VHL), Focus group)

8.3.6.1.2. Decision maker related factors

The modified decision maker framework (Glatzer et al. (89)) splits ‘decision maker related factors’ into three subdomains:

A) Patient specific factors

B) Patient-physician interaction

C) Physician related factors

The themes identified during the focus groups are described within these subdomains.

A) Patient specific factors

Participants recalled feelings and opinions which were grouped under the following themes.

- Patient empowerment

Participants described a need to feel empowered.

"I am proactive. I have a file on the matter. I have dates. If I am not informed, I will speak up and express my thoughts, but I do not want to be a nuisance. I do not want to burden the system, but I do need to know. It wouldn't be rocket science, would it, for them to simply say 'Your plan is as follows.” (Participant from the UK, Focus group)

“I learned that it is important to “get smart” and especially if you are supposed to get talked into something, that you can resist, that you know not to fall for anyone, make the decision which fits to your life and do not just sit back and let them decide for you.” (Participant from Germany, Focus group)

- Health literacy and information needs

The influence of **personal experience and medical knowledge** on treatment decisions was another source for lively discussions. This was specifically highlighted by a VHL disease participant who is very engaged in a kidney cancer patient association.

"Yes, uh, luckily, I have absorbed a lot of knowledge over the years about what the disease exactly is. And what exactly are the treatment methods. And it also helped me in part that I was, on the board (Kidney Cancer Patient Organisation). Yes, that certainly helps, I have also been to the international conferences. So, you know a little more of what is going on and what the possibilities are and, also what to expect. Also, of course, seeing many patients who have undergone the same type of treatment. Yes, of course you learn from that too, so that has been it for me a bit." (Participant from the NL (VHL), Focus group)

"And it is also less threatening. I have already experienced and seen so many things in other patients. And if you then get that rotten cancer yourself, that puts things into perspective, and you do not panic easily. Otherwise, it would have been more challenging." (Participant from the NL, Interview)

Participants also expressed how they felt **passive** in their **treatment decision-making.**

"It was also difficult in the sense that I did not have a chance to ask anything. It was decided by the consultants and there was no other way. There was no alternative and I found out afterwards that there are more treatment options from the charity." (Participant from Germany, Focus group)

"I didn't even ask if there was an alternative because I kind of got the impression that the only alternative was watch and wait." (Participant from the UK, Interview)

Moreover, participants discussed their **comprehension of information,** which was given by the HCPs during the process of diagnosis and its impact on treatment decisions differed across patients.

"Right. And that's doctors' talk, and I did not understand the word of it, but I understood tumours a tumour. So obviously I have gone on to Uncle Google or Doctor Google; googling what is this T1B mean? The M 0, the N 0? What does this mean? This really confused me." (Participant from the UK, Focus group)

"Cancerous cell carcinoma or something, but in layman's terms, that's cancer, right? Kidney cancer. That is what it is. So, if somebody said, look, it is a 70% chance of having kidney cancer. How do you feel about that? That would have helped me to come to terms with it quicker, instead it left me very confused." (Participant from the UK, Focus group)

- Supportive care

Participants highlighted the importance of **psychological/emotional support** in decision-making. They mostly felt supported by HCPs in their physical recovery but felt they were left alone to deal with their mental health.

"I suppose it is a good thing that the consultant was a surgeon because I felt very reassured with him looking at my case. But there wasn't much in terms of (emotional support- nobody asked me:) "OK, how are you going to cope with this information?" I went to see the cancer nurse who gave me a brochure and then I went out in the car park and sat in the hospital car park for 15 minutes wondering how I was going to come back and tell my wife who only lost her dad to COVID." (Participant from the UK, Focus group)

"I can look back and smile, but yes, once you are in the system, dealing with the immediate was ok. Well, there were not many options. You felt safe. Secure. It is the bits before that and certainly the bits after that. You are a bit left alone." (Participant from the UK, Focus group)

To cope with the mental health impact of dealing with the diagnosis, all participants turned to cancer charities, who supported them emotionally during their decision-making.

"They (the NHS) rely on charities to do that, like kidney cancer UK, like Maggie's who provide counselling. They will tell you what you need to know via online and telephone counselling." (Participant from the UK, Focus group)

"I plucked up the courage to pop into our local Maggie Centre and they had loads of time for me. We had a cup of tea and chatted about the other things that were playing on my mind because you do start thinking, you know 'we're not going to live forever'. But you also start thinking right 'How do I get things in order without worrying my family?'. It was a difficult period in my life that I will never forget the mental impact." (Participant from the UK, Focus group)

Involving family in the decision-making can be difficult as expressed below.

> *"My family was so depressed by the diagnosis. However, the joy was great, of course, when we were told that the imaging showed that there was no bone metastasis. But the joy did not last that long, they were frustrated by the cancer diagnosis, my wife, daughter, and mother." (Participant from Germany, Focus group)*

Or helpful to have their families involved.

> *"He (the surgeon) explained to me exactly how it works. I cannot remember that anymore. I was glad that my husband was there and remembered the information given." (Participant from Germany, Focus group)*
>
> *"Of course, my husband is involved- however, preferably from the distance (…) And he also knows that his advice is helping me to take my treatment decisions." (Participant from the NL (VHL), Focus group)*

Both the UK and German group participants discussed feeling **overwhelmed** by their diagnosis and **rushed to make a treatment decision**, indicating that additional time would have supported them in their decision-making process.

> *"Having information to just step back for a minute and look at the information we're presented with, I don't know if it's feasible with the demands of the NHS, but it would have been helpful to have more time." (Participant from the UK, Focus group)*
>
> *"Well, it went almost too fast for me. (…) Of course, you do not want to wait long, but I do not know if when you are confronted with something like that for the first time, whether in the exaggerated sense, diagnosis on Friday and surgery next Friday is the best timeline. If you are diagnosed with cancer for the first time, you need to be able to mentally comprehend the information and this is difficult when the timeline is so tight." (Participant from Germany, Focus group)*

- Fear of recurrence

Participants also described that **fear of recurrence** having a significant impact on their treatment decisions.

"And you have got to think, well, hang on, is it (the tumour) gone. Will it come back after some time? You never know. This is described as the journey, and this is your path going forward for the next five years." (Participant from the UK, Focus group)

"'All we can do is manage it' said the consultant to me. So now this is what my mind said, 'does that mean that one day the cancer is going to come back, it's going to appear somewhere else, and then what are the things that I have to look out for?" (Participant from the UK, Focus group)

- Trust in the treatment option and treating HCP

Trust in the treatment option, (or lack thereof) was highlighted in the German and UK focus groups and interviews.

"It is just monitoring, right? Yes, I would find that a bit scary, to be honest. And the tension of what has happened or what is going to happen. Each time you make a scan and wait for the result if the tumour has grown yes or no. No that does not fit my character/personality." (Participant from the NL, Interview)

Trust in the treating clinician was also discussed during the UK and German focus groups. A participant from the UK shared how different HCPs recommended different treatments.

"The different answers from the different consultants concerning my treatment options did not fill me with confidence. After talking to three different people who told me first to have a nephrectomy, then partial nephrectomy hen suggested a biopsy. I was then referred to the original hospital and spoke with the first consultant again. He would not tell me what he thought was medically best for me, instead, he told me I could have a total nephrectomy or nothing and just keep it under surveillance. This knocked me out for six- I could not process any other information I was told as everybody suggested something else. "(Participant from the UK, Interview)

In Germany, the focus group agreed that a second opinion was very helpful and increased their faith in whether they are making the right decision or not.

"What would have helped me, would have been a second opinion. Surely no one wants to wait a long time for the surgery date. It was ambivalent, but the fact that I was able to get a

second opinion, that I had to use the time because of the infection I had too, helped me a lot." (Participant from Germany, Focus group)

"I received a second opinion. I spoke to the senior physician, and he looked at my pictures and recommended the same treatment as the colleagues in the other hospital. Well, and then the decision was clear for me, it was necessary to have surgery." (Participant from Germany, Focus group)

In the UK and the NL, participants expressed how MDT discussions increased their confidence in the treatment options presented.

"The treating doctor also started consulting colleagues and the initial conclusion was that the kidney had to come out (...) This filled me with confidence, that she still wanted to discuss with the oncology and urology colleagues." (Participant from the NL, Interview)

"They discussed my case at the MDT to decide whether I would have a partial or a full nephrectomy." (Participant from the UK, Interview)

B) Patient-physician interaction

Shared decision-making was the most dominant theme identified as part of the domain decision-maker-related criteria.

- Shared decision-making

The importance of **shared decision-making** in kidney cancer treatment was extensively discussed across the three countries. The NL focus group highlighted how they were actively involved in the treatment decision-making and how it helped to understand side effects and the treatment journey to feel like they made an informed decision.

"She also just simply sketched a realistic picture of the long-term risks. For both cases: If you take out the whole kidney, with the adrenal gland and the tumour, there are advantages e.g., lower chance of metastasis. But of course, as I have already said, removing it completely has also disadvantages, in particular the kidney function. So yes, she clearly said that it is a choice that can also have consequences in the long term. In the end yes, I am 68 years old, and we were concentrating on removing the tumour, and there are no metastases yet." (Participant from the NL, Interview)

"So, that is the big trick. How do you get patients who are suddenly confronted with such news as 'you have cancer', how do you get them well-informed or on the right path. (…) how do I deal with that and how do I go into that treatment. What kind of treatment will I receive? And what choice can I make? (You need that information, since) as an individual patient, you do not have that knowledge at that moment." (Participant from the NL, Interview)

However, this was not the experience in the UK.

"He (the consultant) cannot read my mind. I appreciate that. But I would have hoped that I was asking the questions that indicated that medically I was not qualified, and I needed his input rather than just waiting for me to say I want this, or I want that." (Participant from the UK, Interview)

Another participant described the conversation during the consultation as quite challenging.

"So, you (directed at the consultant) would suggest active surveillance? And he said 'Ohh, no, no. You must choose. No, I cannot choose. But I cannot choose without input from the consultant, but eventually by asking him the question 'What would you suggest if I would be a family member', he finally told me that he would choose Active Surveillance." (Participant from the UK, Interview)

An essential part of shared decision-making is **clear communication** and particularly the use of **lay language**. Most participants described struggling with the HCP's use of medical terminology.

"(…) That is doctors' talk, and I did not understand a word of it, but I understood it was a tumour. So obviously, I went on to Uncle Google or Doctor Google. Then googled 'what does T1B mean? M0, N0? What is that?" (Participant from the UK, Focus group)

"It was the consultant that gave me the information about a Mayo risk score, but in the other hospital, it was another risk score, and I didn't know how comparable it was." (Participant from the UK, Interview)

Participants also expressed that **understanding the next steps** to prepare for treatment was very helpful to decide on a treatment option. They felt better informed and therefore ultimately calmer about their decision.

"There are many patients who are new to this. They should be guided a little more. What is coming and what the procedure looks like. Those are just simple steps. But it would give me some peace of mind." (Participant from the NL (VHL), Focus group)

"I think the information helped me to make the treatment decision because it indicated to me that my cancer is a very small form and although you don't want cancer growing there, if it's not doing any harm and not causing any problems, you probably cause more problems by going in and doing something than you would not have to deal with if you left it well alone." (Participant from the UK, Interview)

Understanding the **side effects** of one's treatment was discussed by all three focus groups.

"Because it had already been shown at that time that there were no metastases yet, not in the lungs, not in the abdomen, not in lymph nodes. I thought, I know it has to come out, but the prospect of having to go on dialysis at my age was more stressful for me than the fact that I had kidney cancer." (Participant from the NL, Interview)

"Another thing patients might find helpful is to know about the pain in the shoulders, which is caused by gas after surgery. I had no idea and it scared me at first as I did not expect it (…) There are tips and tricks that you can notice Facebook and that can be extremely useful to understand how to deal with the side effects." (Participant from the UK, Focus group)

C) Physician-related factors

The following two themes were identified by the participants as physician-related factors.

- Professional interaction

The professional interaction with the clinician played an important role for the participants in physician decision-making.

"Of course, it is nice when you see a doctor and I now also understand this because I am a patient myself (participant has a medical degree). Then you realize how important it is to have an empathetic doctor. Yes, that is how I feel. He or she has to be good too off course. But just someone who looks you in the eye and walks not far ahead in the hallway. That you do not stay behind, and he/she only looks at his/her computer screen. And that is a bit of a personality thing of course; you either have that or you do not. In the first hospital I did not like that that one urologist. The urologist in the next hospital and later also the female

urologist in the hospital, their approach just felt like a warm blanket. And it does not come at an additional cost." (Participant from the NL, Interview)

"If they're on autopilot, they forget the human side to it, they try though." (Participant from the UK, Focus group)

However, they also recognised the impact of **time constraints during consultation** on physicians and acknowledged this as a challenge.

"I can imagine how frustrating it is for them. They want to do more, and they do not have time because they have to see thousands of people." (Participant from the UK, Focus group)

- Personal belief system

The impact of **personal biases and motivations** on treatment recommendations for kidney cancer was expressed by participants.

"A surgeon likes to cut, for example when your car doesn't work anymore, (the answers you receive depend on whom you ask) if you ask the salesman, there is no need to repair the car, he recommends that you get a new one, if you ask the car mechanic in the workshop, then he wants to repair the car." (Participant from Germany, Focus group)

8.3.6.1.3. Contextual Factor

The following themes emerged from the discussions across the three countries: Organisational and Administrative issues.

Most of the patients have been treated or diagnosed during or at the end of the first and/or second COVID-19 wave.

- Organisational issues

The **availability and accessibility of diagnostic and treatment options** for kidney cancer have influenced the treatment decision-making of the focus group participants.

"Doctors predominantly look at what they can do within their hospital. Because in the end it is also just a matter of cost, or income. It still feels that way." (Participant from the NL, Interview)

The importance of **face-to-face vs. online consultations** in kidney cancer treatment was already highlighted in chapter 5.

Some participants expressed a clear preference for online/telephone consultations.

> *"This was all done over the telephone. I did not see any scans. (…) I live an hour and a half drive away from the hospital. Hence, I specifically asked to be notified by phone because whether it is good news or bad news if it's bad news, I didn't want to drive an hour and a half back with all those thoughts going through my head, I would be there on my own." (Participant from the UK, Interview)*

Others felt more comfortable speaking with the HCP in person.

> *"During a physical appointment I find it easier to ask questions and bring up something." (Participant from the UK, Focus group)*

However, other participants highlighted that the method of consultation should be dependent on the information that is being communicated.

> *"Keeping telephone consultations depends on the problem. I would not use it as the default option, no. I think if I am having a new complaint or a new disease, I would certainly want a physical appointment the first time. But once you are in the medical circuit for a certain condition, I think certain results, such as lab results etc. could be communicated by phone. But I find it a requirement that you get to know your doctor/physician a little bit first." (Participant from the NL, Interview)*

- Administrative issues

Participants' experience of their healthcare system had a direct impact on their level of trust, especially episodes of **miscommunication between hospitals and/or departments**.

> *"When I arrived at the hospital, I was given a bed and then about two hours later, they came and said they were sorry, but the two departments hadn't communicated with each other and, although they were expecting me and knew I was there, they didn't know I was there, and I had missed my slot for the biopsy." (Participant from the UK, Focus group)*

How best to **navigate the healthcare system** was picked up by the participants as a factor which impacted their mental health and trust in the system.

"Then he just told me the hospital would get in touch with me and I heard nothing, and I went to our local Maggie's Cancer Centre and broke down crying?" (Participant from the UK, Focus group)

Choosing the 'right' hospital for kidney cancer treatment played a particular role in the experience of participants from Germany and the NL.

"I went to other doctors, other oncologists to get this information. It played a big role for me, I was in a relatively small hospital, but it was the closest and for me, that meant that my family could come every day and that would not have been possible with the next bigger university hospital. And they contributed a lot to my healing by coming. I did not have to rely on nurses to accompany me to the bathroom or anything like that. That was an important aspect for me." (Participant from Germany, Focus group)

"In the end, I did undergo that treatment in a different hospital. This has worked out positively for me. I am glad I did not do it in the hospital closer to my home, because they would have performed open surgery." (Participant from the NL, Interview)

The impact of financial concerns linked to **social benefits and sick leave** on kidney cancer treatment and recovery also played an important role in the discussions.

"I wish I had known someone to get the correct information about my pension, about monetary things. It took me about a year to find out." (Participant from the UK, Focus group)

"At the moment, that is still regulated by the sickness benefit. It is practically for so and so many weeks, and I'm still within the time limit, but at the end of the day, I'm already thinking about starting to work again, but I don't know to what extent I'll be able to manage it. I have applied for rehabilitation, and it has been approved." (Participant from Germany, Focus group)

8.3.6.2. Identified Themes Suggested Care Needs

A range of factors across the three decision-making domains were described by focus group participants and interviewees. One of the aims of the focus groups/interviews was to determine and explore what would have made the participants feel better supported; seven themes emerged, based on these discussions.

Offer access to support and information through **cancer charities**; offer access to **stage-specific support groups**; offer access to **peer support**; and provide access or signposting to support groups for **spouses and family members** of kidney cancer patients.

Offer access to a **Clinical Nurse Specialist**; offer referral to **psycho-oncological sessions**; and access to **digital and non-digital information resources.**

- Offer access to support and information through cancer charities

The most dominant theme identified across all three countries was **direct access to patient organisations**. Participants expressed the significantly positive impact that patient organisations had on their treatment decision-making.

> *"I was so confused by all the options, but I was able to talk through all the options at my local Maggie's. They could not give me medical advice, but then I could say what I thought, and they said that was sensible or you are missing such and such a point. And that was very, very helpful." (Participant from the UK, Interview)*
>
> *"Kidney Cancer UK have a helpline and I have spoken to them; this was very helpful." (Participant from the UK, Focus group)*

- Offer support groups for patients with a similar diagnosis (i.e., localised kidney cancer)

German and UK participants expressed that they would prefer to be involved in a **support group surrounded by people with the same diagnosis**.

> *"I did not feel I had a valid place in the group because I've sort of had my cancer removed, as far as I know. And interestingly, they all looked at me as if I were crazy and they said, they felt, they were in a better position because they either had radiotherapy, chemo or going through active treatment." (Participant from the UK, Focus group)*

- Offer peer support for kidney cancer patients

Participants who attended the focus groups in the different countries were connected via the respective kidney cancer association and therefore valued the idea of **peer support**. However, they connected through different formats such as peer support groups or Facebook groups.

“I think that peer contact, so to speak, where you are speaking with patients who have experiences with this hassle, is very important. And, that you talk on a more equal level. A doctor is someone who will tell you how everything should be done, so to speak. While when you are with fellow patients, you share other things more naturally than when there is some kind of hierarchy and a sense of 'that doctor will know.” (Participant from Germany, Focus group)

“I mean, we were on the Facebook group. So, we've sort of almost created our buddy scheme, haven't we? By connecting with fellow cancer patients. So yes, you kind of self-identify with those that are having a similar journey, about the same time, as you because when you are posting about it or reading about it.” (Participant from the UK, Focus group)

- Offer support groups for spouses and family members of kidney cancer patients

Men especially highlighted the need to **offer access to support groups for spouses and family members**.

"The General Support group I went into the surgical one because my wife joined the first group before I did, and I didn't want this thing. I did not want to discuss that, not with her, involved with the best wishes in the world. But then again, there is so many. And they are not many husbands who say I am on this group because my wife's got kidney cancer. But it seems a small army of women who are on because their husbands have got it " (Participant from the UK, Focus group)

- Offer access to Cancer Nurse Specialists (CNS)

To offer **access to a CNS** is very common in the UK and has been identified across cancer care as a very important supportive approach. Conversely, in the NL and Germany, this is less common. However, Dutch, and German patients expressed the feeling that CNSs would have a positive impact on their treatment journey.

“I think it would be great if there was someone, a companion, whatever you want to call it, these onco-nurses that sometimes exist or something like that or a therapy companion, disease manager” (Participant from Germany, Focus group)

Whereas the UK patients wanted more access and continuity of care:

"I discovered that the specialist nurse that I had been given, had moved on and I was not given another one. So, there have been times since when I needed to speak to somebody and there was not anybody I could speak to at the hospital." (Participant from the UK, Focus group)

"I was given the contact details of a specialist nurse, but she was so busy all the time." (Participant from the UK, Interview)

- Offer access to psycho-oncological sessions in kidney cancer treatment

Participants often felt alone during their cancer experience and suggested that psycho-oncological support from the point of diagnosis would be helpful.

"Being confronted with a cancer diagnosis is dramatic and you would just need some sort of psychological support, not only technical information. You and your family are left alone, so that you do not lose yourself somewhere, you need support." (Participant from Germany, Focus group)

- Establish a format of shared decision-making in consultations

To empower patients to be able to actively take part in the decision-making process, participants suggested seeking clarification on various topics.

For example, it was suggested that it may be helpful to look at the imaging.

"*It feels helpful to look at the CT images together with the doctor." (Participant from the UK, Interview)*

Participants also expressed that they would have felt more supported if they were given the opportunity to ask further questions *after* the initial diagnosis.

"If you get information material right now (during the diagnosis), you cannot read it, like you need to process everything first. And then afterwards you have questions because in that moment, I personally I did not have questions. It is when you go home and you think ohh, why didn't I ask that?" (Participant from the UK, Focus group)

Participants also felt that different types of questions would have helped them to navigate the treatment journey.

"There's probably different aspects to asking questions: the pre-op questions and post op." (Participant from the UK, Focus group)

- Access to digital and non-digital information resources

Participants mentioned different types of apps they used during their treatment decision-making process. A participant from Germany highlighted a helpful app.

"I have this digital health app myself; it is called Mika- I can find psycho-oncology and all these contributions. It has helped me personally a lot because in the village you cannot get anywhere quickly. It is just that you can really comprehensively deal with the illness and then understand everything bit by bit, understand your body better and listen to yourself when something does not work." (Participant from Germany, Focus group)

However, a UK participant expressed that it might be difficult to personalise the information using an app.

"I am unsure how an app can work- The app might tell you to sort of drink two litres. But the cancer diagnosis is quite individual, isn't it?" (Participant from the UK, Focus group)

Participants also found information material very helpful but commented that the access to this type of information should be more coordinated on a higher level e.g., NHS webpages.

Good patient material would already help if you had it right at the time of diagnosis. It is just a question of who hands it out? I mean, sometimes it is the family doctor, sometimes it is the urologist, sometimes it is, I think that's the difficulty with the disease. It is easier with breast cancer. There is the gynaecologist, and he can give you a booklet straight away. And with kidneys, it is a bit more complex." (Participant from Germany, Focus group)

"It would be better if you were given a list of reputable sites, you know you can go on, not just start to google. (…) on the NHS pages for examples, therefore you know that it has been verified and that the information was provided by the professionals." (Participant from the UK, Focus group)

Overall, the navigation of the information landscape is an essential factor as underlined by one of the participants in a negative experience.

"I watched one or two of those (kidney cancer videos) and they were a little, a little bit reassuring, but one of them wasn't because it had a like a postscript underneath that said that young lady had passed away." (Participant from the UK, Focus group)

8.4. Discussion

This study explored "decision maker-related factors" by delving into the perspectives of the treatment decision-making process of patients across the UK, the Netherlands, and Germany. Eleven themes across three domains were identified (see Figure 30). The most discussed themes were: Shared decision-making and supportive care, followed by patient empowerment. Having reviewed and summarised the data below further questions were identified to add to a future interview guide after each theme. Table 19 provides a visual representation of the areas that require policy changes, as well as the identified themes that can be modified through research for effective implementation in clinical practice. The ensuing discussion delves into a comprehensive exploration of these themes, offering a more detailed understanding of their implications.

Table 19: Need for action to be implemented in practice

Need for policy change		Need for additional research	
Theme	**Modifiable by Policy: Need for policy action**	**Theme**	**Modifiable by Research: Research questions**
		Incidental findings	*What specific types of communication and support would be most helpful to patients during the diagnostic process to better prepare them for potential incidental findings and help them select the right treatment?*
		Diagnostic option	*What are the reasons for the underutilization of biopsies as a diagnostic option in cancer treatment decision-making, and how can this be addressed?*
		Patient characteristics	*A) How can medical professionals better incorporate patient characteristics such as age, comorbidities, and genetic disorders into the treatment decision-making process?* *B) What factors contribute to VHL patients being more informed about less invasive treatments, and how can this knowledge be shared with other patients?*

		Health literacy and information needs	*What strategies can be used to improve patient understanding of diagnosis and treatment options?*
		Supportive care	
Fear of recurrence	*Incorporate psychological care in the patient pathway*	**Fear of recurrence**	*What types of psychological support are most effective? What are the key components to be successful in clinical practice?*
		Trust in the treatment option	*A) Set up prospective registries to improve e.g. AS protocols to create evidence to increase trust of HCP in treatments.* *B) What communication strategies can healthcare professionals use to build trust with patients and improve their confidence in treatment options?*
Trust in the treating HCP	*Offer 'second opinions' to patients; Ensure that MDMs have supported the decision*		
Shared decision-making	*The patient pathway needs to be adapted to incorporate e.g. decision aids, give the patient more time to comprehend the information, incorporate time to ask more questions.*	**Shared decision-making**	*A) How can healthcare providers better facilitate shared decision-making among patients with localised kidney cancer to be successful in clinical practice?* *B) How can decision aids be effectively utilised to enhance shared decision-making?*
Professional interactions	*The system needs to support HCPs to ensure more focus on patient-physician interaction*		
		Personal belief system	*A) How can default bias be mitigated in HCPs when presenting treatment options to patients, especially when there is a preference for a specific treatment option?* *B) How can HCPs be trained to recognise and address their own biases when presenting treatment options to patients, and what impact does this have on shared decision-making and patient outcomes?*
		Organisational factors	*How can healthcare systems work to address these barriers moving forward?*
		Administrative issues	*What are some potential interventions that could be implemented to help patients regain a sense of control over their healthcare journey?*

8.4.1. Identified Themes that Impacted the Decision-making Process

8.4.1.1. Kidney cancer-specific characteristics

The impact of **incidental findings** on decision-making was significant for the participants, who were overwhelmed by an unexpected kidney cancer diagnosis, and who struggled to comprehend the given diagnosis. Equally, around one-third of the participants felt pressured to make a treatment decision. Similarly, Reyna et al. stressed in their research, that the emotional burden triggered by a sudden cancer diagnosis may influence the decision-making process. Moreover, making decisions related to cancer often involves predicting how different courses of action will make one feel, which can be challenging when faced with a sudden diagnosis and unfamiliar treatment options (215). This emphasizes the need for improved communication and support during the diagnostic process to better prepare patients for potential incidental findings and help them select a treatment which is right for them. Additional research is needed to understand the way incidental findings are communicated and how to better support patients to comprehend the information.

One-third of participants noted that biopsies (**diagnostic option**), were not available to assist in making treatment decisions. This aligns with the findings from the mixed methods systematic review on the barriers and facilitators to treatment decision-making. The review highlighted that biopsies can act as a facilitator to making informed treatment decisions, thus avoiding overtreatment and complications. Despite this, biopsies are not commonly utilised as suggested by our results, which should be further investigated.

Less than a third of participants described **patient characteristics** such as **'age'**, **'comorbidities'** and **'genetic disorders'** (i.e., VHL) as a factor influencing treatment decision-making. One participant shared his decision to choose a less invasive treatment due to his age and co-morbidities. Age was previously identified in the mixed methods systematic review, where it was emphasised that age should not be used as a proxy for clinical decision-making. VHL patients in particular seemed more informed about less invasive treatments (PN and ablation), perhaps because of their genetic disorder.

8.4.1.2. Decision maker related factors

Patient specific factors

Patient empowerment was identified as a trigger to treatment decision-making in the mixed methods review, however, only a limited evidence base was provided due to limited literature in localised kidney cancer. Across cancer care, patient empowerment has been shown to positively impact patient satisfaction with care, increase adherence to treatment self-management, and result in better clinical outcomes (216, 217). This was echoed by the participants of the focus groups/interviews who emphasised the importance of being an active participant, understanding their treatment options and sharing the decision-making responsibilities with the treating HCP. However, further research needs to be implemented to understand how to support patients better to feel impowered.

Health literacy and information needs is an important factor in treatment decision-making as reported by the participants across all three countries. Patients from the UK and Germany often only felt passively involved in the treatment decision-making process due to limited information and unfamiliarity with medical terminology. Across all countries participants agreed that to enable them to make an informed treatment decision, it is crucial to understand the diagnosis, all treatment options, and the consequences of each choice (i.e., a “shared decision-making” consultation). Across cancer care, literature suggests that many patients struggle to comprehend the information presented to them in medical consultations, leaving them with a feeling of disempowerment (218, 219). This is especially prevalent in cases where healthcare professionals use a paternalistic communication style (219). According to Edwards et al., it is crucial to educate healthcare professionals about the importance of tailoring health information in a way that best facilitates patients' understanding of their diagnosis and possible treatment options (219). Edwards et al. also agrees that by fostering a collaborative relationship between healthcare professionals and patients (i.e., through shared decision-making), it is possible to overcome the barriers to health literacy and facilitate better health outcomes (219).

The most prominent theme across participants (as part of the patient specific factors) related to **supportive care**. They stressed the importance of receiving psychological support, as they often felt isolated, have difficulty communicating their diagnosis to their friends and

families, and/or feel pressured to make a quick treatment decision without the appropriate support. A recent study in the field of prostate cancer revealed that time pressure shortly after diagnosis predicted long-term decisional regret in their research participants (220). Therefore, in order for patients to be able to better cope with a kidney cancer diagnosis, research suggests the provision of additional psychological support as it conveys a feeling of control in the treatment decision-making process (221-223).

The **fear of recurrence** has been identified as a prevalent unmet need among cancer patients, which results in emotional and physical distress and reduced quality of life (224). In the focus groups, two patients were particularly concerned about recurrence and therefore decided to choose surgery instead of ablation. The literature stresses the importance of early recognition and support in dealing with these fears during cancer diagnosis. According to the literature, patients exhibiting signs of "fear of recurrence" may require additional support e.g. a psychologist supporting the patient, to make informed treatment decisions that are not solely motivated by fear (224). Additional research is also needed to better understand how to best support this patient group.

One-third of participants reported **trust in the treatment option and trust in the treating HCP** as important factors that influenced their treatment decision. One Dutch participant expressed that he would not trust AS and described the option of surveillance as ‘scary’ and unclear. To avoid mistrust in a treatment option, Beckmann et al. highlighted clear communication as the corner stone to building faith in AS in the prostate cancer setting (225), however, further research needs to be conducted in localised kidney cancer

Trust in HCPs was deemed crucial across all three countries to not feel overwhelmed and confused by the treatment options presented. Interestingly, all participants from Germany stressed how a ‘second opinion’ helped or would have helped their trust in the treatment proposal and treating clinician. ‘Second opinions’ are described in the literature as helpful in enabling patients to make more informed decisions and increase their understanding of the disease, but as a result can also lead to changes in the treatment (226). ‘Second opinions’ have been reported to also reduce the number of surgeries as shown by the results of the Cornell Elective Surgery Second Opinion Program, where 27.6 % of recommendations for surgery were not upheld by the second opinion clinician (226). Many countries such as Germany, the Netherlands, Israel, and Albania have introduced programs which help

patients seek a second opinion (227-230). Nevertheless, Greenfield et al. identified that the need for patients seeking a second opinion often stems from unsatisfactory communication with the first doctor. They argue that if doctor-patient communication improves, the trust of the patient increases in their HCP and ultimately, there is no need for a second opinion (231). In addition, consistent with the results of the mixed methods systematic review, participants from the focus groups also agreed regarding the effectiveness of implementing a multidisciplinary team meeting (94) as it helped them to improve their level of trust during the treatment recommendation process.

Patient-physician interaction

The theme of **shared decision-making** was considered to be a significant topic among the participants and has been accepted across cancer care as having a positive impact on patient satisfaction and clinical outcomes (80, 82). Specifically, Dutch patients communicated their positive shared decision experiences. Conversely, German and UK participants shared examples of either not experiencing shared decision-making or feeling overwhelmed by the decision-making process due to a limited understanding of the treatment options presented.

These results add to the findings of the mixed methods systematic review, where clear communication and the use of lay language was stressed as being more critical in shared decision-making than the person who makes the decision. The American Society of Clinical Oncology (ASCO), through Gilligan et al., supports this idea and recommends that clinicians communicate effectively, including the use of medical interpreters and plain language for patients with low health literacy. Visual aids should also be used to help patients to understand their diagnosis and treatment options. In addition, family involvement in discussions should be encouraged, especially during crucial points in care (232).

Through the mixed methods review, it was discovered that decision aids are effective tools when informing patients about their treatment options (94). Furthermore, the literature indicates that decision aids across cancer care are valuable and enhance shared decision-making (233), however, participants in the focus groups had not yet experienced their use and there is no research available in localised kidney cancer. Therefore, further research is

needed to identify how the use of decision aids can enable shared decision-making in the context of localised kidney cancer.

Physician related factors

Professional interactions with HCPs were deemed significant across the board. Participants appreciated when HCPs dedicated time to clearly explain their diagnosis and the consequences of different treatment options. Gilligan et al., presenting ASCO's consensus report, suggested that HCPs should engage in behaviours that actively foster trust and confidence in patient-physician interactions (232).

The mixed methods systematic review identified that the **personal belief system** of HCPs can be a facilitator to treatment decision-making, however, clinician bias can be a barrier (94, 166). Therefore, confidence in a particular treatment option is a key factor to enable an unbiased treatment decision. One study participant highlighted that surgeons may prefer surgical intervention, resulting in a lack of consideration of other options. This phenomenon is referred to as "default bias" in the literature cited in the review, wherein HCPs present one option that aligns with their personal preference (94, 166). Shared decision-making environments as well as MDT decisions can help to prevent default bias.

8.4.1.3. Contextual Factor

Organisational factors, such as the **availability and accessibility of diagnostic and treatment options**, play a crucial role for patients in their kidney cancer treatment decision-making. Lack of availability and accessibility to certain diagnostic options and treatments can force patients to choose alternative options that may not be as effective or have a lower success rate (232, 234). This was raised by one participant, who highlighted that HCPs may only offer treatments that are available within their own hospital. However, this was not representative across all countries, as participants often reported being referred to other hospitals where the treatment was available or were able to self-refer.

Approximately one-third of participants reported a lack of support in their journey, primarily due to **administrative issues** like miscommunication between healthcare facilities, causing delayed follow-ups. This experience is reflected across documented cancer experiences (235, 236). Balio et al. emphasized its significant impact on the mental well-being of patients, who experience a sense of loss of control over their healthcare journey (235).

8.4.2. Supportive Care Needs

A range of recommendations were described by the participants of the focus groups/interviews. The most prominent themes were access to charities, support groups, and peer support. Additionally, the importance of CNS and psycho-oncology support availability, as well the importance to create a shared decision-making environment were recommended. Lastly, the participants explored different digital and non-digital tools to gather information.

Table 20 outlines the interventions that warrant further exploration to facilitate the seamless integration of the theme into clinical practice. These interventions may involve advocating for policy changes or conducting additional research to address any gaps or uncertainties.

Table 20: Supportive care needs

Need for policy change		Need for additional research	
Theme	**Modifiable by Policy: Need for policy action**	**Theme**	**Modifiable by Research: Research questions**
		Support through charities	*Which patient group benefits from support through charities?*
		Online support groups	*What are the key factors that influence the effectiveness of support groups for kidney cancer patients?*
Establish a format of shared decision-making in consultations	*Policy needs to enable a shared decision-making environment.*	**Establish a format of shared decision-making in consultations**	*A) What are the key components for integrating psycho-oncological care and CNS support into standard cancer care to address the disparity between the need for these services and their implementation?* *B) What are the potential benefits and challenges of providing access to digital health solutions in localised kidney cancer treatment?* *C) How can these solutions be tailored to meet the needs and preferences of individual patients in clinical practice?*

		Access to digital and non-digital information resources	*A) What are the key components for integrating psycho-oncological care and CNS support into standard cancer care to address the disparity between the need for these services and their implementation?* *B) What are the potential benefits and challenges of providing access to digital health solutions in localised kidney cancer treatment?* *C) How can these solutions be tailored to meet the needs and preferences of individual patients in clinical practice?*

Offer access to support and information through cancer charities, support groups and peer support for patients and families

Participants in the study reported that receiving support **from charities** and particularly **support groups** had a positive impact on their understanding and ability to cope with their kidney cancer diagnosis and treatment. This finding is consistent with existing literature which has indicated that support groups and peer support can address various supportive care needs with a direct impact on physical and mental health (237-239).

Our participants predominantly sought support from **online support groups**, such as independent discussions within established groups or forums on social media platforms like Facebook or Twitter. Previous studies have demonstrated that online support groups can alleviate feelings of isolation, depression, and anxiety, and improve knowledge, coping, and self-management skills (238, 239). However, despite the benefits of online support groups, there is still a need to understand why and how support groups work best to optimise their effects for kidney cancer patients and their families. Research has shown that support groups are complex, and what works for some may not work for others (i.e. digital vs non digital) (237). Therefore, further investigation is necessary to determine how to maximise the benefits of support groups for localised kidney cancer patients.

Establish a format of shared decision-making in consultations

Shared decision-making as identified above has been recognised as a crucial component in enhancing treatment decision-making, but despite advocacy over the last three decades, there is still a clear gap between research settings and practice (240-243). This was also identified by the participants, who wanted to be involved in the treatment decision process.

The literature emphasizes that enabling a shared decision-making environment entails changes to the treatment pathway, and study participants highlighted three main components: CNS involvement, psychological support and access to information resources.

The importance of the role of the **CNSs** was supported by the participants from the UK. They reported a high level of appreciation for this support. CNSs helped the participants to feel more empowered, however, the participants also discussed the current staffing concerns which impacted the continuous patient-nurse relationship. The Royal College of Nursing in the UK highlights that successful cancer treatment encompasses a holistic approach. This is where the pivotal role of the CNS comes into play, as they not only perform clinical tasks and check-ups but also help patients comprehend their treatment options. Furthermore, CNSs provide consistent support throughout the entire treatment process, allowing patients and their loved ones to receive extensive support for both their mental and emotional well-being. This fosters trust, cultivates a strong patient-nurse-physician relationship (184), and is even occasionally associated with improved clinical outcomes (244). The desire to access such services was expressed by the German participants, where the role of CNSs as described above, is not well established. It is traditionally the role of the treating doctor to counsel patients with their treatment decisions (245).

To address the psychological distress associated with a cancer diagnosis and treatment, the participants of the focus groups/interviews expressed the importance of **psycho-oncological care**. However, in the NL, due to the way psycho-oncological care was organised (e.g., inconsistent availability of psychologists), psycho-oncological care did not add any meaningful value for the participants. Across cancer care, research reveals a disparity between the need for psycho-oncological sessions and their implementation (246, 247). To bridge this gap, an integrated care approach that includes psycho-oncological care as a standard part of cancer care may be a viable solution. This can be a digital or non-digital format dependent on the patient’s preference (246).

In addition, it was recommended by the literature that healthcare professionals should normalise the psychosocial impact of cancer on patients' daily lives and provide tailored support and information to patients. This may entail communication skills training for healthcare professionals to facilitate discussions about psychological symptoms in their daily practice (246).

During the focus groups, **access to digital and non-digital information resources** in different formats was heavily discussed to empower patients to be more informed about their treatment options and health status. While most participants were in favour of accessing digital healthcare, personalisation was a prominent concern.

For more than a decade, the literature increasingly recommends digital healthcare as a means to improve patient management (248). The goal of providing access to E-Health is not only to improve clinician-reported outcomes like overall survival but also patient-reported outcomes and overall quality of life of the patient (249, 250). E-Health refers to the provision of healthcare services supported by digital technology, which includes telemedicine (providing medical services remotely to patients), telemonitoring (using digital technologies to monitor patients, e.g., ePROs), and digital therapeutics (algorithms based on medical guidelines and practices). Research shows that these solutions can improve communication, education, clinical assessments, and monitoring with ePROs, and patient empowerment (248). However, a gap remains between the evidence and the use of digital health solutions in practice. For optimal supportive care in oncology in line with appropriate guidelines, digital health solutions need to be integrated into the patient pathway and healthcare team practices. Aapro et al. highlight that while E-Health approaches are promising, successful implementation in clinical practice requires guidance from the treating healthcare professional (248). Further research should try to identify how to best implement digital health in the localised kidney cancer treatment pathway to enable a shared decision-making environment.

8.4.1. Strength and limitations

With the finalisation of the codebook, it is now possible to expand the evidence base and present a more comprehensive research output in this thesis.

The main limitation of the focus groups/interviews was the self-selection of participants. Only patients who were in contact with the patient association were recruited. This might have influenced the health literacy of patients suggesting they might be better informed than the ‘average’ patient and therefore might undermine the representability of the sample. The decision of recruitment, however, was heavily impacted by the COVID-19 pandemic. During the initial stages of the pandemic, from its onset until 2022, the process

of obtaining ethics approval through the NHS Trust ethic committee became challenging. Due to the impact of the pandemic, the ethics approval process was temporarily halted, resulting in a backlog of studies and a need for prioritisation.

Consequently, we made a strategic decision to recruit participants for our study through patient organizations rather than relying on hospitals. By collaborating with patient organizations, we were able to circumvent the hurdles posed by the disrupted ethics approval process.

By adapting our recruitment strategy to the circumstances at hand, we aimed to maintain the momentum of our research despite the challenges imposed by the pandemic. Through this alternative approach, we could continue making progress and gathering valuable data, contributing to the advancement of knowledge in our field of study.

8.5. Conclusion

The experiences shared by participants in the focus groups and interviews offer insights into the complex components of decision-making that localised kidney cancer patients face. All participants expressed a desire to be involved in their decision-making process. However, due to the emotional toll of the cancer journey, which often requires quick decisions, actively engaging in the decision-making process was described as challenging.

Research in cancer care stresses the importance of shared decision-making and clear communication as key elements of effective decision-making. These themes were reflected in the present study, but there appears to be a gap between research recommendations and practice. It seems that concepts which seem to support treatment decision-making in research settings, are often not implemented in practice. It is crucial to identify how best to translate research into practice and highlight the essential components of research recommendations that will benefit patients. The additional exploratory questions can help to further investigate this gap.

8.5. Summary of Chapter 8

The focus groups, and additional interviews investigated the decision-making process from a patient perspective. This helped to produce a codebook by utilising a thematic analysis across three countries. Some of the factors identified were also identified in the systematic review on barriers and facilitators to treatment decision-making, as well as the COVID-19 survey (Chapter 5). Overall, eleven themes across three domains were identified (kidney cancer-specific decision-making, decision maker related factors, and contextual factors), which impacted the treatment decision-making of the participants across all countries (see Figure 28/ Table 19).

Participants in the focus groups and interviews also expressed their need for support and recommended various methods to enable this. Seven themes emerged based on their recommendations (see Figure 29/ Table 20).

This awareness will form the basis of a semi-structured thematic approach to subsequent focus groups, which solely focus on supportive care recommendations.

Chapter 9: Overall Conclusion and Future Directions

This chapter describes a summary of the overall conclusions of the thesis and proposes potential future work to be taken forward in this area of research.

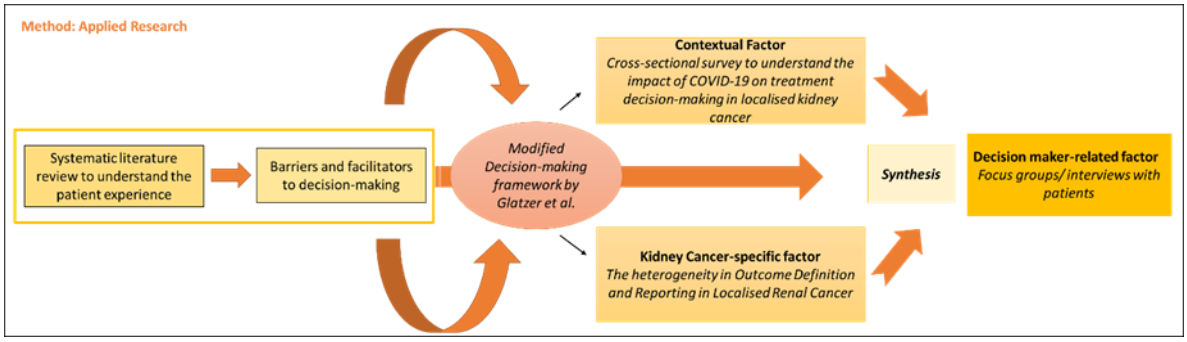
9.1. Summary of the Thesis

This thesis has addressed the need to improve the understanding of treatment decision-making in localised kidney cancer. Over the last decades, the incidence of localised kidney cancer has increased, and the treatment options have expanded from only using invasive treatments (i.e., surgery), to also including less invasive treatment options (ablative treatments and AS) (5). However, there has been limited research to improve the evidence on the different treatment options and the research conducted to date has been criticised based on design, sample size, and other factors influencing the validity and reliability of the research (14, 161).

Additionally, decision-making across cancer care has been promoted to change from primarily paternalistic models to decision-making models, which are based on shared decision-making (251). The focus of how decisions should be taken has shifted towards understanding the patient perspective and trying to empower patients; however, little has been done to reflect this in localised kidney cancer (78, 83, 251).

This has shown the need to understand the factors that influence the treatment decision-making process in localised kidney cancer. This final chapter summarises the thesis and highlights future research opportunities (Figure 32).

Figure 31: Methodology overview: Overall conclusion and future directions



Chapter 4 was split into two stages. A first systematic review on patient decision-making confirmed that there is limited research available to fully understand the process of

treatment decision-making in patients with localised kidney cancer from a patient perspective. The current literature is predominantly concerned with the support of HCPs in their treatment decision-making process based on clinical factors.

A second mixed methods systematic review then identified the barriers and facilitators to treatment decision-making. Key themes were identified and categorised into the three domains of Glatzer et al.'s decision-making framework: 1) kidney cancer specific characteristics; 2) decision maker related criteria; and 3) contextual factors. The main facilitators identified within these domains were size at diagnosis, age, comorbidities, body mass index, gender, nephrometry scoring systems, biopsy, socioeconomic status, family history of cancer, year of diagnosis, geographic region, and practice pattern. The key barriers were race, gender, patient anxiety, low confidence in diagnostic and treatment options, cost of procedure, and practice patterns.

Chapter 5 then evaluated the significance of contextual factors i.e., the impact that the COVID-19 pandemic had on the practice and perspectives of HCPs working in kidney cancer in the NHS during the first six months of the outbreak. It revealed that the pandemic affected treatment decision-making in the healthcare system and that HCPs expressed high levels of dissatisfaction with the standard of care being delivered. The policy impact of COVID-19 on treatment decision-making is particularly important for this work as it has affected decision makers across the entire treatment decision-making pathway.

Kidney cancer specific factors were further assessed in **Chapter 6** by evaluating outcome reporting heterogeneity. This systematic review of the literature highlighted the ongoing problem of outcome reporting heterogeneity in localised kidney cancer studies, with multiple terms used to refer to similar outcomes and the variation in definitions used. This makes it difficult to interpret the evidence basis for clinical decision-making and hence, to create clinical practice recommendations. In addition, there is a lack of PROs in localised kidney cancer studies, due to a limited number of specific tools available to capture quality of life outcomes in this population.

The evidence obtained in Chapters 4 to 6 was then used in **Chapter 7** to develop a semi-structured interview guide to gain a deeper understanding of how patients make treatment

decisions. Kallio et al.'s methodology was employed to ensure the reliability of the focus groups and interviews and guarantee the study's credibility (as described in Chapter 8).

The interview guide developed in Chapter 7 was then used in **Chapter 8** to run focus groups and interviews to test the interview guide and identify the factors that impacted patients diagnosed with localised kidney cancer in their treatment decision-making. As part of the study, a codebook was developed for the qualitative data analysis. Eleven themes across the three domains (kidney cancer specific decision-making, decision maker related factors, and contextual factors) impacted the treatment decision-making of the participants from the UK, Germany, and the Netherlands. The most prominent themes were related to shared decision-making, supportive care, and patient empowerment.

The participants in the focus groups and interviews also expressed a need to feel better supported in their treatment decision-making. Seven themes emerged based on their recommendations: access to charities, support groups, peer support, CNS and psycho-oncology support, a shared decision-making environment, and digital and non-digital information tools.

It is crucial to acknowledge that the method of recruitment employed in this study may have introduced a potential sampling bias, as discussed in detail in Chapter 8. To address this concern and enhance the representativeness of the participant pool, a deliberate effort will be made to recruit patients through Erasmus Medical Centre. By utilising this recruitment strategy, the study aims to broaden the diversity and inclusion of participants, thereby reducing the potential bias associated with the initial recruitment method presented.

Throughout the research process, the advantages of interviews over focus groups became increasingly evident, following the completion of three focus groups and four interviews. Initially, focus groups were chosen as the preferred method to foster group discussion and encourage participants to think creatively. However, upon careful analysis of the outcomes and considering the comprehensive discussion guide developed in stages 1-4 of the research, it became apparent that interviews provided a more profound exploration of the subject by allowing for more detailed and targeted questioning.

The interview format offered a valuable opportunity to engage with participants on an individual level, facilitating a focused and in-depth examination of their perspectives, experiences, and decision-making processes. This was supported by LV, who conducted the Dutch interviews. We

both felt that the one-on-one setting created an intimate and personalised interaction, enabling a deeper understanding of the multifaceted factors that influence treatment decisions in cases of localised kidney cancer.

Furthermore, interviews proved to be instrumental in capturing nuanced and context-specific information which has been more challenging to elicit within the group setting.

By incorporating interviews alongside the initial focus groups, the research process benefitted from a complementary methodology that allowed for an understanding of the research subject and helped me to understand the two settings in detail. The combination of focus groups and interviews ensured that both the broader group dynamics and individual perspectives were thoroughly considered, thereby enhancing the overall rigour and depth of the study's findings. Nevertheless, for future work, we recommend interviews using the discussion guide and codebook developed. **In summary** this thesis gives insights into the complex components of the treatment decision-making process in the field of localised kidney cancer. Factors that influence decision-making have been identified using a multidimensional approach. These factors need to be considered and awareness should be raised to help HCPs and their patients decide on the most optimal treatment given their specific circumstances. Moreover, patients are keen to actively participate in this decision-making process, but various factors such as COVID-19 can make it challenging. The emotional toll of the cancer journey, the current infrastructure of healthcare settings, and the heterogeneity of outcome reporting in clinical guidelines require consideration.

9.2. Future Research Direction

In order to expand on the research conducted, the following recommendations for future research are proposed.

- **Patient-HCP communication**

Given the scarcity of research on shared decision-making in localised kidney cancer and its established significance in enhancing patient care, it would be valuable to assess the degree of communication between patients and their treating HCP. This goal could be achieved through the use of the EORTC Patient-Reported Outcome Measurement on Communication (COMU26) tool, designed to provide a deeper insight into patient-physician communication. This will help to further improve shared decision-making in localised kidney cancer.

- **Understanding the policy angle**

The proposed multidimensional factors must also be taken into account by policymakers. Healthcare systems face significant barriers that make it challenging to empower patients and establish a shared decision-making environment, even when desired.

Addressing this challenge requires an understanding of how to effectively utilise well-established support systems, such as CNS support, patient support groups or psychologists, within the patient pathway. Restructuring the patient pathway becomes essential to enable shared decision-making in this context. By restructuring the pathway using a top-down approach, it becomes possible to integrate the necessary resources and expertise, facilitating a collaborative decision-making process between patients and HCPs.

Furthermore, as identified in this thesis, shared decision aids serve as valuable tools to support both patients and HCPs in the decision-making process. However, further research is needed to explore how the combination of restructuring clinical pathways and utilizing decision aids can have the greatest impact. Understanding the optimal integration of these tools and strategies can contribute to the successful implementation of shared decision-making in the management of localised kidney cancer.

Therefore, it is crucial for policymakers to recognize the importance of overcoming the barriers in healthcare systems and actively support the restructuring of patient pathways to facilitate shared decision-making. Additionally, allocating resources for the development and implementation of effective shared decision aids is essential to empower and enable patients to make informed choices regarding their treatment options. By addressing these considerations, policymakers can promote patient-centred care and improve outcomes for individuals with localised kidney cancer.

- **MDT's role in decision making in localised kidney cancer**

Kidney cancer patients' decision-making process is complex. It has been recognised in recent years that a multidisciplinary approach is important to ensure optimal quality of care. MDT conferences do not only serve to guide one's management, but also to ensure the adherence to the latest clinical guidelines and its implementation considering the local context has been implemented (168, 169). To better understand treatment decision-making, a real-world evidence study could investigate the correlation between MDT

decisions and treatment received by the patient. In the context of localised kidney cancer, there is often more than one option available, and it would be interesting to understand whether patient preference affects this correlation. The study would not explain why a certain treatment option was chosen, but it would begin to quantify the decision-making progress.

To expand the results identified in Chapter 8, a follow-up study has been developed which will be conducted in collaboration with the team at the Royal Marsden Hospital and my future employer at Erasmus University in Rotterdam. Using a semi-structured thematic approach to subsequent interviews, which focuses on supportive care recommendations while highlighting the themes identified in Chapter 8, is the proposed approach. An ethics application has been submitted to the Royal Marsden Hospital in London and Erasmus MC in Rotterdam. Attempts to encourage and engage with further collaborators to identify a centre in southern Europe, the Nordic countries and eastern Europe will be made to ensure a wider representation of Europe.

Addendum: The Impact of the COVID-19 pandemic on this thesis

The timeframe of the thesis, spanning from 2019 to 2023, coincided with the occurrence of the COVID-19 pandemic, which significantly impacted the project in multiple ways. During the two years affected by the pandemic, it became evident that both patients and HCPs experienced substantial disruptions in the treatment decision-making process. Many patients encountered delays in diagnosis and the initiation of their chosen treatment plans. As an immediate solution, AS was often introduced, with varying recommendations from different medical societies across the EU of the period which was considered 'a safe delay', this data should be used for the future to further assess AS for localised kidney cancer.

The COVID-19 pandemic also prompted the adoption of new consultation methods across most EU countries, transitioning from traditional face-to-face consultations to phone or video consultations. While this shift created new opportunities, it also presented challenges that require further investigation to enhance communication and ensure patient-centred care. This was already introduced in Chapter 9 but should be further investigated to enable patients to benefit from the new way of consultation post COVID-19 pandemic.

As discussed in Chapters 5 and 8, I also encountered challenges in obtaining ethics approval, ultimately requiring approval from KCL. This necessitated the adoption of novel recruitment methods, such as utilising Twitter or collaborating with patient organizations. Although these approaches introduced a potential recruitment bias, they compelled me to think creatively and incorporate innovative methodologies that were previously less commonly employed.

In summary, the COVID-19 pandemic introduced numerous challenges but also unveiled opportunities that are reflected in this thesis. The pandemic's influence will continue to shape future research endeavours in the field of translational urology and oncology. By adapting to the unique circumstances imposed by the COVID-19 pandemic, this PhD thesis not only shed light on the impact of the pandemic on decision-making processes but also paved the way for novel approaches and methodologies in conducting research.

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Appendix 1: Factors that influence patients' view on treatment decision-making in localised kidney cancer (Poster)

The current evidence for factors that influence patients' choice of treatment in stage I kidney cancer: a systematic review

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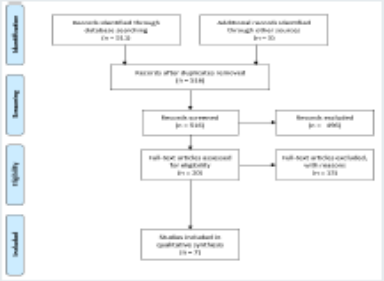
Background

- An increasing number of management options for stage 1 renal cancer presents a unique challenge for both patients and clinicians. These treatment options now include active surveillance, surgery, cryotherapy and RFA.
- Various guidelines and scientific papers recommend shared decision making to improve the decision-making process.
- We therefore aimed to understand the factors that influence the patients' decision-making process focusing on decision maker related criteria.

Methodology

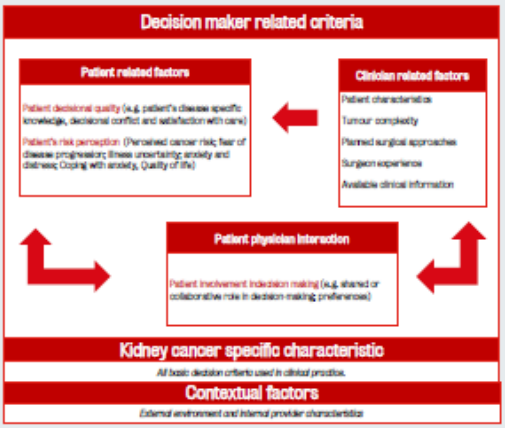
- We conducted a systematic review of interventions for localised RCC (stage 1) offered in the European Union
- Published between the 1st of January 2004 and 26th of June 2019
- Articles with a qualitative or quantitative design generating data on decision-making were included.
- Studies were selected on the basis that:
  - they explore patient views on treatment decision-making
  - they are of sufficient methodological quality
  - their findings can be translated into suggestions for clinical care



- The information was extracted following a Bayesian approach.
- We used the Glatzer et al framework for 'Decision Making Criteria in Oncology' to structure the identified themes.

Results

- Most of the studies identified addressed healthcare professionals' provision of information with respect to treatment choice (e.g. quantitative RWE data).
- Three studies identified assessed interventions (interdisciplinary counselling, use of decision aid tool) which directly involved patients in decision-making.
- Factors which influenced patients' decision-making quality included: patient involvement in decision-making; and decisional quality (i.e. patient's disease specific knowledge, decisional conflict and satisfaction with care).



Conclusion

- This systematic review shows that involving patients in decision-making using a decision aid tool or interdisciplinary counselling services; including these tools for shared decision-making may increase decisional quality in both patients and clinicians. This improves patient satisfaction and may even lead to change of treatment.
- We are now updating the current systematic review by extending the study selection basis to ' views on treatment decision-making' to get a better understanding of the overall process looking at the decision-making criteria in localised kidney cancer.

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Appendix 2: Factors that influence patients' view on treatment decision-making in localised kidney cancer

Editorial Commentary on Expectant Management in Genitourinary Malignancies (Prostate, Bladder, Kidney)

Factors that influence patients' views on treatment decision-making in localised kidney cancer

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The increasing number of treatment options for localised kidney cancer presents a unique challenge for both patients and clinicians during the decision-making process (1). Current treatment options for localised tumours (T1b, T2, T3), which comprise the largest group of patients, include active surveillance, surgery and minimally invasive ablative procedures (1,2). These differ with respect to morbidity and individual patient confidence with respect to long term outcomes and potential implications.

International guidelines on treatment decision-making in cancer-care recognise the importance of involving patients in the treatment decision-making process (3). The American Urological Association and the NICE guidelines in the UK highlight that treatment decisions are 'preference sensitive' and recommend implementing shared decision-making (1,4). In order to implement this, it is first important to understand what factors influence a patient's decision-making.

We conducted a systematic review of the evidence following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (5). A computerised literature search of databases (PubMed, Cochrane) was performed to identify full text and abstracts published between 1st of January 2004 to September 2020 (*Figure 1*). Studies were selected on the basis that: (I) they explored patient views on treatment decision-making; (II) they were of sufficient methodological quality; and (III) their findings could be translated into suggestions for supportive care.

After screening titles and abstracts we identified 534 studies of which 22 met the inclusion criteria. Full text review of these by two authors (NK and KB) five studies were identified as relevant (*Figure 2*). Data was extracted following a Bayesian approach where data is codified into themes and presented in a meta-aggregation generating summative statements of the evidence (6). For each identified study we extracted information on treatment decision-making factors identified by patients.

One study evaluated an interdisciplinary service for renal malignancies (7), whereas another conducted an assessment of patients'/caregivers' perception of information provided in renal cancer treatment (8). The third study used a survey to measure the patients' decisional quality (e.g., emotional impact or knowledge of the decision to take) in patients diagnosed with localised kidney cancer (1). The fourth and fifth study developed a patient decision aid for surgical treatment and active surveillance in localised renal cancer (9).

A summary of the factors identified to influence patient decision-making in these five studies is shown in *Table 1*. Key themes emerged around 'Patient-related criteria' and 'Patient-physician interaction'. The patient-related criteria included: decisional quality and patient's risk perception (e.g., anxiety, concerns about cancer) (1,7-9). Factors contributing to the patient-physician interaction centred around patient involvement in decision-making, perceived shared decision-making and the negative influence of paternalistic care (1,7,8).

The five studies also identified gaps in supportive care during the decision-making process and recommended a move away from a paternalistic decision making model. Shirk

Table 1 Summary table: factors influencing patient decision-making

Decision maker criteria	Factors	Supportive care suggestions	Why is this important in clinical practice	Ref
Patient-related criteria'	Patient decisional quality: (= education level; age; patient satisfaction with care; knowledge of kidney cancer; decisional conflict; emotional impact of decision making; emotional impact of decision making)	Introduce clinical decision aids to increase patient involvement and knowledge about their disease	Will reduce decisional conflict of the patient and shared decision making; however, it does not replace counselling	(1,9,10)
	Patient's risk perception: (= fear of recurrence; fatigue; anxiety; concerns about cancer; depression; aches; decreased interest in previously enjoyed activities; decreased interest in previously enjoyed events; decreased interest in previously enjoyed events; reluctance to start new relationships)	Providing patients/ caregivers with an electronic or written document to act as a reminder/resource	Will ensure that physicians do not omit or 'gloss over' important issues and patient can access information provided in a less stressful environment	(8)
		Educational videos and online modules before the appointment	Will prepare patients for an interactive consultation regarding their care	(1)
Patient-physician interaction	Patient involvement in decision making: (= interaction with different specialities; perceived shared decision making; paternalistic care, (clear) information provided by the doctor; psychological support)	Interdisciplinary counselling service	Will enable patient to receive a complete picture	(7)
		Provide more information about their cancer, long term follow-up and potential complications	Setting the scene for decision making and setting patient expectations	(8)
		Shared decision-making modelling	Consider use in reimbursement models (US) and private consultations. Increases adherence to clinical management guidelines.	(1)

Customise: Date, species, Language
((kidney) OR (renal))
AND
((cancer) OR (malignant) OR (carcinoma) OR (malignancy) OR (tumour) OR (tumor) OR (neoplasm) OR (neoplastic) OR (neoplasia) OR (RCC))
AND
((treatment) OR (intervention) OR (therapy) OR (surgery) OR (chemotherapy) OR (nephrectomy) OR (radiotherapy) OR ("active surveillance") OR (ablation) OR (ablative) OR (cryotherapy) OR (RFA))
AND
(("patient preference") OR ("patient choice") OR ("patient view") OR ("patient decision") OR ("patient opinion") OR ("patient perspective") OR ("patient perception") OR ("patient attitude") OR ("patient motive") OR ("patient motivation") OR ("patient bel*"))

Figure 1 Key word search terms.

(in 2018) and Moretto (in 2014) concluded that patients lack knowledge even after counselling (1,8), and consequently are heavily influenced by paternalistic care (1). To enable the patient to actively participate in their own care, Huber *et al.* (in 2018) introduced interdisciplinary counselling in which the patient was encouraged to attend the tumour board (i.e., Multi-Disciplinary Team meeting) (7). This led to a significant shift in treatment decision-making, with documented change in treatment decisions alongside improved satisfaction with care (7). McAlpine *et al.* (in 2019) developed two patient decision aids for patients with localised renal cancer, which aimed to improve decisional quality (9,10).

This short review captures the complexity of

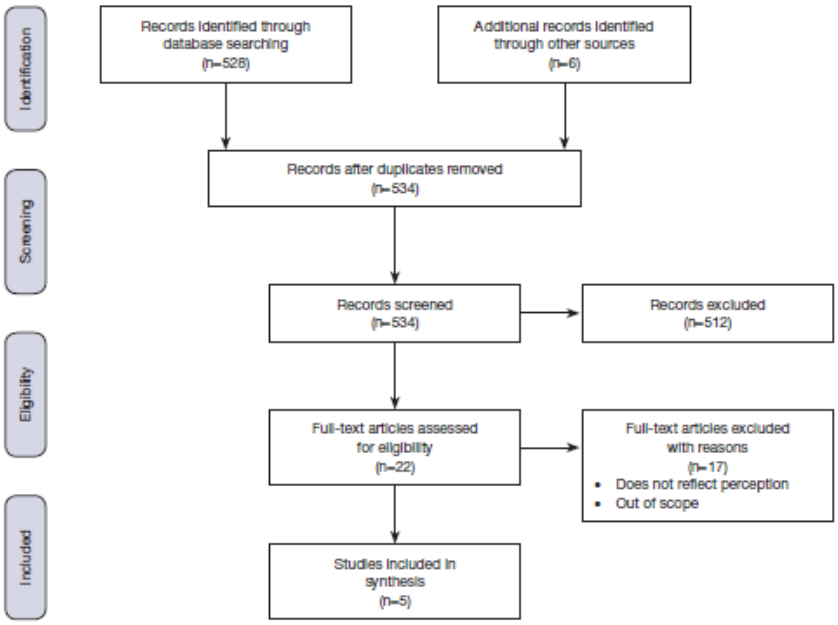

Figure 2 PRISMA.

decision-making purely from the patient perspective. An understanding of these factors is required to reduce paternalistic decision-making models of care and empower patients to take an equal and active part in the treatment decision-making process. However, we recommend future research of all factors influencing the treatment decision making process (e.g., physician-related factors) to increase guideline adherence, improve satisfaction of care and in particularly help to capture the complexity of decision making.

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Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Appendix 3: The Current Evidence For Factors that Influence Treatment Decsion Making in Localized Kidney Cancer: A Mixed Methods Systematic Review

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The Current Evidence for Factors that Influence Treatment Decision Making in Localized Kidney Cancer: A Mixed Methods Systematic Review

Katharina Beyer, Ravi Barod, Louis Fox et al.

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Full-length article available at www.auajournals.org/doi/10.1097/JU.0000000000001901.

Study Need and Importance: With a growing number of treatment options for localized kidney cancer, patients and their health care professionals have both the opportunity and the burden of selecting the most suitable management option. Current evidence suggests equipoise in oncological outcomes among these treatment options; however, a recent BAUS audit recorded that 60% of patients underwent surgery, suggesting a weighting given to surgical intervention. In the absence of clear clinical guidance on best treatment, there is therefore a need to understand the process and supportive care needs making these treatment decisions.

What We Found: We identified 42 articles for synthesis in a systematic review. Using a modified version of Glatzer's framework on "Decision Making Criteria in Oncology," we presented key themes emerging from the systematic review. These were divided into 3 main levels with 10 sub levels (see figure).

Limitations: Our mixed methods systematic review captured a wide range of both quantitative and qualitative literature. However, the included studies were rather heterogeneous, reflecting the current research portfolio. The majority of the quantitative studies were of an observational nature and the decision making was retrospectively analyzed. We mitigated this by assessing the strength of the studies using the Purpose, Respondents, Explanation, Findings and Significance (PREFS) and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) quality criteria checklist.

Interpretation for Patient Care: This is the first published systematic review of factors influencing treatment decision making in localized kidney cancer. Of greatest significance was the paucity of evidence reflecting the patient voice, which highlighted a lack of understanding as to what supportive care needs patients have. With this review, we aim to initiate a wider conversation on the importance of including shared decision making in future guidelines for the management of kidney cancer. We recommend that future research should focus on deploying robust qualitative methods to understand the patient experience of treatment decision making.

Figure. Framework of decision making in localized kidney cancer.

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The Current Evidence for Factors that Influence Treatment Decision Making in Localized Kidney Cancer: A Mixed Methods Systematic Review

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Abbreviations and Acronyms

AS = active surveillance
HCP = health care professional
HRQoL = health related quality of life
PN = partial nephrectomy
PREFS = Purpose, Respondents, Explanation, Findings and Significance
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QL = qualitative analysis
QN = quantitative design
SR = systematic review
STROBE = Strengthening the Reporting of Observational Studies in Epidemiology

Purpose: With a growing number of treatment options for localized kidney cancer, patients and health care professionals have both the opportunity and the burden of selecting the most suitable management option. This mixed method systematic review aims to understand the barriers and facilitators of the treatment decision making process in localized kidney cancer.

Materials and Methods: We searched PubMed®, Embase® and Cochrane Central databases between January 1, 2004 and April 23, 2020 using the Joanna Briggs Manual for Evidence Synthesis and the Preferred Reporting Items for Systematic Review and Meta-analysis statement. We identified 553 unique citations; of these, 511 were excluded resulting in 42 articles included for synthesis. The Purpose, Respondents, Explanation, Findings and Significance and the Strengthening the Reporting of Observational Studies in Epidemiology checklist was applied.

Results: The key themes describing barriers and facilitators to treatment decision making were identified and categorized into 3 domains: 1) kidney cancer specific characteristics, 2) decision maker related criteria and 3) contextual factors. The main facilitators identified within these domains were size at diagnosis, age, comorbidities, body mass index, gender, nephrometry scoring systems, biopsy, socioeconomic status, family history of cancer, year of diagnosis, geographic region and practice pattern. The key barriers were race, gender, patient anxiety, low confidence in diagnostic and treatment options, cost of procedure, and practice patterns.

Conclusions: Future interventions designed to improve the decision making process for localized kidney cancer should consider these barriers and facilitators to ensure a better patient experience.

Key Words: carcinoma, renal cell; decision making; kidney neoplasms; clinical decision-making

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References 51 through 77 can be obtained at https://www.jurology.com.

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KIDNEY cancer accounts for 2.2% of all new cancer cases worldwide.[1] It is estimated that in the United Kingdom 56% of all kidney cancers present as stage I or stage II.[2] The most widely used treatment options for localized kidney cancer are surgery, ablation, and active surveillance (AS), which have a diverse range of morbidities to consider, ranging from the risk of anesthetic to the psychological morbidity of surveillance.[2–4] Current guidelines do not give a clear recommendation on the best option.[4] Instead, to enable clinicians to recommend an appropriate management plan, guidelines highlight the importance of considering objective metrics including oncological outcomes, potential harms/side effects and overall survival. However, these guidelines do not include any direction on supportive care focused on managing and enabling treatment discussions.

In order to enable robust treatment discussions, there is a need to identify and understand the barriers and facilitators to treatment decision making. This would provide means for future research themes to study interventions aimed at facilitating and supporting patients and health care professionals (HCPs) during this decision making process.

Therefore, the purpose of this paper is to systematically evaluate the literature for factors influencing treatment selection as a management strategy for localized kidney cancer.

METHODS

This mixed methods systematic review (SR) followed the Joanna Briggs Manual on mixed methods SRs[5] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[6]

Search Strategy

Studies published between the January 1, 2004 and April 23, 2020 were identified through a systematic search of electronic databases (PubMed® and Cochrane Library). The search strategy focused on the use of key word search terms to identify studies focusing on factors that influence treatment decision making in localized kidney cancer; kidney OR renal AND cancer AND treatment OR intervention OR decision-making OR barriers OR facilitators (supplementary table 1, https://www.jurology.com).

Study Eligibility and Selection Criteria

We followed the inclusion criteria recommendations of the Joanna Briggs Manual for systematic mixed methods reviews.[5] We included studies in which the participants were adults (≥18 years of age) diagnosed with localized kidney cancer (T1, T2, T3 N0M0)[4] and excluded studies before 2004 based on the updated World Health Organization classification on kidney tumors in adults.[7] Therein, the categorization of kidney tumors was expanded, which consequently impacted on treatment options and decision making. Studies were selected on the basis that 1) they explored views on treatment decision making, 2) they were of sufficient methodological quality and 3) their findings could be translated into suggestions for supportive care.

Qualitative analysis (QL) studies with fewer than 20 participants[8] or without a specific statement on thematic data saturation, as well as quantitative design (QN) studies with fewer than 100 participants, were excluded.

Data Quality

The included QL and QN studies focusing on patients preferences were evaluated for quality using the Purpose, Respondents, Explanation, Findings and Significance (PREFS) quality checklist, which focuses on 5 areas: 1) purpose, 2) respondent, 3) explanation, 4) findings, 5) significance.[9]

The quality score was calculated by adding 1 point for each "yes" answer on the PREFS checklist, with a maximum potential score of 5. From this we calculated the mean PREFS quality score (table 1).

Cohort/registry papers were assessed for strength of evidence. A modified version of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist[10] was used. The following items were assessed: clear explanation of all outcomes, exposures and potential confounders, data source, bias, statistical methodology, descriptive data, and characteristics of individuals given. In each of the 11 categories, 1 point was assigned to each positive response, giving a possible total score of 11 (table 2).

All QN studies included outcome, exposure, descriptive and clinical data and only 1 study did not report potential bias. However, there was a high level of variability found in relation to confounder variables, assessment of bias, missing data, sensitivity analyses and the characteristics of individuals given social data.

RESULTS

We identified 553 unique citations, of which 447 were excluded as review articles, commentaries or narratives. Full-text screening was carried out on 106 articles. Four of these papers were SRs, resulting in an additional 30 papers for review. Eventually 79 studies were excluded, resulting in 42 articles included for synthesis (fig. 1). Of the articles 17 were QL and QN studies focusing on patient's preferences, while 25 were cohort/registry studies. Given the heterogeneous study designs, no statistical comparisons were made.

For this mixed method analysis, a meta-aggregation of data was presented using a Bayesian approach, whereby all data were codified into themes. This approach generates summative statements of the evidence to equally inform the topic in a mutually compatible format (table 3). While the identified papers may be looking into outcomes, the purpose of this mixed methods SR was to capture information on decision making.

The themes identified were presented using a modified version of Glatzer et al's framework "Decision Making Criteria in Oncology" (fig. 2).[11] Glatzer et al's framework has been developed to capture the broad range of factors which influence decision making in oncology. It is based on the following 3 "domains of influence": 1) decision specific criteria, which describe factors that involve clinical criteria; 2) decision maker related characteristics,

Table 1. *PREFS checklist*

References	Type of Study	Categorization	Score	Purpose	Respondence	Explanation	Findings	Significance
Alam R et al (2019)	QN	HRQoL	5	x	x	x	x	x
Barwari K et al (2012)	QL	Survey	5	x	x	x	x	x
Bhindi B et al (2018)	QN	Comparison of treatments	2	-	-	-	x	x
Dash A et al (2006)	QN	Comparison of treatments	5	x	x	x	x	x
Desai MM et al (2005)	QN	Comparison of treatments	3	x	-	x	-	x
Golan S et al (2018)	QL	Survey	4	x	x	x	x	-
Gong EM et al (2008)	QN	Comparison of treatments	3	x	x	x	-	-
Gratzke C et al (2009)	QN	HRQoL	4	x	x	x	-	x
Guillotreau J et al (2012)	QN	Comparison of treatments	3	x	-	x	-	x
Huber J et al (2015)	QL	Interview and focus group	4	x	-	x	x	x
Kwon T et al (2015)	QN	Preference	5	x	x	x	x	x
Larcher A et al (2017)	QN	Comparison of treatments	5	x	x	x	x	x
Marszalek M et al (2009)	QN	Comparison of treatments	4	x	x	x	-	x
Medina-Polo J et al (2011)	QN	Comparison of treatments	3	x	-	x	-	x
Moretto et al (2014)	QL	Survey	4	x	x	x	-	x
Naya Y et al (2015)	QN	Comparison of treatments	4	-	x	x	x	x
Shirk JD et al (2018)	QL	Survey	5	x	x	x	x	x

Purpose: whether preference assessment was a core and clearly defined objective of the study. Respondence: an assessment of the risk of selection bias that might be present if respondents differ from nonrespondents. Explanation: whether the methods are explained in sufficient detail and clarity to enable replication of a study. Findings: assessing the potential biases arising from excluding data from the findings. Significance: whether key results were reported stochastically and with tests of significance. x, reported. -, not reported.

which include factors that influence the patient and HCP; 3) contextual factors, which was described as factors that include in the context of medicine the environment (including government policies).[11] We used and modified these 3 domains to present the factors identified in the literature as barriers or facilitators of treatment decision making.

All abstracts and full texts were screened independently by 2 reviewers (KB, NK). One researcher extracted the data, after which it was reviewed by a second. Any disagreements arising were resolved through consultation with a third clinical researcher (MVH). The following data were collected: author, year of publication, type of study, patient population and aim of the study, as well as all factors that were identified as influencing decision making.

Study Design of Included Studies

Supplementary table 2 (https://www.jurology.com) summarizes the 36 included QN studies and 6 QL studies. Of the 36 QN studies, 24 studies took place in the United States of America, 6 in Europe, 2 in China, 2 in Japan and 2 in South Korea. The number of study participants was below 500 in 24 studies, below 1,000 in 4 studies and above 1,000 in 8 studies. Only 10 studies collected data across multiple institutions. Of those, 3 studies used the Surveillance, Epidemiology, and End Results (SEER) database, 2 the DISSRM registry, 1 the National Cancer Registry, and 4 studies collaborated with other institutions to collect data. The single-institution studies used their own hospital registry to assess the data collected. Three studies reported HRQoL and 2 of those used validated questionnaires/tools.

Of the included 6 qualitative studies, 3 were solely surveys, 1 a mixed method survey, 1 study performed a survey and interviews, and 1 conducted interview and a focus group.

Quality Scores

The PREFS quality scores ranged from 2 to 5 and mean PREF score of the included papers was 4 (SD 0.88). We further categorized the assessed paper using Joy et al suggested categories.[9] Four papers fell under the category contingent evaluation (ie survey) with the mean score for this category being 4.5 (SD 0.45); 10 papers stated preference/choices of treatment with the mean score of 3.7 (SD 0.96); 1 paper fell under the category qualitative (ie interviews, focus groups) with the score 4. Two studies used a validated HRQoL tool and scored a mean quality score of 4.3 (SD 0.46; table 1).

The mean quality score of papers assessed with the STROBE checklist[10] was 6.44 (SD 1.5), with scores ranging from 4 to 11 (table 2).

EVIDENCE SYNTHESIS

Within the 3 domains identified by Glatzer et al,[11] we identified numerous barriers or facilitators to treatment decision making in kidney cancer, which are summarized below and in figure 2.

Kidney Cancer Specific Characteristics

Kidney cancer specific characteristics were divided into 3 domains: prognostic factors, patient demographic factors and predictive tools.

Prognostic factors.

Facilitators. 50% of included papers highlighted prognostic factors such as anatomical, histological, clinical and molecular factors. These papers highlighted tumor size at diagnosis as a facilitator to treatment decision making,[12–32] with larger tumors being more likely to be of malignant potential.[12,14]

Table 2. *Strength of confidence in quality of QN Cohort/Registry studies (Modified STROBE checklist)*

			No. Participants (variables)			Bias			Statistical Methodology		Descriptive Data		
References	Study Design	Score	Outcome	Exposure	Confounder	Documented	Addressed	Full Description	Missing Data	Sensitivity Analysis	Demographic	Clinical	Social
Ambani et al (2016)	QN	8	x	x	-	x	x	-	x	x	x	x	-
Audenet et al (2014)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Bjurlin MA et al (2017)	QN	11	x	x	x	x	x	x	x	x	x	x	x
Chang X et al (2015)	QN	8	x	x	-	x	x	x	x	-	x	x	-
Corradi R et al (2017)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Ghanie A et al (2018)	QN	6	x	x	-	x	-	x	-	-	x	x	-
Haramis G et al (2012)	QN	6	x	x	-	x	-	x	-	-	x	x	-
Kim CS et al (2014)	QN	7	x	x	x	x	-	x	-	-	x	x	-
Klatte T et al (2011)	QN	6	x	x	-	x	x	-	-	-	x	x	-
Kowalczyk KJ (2012)	QN	7	x	x	x	x	-	-	-	x	x	x	-
Maturen KE et al (2007)	QN	7	x	x	-	x	x	-	x	-	x	x	-
McIntosh AG (2018)	QN	9	x	x	-	x	x	-	x	x	x	x	x
O'Malley RL et al (2013)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Parker PA et al (2013)	QN	8	x	x	-	x	x	x	-	-	x	x	x
Peyton CC et al (2017)	QN	7	x	x	x	x	-	x	-	-	x	x	-
Pierorazio PM et al (2015)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Shin SJ et al (2015)	QN	6	x	x	-	x	x	-	-	-	x	x	-
Tan HJ et al (2012)	QN	8	x	x	x	x	-	x	-	-	x	x	x
Tanagho YS et al (2013)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Tomaszewski JJ et al (2014)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Woldu SL et al (2014)	QN	6	x	x	-	x	-	-	x	-	x	x	-
Yang C et al (2019)	QN	6	x	x	-	x	-	-	-	-	x	x	-
Yasuda Y et al (2013)	QN	4	x	x	-	-	-	-	-	-	x	x	-
Zhou HJ et al (2017)	QN	5	x	x	-	x	-	-	-	-	x	x	-
Zondervan PJ et al (2016)	QN	6	x	x	-	x	-	-	-	-	x	x	-

x, reported. -, not reported.

Patient demographic factors.

Facilitators and Barriers. 71% of papers found that particularly age, comorbidities, body mass index and gender influenced treatment decision making representing the factors as either a barrier and/or facilitator based on how they were presented in the paper.[12–16,18,21,23,24,26–31,33–47] Of those, 5 papers highlighted that younger patients were identified as more likely to undergo partial nephrectomy (PN) or nephron sparring surgery (including, laparoscopic PN, or robotic PN),[24,29,34,43,46] whereas those undergoing ablation or AS were older with more comorbidities.[15,24,29,34,35,43–46]

Three papers identified race and gender as important barriers to take into consideration.[13,14,40] O'Malley et al highlighted in their research that women had a superior comorbidity profile, which would make them better candidates for PN.[13] In addition, 3 studies showed that women were more likely to have benign disease,[13,14,40] while men were diagnosed with a more aggressive histology, larger tumors and higher grade.[14] Despite this, women were found to be more likely to receive radical nephrectomy, with Black women having the highest rate in the presented study.[13]

Predictive tools.

Facilitators. Eleven papers described predictive tools to support decision making.[12,13,15,17,20,22,27,33,35,44,48] The RENAL (radius, exophytic/endophytic, nearness of tumor to collecting system, anterior/posterior, location relative to polar line) nephrectomy score was used to help overcome selection bias,[31] assist surgeons in preoperative decision making[48] and correlate with tumor histology and grade.[35,44] Similarly, the PADUA score was reported to support the process of decision making by identifying the tumor complexity. Four papers highlighted that biopsy results significantly influenced treatment decision making in the majority of patients.[15,27,33,44]

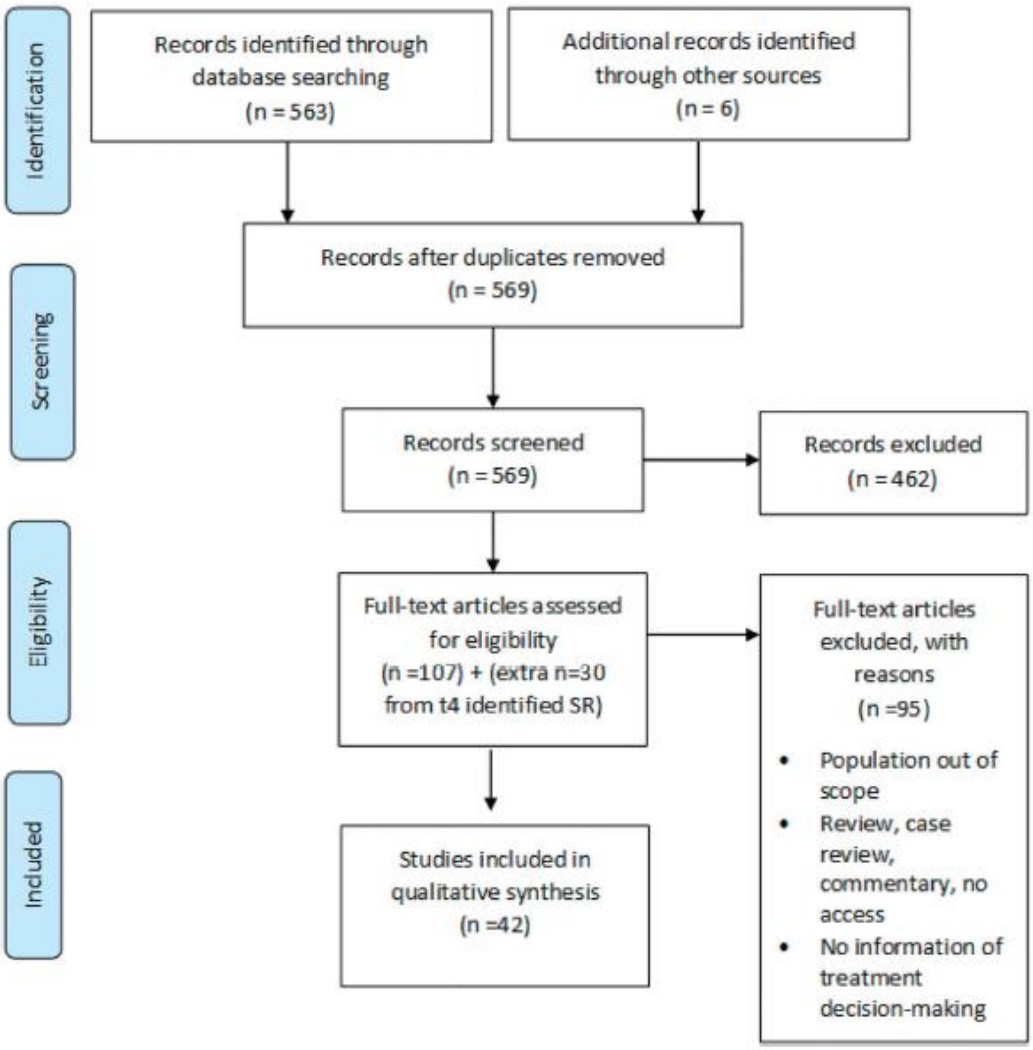

Figure 1. PRISMA flow diagram.

Maturen et al reported that in their sample 61% of the biopsies performed resulted in alteration in management and substantive change of treatment.[27] Bjurlin et al noted that, while controlling for demographic and disease characteristics and comorbidity, 61% of patients were more likely to be managed nonsurgically than those who received a diagnostic biopsy.[15]

Decision Maker Related Criteria

Decision maker related criteria were divided into patient related criteria, physician related criteria and patient physician interaction.

Patient related criteria.

Facilitators or Barriers. 4 papers suggested education status, socioeconomic status and family history of cancer were all facilitators or barriers to a patients' treatment decision making.[13,22,30,36] One study reported that having an academic degree might be a facilitator in treatment decision making.[22]

Barriers. Cancer anxiety, related to personal as well as family history or the fear of missing a tumor, was reported as a strong barrier to AS in the context of repeating biopsies.[22,30]

Table 3. *Domains and factors that influence treatment decision making*

Domain	Factor	Details	References
Kidney cancer specific characteristics	Prognosis factors	Pathological tumor size; tumor stage/TNM/anatomical classification; location of tumor/accessibility.	11-31
	Anatomical, histological, clinical and molecular factors influence decision making	Grade/Fuhrman nuclear grade/growth rate; growth pattern; histology; pathological diagnosis/data/stage/outcome; tumor vol IC; benign vs malignant; indolent vs aggressive; type of tumor/RCC subtypes; nephrometry radius; exophytic vs endophytic; anterior/posterior; complexity score/anatomical complexity; multifocal disease/number of lesion; mass composition; tumor side; state of disease; pain level; single kidney; solidary kidney; kidney function (estimated glomerular filtration rate)/preop kidney function/kidney function values; American Society of Anesthesiologists® score.	
	Demographic characteristics	Age; Charlson comorbidity score/comorbidities; body mass index; gender; race; marital status; socioeconomic status; education; smoking history; family history of RCC; prior RCC diagnosis/kidney medical history; employment status; education.	11-15,17,20,22,23,25-30, 32-46
	Predictive tools	Scoring systems: NePhRO scores; C-index; The Predictive Tool to Determine Renal Function Benefit of Nephron Sparing Surgery Compared to Radical Nephrectomy online calculator, RENAL nephrometry score; The PADUA classification.	11,12,14,16,19,21,26,32,47
		Diagnostic tools: Imaging (MRI)/CT Diagnostic accuracy of CT or MRI; Biopsy (Biopsy, CT diagnosis, Biopsy technique & Biopsy Result; Biopsy sensitivity; Biopsy specificity; Biopsy technique; Probability of nondiagnostic biopsy; Probability of biopsy track seeding with malignant cells; clinical behavior by abdominal imaging).	
Decision maker related criteria	Patient related criteria	socioeconomic status; level of education; having an academic degree; history of Ca; history of invasive procedures and history of procedural complications; personal or family history of Ca; anxiety associated with missing a Ca; concern about potential biopsy complications was the primary reason to decline renal mass biopsy among surveillance patients; reluctance to undergo biopsy; concern about potential biopsy complications; patient preference; quality of life.	12,21,29,35
	Physician related criteria	Surgeon preference/surgical modality was chosen at the discretion of the surgeon; surgeon's experience level confidence in the management option.	14,15,18,21,24,34,35,48
	Patient—physician interaction	Patient—physician interaction; clinical decision aids; interdisciplinary discussion.	12,16,21,22,30,32,43,49, 50,51-52
Contextual factors	Economic variables	Insurance; Income by ZIP code; cost of procedure.	32,43,45
	Access to health care	Geographic region; Urban vs Rural; Travel distance; Medicare A or B; shared decision making in included reimbursement models.	14,51
	Health care organization	Facility type; facility location; shared decision making; infrastructure available.	12,15,32,48,51

RCC, renal cell carcinoma. *MRI*, magnetic resonance imaging. *CT*, computerized tomography.

Physician related criteria

Facilitators. Clinical experience, preference, confidence in management option and evidence-based recommendations were factors identified in the literature as influencing HCPs' treatment decisions.[16,19,25,35,36,49] Clinical experience of the surgeon was suggested as a factor to facilitate treatment decisions.[16] Shin et al reported that surgeons with more experience are more likely to choose PN, even for complex cases.[16]

Barriers. Bjurlin et al reported that 30% of patients who saw a urologist first were less likely to have a diagnostic biopsy than those who first saw a nonurologist physician.[15] The confidence in the management option of HCPs was also reported as a barrier. Golan et al reported that 40% of their participating urologists totally opposed a kidney mass biopsy.[22] In a study by Barwari et al 50% of urologists indicated that small kidney masses were the least important reason to perform a biopsy and 73% of the urologists very rarely or never recommended kidney mass biopsy for treatment decision making.[49]

Patient-physician interaction

Facilitators. 8 articles reported the importance of shared decision making as a facilitator.[17,23,33,44,48,50,51–52] Two papers introduced a clinical decision aid to empower the patient to take a definitive decision and to reduce decisional conflict.[51,52] A Canadian survey highlighted the importance to provide additional electronic or written documents to empower the patient to a meaningful discussion.[53]

Contextual factors

We divided contextual factors into economic variables, access to health care, and the health care organization such as type of practice.

Economic variables

Barriers. Cost of procedure was identified as a barrier or facilitator for treatment decision making in localized kidney cancer by 2 studies based in the U.S.[44,46] Open radical nephrectomy and open PN have been reported to be costlier than less invasive treatments. AS and ablation have been presented as least costly. Understanding the chances of progression could lower costs.[44]

Access to health care

Facilitators. Geographic region was identified by Bjurlin et al as a facilitator to getting biopsied.[15] Being insured under a certain system contributes to

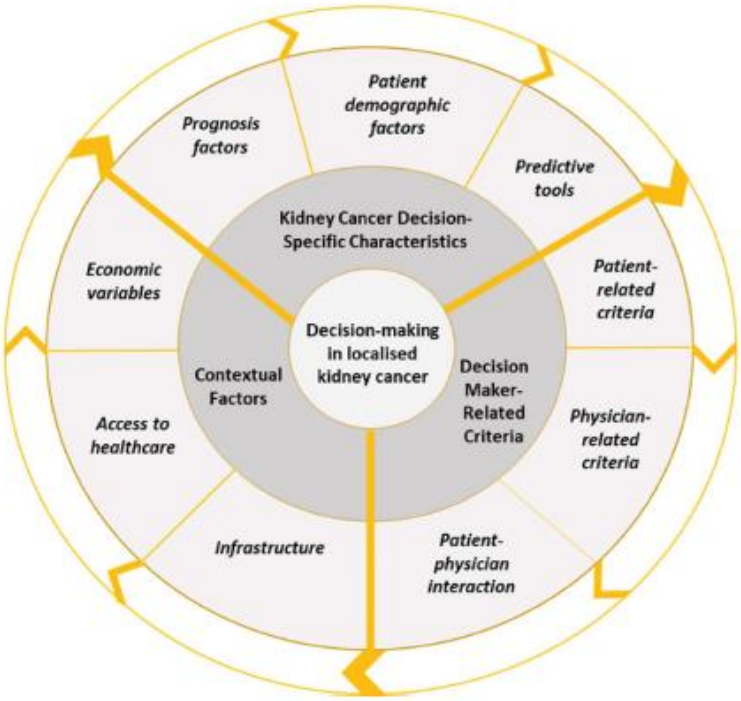

Figure 2. Domains that influence treatment decision (modified framework of Glatzer et al).[11]

access to health care as either a facilitator or a barrier.[46]

Health care organization

Facilitators and Barriers. 5 studies described practice patterns of institutions and type of practice as potential factors influencing treatment decisions.[13,16,33,49,52] One study identified a significant difference between "never perform a biopsy" amid HCPs practicing in a university hospital compared to other types of practices.[49] A similar observation was identified by 2 studies that reported greater nephron sparing surgery usage in centers of excellence or tertiary centers of excellence.[13,16] Ensuring that a system of shared decision making is in place can also be interpreted as a facilitator for decision making in localized kidney cancer.[52]

DISCUSSION

This review has identified a multitude of barriers and facilitators to treatment decision making in kidney cancer, spanning all domains of Glatzer et al's "Decision Making Criteria in Oncology" framework.[11] The literature reviewed has shown that the ability of kidney cancer patients to reach decisions about their treatment is affected by kidney cancer specific criteria, decision maker related criteria and contextual factors which are consistent themes within the framework.

Kidney Cancer Specific Factors

Prognostic factors. Prognostic factors including anatomical, histological, clinical and molecular factors were found to be facilitators to decision making in kidney cancer in this review.[12–32] This is similar to the findings reported in Campi et al's SR: they identified most decisions are based on tumor related factors and renal mass growth was the most influential trigger.[54] This was consistent with our findings, where prognostic factors were identified as facilitators to clinical decision making.

Demographic factors. Some studies included in this review found that age, comorbidities and body mass index may have influenced treatment decision making.[12–16,18,21,23,24,26–31,33–47] Patient age has long been highlighted as the most controversial patient demographic factor on which to base decision making across cancer care.[55] A scoping review by Tranvåg et al highlighted that it is important to accept the relevance of patient age in a clinical setting; however, discussion with the patient should be transparent.[55] Puts et al

further suggested that individual geriatric assessments in a multidisciplinary diagnostic environment should include psychological, social and functional capacity instead of using age as a proxy on which to base clinical decision making.[56]

This review also found that patients' gender and ethnicity can have an indirect influence to treatment decision making in kidney cancer.[13,14,40] Being Black and/or female has been found to be associated with higher use of radical nephrectomy,[13] despite the fact that this ethnic group is at higher risk of chronic kidney disease progressing to end-stage renal disease.[57] In support of this finding, Mancini et al found that gender influences treatment option selection and identified that men were more likely to receive AS or nephron sparing surgery treatments.[58] This further supports the findings of our review that potential indirect barriers are linked to demographic factors including race and gender and due to the current observation design of the studies, we recommend that future studies need to further investigate how demographic factors like age and gender influence choice.

Predictive tools. Our literature review suggests that predictive tools facilitate decision making. The PADUA or RENAL score can act as a facilitator to decision making to support HCPs when quantifying tumor complexity.[15,27,33,35,44,48] Alvim et al, who compared the predictive accuracy of nephrometry scores to assess PN complexity, did not suggest a preference for a single nephrectomy scoring tool,[59] which is also reflected in the results of our review.

We further identified that performing a biopsy is a facilitator to treatment decision making. Across cancer care, biopsies have long been used to contextualize a cancer diagnosis in respect to type, grade and potential treatment options.[60] A recent study by Finelli et al confirmed the importance of biopsies in respect to progression rates amongst kidney cancer subgroups,[61] which ultimately may enable clinicians to present patients with options to avoid overtreatment and treatment complications.[61,62]

Decision Maker Related Criteria

Patient related criteria. We found that education status, socioeconomic status, a family history of cancer, and cancer anxiety can be barriers to treatment decision making in kidney cancer.[13,22,30,36] Consistent with this review, Campi et al identified patient preference as a trigger to treatment decision making in the context of AS. However, they concluded there was a clear lack of evidence exploring the process of patient preference in detail.[54] Our review identified cancer anxiety as a strong barrier.[22,30] Numata et al showed in their research on early stage malignant brain tumor that patients experiencing anxiety during treatment decision making are often driven by the fear of uncertainty of prognosis, their future quality of life and loss of the self.[63]

According to the studies reviewed, most patients appear to prefer to be involved in their decision making. However, Laviana et al found that in most tumor groups patients do not receive sufficient information to educate them on their treatment options.[64] They recommended that structured decision aids aimed at guiding and supporting the patient through this process, ultimately reduce anxiety[64] and improve concordance between patient and clinician.[65,66] Given that anxiety has been identified as a barrier in our review, implementing such decision aids will support the decision making process. The International Kidney Cancer Coalition has hence developed and validated a decision making tool, which can be used to support/share treatment decision making.[51]

Clinician related criteria. Clinician confidence in particular management options and the provision of evidence-based recommendations have been suggested as facilitators to treatment decision making in the studies included in our review.[15,16,19,22,25,35,36,49] It should be noted that clinician bias was highlighted as an influencing factor. Across cancer care, this has been identified in a literature review as "default" bias, which referred to HCPs presenting a default option relating to the preference of the treating physician.[67] In the UK, the implementation of a multidisciplinary team meeting, where all new patients are discussed by the team of treating cancer clinicians, was suggested to reduce clinician bias in the treatment recommendation process.[68] The literature for breast and prostate cancer has shown that multidisciplinary team discussions also improve guideline adherence.[69] Stewart et al reported that over a period of 6 years AS in prostate cancer increased by 80% as a result of multidisciplinary team discussion prior to patient consultation.[70]

Patient–physician interaction. Patient–physician interaction factors in decision making were identified, with studies suggesting that shared decision making is a facilitator in kidney cancer and that clinical decision aids providing information to patients can also be useful.[13,17,22,23,31,33,44,50,51–53] There is a clear link between shared decision making, patient related criteria, physician related criteria and patient–physician interaction. Bomhof-Roordink et al emphasized choice awareness as a pivotal concept of shared decision making.[71] Their review also highlighted that it is of less importance who is making the final decision in a shared decision making environment, but all stakeholders should be equally educated and mutually agree on the decision. In addition, it was suggested in 1

study that the provision of additional electronic or written documents to the patient can empower the patient to discuss treatments with their physician in a meaningful way.[53]

Contextual Factors

Economic variables. Economic variables were identified as an important facilitator or barrier to treatment decision making.[33,44,46] However, this is highly dependent on the health care system's financing approach, as there are variations at the national and local level. The studies identified looked at the U.S. health care system, where disparities in costs of different treatments have been suggested to affect treatment decision making. Chien et al indicated that costs appeared to rise with aggressiveness of the local treatment in the U.S.[72] Nevertheless, there is significant inequality in access to health care and insurance in the U.S.,[73] which introduces an additional systemic factor that may affect treatment decision making which may not apply to other countries.

Access to health care. This SR highlights that limited access to health care could potentially affect treatment the decision making ability.[15,52] This includes regional geographic variation in the offering of kidney cancer diagnosis, treatments and services.

The relationship between cancer survival and hospital districts was reviewed by Seppä et al, who identified substantial variation across geographical locations in Finland and concluded that the differences were explained by the availability of cancer services and treatment.[74] This phenomenon has also been described in other urological cancers.[10] Kinsella et al highlighted the differences in uptake of AS for prostate cancer ranged from 27%−80%, further suggesting that this variability is linked to the availability of the technology to deliver surveillance imaging and treatment protocols.[10]

Thorstenson et al recommended that national cancer registries such as the National Swedish Kidney Cancer Register could help to facilitate benchmarking of contextual factors related to health care access across geographical regions.[75] Again, this is reflective of research carried out in prostate cancer where population based registries have been used to benchmark the uptake of treatments across regions and countries to facilitate the distribution of health care services.[76]

Health care organization. Treatment decisions in kidney cancer can vary by health care center, eg the use of biopsy or surgical techniques.[13,16,33,49,52] As part of Tran et al's observational study, the positive association between type of surgery and complication rate with hospital volume was evaluated in the UK.[77] They found a positive association between hospital volume and the proportion of T1 tumors that were treated with PN rather than radical nephrectomy. They also identified that the complication rate decreased with rising hospital volume.[77]

Limitations

This mixed methods review captures a wide range of both QN and QL literature. Furthermore, the application of a recently published quality assessment tool specifically developed to assess papers focusing on barriers and facilitators further strengthens our results.[9] However, the included studies were rather heterogeneous and single center based, reflecting the current research portfolio in this field. The majority of the QN studies were of an observational nature and the decision making was retrospectively analyzed. Most of the real-world evidence studies reported selection bias; however, we mitigated this by assessing the strength of the studies using the PREFS and STROBE checklists. Nevertheless, additional qualitative research should be performed to ensure the HCP's and patient's voice is adequately captured.

CONCLUSION

When HCPs and patients are deciding on the most suitable treatment, they are confronted with multiple factors which influence the process. The clear recommendation from this SR is to consider the multitude of barriers and facilitators to treatment decision making. Our results will inform health care providers when designing future interventions aimed at facilitating kidney cancer treatment decision making.

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EDITORIAL COMMENTS

Treatment decision making plays a critical role in the care of patients with cancer. This study evaluated key barriers and facilitators to treatment decision making among patients with localized kidney cancer, their family and their physician. Utilizing a mixed method systematic review, Beyer et al identified 42 articles published between 2004 and 2020. Three major domains were identified: kidney cancer decision specific characteristics (demographic characteristics, prognosis and predictive tools), decision maker related criteria (patient and physician criteria, and patient-physician interaction) and contextual factors (economic variables, access to health care and infrastructure). A deeper exploration of these domains showed that prognostic factors, predictive tools, geographic region, clinician confidence and shared decision making were facilitators to clinical decision making, while in contrast race, education status, access to health care and cancer related anxiety were noted as barriers. Age, gender, socioeconomic status, body mass index, comorbidities, family history of cancer, practice patterns of institution, type of practice and economic variables (eg cost of procedure) were identified as both possible facilitators and barriers. For example, age can be a major determinant of the aggressiveness of a procedure that patients may be willing to undergo, with younger patients electing for nephrectomy while older patients may undergo ablation or active surveillance.

These findings warrant further investigations to ensure patients possess an accurate understanding of their treatment options. Specific tools to address the disparities and barriers of age, gender and race need to be developed. With the emergence of a myriad of novel and complex treatment modalities, better strategies are needed to help patients understand their options of treatment, likely adverse events, possible outcomes and, ultimately, prognosis. This study may be the launching pad for prospective evaluation of the factors that matter to fulfill patient expectations of cure in localized kidney cancer.

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The armamentarium for management of localized (frequently defined as T1-2N0M0) renal cell carcinoma (RCC) is broad, with active surveillance, ablative therapy, and surgical intervention with open, laparoscopic, or robotic approaches available in addition to evolving roles for biopsy and novel imaging modalities. Personalizing treatment intensity and treatment modality for localized RCC is paramount given the increased incidence of predominantly nonaggressive disease.[1] Shared decision making is valuable because no single management option is superior across all outcomes. This review identifies factors associated with treatments or outcomes and attempts to categorize them as facilitators or barriers to decision making grouped by a framework of 3 broad categories.

The utilized framework was originally adapted by Glatzer et al (reference 11 in article) from strategic decision making (SDM) in management research.[2] Interestingly, the conclusion from SDM was that decision specific characteristics most strongly influenced the specific decision processes that were utilized, a conclusion that may also apply in the present setting. The included RCC literature, the bulk of which is retrospective, largely concerns the decision specific factors of prognosis and patient demographics (with the authors including comorbidity profile under "demographics"), and the closely related predictive tools derived from such factors. Additionally, most of the references regarding patient engagement and experience and the decision making process were drawn from literature outside of RCC.

These findings and those of others[3] highlight the dearth of research into decision making beyond the clinical factors largely grouped as decision specific factors here. Multiple relevant outcomes, such as oncologic control, renal functional decline, and postoperative complications, have been enumerated previously. Improved biological risk stratification and prognostication may better elucidate probabilities of these potential outcomes. Even so, the physician and patient still must interpret such probabilities in the context of their own preferences, values, and risk tolerance and then apply that interpretation to a decision.

Shared decision making has become the mantra for management of early stage RCC. Unfortunately, evaluation of the perspectives, values, and processes inherent to that decision making hasn't kept pace with our expanding treatment options or opportunities to use them. Ongoing work to alleviate the uncertainty surrounding tumor biology is critical, but achieving truly patient centered, high value

care, and making shared decision making a reality, will also require further study into the entire decision making process in addition to defining patient centric outcomes.

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REPLY BY AUTHORS

In their editorials, Decat Bergerot and Vaishampayan, and Meredith rightly point out that shared decision making has become the mantra across cancer care. In our review, we point out the importance of patient preference; however, with virtually no research evidence reflecting a patient voice there is a lack of understanding as to what supportive care needs patients have during the decision making process and therefore what shared decision making looks like in the context of kidney cancer.

We used examples from other urological tumor groups to illustrate where the interrogation of patient experience was used to gather evidence and subsequently inform multi-stakeholder engagement events to design shared decision making aids/pathways to limit the decisional regret of patients (references 10 and 64 in article). Future research should therefore focus on robust qualitative methods to establish the current experiences of patients during treatment decision making and any unmet supportive care needs.

This review therefore aims to initiate a wider conversation on the inclusion of shared decision making in future guidelines for the management of kidney cancer.

Appendix 4: How does COVID-19 impact treatment decision-making for clinicans in localised kidney cancer

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RESEARCH COMMUNICATION

BJUI COMPASS

How does COVID-19 impact treatment decision-making for clinicians in localised kidney cancer

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Kidney cancer (KC) is the seven most common cancer in the United Kingdom; about 56% of new cases classified as localized disease. Although there are several treatment options which achieve similar oncological outcomes for those with localized disease, they all present different side effect profiles,[1] making appropriate treatment selection paramount to optimize quality of life.

The COVID-19 pandemic has complicated the process of decision making. Official guidance called for non-urgent cancer care to be rationed, delayed and/or adapted. Hence, the British Association of Urological Surgeons (BAUS) recommended that patients diagnosed with localized KC were offered a period of surveillance rather than curative treatment.[2]

The impact of COVID-19 medical guidance on patients was described by kidney patient associations in the United States and United Kingdom (KCCURE and KCUK) in small snapshot surveys, exploring patient experience, anxiety, and their management.[3,4] They found that anxiety was high in respect to both cancer and COVID-19 and its implications for treatment and follow-up.

Building on these initial observations, we conducted a cross-sectional, web-based survey amongst health care professionals (HCPs) delivering localized KC treatments, to understand the barriers and facilitators to supporting patients in their treatment decisions. Our multidisciplinary research team followed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). The ethics board of King's College London approved the survey as a Minimal Risk Study.

The survey (28 questions) was distributed via Twitter on May 16th, 2020 for 22 days using SmartSurvey. Fifty-eight respondents (36 from the United Kingdom and 22 from outside of the United Kingdom) completed the survey, of which 43% were United Kingdom doctors, 19% were United Kingdom nurses and 38% non-UK doctors. 31% of the UK participants were working at Specialist Centres tertiary referral hospitals, 47% at District General or Teaching hospitals and 22% only indicated NHS Trust.

Five main themes emerged from the survey: diagnostics, treatment, consultations and supportive care, HCP satisfaction, and delivery of future KC care. Due to disparities in healthcare guidelines followed by each country, we have focused our report on the United Kingdom.

In the context of diagnostics, Oderda et al noted that the delays observed during the pandemic have severely impacted on patients through lengthening of both diagnostic and treatment waiting lists. They emphasized the need for healthcare authorities to develop strategies to catch up with diagnostics.[5] This was confirmed in our survey as 75% of survey respondents highlighted disruption to the diagnostic pathway in the United Kingdom, compared to only 27% for non-UK respondents: reduced access to imaging (69%), reduction or no access to kidney biopsy (78%), delivering diagnostic consultations via phone (83%) and video call (25%). Moreover, the discussion of those patients newly diagnosed in the Multidisciplinary Team meeting (MDT) posed another problem. During COVID-19 these were moved to virtual platforms overnight. The MDTs are a forum for discussion, knowledge transfer, and learning. When asked whether these should remain as virtual events, 55% of nurses in the UK felt that these should revert to face-to-face meetings, compared to only 28% of UK doctors.

The opportunity to connect with the wider team is a unique experience with virtual MDTs possibly leading to a loss of professional understanding and social interaction.

With respect to treatment during Covid-19, the EAU Guidelines Office Rapid Response Group is recommending postponement of surgery by 6 months where progression is unlikely.[6] Fifty-eight percent of UK respondents reported that deferring treatment for 0-12 months for T1a disease or deferring treatment for 3-6 months in T1b disease (53% of respondents) or a delay of 0-6 month for T2 lesions (83% of respondents) would adversely affect the oncological outcomes. This might also in part explain the high level of dissatisfaction in respect to available treatment options, where none of the UK nurses who responded and only 28% of UK doctors were satisfied with the treatment options.

For consultations and supportive care, the main patient focus has been to prevent unnecessary risk of exposure to COVID-19. To this end, telephone and video consultations were implemented across the United Kingdom in line with BAUS guidance. Boehm et al assessed the willingness of patients to telemedicine (video consultations) and their results suggested that 54% were willing to undertake telemedicine consultations.[7] However, this survey identified that the majority of treatment consultations in the United Kingdom were carried out via telephone during COVID-19 (86% for treatment consultation) instead of video consultations (22%). It is, therefore, not possible to understand if HCPs would have felt more satisfied and prepared to provide supportive care using telemedicine consultations.

The UK's deferred treatment plan was reported by the respondents as a contributor to HCP dissatisfaction. Only 36% of UK respondents were able to perform partial nephrectomies and 8% ablation. As reported by KCCURE's and KCUK's snapshot surveys, patients reported experiencing a high level of anxiety during the COVID-19 period. Therefore, it is not surprising that 47% of UK respondents confirmed an increase in the number of patients contacting their service. This, combined with widespread re-deployment of health care professionals (56% of the medical team and 81% of the nursing team) may explain the reason why only 47% of UK nurses and doctors felt satisfied to very satisfied with the service they provided during the peak of the pandemic. With a demonstrable increase in cancer patient anxiety,[3,4] consideration should, hence, be given to the merits of staff redeployment versus patient safety if a second wave pandemic was realized.

For the delivery of future KC care, 78% of UK respondents agreed there is a need for additional imaging (78%), theatre (100%), inpatient (78%), outpatient capacity (69%) and manpower resources (58%). Responding to the additional needs will be challenging, but necessary.[5] This includes a stratified approach to patient assessment in relation to anxiety and depression, as a result of the increase in waiting times. Moreover, both doctors and nurses reported a high level of moral distress. 67% of respondents felt distressed to worst possible distress. This should be taken seriously by policy makers and hospital executives going forward.

A limitation was the distribution of the survey via twitter, however the CHERRIES statement, which aims to reduce selection bias, guided our understanding of the sample (self)selection (see online Appendix).[8]

Our survey has shown high levels of dissatisfaction among HCPs regarding the standard of care delivered during the COVID-19 pandemic in the United Kingdom, suggesting that there is a need to re-visit the guidelines. It is important to ensure the diagnostic pathway is not disrupted, ensure the ability to use video consultations is available, prevent the medical team and particularly CNSs to be redeployed and all available treatment options such as the ability to perform surgery in COVID-19 cold sites are assured. Our findings should be used to inform policy on KC care provision in the event of a second wave or a future healthcare crisis.

CONFLICT OF INTEREST

Grants were received from Kidney Cancer UK and the Royal Marsden Charity.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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Appendix 5: A Systematic Review of Heterogeneity in Outcome Definition and Reporting in Localised Renal Cancer

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European Association of Urology

Review – Renal Disease

A Systematic Review of Heterogeneity in Outcome Definition and Reporting in Localised Renal Cancer

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Abstract

Context: Outcomes in renal cell carcinoma (RCC) are reported inconsistently, with variability in definitions and measurement. Hence, it is difficult to compare intervention effectiveness and synthesise outcomes for systematic reviews and to create clinical practice guidelines. This uncertainty in the evidence makes it difficult to guide patient-clinician decision-making. One solution is a core outcome set (COS): an agreed minimum set of outcomes.
Objective: To describe outcome reporting, definitions, and measurement heterogeneity as the first stage in co-creating a COS for localised renal cancer.
Evidence acquisition: We systematically reviewed outcome reporting heterogeneity in effectiveness trials and observational studies in localised RCC. In total, 2822 studies (randomised controlled trials, cohort studies, case-control studies, systematic reviews) up to June 2020 meeting our inclusion criteria were identified. Abstracts and full texts were screened independently by two reviewers; in cases of disagreement, a third reviewer arbitrated. Data extractions were double-checked.
Evidence synthesis: We included 149 studies and found that there was inconsistency in which outcomes were reported across studies and variability in the definitions used for outcomes that were conceptually the same. We structured our analysis using the outcome classification taxonomy proposed by Dodd et al. Outcomes linked to adverse events (eg, bleeding, outcomes linked to surgery) and renal injury outcomes (reduced renal function) were reported most commonly. Outcomes

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related to deaths from any cause and from cancer were reported in 44% and 25% of studies, respectively, although the time point for measurement and the analysis methods were inconsistent. Outcomes linked to life impact (eg, global quality of life) were reported least often. Clinician-reported outcomes are more frequently reported than patient-reported outcomes in the renal cancer literature.

Conclusions: This systematic review underscores the heterogeneity of outcome reporting, definitions, and measurement in research on localised renal cancer. It catalogues the variety of outcomes and serves as a first step towards the development of a COS for localised renal cancer.

Patient summary: We reviewed studies on localised kidney cancer and found that multiple terms and definitions have been used to describe outcomes. These are not defined consistently, and often not defined at all. Our review is the first phase in developing a core outcome set to allow better comparisons of studies to improve medical care.

1. Introduction

Renal cell carcinoma (RCC) represents 2.2% of all new cancers worldwide [1,2]. With the increase in reporting of incidental findings, a greater proportion of patients newly diagnosed with renal cancer currently present with stage I disease [3,4]. Historically, surgery has been the standard of care for localised renal cancer, but international guidelines have more recently proposed ablative treatments and active surveillance as alternative options [5,6]. Currently, oncological outcomes across treatments are similar and treatment decision-making is multifactorial [7].

Across many clinical areas including urology, patient-reported outcomes and clinical outcomes are reported inconsistently, with variability in definitions and measurement, for instance in the settings of localised prostate cancer and bladder cancer [8–10]. This makes it very difficult to compare and synthesise outcomes to improve guidelines to better direct and support patients and clinicians during treatment decision-making and ultimately improve results in clinical practice [11,12]. A core outcome set (COS) is a standardised set of prioritised outcomes and is proposed by current research as a solution to decrease heterogeneity in collection, reporting, and analysis of outcomes. COS in urology are needed because inconsistencies and variability cause not only frustration but also potentially problematic conclusions [9]. This issue is also clearly apparent for localised renal cancer, and ultimately results in barriers for the multifactorial process of decision-making [7].

The aim of this systematic review was to identify which outcomes are reported in intervention effectiveness research in localised kidney cancer and to assess heterogeneity in outcome definitions and measurements. It constitutes the initial stage in the development of a COS for localised renal cancer with the intention of identifying a minimum set of outcomes that are potentially important to health care professionals and patients. The outcomes identified in this systematic review are organised under the taxonomy developed by Dodd et al. [13], which helps to structure general health research vocabularies to reduce inconsistencies. It is embedded in a larger project registered in the Core Outcome Measures in Effectiveness Trials (COMET) database [14], and uses the same robust methodology that was already followed for the prostate cancer COS [15] developed in collaboration with the European Association of Urology.

2. Evidence acquisition

This systematic review followed the guidelines of the COMET initiative, an international expert body that established guidelines on how to develop methodologically robust COS. We report our study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the COS-STAR reporting guidelines, which are relevant to this stage of COS development [16]. A project steering committee (S.M., M.V.H., P.Z., A.B., L.M., S.D., R.B., N.K.) supported the development from a methodological and clinical perspective. The study protocol was registered on PROSPERO (ID: CRD42020198605).

2.1. Aims and objectives

The aim of this project was to systematically review which outcomes have been reported in effectiveness trials and observational studies in localised renal cancer, and how they were defined and measured.

2.2. Identification of relevant studies

We searched Medline, EMBASE, Cochrane CENTRAL, and Cochrane Database of Systematic Reviews (via Ovid) from inception to June 2020. We worked with an information scientist to design the search strategy (Supplementary Fig. 1). To balance the feasibility and precision of the search, we used a two-step approach. First, we identified all published systematic reviews and intervention trials related to RCC without limiting the search to localised renal cancer, and we screened the reference lists in all the articles as a pragmatic way to identify primary studies potentially meeting our inclusion criteria. Second, we searched for and screened

all interventional studies on localised RCC from 2015 onwards without limiting the study design. We included randomised controlled trials (RCTs), cohort studies, and case-control studies that reported on eligible interventions for localised renal cancer. We excluded case studies owing to their low level of evidence according to the Oxford Centre for Evidence-Based Medicine (level of evidence 4 or lower [14]) and the unlikelihood of changing clinical practice. We also excluded conference abstracts.

2.2.1. Study participants

Adults (male and female) with suspected localised renal cancer (N0M0 according to the TNM classification; all versions of the TNM staging system) on magnetic resonance imaging, computed tomography, or ultrasound imaging were included.

Those undergoing treatment for renal metastasis or other tumours were excluded.

2.2.2. Intervention and comparator

Studies reporting on any intervention for localised renal cancer were retained, including but not limited to active surveillance, radical nephrectomy (all modes and approaches), partial nephrectomy (all modes and approaches), cryoablation, radiofrequency ablation, microwave ablation, irreversible electroporation, watchful waiting, high-intensity focused ultrasound, or radiotherapy.

2.2.3. Eligibility of studies

All abstracts and full texts were screened independently by at least two reviewers (C.W., K.B.). Any disagreements were arbitrated by a third review author (S.M).

2.3. Data extraction

Data were independently extracted from the studies included by two researchers (C.W., K.B.) and checked for accuracy by another reviewer (S.M.). We extracted data on study design; author details; year and journal of publication; intervention(s) under investigation; each effectiveness outcome reported; whether the outcome was defined or not; the definition used; the indicators and/or tool(s) used to operationalise or measure the outcome; the time point or period for outcome measurement; and how the outcome was reported.

2.4. Data analysis and synthesis

The outcome names extracted were coded and categorised according to the outcome reporting taxonomy developed by Dodd et al. [13], which has been suggested by COMET for classification of outcomes and group domains.

2.5. Assessment of risk of bias

A risk-of-bias assessment was not conducted, as no estimation of the effect size of treatments was conducted and only qualitative information containing terminology was extracted.

3. Evidence synthesis

3.1. Characteristics of the studies included

Our initial search returned 2785 abstracts. Of these, we assessed 319 full-text articles, of which 149 were included (Fig. 1). Of the 149 studies included, 97% were observational studies and five (3%) were RCTs.

3.2. Heterogeneity in outcome reporting, detection, and definitions

A suitable outcome taxonomy for health research must differentiate between high-level outcome domain classifications, and comprehensively classify all outcomes, while also proposing a standardised terminology. Therefore, we reported and organised the outcomes in the studies under the taxonomy developed by Dodd et al. [13] and recommended by the COMET initiative. Taxonomies help to

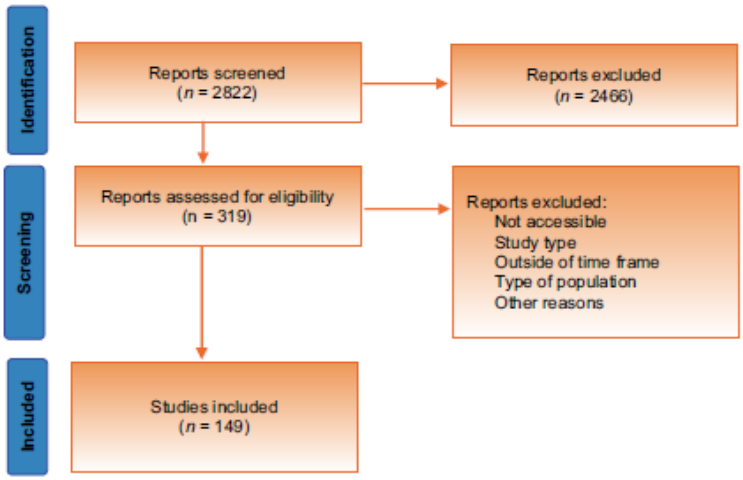

Table 1 – Outcomes classified according to the taxonomy of Dodd et al. [13]

Death	Adverse events/effects	Physiological or clinical	Resource use	Life impact
Mortality/survival	38. Adverse events/effects	2–24. Physiological/clinical	Resource use	Functioning
Mortality/survival *Overall survival* • OS rate • Cumulative survival • Stage-related OS • Mean OS • Survival probability 1 yr *Deaths* • Deaths • Death from any cause *Mortality* • Other-cause mortality • Mortality events • Overall mortality • Total mortality • X-day mortality *Cancer-specific survival* • RCC-specific survival • Recurrence-free survival *Death from kidney cancer* • Number of patients deceased at last follow-up • Death from kidney cancer • RCC death • Death from RCC • Death due to cancer *Cancer-specific mortality* • Cancer-specific mortality • Death from nonRCC, other-cause mortality	**38. Adverse events** *Complications* • Surgical complications • Intraoperative complications • Conversion to nephrectomy • Short-term complications • Conversions • Grade 1 and grade II complications • Highest complication grade • Overall complications • 30-d postoperative complications *Bleeding* • Bleeding severity • Units of blood transfused during hospitalisation • Estimated bleeding • Bleeding-related complications • Haemoglobin postoperatively ***Perioperative*** *Surgical margins* • Surgical margins • Negative margins • Positive surgical margins *Outcomes linked to surgery* • Operation time • WIT • Surgical time • Drainage time • Procedure time • Pneumoperitoneum time • Suture time • WIT ≤25 min • Conversions • Open conversion • Average clamping time • Haemoglobin after surgery • Postoperative drainage time • Intra-abdominal pressure • Adverse health outcomes • Clampless rate *Blood loss* • Mean estimated blood loss • Estimated blood loss • Changes in estimated blood loss • Units of blood transfused during surgery • Transfusion requirement • Transfusion rate • Intraoperative transfusion • Intraoperative ES transfusion • Transfusions received • Perioperative allogenic blood transfusion	**19. Renal and injury outcomes** *New CKD* • CKD probability *CKD stage* • CKD stage • Upgrading to CKD grade III–V • CKD upstaging • No CKD upstaging • Postoperative CKD stage • Postoperative new onset of stage III or IV CKD • Final CKD stage • Patients with acquired stage III–V CKD at follow-up, compared to preoperative *Time to CKD* • Decline in CKD stage • Progression to CKD • CKD upstaged–free survival • De novo CKD stage III • Survival without CKD upstaging • Time to diagnosis of CKD *Outcomes linked to procedure* • Mean ablation time • Laser excision time • Median procedure time • Renal outcomes • Urinary function • Oncological outcomes • Collecting system entry • Haemostatic agent *eGFR* • Mean eGFR change • Median eGFR preservation • Median percentage eGFR change • Change in GFR • eGFR preservation (%) • Latest eGFR preservation • Δ GFR change • Last eGFR • eGFR 1-yr post operation • Percentage change in eGFR • eGFR decrease • Postoperative eGFR change (%) from baseline to 1-yr follow-up *Serum creatinine* • Preoperative creatinine • Creatinine level • Serum creatinine • Difference in serum creatinine between preoperative and postoperative levels • Postoperative creatinine level • Postoperative creatinine • Latest creatinine level • Percentage change in creatinine • Variation of creatinine	**34. Economic** *Cost* • Health care expenditure • Medical cost • Total cost • Imaging (linked to costs) • *Medications?* **36. Need for further intervention** • Readmission **35. Hospital** • Length of stay • Postoperative HSP time • HSP time • Hospital stay • Average hospital stay • Duration of HSP • Duration of postoperative hospital stay • Median hospital stay • Surgical supplies and devices • Operating room	**31. Perceived health status** • Perceived health • Pain • Adverse health outcomes **30. Global quality of life** • Health-related quality of life

(*continued on next page*)

Table 1 (*continued*)

Death	Adverse events/effects	Physiological or clinical	Resource use	Life impact
	• Percentage blood transfusion • BUN after 1 d and 1 mo *Trifecta/pentafecta* • Trifecta • Trifecta rate • Pentafecta reached • Highest complication grade • Low-grade complication	• Δ creatinine *Recurrence-free survival* • RFS + time		
	38. Adverse events/effects or 35. Resource use: hospital • Dialysis free probability • No. requiring dialysis • Temporary dialysis • Permanent dialysis	**16. Outcomes relating to neoplasms: benign, malignant and unspecified (including cysts and polyps)** *Metastasis* • Distant metastasis–free survival • Distant metastasis • Extrarenal metastasis *Follow-up* • Follow-up • Long-term outcomes • Median postoperative follow-up time • Average length of follow-up • Median follow-up time *Progression-free survival* • PFS • Systemic PFS • Clinical PFS *Progression* • Local tumour progression • Disease progression *Recurrence* • Local recurrence • Disease-free survival • Recurrence rate • Recurrence-free survival • Recurrence result *Recurrence linked to time* • Time to local recurrence • Events of local recurrence • Delayed recurrence • Time to recurrence • Local recurrence rate • Local recurrence-free survival • Recurrence (local or metastatic) • Local ipsilateral recurrence • Disease-free survival		

BUN = blood urea nitrogen; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ES = erythrocyte suspension; HSP = hospitalisation; OS = overall survival; PFS = progression-free survival; RCC = renal cell carcinoma; WIT = warm ischaemia time.

Table 2 – Outcomes reported in each study after classification according to the taxonomy suggested by Dodd et al. [13]

First author	Design	Location	Death		Adverse events		Physiological or clinical		Resource use			Life impact	
			OS	CSS	AEs	AEs/ ERUH	RIO	ORN	E	H	NFI	PHI	GQL
Patel	OBS	US	X				X	X					
Li	OBS	China			X		X			X			
Wang	OBS	China			X		X			X			X
Morkos	OBS	USA	X	X		X	X	X					
Alshyarba	OBS	Saudi Arabia	X		X								
Wu	OBS	China			X		X			X			
Packiam	OBS	USA			X		X			X			
Yang	OBS	Not stated	X		X					X			
Rembeyo	OBS	France	X	X	X		X	X					
Uhlig	OBS	USA	X										
Yu	OBS	China	X	X	X		X	X					
Kartal	OBS	Turkey	X		X		X	X					
Jalbani	OBS	Pakistan			X		X			X			
Seon	OBS	South Korea	X	X	X		X	X					
Choi	OBS	South Korea			X		X			X			
Tan	OBS	USA, Puerto Rico	X										
Grant	OBS	USA	X										
Chen	RCT	China			X		X			X			
Liu	OBS	China			X		X			X			
Sandbergen	OBS	Netherlands			X								X
Shapiro	OBS	USA		X	X		X	X					
De Cobelli	OBS	Italy			X		X						
Nayan	OBS	Canada	X	X			X	X					
Jin	OBS	China			X		X			X			
Mourao	OBS	USA, Spain	X	X	X		X			X			
Anglickis	OBS	Lithuania			X		X	X		X		X	
Marchioni	OBS	USA	X	X									
Li	OBS	China		X									
Liao	OBS	USA	X	X									
Simone	OBS	Italy	X	X	X		X	X					
Shao	OBS	Taiwan			X			X		X			
Antonelli	RCT	Italy			X		X			X			
Kitley	OBS	USA	X										
Zhou	OBS	China			X		X						
Andrews	OBS	USA		X				X					
Zhou	OBS	USA		X			X	X					
Fraisse	OBS	France	X		X			X				X	
Hu	OBS	China			X								
Abu-Ghanem	OBS	Israel	X	X			X	X					
Kavaric	OBS	Montenegro			X		X			X			
Ziegelmueller	OBS	Germany	X				X	X					
Talenfeld	OBS	USA	X	X	X								
Bhindi	OBS	USA	X	X	X		X	X					
Larcher	OBS	Netherlands, Italy	X		X		X	X		X			
Xing	OBS	USA	X	X								X	
Ristau	OBS	USA, Puerto Rico	X										
Zhao	OBS	China			X		X	X		X			
Gershman	OBS	USA	X	X			X	X					
Benoit	OBS	France			X		X	X		X			
Paulucci	OBS	USA			X		X	X		X			
Abdel Raheem	OBS	South Korea		X	X		X	X		X			
Lourenco	OBS	Canada	X		X		X	X		X			
Hasegawa	OBS	Japan					X	X			X		
Streja	OBS	USA		X			X						
Borghesi	OBS	Globally			X		X			X			
Uhlig	OBS	USA	X							X	X		
Ye	OBS	China			X			X		X			
Park	OBS	Not stated											
Venkatramani	OBS	USA	X							X			
Uhlig	OBS	USA		X									
Zhang	OBS	USA	X	X									
Lee	OBS	South Korea	X	X	X			X					
Chong	OBS	USA			X			X			X		
Chang	OBS	Taiwan			X				X	X			
Yang	OBS	China			X			X		X			
Veys	OBS	Belgium	X	X	X		X	X					
Banapour	OBS	USA			X		X			X			
Cai	OBS	China	X	X			X						
Lanchon	OBS	France			X		X			X			
Venkatramani	OBS	USA	X								X		
Karalli	RCT	Sweden										X	

(continued on next page)

Table 2 (*continued*)

First author	Design	Location	Death		Adverse events		Physiological or clinical		Resource use			Life impact	
			OS	CSS	AEs	AEs/ ERUH	RIO	ORN	E	H	NFI	PHI	GQL
Dong	OBS	Not stated					X						
Wang	OBS	USA	X										
Tang	OBS	USA	X	X									
Yin	OBS	China	X					X					
Shah	OBS	USA					X						
Annino	OBS	Italy			X			X					
Wang	OBS	China	X					X					
Shum	OBS	USA	X					X		X	X		
Luo	OBS	USA	X	X									
Lee	OBS	South Korea	X	X	X			X					
Caputo	OBS	USA	X	X	X		X						
Lu	OBS	China			X		X			X			
Maric	OBS	Serbia			X								
Matei	OBS	Italy			X	X	X	X		X			
Paulucci	OBS	USA			X		X						
Rassweiler	OBS	Germany			X								
Larcher	OBS	USA	X		X			X	X	X	X		
Lenis	OBS	USA	X		X								
Wang	OBS	USA			X					X			
Peng	OBS	China		X	X		X	X		X			
Malkoc	OBS	USA			X			X		X	X		
Long	OBS	France	X	X	X	X	X	X		X			
Yoo	OBS	South Korea					X						
Redondo	OBS	Spain			X					X			
Carrion	OBS	Spain			X		X						
Shah	OBS	USA			X		X						
Moskowitz	OBS	USA	X										
Huang	RCT	China			X		X			X			
Larcher	OBS	USA		X									
Jang	OBS	South Korea	X	X	X		X	X					
Forbes	OBS	Canada	X		X		X	X					
Kara	OBS	Not stated			X		X	X		X			
Takagi	OBS	Not stated			X		X	X		X			
Oh	OBS	Not stated			X								
Andrade	OBS	Not stated			X	X			X	X			
Dong	OBS	Not stated	X		X		X	X		X			
Trudeau	OBS	USA	X		X								
Lai	OBS	China	X	X	X					X			
Liu	OBS	China	X		X		X			X			
Pantelidou	OBS	UK			X		X	X		X			
Liu	OBS	China	X		X		X	X					
Larcher	OBS	USA			X		X						
Hossein	OBS	Iran			X		X						
Komatsuda	OBS	Japan			X		X						
Janicic	OBS	Serbia	X	X									
Lyon	OBS	USA			X					X			
Satkunasivam	OBS	USA	X		X	X	X			X			
Thompson	OBS	USA	X				X	X					
Tabayoyong	OBS	USA						X					
Alanee	OBS	USA		X									
Zargar	OBS	USA			X		X	X					
Mano	OBS	USA	X		X		X	X		X			
Chang	OBS	China	X	X	X		X	X		X			
Serni	OBS	Italy	X	X	X		X	X					
Chung	OBS	Korea	X	X			X						
Yu	OBS	Not stated	X		X								
Weinberg	OBS	USA			X				X	X			
Park	RCT	South Korea			X					X		X	X
Balasar	OBS	Turkey			X		X						
O'Malley	OBS	USA	X	X			X						
Kim	OBS	South Korea			X		X						
Chang	OBS	China	X		X								
Cooper	OBS	USA			X		X						
Alam	OBS	USA	X	X			X						
Çömez	OBS	Turkey			X		X			X			
Kopp	OBS	USA			X		X	X		X			
Danzig	OBS	USA			X		X						
Hussein	OBS	Egypt					X						
Simsek	OBS	Turkey			X		X			X			
Fossati	OBS	Italy		X	X					X			
Ji	OBS	Italy, China	X	X	X	X	X	X		X			

Table 2 (*continued*)

First author	Design	Location	Death		Adverse events		Physiological or clinical		Resource use			Life impact	
			OS	CSS	AEs	AEs/ ERUH	RIO	ORN	E	H	NFI	PHI	GQL
Mason	OBS	USA					X						
Chehab	OBS	Not stated			X								
An	OBS	USA			X					X			
Rosen	OBS	USA			X		X						
Ramirez	OBS	USA			X		X						
Malkoc	OBS	Turkey			X		X				X		

AEs = adverse events; CSS = cancer-specific survival; E = economic resource use; ERUH = effects or resource use: hospital; GQL = global quality of life; H = hospital resource use; NFI = need for further intervention; OBS = observational study; ORN = outcomes relating to neoplasms; OS = overall survival; PHI = perceived health impact; RCT = randomised controlled trial; RIO = renal and injury outcomes.

studies (3%) as mean or median costs), "need for further intervention" (eg, readmission; reported in eight studies [5%] as a binary yes/no result or median value), and "hospital" (eg, length of hospital stay, reported in 58 studies [39%] as mean or median length of hospital stay in days).

3.8. Discussion

To the best of our knowledge, this is the first systematic review of outcome reporting heterogeneity in the literature on localised renal cancer. Our results build a framework for developing a COS for localised renal cancer with the aim of reducing heterogeneity for outcome definitions, measurement, and reporting.

Our systematic review highlights the persisting problem of outcome reporting heterogeneity in studies on localised renal cancer. Multiple terms are used to refer to conceptually similar outcomes, and there is variation in the outcome definitions used. This has not improved over time and is problematic when summarising the evidence base for treatment effectiveness to inform decision-making, because it is not advisable to synthesise data with different outcome definitions within a meta-analysis. Such a practice can produce meaningless summary statistics that may be given more credibility than they are due. Therefore, a cumbersome and often less-informative narrative synthesis must be undertaken instead. Furthermore, our work highlights variety in data reporting and measurement. For instance, if dichotomous outcomes such as OS and CSS are reported using different methods (eg, some studies report adjusted and some unadjusted hazard ratios, others report a rate at median follow-up or at specified time points such as 1 yr or 5 yr), then these data cannot be easily or reliably synthesised in a meta-analysis. When these problems all occur together, then it is difficult to interpret the body of evidence and clinical practice guideline panels encounter challenges in drawing up recommendations and applying certainty-of-evidence attributes such as those proposed by the GRADE working group [17].

Worryingly, we identified very few patient-reported outcomes (PROs), which might be related to the limited number of specific tools available for capturing QoL for renal cancer. In their systematic review, Rossi et al. [18] identified three generic PROMs (RAND medical outcome survey SF-36 and SF-12, EuroQol [EQ-5D], Convalescence and Recovery Evaluation [CARE]) and eight cancer-specific PROMs (Cancer Rehabilitation Evaluation System-Short Form [CARES-SF], European Organisation for Research and Treatment of Cancer [EORTC] Quality of Life Questionnaire [QLQ]-C30, Functional Assessment of Cancer Therapy-General [FACT-G], FKSI, Renal Cell Carcinoma-Symptom Index [RCC-SI], Instruments to assess psychological wellbeing Impact of Events Scale [IES], Hospital Anxiety and Depression Scale [HADS], Mishel Uncertainty in Illness Scale (MUIS)) which are currently being used in renal cancer. However, of the PROM instruments used, only two are specific to renal cancer and are not stage-specific (FKSI, RCC-SI) [18].

In their study of the symptom index most commonly used for renal cancer, Rosenblad et al. [19] assessed the psychometric properties of the FKSI-19 (which captures physical and emotional disease-related symptoms, function/wellbeing, and treatment side effects) among patients with RCC and reported that it is barely fit for this purpose. Decat Bergerot et al. [20] conducted a patient survey that identified many of the FKSI-19 questions as irrelevant from a patient perspective and stressed the need to incorporate patients in the development of PRO tools to determine areas of importance to them. The EORTC Quality of Life group is currently developing an RCC-specific module to be used in combination with their QLQ-C30 instrument.

Our project steering group includes clinical RCC experts, patient advocacy groups, methodologists, and guideline developers from the European Association of Urology (most are co-authors of this study). We aim to use these networks to improve recruitment to our research stages, and to subsequently endorse and disseminate the final COS as part of our implementation strategy.

We curated the different terms used and collated them using a standardised outcome classification taxonomy [13] as a first step in creating a COS for localised renal cancer. In the next step we will use consensus processes in a multistakeholder group to prioritise which outcomes are core and to recommend definitions for each outcome. Once we know which outcomes are considered core by our stakeholders, we will systematically review the psychometric properties of PROMs available, with coverage of core outcomes using the COSMIN criteria [21,22] and will recommend one to be used in future research on treatment effectiveness. This is a medium- to long-term vision to standardise the definition, measurement, and reporting of

outcomes in research on localised renal cancer, with the ultimate aim of improving the decision-making process at all levels.

3.9. *Limitations*

We may have missed studies reporting PROs and/or QoL because we did not search specifically for primary qualitative studies of patient experiences of renal cancer treatment. However, we will supplement the list of outcomes presented here with outcomes identified in our own primary interview study with patients who have been treated for renal cancer, and further review work. Furthermore, as part of our prioritisation process, participants will be able to propose outcomes they think are missing from our list.

4. Conclusions

Our review indicates that clinical research on localised renal cancer is impeded by heterogeneity in outcome selection, definitions, and reporting. This work represents the first step in the development of a COS that will ultimately improve the evidence basis for treatment of patients with localised renal cancer and the process for creating clinical practice guidelines, and will facilitate treatment decision-making by health care professionals and patients.

Author contributions: Katharina Beyer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Beyer, Widdershoven, Van Hemelrijck, Bex, Zondervan, MacLennan.
Acquisition of data: Beyer, Widdershoven, MacLennan.
Analysis and interpretation of data: Beyer, Zondervan, MacLennan.
Drafting of the manuscript: Beyer, Zondervan, MacLennan.
Critical revision of the manuscript for important intellectual content: Beyer, Widdershoven, Wintner, Dabestani, Marconi, Moss, Kinsella, Yuan, Giles, Barod, Van Hemelrijck, Bex, Zondervan, MacLennan.
Statistical analysis: None.
Obtaining funding: None.
Administrative, technical, or material support: Beyer, Widdershoven, Yuan.
Supervision: Zondervan, MacLennan.
Other: None.

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Funding/Support and role of the sponsor: None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.11.014.

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Appendix 6: Ethics application KCL

Research Ethics
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Waterloo Road
London SE1 9NH
Telephone 020 7848 4020/4070/4077
reo@kcl.ac.uk

KING'S College LONDON

Katharina Beyer

16/06/2021

Dear Katharina,

LRS/DP-20/21-22307: Treatment decision making in localised kidney cancer: qualitative study

Ethical Clearance

Thank you for submitting your application for the above project. I am pleased to inform you that full approval has been granted by the BDM Research Ethics Panel

Important COVID-19 update: Please consult the latest College guidance (linked below) and ensure you have completed the risk assessment procedure prior to any data collection involving face-to-face participant interactions.

https://internal.kcl.ac.uk/innovation/research/ethics/applications/COVID-19-Update-for-Researchers

Ethical approval has been granted for a period of **three years** from 16 June 2021. You will not be sent a reminder when your approval has lapsed and if you require an extension you should complete a modification request, details of which can be found here:

https://internal.kcl.ac.uk/innovation/research/ethics/applications/modifications.aspx

Please ensure that you follow the guidelines for good research practice as laid out in UKRIO'sde Code of Practice for research: http://ukrio.org/publications/code-of-practice-for-research/

Any unforeseen ethical problems arising during the course of the project should be reported to the panel Chair, via the Research Ethics Office.

Data Protection Registration

As you have indicated in Section E that personal data will be processed as part of this research project, this letter also confirms that you have also met your requirements for registering this processing activity with King's College London. This is required in line with the College's role as a Data Controller, in accordance with the General Data Protection Regulation (GDPR).

Please note it is the responsibility of the researcher(s) to ensure compliance with other aspects of the GDPR, more information about this can be found here: https://internal.kcl.ac.uk/innovation/research/Research-Governance/how-does-GDPR-affect-research/How-does-GDPR-affect-research

You are required to adhere to all research data/records management and storage procedures agreed to as part of your application. This will be expected even after the completion of the study.

If there are any changes to the project that will impact on how you will you collect, manage or otherwise use your data, these must also be reflected in a modification request as outlined above.

Please note that we may, for the purposes of audit, contact you to ascertain the status of your research.

We wish you every success with your research.

Yours sincerely,

Mr James Patterson

Senior Research Ethics Officer

For and on behalf of:

BDM Research Ethics Panel

Appendix 7: COREQ checklist

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	KB, LV
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	MD, PhD
Occupation	3	What was their occupation at the time of the study?	PhD student
Gender	4	Was the researcher male or female?	Female
Experience and training	5	What experience or training did the researcher have?	Qualitative r
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	no
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	We shared a
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	n/a
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Decision ma
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	purposive
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	email
Sample size	12	How many participants were in the study?	16
Non-participation	13	How many people refused to participate or dropped out? Reasons?	6 from Innsb
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	online
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	na
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	all localised
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	semistructur
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	no
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	Microsoft te
Field notes	20	Were field notes made during and/or after the inter view or focus group?	Yes
Duration	21	What was the duration of the inter views or focus group?	around 1-2 h
Data saturation	22	Was data saturation discussed?	Yes
Transcripts returned	23	Were transcripts returned to participants for comment and/or	no

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	2
Description of the coding tree	25	Did authors provide a description of the coding tree?	Yes- Nvivo w
Derivation of themes	26	Were themes identified in advance or derived from the data?	we used a in
Software	27	What software, if applicable, was used to manage the data?	Nvivo, Excel
Participant checking	28	Did participants provide feedback on the findings?	no
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	Quotes were
Data and findings consistent	30	Was there consistency between the data presented and the findings?	Yes
Clarity of major themes	31	Were major themes clearly presented in the findings?	Yes
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	Yes

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

Appendix 8: Semi-structured Topic guide

Confidential: Anything you say here will be confidential in that none of you will be identified in any report about the meeting.

Consent: You have signed and returned the consent sheet which outlined in detail on how we handle your data.

Background: As described in the patient information sheet, the current guidelines do not give a clear recommendation of which treatment option to use in localised kidney cancer. There is therefore a need to identify and understand the barriers and facilitators to treatment decision-making in localised kidney cancer.

Prior to this project, we performed research on barriers and facilitators to treatment decision-making. The themes are linked to Kidney Cancer Specific Characteristics Decision Maker (i.e., size of the cancer), Decision Maker- related criteria (i.e., patient preference) and Contextual factors (i.e., access to the hospital).

After completing the systematic review, we identified a clear gap in the literature. Despite the recommendation across cancer care to empower patients in their decision-making, the literature in this field, does currently not explore the view of patients. We therefore want to build on the identified themes (i.e., Kidney Cancer Specific Characteristics Decision Maker-related criteria, Contextual factors) around barriers and facilitators of treatment decision-making, validate these themes during the focus group, understand if there are additional barriers and facilitators and finally discuss ways and methods to better support patients to improve the decision-making process.

Introduction – Ask the pt. to introduce themselves
1. How long ago was your diagnosis?
2. How did you get diagnosed?
3. How much time was there between when you first experienced symptoms and visiting your GP?
4. How much time was there between your visit to your GP and your referral to hospital?
Kidney Cancer Specific Characteristics
Prognosis factors, Demographic characteristics, Predictive tools
5. Thinking back to your consultation where you were given your diagnosis, can you tell me what you were told about your cancer, how you felt and how you were supported through that consultation?
6. Was the consultation F2F, Tel, Video? Did you think this medium was appropriate?

7. What tests/investigation did you receive to enable you and your physician to make the decision on treatment?
8. Do you have any other health conditions that impacted on your treatment decision?
9. Did your age influence your choice of treatment?
10. Did any other factors influence your treatment decision?
Decision Maker- related criteria
Patient related criteria
11. What helped you decide on the treatment you had for your kidney cancer?
12. Do you feel your personal treatment preference was acknowledged by the cancer team?
13. (How) did your family influence your treatment decision?
14. Were there other influences outside of the healthcare system that helped you come to a treatment decision e.g., church, contact with a charity, friends?
15. How did your native language i.e., when English is not the native language had an impact?
16. If your native language is not English, were you offered information in another language? Was this helpful?
Physician related criteria
17. Did you have enough opportunities/time to talk with your cancer team about what treatments are available?
18. Were you encouraged to ask questions?
19. Has your physician explained to you the aims of the treatment (for example to treat cancer) in a way you understood?
20. Did you have a dedicated CNS to support you through treatment decision-making? Were they hard/easy to contact?
Patient physician interaction
21. How easy is it for you to discuss your cancer and the treatment with your cancer team?
22. Did your cancer team make it easy for you to talk openly about issues that concern you?
23. How easy is it to contact your doctor to discuss any concerns?
Contextual factors
Economic variables
24. Did financial concerns have any impact of your treatment decision (e.g., the need to work, look after children)?
Access to healthcare
25. Did your access to the treatment (e.g., travel time/mode of travel to the hospital) have an impact on your treatment decision?
Healthcare organisation
26. Would telephone/virtual clinics have been helpful?
27. Can you think of other ways the hospital could have supported you to take a treatment decision? (i.e., additional reading/video material? Support group if not already attended)
Evidence basis

28. Were you offered other material to support your treatment decision-making e.g., video, DVD, support group access, virtual educational seminar?
End task: Supportive care recommendations
29. Do you feel anything was missing (or left out) in the decision-making process?
30. If you could change one thing about your treatment decision-making pathway, what would it be?
31. Did anything about the decision-making process does not meet your expectations?
32. How can we improve the support for decision-making for patients?
33. If you were speaking to someone considering treatment for this same condition and you had to give them advice, what would you say?

Ending: Thank you for taking part in this discussion. We are holding a number of discussions like this one and aim to publish our results in a peer reviewed journal. The overall aim of my PhD is to create supportive care recommendations to support patients better during treatment decision-making in localised kidney cancer.

Appendix 9: Invitation letter patients

Dear Sir/ Madam,

We would like to invite you to participate in a research study, which aims to improve treatment decision-making in localised kidney cancer. The study is being conducted by King's College London.

We are contacting you because you are someone who has had to decide on your treatment for localised kidney cancer. Therefore, you may be able to participate in this study. If you choose to take part, you will take part in a focus group run by a study researcher. The focus group will last approximately two hours. In the focus group you would be asked about your experiences of your treatment decision-making process for localised kidney cancer and particularly.

If you are interested to participate, we will share a Participant Information Sheet, containing more detailed information about why we are doing this study, what your participation would involve, and other details. If you are interested in participating in the study, please read the enclosed Participant Information Sheet carefully.

A researcher from King's College London will contact you within the next 7 days, to have a further conversation about this study.

If you would like to speak to the research team, please contact: Katharina Beyer (Katharina.beyer@kcl.ac.uk)

Thank you for taking the time to consider this invitation.

Yours sincerely,

Katharina Beyer, Netty Kinsella, Ravi Barod and Mieke Van Hemelrijck

Appendix 10: Information Sheet for Participants

INFORMATION SHEET FOR PARTICIPANTS

Ethical Clearance Reference Number: **22307**

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of project

Treatment decision-making in localised kidney cancer- a qualitative study.

Invitation Paragraph

We would like to invite you to participate in this thesis which forms part of a larger project funded by Kidney Cancer UK and endorsed by the National Cancer Research Institute. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. If there is anything that is not clear or if you would like more information, contact the research team using the contact details at the bottom of this form.

What is the purpose of the project?

There are several treatments for localised kidney cancer all offering similar rate of cancer control/cure. There is therefore a need to identify and understand the barriers and facilitators to treatment decision-making in localised kidney cancer.

Prior to this project, we performed a review of the current research evidence looking for the barriers and facilitators to treatment decision-making. After completing this review, we identified a clear gap in the literature. Despite a national recommendation across cancer care to empower patients in the cancer treatment decision-making process, the literature, does currently not explore the view of patients. We therefore want to build on the identified themes around barriers and facilitators of treatment decision-making, to include the patient perspective. We will also discuss the supportive care needs of patients to improve the decision-making process.

Why have I been invited to take part?

You are being invited to participate in this project because you have been identified as someone who has been diagnosed with localised kidney cancer or are a partner of someone diagnosed with kidney cancer. Your experiences will be invaluable in helping us redesign the treatment decision-making process.

What will happen if I take part?

If you choose to take part in the project you will be asked to take part in an online focus group, which will be conducted by an experienced researcher. The focus group will take around 2 hours in total.

Participation will take place from your home, over an online secure video call. This ensures that we can conduct the research safely, given the ongoing situation with coronavirus (COVID-19).

As part of participation, you will be asked to provide your age, and we will also ask for your consent to use the information you have provided in our analysis.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in anyway. Once you have read the information sheet, please contact us if you have any questions that will help you decide about taking part. If you decide to take part, we will ask you to sign a consent form and you will be given a copy of this to keep.

What are the possible risks of taking part?

While some people find it helpful to think about and talk about their patient journey, a few people may find this upsetting. If you did find that you were upset at the end of the focus group, someone who is independent from the study would be available to talk with you further. Information on free support services will be provided to you.

If you become distressed during the focus group, you will be offered a short break (5-10 minutes, or however long you desire) and you will be prompted to switch off your camera and microphone during this break and get a drink or a snack if you wish to do so. After the break, you will then be asked if they would like to continue the discussion or terminate the participation of the focus group.

Regardless of whether you become distressed in the interview or not, breaks in the interview will be offered to you at periodic intervals.

What are the possible benefits of taking part?

There are no intended benefits to you personally from taking part in this study. Some people find it helpful to speak about their experiences, but this is not the objective of the study. In addition, a clear benefit will be the aim to shape the experiences of patients in the future. It will enable you to have your patient voice heard to improve the journey of other patients.

Data handling and confidentiality

All electronic data (recordings) will be stored on KCL secure servers, will be password protected and will only be accessed by core members of the research team. This data will include compiled excel/NVivo worksheets as well as text documents for transcriptions. Manual data encompasses the Site File and will include consent forms and notes from interview. The Site File will be stored in a locked cabinet in a secure KCL office and will only be accessed by the Research team.

Your data will be processed in accordance with the General Data Protection Regulation 2016 (GDPR). All identifiable information which is collected about you during the research would be kept strictly confidential and will be shared with no-one besides the *Research Team*, which is made up of four individuals in the Translational Oncology and Urology Research (TOUR) group at KCL. The four individuals that make up the *Research Team* will have access to a password-protected spreadsheet containing the data identifying you. No-one else will have access to this spreadsheet, and the information in it will not be shared with anybody else aside from the *Research Team*. Upon conclusion of the data analysis, this spreadsheet will be destroyed, meaning your personal data will be erased. It will not be possible to identify you in any publication of the research findings. The data you have provided will be stored at KCL, in a fully anonymised format, for 7 years following the conclusion of the study, in line with KCL's Records and Data Retention Schedule.

The video call software that we will be using to conduct your interview uses a secure connection, meaning that no third parties can access the content of the video call (in other words, no-one can hack into the call to access its contents).

Data Protection Statement Your data will be processed in accordance with the General Data Protection Regulation 2016 (GDPR). If you would like more information about how your data will be processed in accordance with GDPR please visit the link below:

https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research

What if I change my mind about taking part?

You are free to withdraw at any point of the project, without having to give a reason. Withdrawing from the project will not affect you in any way. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. **If you withdraw from the project, we will keep the information about you that you have already provided.** To safeguard your rights, we will fully anonymise this information upon your withdrawal from the study (i.e., the personal identifiable information we hold on you will be fully erased; we will only keep your interview contributions in an anonymous format).

How is the project being funded?

This project is being funded by Kidney Cancer UK and the Royal Marsden Charity.

What will happen to the results of the project?

The results of the project will be summarised in a manuscript which will be submitted for peer-review in an academic journal. The results will be used to inform a further study on how to improve treatment decision-making in localised kidney cancer.

Who should I contact for further information?

If you have any questions or require more information about this project or would like to contact the clinical team, please contact us using the following contact details, and ask for Katharina Beyer.

TOUR Research Team

Saran Green

Saran.green@kcl.ac.uk

TOUR office

Research Oncology

Third floor, Bermondsey Wing

Guy's Hospital

Great Maze Pond

London SE1 9RT

What if I have further questions, or if something goes wrong?

If this project has harmed, you in any way or if you wish to make a complaint about the conduct of the project you can contact King's College London using the details below for further advice and information:

The Chair, Biomedical and Health Sciences Subcommittee (BDM RESC)

Tel: 020 7848 4070

Email: rec@kcl.ac.uk

Thank you for reading this information sheet and for considering taking part in this research.

Appendix 11: Consent

CONSENT FORM FOR PARTICIPANTS IN RESEARCH PROJECTS

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research

Title of project: Treatment decision-making in localised kidney cancer		
Ethical review reference number: 22307	Version 1.0 05/01/2021	
		Tick or initial
1. I confirm that I have read and understood the information sheet Version 1.0, dated 05/01/2021 for the above project. I have had the opportunity to consider the information and asked questions which have been answered to my satisfaction.		
2. I consent voluntarily to be a participant in this project and understand that I can refuse to take part and can withdraw from the project at any time, without having to give a reason, up until 01/12/2021.		
3. I consent to the processing of my personal information for the purposes explained to me in the Information Sheet. I understand that such information will be handled in accordance with the terms of the General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018.		
4. I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes.		
5. I understand that confidentiality and anonymity will be maintained, and it will not be possible to identify me in any research outputs		
6. I understand that the confidentiality of my contributions cannot be absolutely guaranteed. This is due to the interactive and interdependent nature of focus group participation.		
7. I agree that the research team may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would not be identifiable in any report).		
8. I consent to my participation in the research being audio recorded.		
9. I understand that I must not take part if I fall under the exclusion criteria as		

detailed in the information sheet and explained to me by the researcher.	
10. I agree to maintain the confidentiality of focus group discussions	
11. I understand that the information I have submitted will be published as a report	
12. I wish to receive a copy of the final report.	
13. I agree to be re-contacted in the future by King's College London researchers regarding this project.	
14. I agree that the researcher may retain my contact details so that I may be contacted in the future by King's College London researchers who would like to invite me to participate in future studies of a similar nature.	

_____ _____ _____

Name of Participant Date Signature

_____ _____ _____

Name of Researcher Date Signature