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How to live well with Chronic Kidney Disease

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British Geriatrics Society Autumn Meeting
November 2019

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Living well with CKD

- Some CKD epidemiology
- Living with CKD – what patients tell us
- Living *well* with CKD – challenges and suggestions

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CKD classification

Two measures of eGFR at least 3 months apart

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Many causes, but can broadly be considered vascular condition

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter., Suppl. 2013; 3: 1-150.

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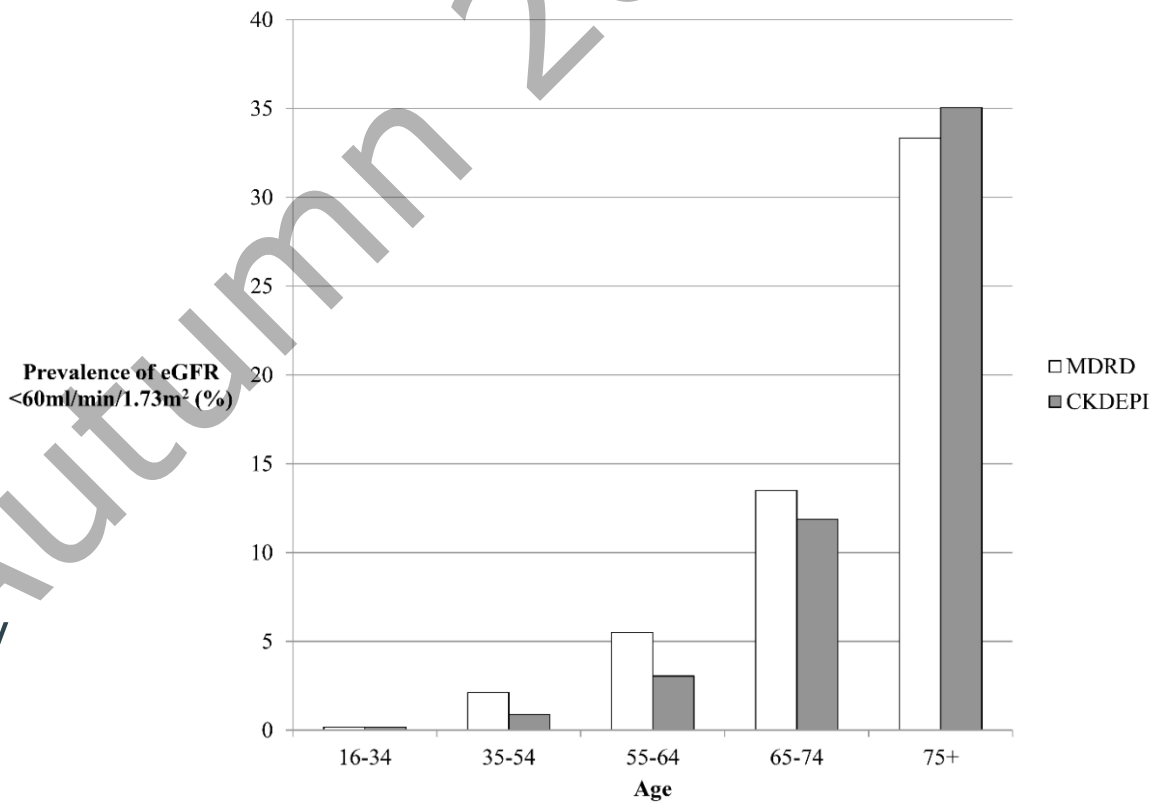
CKD is common

- Prevalence estimates vary. Depends on measures/equations / population
- Stage 3 – 5 CKD in Health Survey for England (population representative but only one eGFR)
- Prevalence seems relatively stable (although the population is ageing)



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Fraser SDS, Aitken GR, Taal MW, Mindell JS, Moon G, Day J, O'Donoghue D, Roderick PJ. Exploration of chronic kidney disease prevalence estimates using new measures of kidney function in the Health Survey for England. PLOS ONE 2015; 10(2): e0118676

Aitken GR, Roderick PJ, Fraser SDS, Mindell JS, O'Donoghue D, Day J, Moon G. Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010. BMJ Open 2014;4:e005480.

CKD is common

- Data from 485 participants >60 in the Oxford Renal Cohort Study (primary care)
- At least two eGFR tests
- Prevalence CKD 1-5 using CKD-EPI = 38%, but CKD 3 or worse 16%
- Concluded:
  - single measure eGFR overestimates prevalence by about 25%
  - current guidance for at least two measures is appropriate

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Hirst JA, Montes MDV, Taylor CJ, Ordóñez-Mena JM, Ogburn E, Sharma V, Shine B, James T, Hobbs FR. Impact of a single eGFR and eGFR-estimating equation on chronic kidney disease reclassification: a cohort study in primary care. Br J Gen Pract. 2018;68(673):e524-e530

CKD outcomes

- CKD Prognosis Consortium: collaborative meta-analyses of general population and high risk cohorts
- Strong evidence of independent association between both lower eGFR and albuminuria all-cause and cardiovascular mortality, end stage renal disease, acute kidney injury and progressive CKD

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Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, Coresh J, Gansevoort RT. Lancet 2010 12;375(9731): 2073-81.

Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts. Gansevoort RT, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, Jong PE, Coresh J; the Chronic Kidney Disease Prognosis Consortium. Kidney Int 2011;80(1): 93-104.

Hallan SI, Matsushita K, Sang Y, Mahmoodi BK, Black C, Ishani A, Kleefstra N, Naimark D, Roderick P, Tonelli M, Wetzels JF, Astor BC, Gansevoort RT, Levin A, Wen CP, Coresh J; Chronic Kidney Disease Prognosis Consortium. Age and association of kidney measures with mortality and end-stage renal disease. JAMA. 2012;308(22):2349-60.

CKD outcomes

Mortality risk – risk varies with age:

Age	eGFR 45 mL/min/1.73 m2 vs. 80 mL/min/1.73 m^2	
	Relative (adjusted HR (95%CI))	**Absolute (excess deaths per 1000 person-years (95%CI))**
18-54	3.50 (2.55-4.81)	9.0 (6.0-12.8)
55-64	2.21 (2.02-2.41)	12.2 (10.3-14.3)
65-74	1.59 (1.42-1.77)	13.3 (9.0-18.6)
≥75	1.35 (1.23-1.48)	27.2 (13.5-45.5)

Similar picture for albuminuria

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Hallan SI, Matsushita K, Sang Y, Mahmoodi BK, Black C, Ishani A, Kleefstra N, Naimark D, Roderick P, Tonelli M, Wetzels JF, Astor BC, Gansevoort RT, Levin A, Wen CP, Coresh J; Chronic Kidney Disease Prognosis Consortium. Age and association of kidney measures with mortality and end-stage renal disease. JAMA. 2012;308(22):2349-60.

CKD and hospitalization

15,336 participants 75 years and older from 53 UK general practices

Showed that dipstick-positive proteinuria and/or eGFR<30ml/min/1.73m^2 is associated with an increased risk of single and multiple hospitalization after adjustment for age, sex and cardiovascular risk factors

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Nitsch D, Nonyane BA, Smeeth L, Bulpitt CJ, Roderick PJ, Fletcher A. CKD and hospitalization in the elderly: a community-based cohort study in the United Kingdom. Am J Kidney Dis. 2011 May;57(5):664-72.

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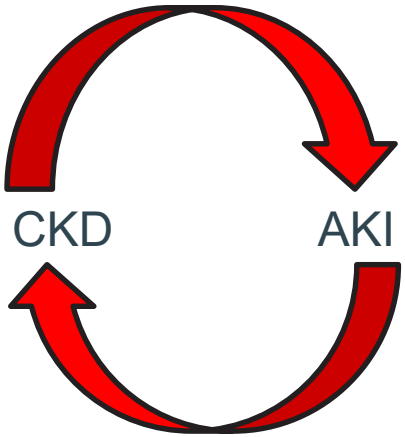
CKD and acute kidney injury

CKD prognosis consortium study:

- Lower eGFR and higher ACR strongly associated with AKI.
- Compared with eGFR of 80mL/min/1.73m^2, the adjusted HR of AKI at eGFR of 45mL/min/1.73m^2 was 3.35 (95% CI, 2.75-4.07).
- Older age associated with higher risk of AKI.
- AKI also associated with higher risk of subsequent CKD / End Stage Kidney Disease



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Grams ME, Sang Y, Ballew SH etl al. A Meta-analysis of the Association of Estimated GFR, Albuminuria, Age, Race, and Sex With Acute Kidney Injury.. AJKD 2015;66(4): 591-601.

CKD and comorbidities

Tonelli M et al, Canadian study in the Alberta Kidney Disease Network database.

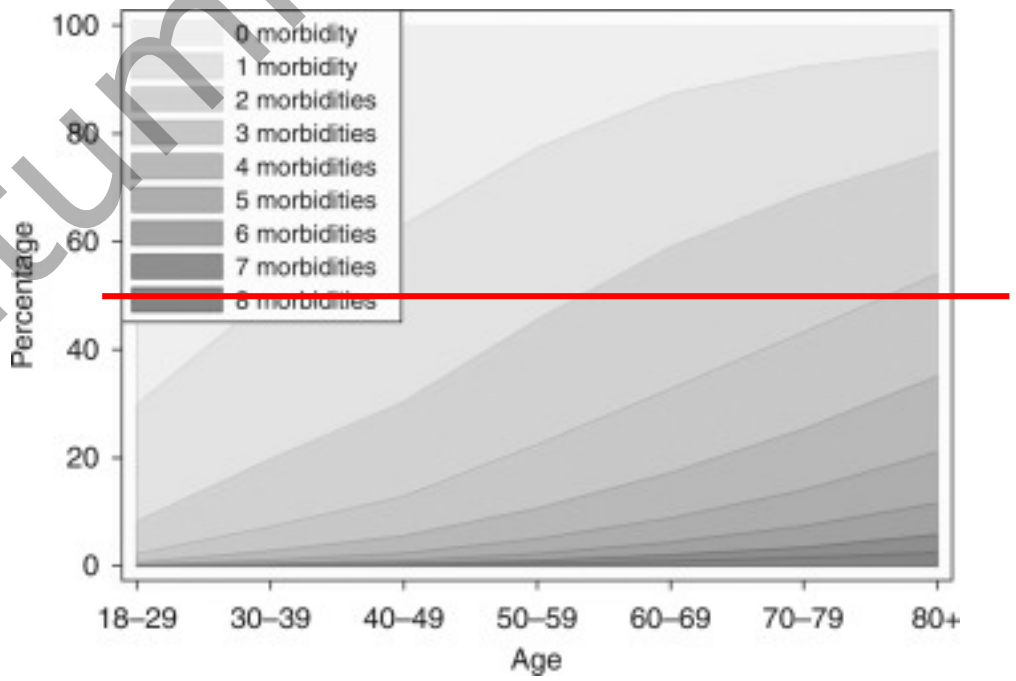
530,771 participants with CKD

Median age 56 (IQR 38-72)

List of 29 comorbidities

'Usual suspects' – hypertension, diabetes, CVD

But others – depression (11%), chronic pain (11%), COPD (14%) quite common



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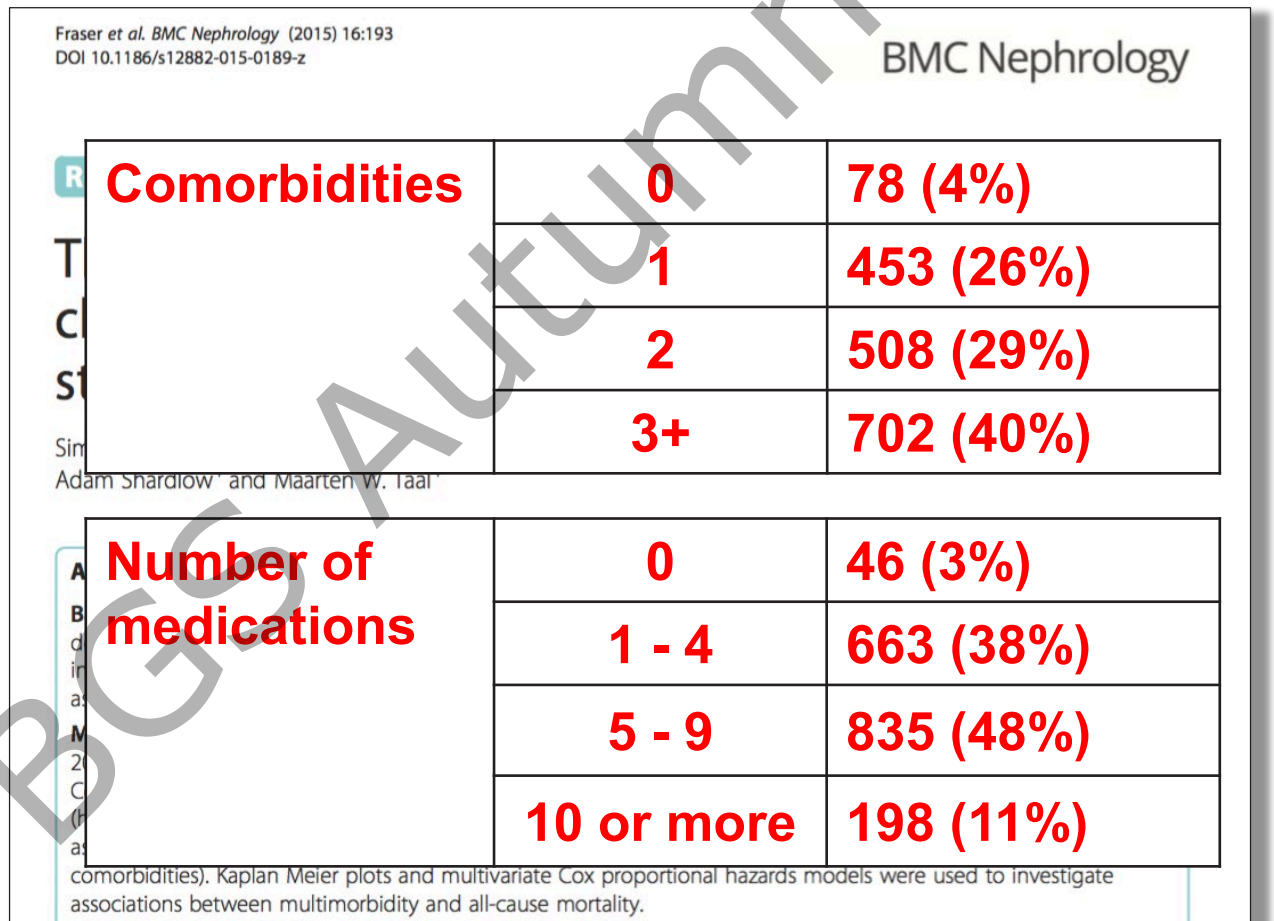
Tonelli M, Wiebe N, Guthrie B et al. Comorbidity as a driver of adverse outcomes in people with chronic kidney disease. Kidney Int. 2015;88(4):859-66

CKD and comorbidities

UK cohort of 1741 people with CKD stage 3 in primary care (mean age 73)



Fraser *et al. BMC Nephrology* (2015) 16:193
DOI 10.1186/s12882-015-0189-z

BMC Nephrology

Adam Shardlow and Maarten W. Taal

comorbidities). Kaplan Meier plots and multivariate Cox proportional hazards models were used to investigate associations between multimorbidity and all-cause mortality.

Comorbidities	**0**	**78 (4%)**
	1	**453 (26%)**
	2	**508 (29%)**
	3+	**702 (40%)**

Number of medications	**0**	**46 (3%)**
	1 - 4	**663 (38%)**
	5 - 9	**835 (48%)**
	10 or more	**198 (11%)**

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CKD and pain

Prevalence of pain in people with CKD stages 1- 4 is ~70%, with musculoskeletal most common (2 US studies)

Renal Risk in Derby study:

- ‘painful condition’ prevalence at baseline based on repeat analgesia prescribing ~30% - probably an under-estimate
- Pain/discomfort domain of EQ5D in year 5 survivors in this cohort ~70% (unpublished data) vs. ~60% in general population >65yrs (HSE)

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Davison SN, Koncicki H, Brennan F. Pain in chronic kidney disease: a scoping review. Semin Dial. 2014;27(2):188-204

Fraser SDS, Roderick PJ, May C, McIntyre N, McIntyre C, Fluck RJ, Shardlow A, Taal MW. The burden of comorbidity in people with chronic kidney disease stage 3: a cohort study. BMC Nephrology 2015, 16:193

Feng Y, Devlin N, Herdman M. Assessing the health of the general population in England: how do the three- and five-level versions of EQ-5D compare? Health Qual Life Outcomes 2015;13:171

CKD and depression

- 8 studies, stage 2 – 5 CKD
- Depression prevalence 21 – 47%

Renal Risk in Derby study:

- Anxiety / depression domain of EQ5D in year 5 survivors in this cohort ~32% (unpublished data) vs. 27% in over 65 year olds in the general population (Health Survey for England 2012 data).
- Age UK estimate of 22% men and 28% women >65 have depression

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Shirazian S, Grant CD, Aina O, Mattana J, Khorassani F, Ricardo AC. Depression in Chronic Kidney Disease and End-Stage Renal Disease: Similarities and Differences in Diagnosis, Epidemiology, and Management. Kidney Int Rep. 2017; 2(1): 94–107.

Feng Y, Devlin N, Herdman M. Assessing the health of the general population in England: how do the three- and five-level versions of EQ-5D compare? Health Qual Life Outcomes. 2015;13:171

Age UK, Later Life in the United Kingdom, February 2016

CKD and functional limitation

- CKD has adverse impact on Activities of Daily Living e.g. Korean cohort of 984 with varying degree of renal function followed for 5 years:
  - incidence of ADL/ instrumental activities of daily living (IADL) decline was 13%, 12.5% and 29.5% in participants who showed improvement, no change, and decline in renal function, respectively (p = 0.01)
- Alabama cohort over 2 years – similar findings
- Clinician-observed functional impairment

(Karnofsky score ≤70) ~23% (unpublished data)

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Bowling C, Sawyer P, Campbell R, Ahmed A, Allman RM. Impact of chronic kidney disease on activities of daily living in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2011;66(6):689-94.

Chin H, Ahn S, Ryu J, Kim S, Na KY, Kim KW, Chae DW, Kim CH, Kim KI.. Renal function and decline in functional capacity in older adults. Age Ageing 2014;43:833-8.

CKD and frailty

Frailty - ?more common among people with CKD than people with normal renal function

5808 adults in cross sectional US study. Prevalence of frailty 15% in people with CKD versus 6% in those without ($p < 0.001$)

After multivariate adjustment for comorbidity, CKD remained significantly associated with frailty
(odds ratio 1.76; 95%CI 1.28 to 2.41)

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Shlipak MG, Stehman-Breen C, Fried LF, Song X, Siscovick D, Fried LP, Psaty BM, Newman AB: The presence of frailty in elderly persons with chronic renal insufficiency. Am J Kidney Dis 43 : 861– 867, 2004

Advanced CKD and fatigue

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Prevalence of fatigue around 50% in people on dialysis (whether haemodialysis or peritoneal)

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Artom M, Moss-Morris R, Caskey F, Chilcot J. Fatigue in advanced kidney disease. Kidney International 2014; 86 (3): 497-505

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Public understanding of kidneys

In 2014, 2005 UK residents aged 15+ were surveyed, results were weighted for key demographic characteristics

- 51% knew that kidneys make urine (59% of graduates)
- 60% knew that the kidneys help remove waste
- 12% knew that kidneys have a role in processing medicines
- 1% thought that smoking endangers kidney health
- >60% thought alcohol endangers kidney health

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Slevin J, Taylor A. Understanding what the public know about their kidneys and what they do. Findings from Ipsos MORI survey 2014. Think Kidneys programme 2015.

The University of Nottingham

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Awareness of CKD diagnosis

Renal Risk in Derby study:

- 41% were unaware of their CKD diagnosis
- higher educational qualifications
- younger age
- lower eGFR
- significant albuminuria

} more likely to be aware of their diagnosis

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McIntyre NJ, Fluck R, McIntyre C, Taal M. Treatment needs and diagnosis awareness in primary care patients with chronic kidney disease. Br J Gen Pract. 2012;62(597):e227-32

Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- a challenging diagnosis
  - feeling well and asymptomatic when first diagnosed
  - feelings of shock and incomprehension about the diagnosis
  - uncertainty about CKD permanence

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Teasdale E, Leydon G, Fraser SD, Roderick PJ, Taal MW, Tonkin-Crine S. Patients' Experiences after CKD Diagnosis: A Meta-ethnographic Study and Systematic Review. American Journal of Kidney Diseases 2017;70(5):656-665.

Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- diverse beliefs about causation
  - believing CKD was a result of their own actions e.g. poor eating habits and alcohol or long-term medication use.
  - others attributed CKD to external factors such as heredity or as the result of having other conditions such as diabetes

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Teasdale E, Leydon G, Fraser SD, Roderick PJ, Taal MW, Tonkin-Crine S. Patients' Experiences after CKD Diagnosis: A Meta-ethnographic Study and Systematic Review. American Journal of Kidney Diseases 2017;70(5):656-665.

Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- anticipated concerns about progression
  - concerns about future treatment
  - anticipated social and financial burden
  - being unable to continue working and/or inability to care for significant others

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Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- delaying disease progression
  - making adjustments to daily life to try and delay disease progression e.g. lifestyle changes

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Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- unmet informational needs
  - common viewpoint: participants believed they had received insufficient information about CKD and its progression from health professionals.
  - some perceived this as a deliberate attempt to withhold information

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Teasdale E, Leydon G, Fraser SD, Roderick PJ, Taal MW, Tonkin-Crine S. Patients' Experiences after CKD Diagnosis: A Meta-ethnographic Study and Systematic Review. American Journal of Kidney Diseases 2017;70(5):656-665.

Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- psychosocial impact
  - loss of freedom / restricted choices (esp CKD 5) due to treatment regimens, fatigue, dietary restrictions and/or dependence on others

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Living with CKD – what patients tell us

Systematic review and meta-ethnography of 10 qualitative studies involving 596 patients with CKD identified 7 themes:

- adjustment to life with CKD
  - greater involvement with decision making
  - importance of community/social support
  - trying to live life to the full, 'carry on as normal', be positive

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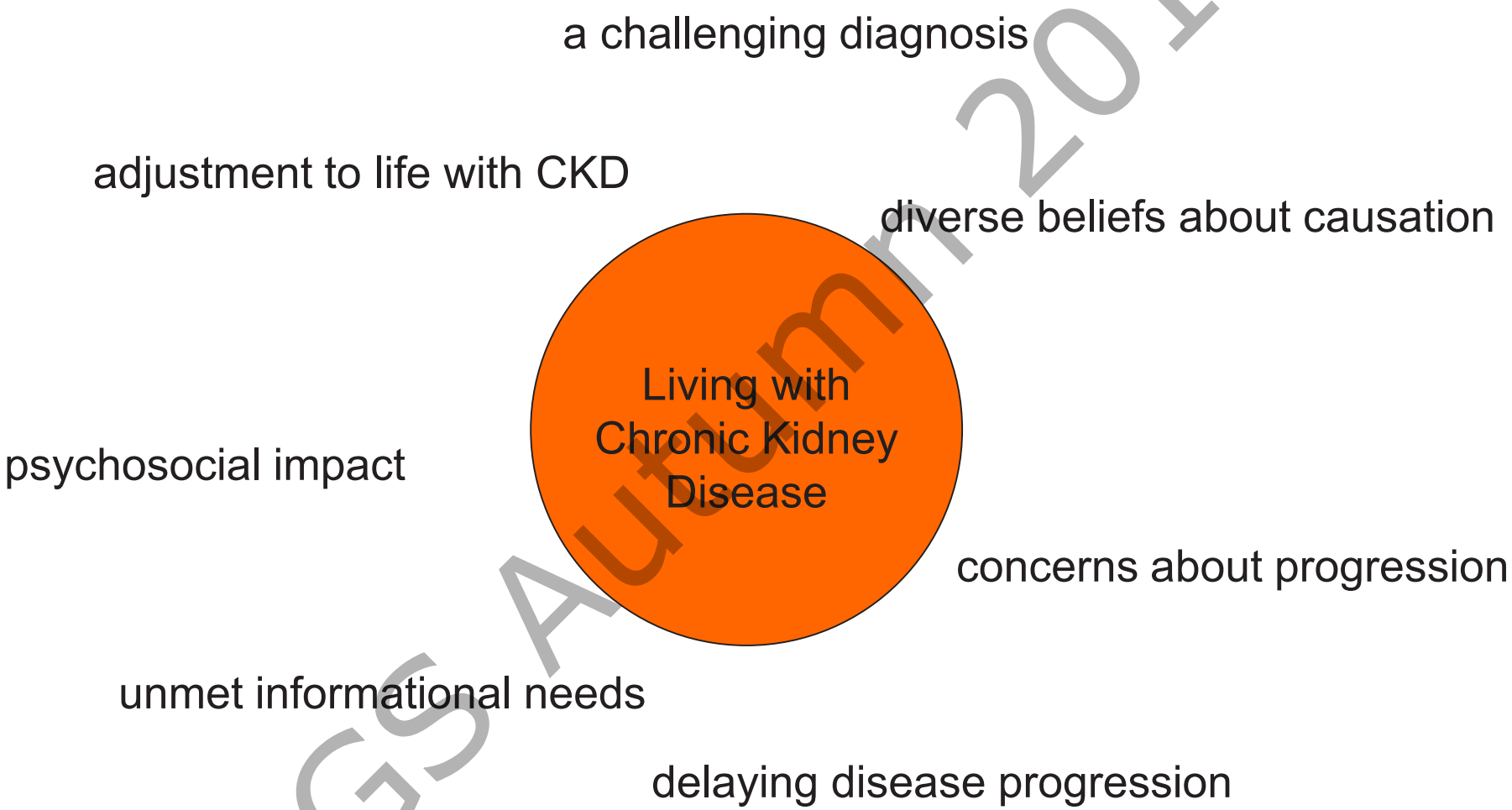
Teasdale E, Leydon G, Fraser SD, Roderick PJ, Taal MW, Tonkin-Crine S. Patients' Experiences after CKD Diagnosis: A Meta-ethnographic Study and Systematic Review. American Journal of Kidney Diseases 2017;70(5):656-665.



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Emerging themes on treatment burden in pre-dialysis CKD…

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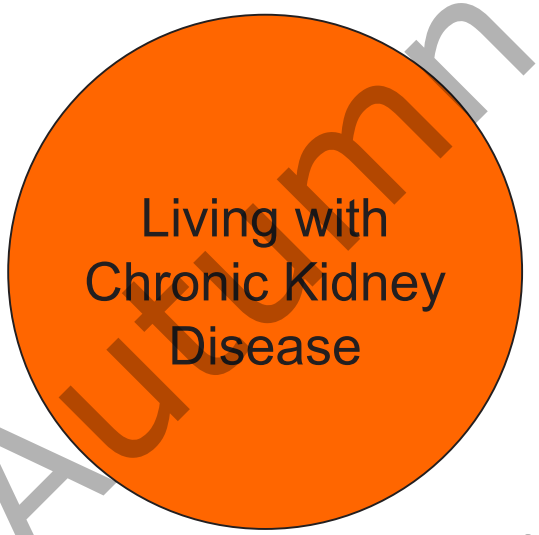
‘workload’ – medications, tests, appointments, parking

medication issues – renal function complicating,

understanding the purpose of meds



practical aspects -

e.g. when and how to seek advice,

getting results

symptoms – e.g. fatigue, mobility

‘complexity’ – loss of continuity, conflicting advice, care coordination

concerns about progression

finance

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Kidney Care UK

BRS British Renal Society Multi-professional working

Quality of life

- Quality of life tends to be poorer for people with CKD (not on dialysis) than their general population peers
- Quality of life scores tend to decline with decreasing renal function

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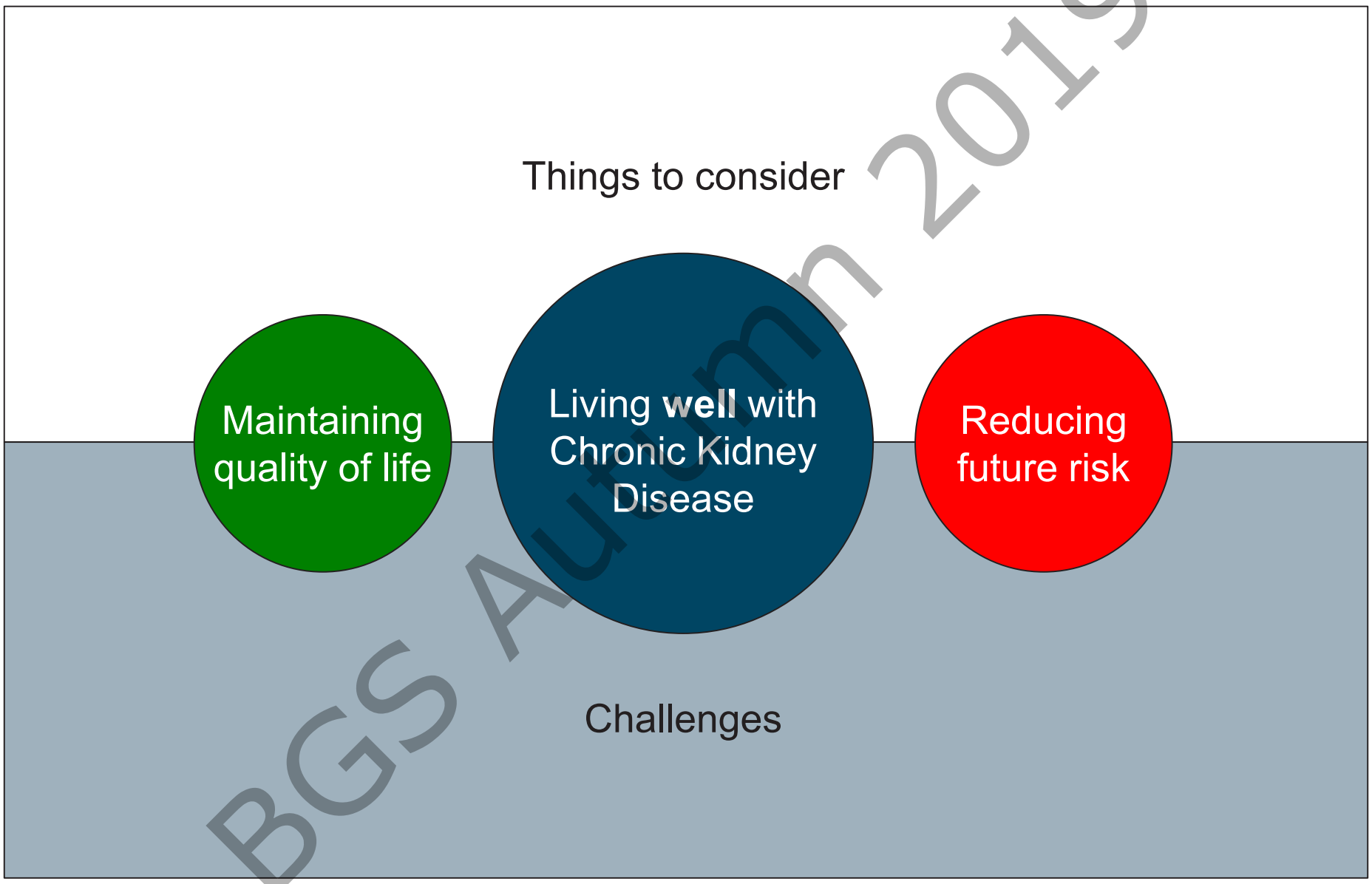
Mujais SK, Story K, Brouillette J, Takano T, Soroka S, Franek C, Mendelssohn D, Finkelstein FO. Health-related quality of life in CKD patients: Correlates and evolution over time. Clin J Am Soc Nephrol 2009; 4: 1293–1301

Perlman RL, Finkelstein FO, Liu L, Roys E, Kiser M, Eisele G, Burrows-Hudson S, Messana JM, Levin N, Rajagopalan S, Port FK, Wolfe RA, Saran R. Quality of life in chronic kidney disease (CKD): A cross-sectional analysis in the Renal Research Institute-CKD study. Am J Kidney Dis 2005; 45: 658–666



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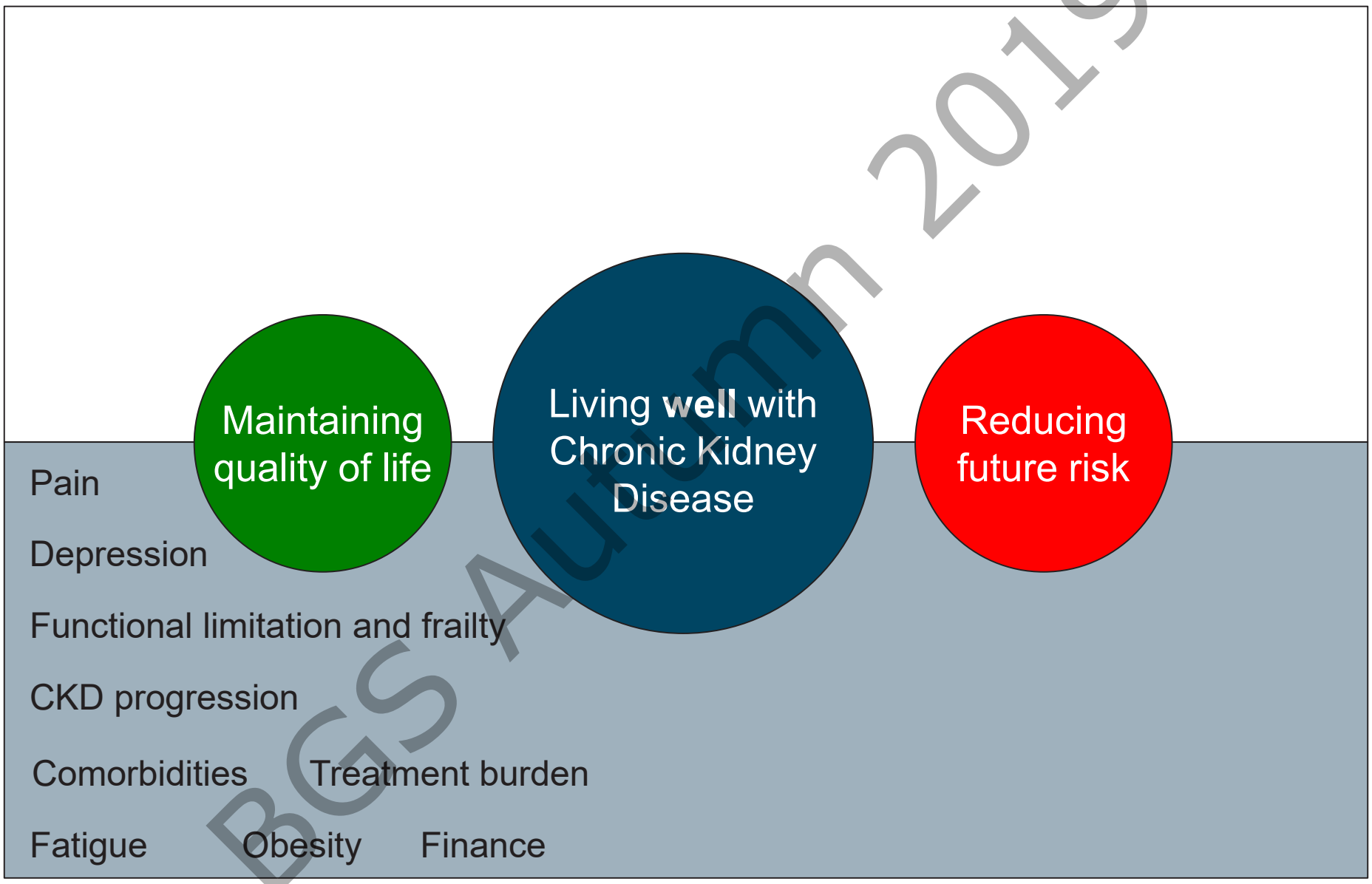

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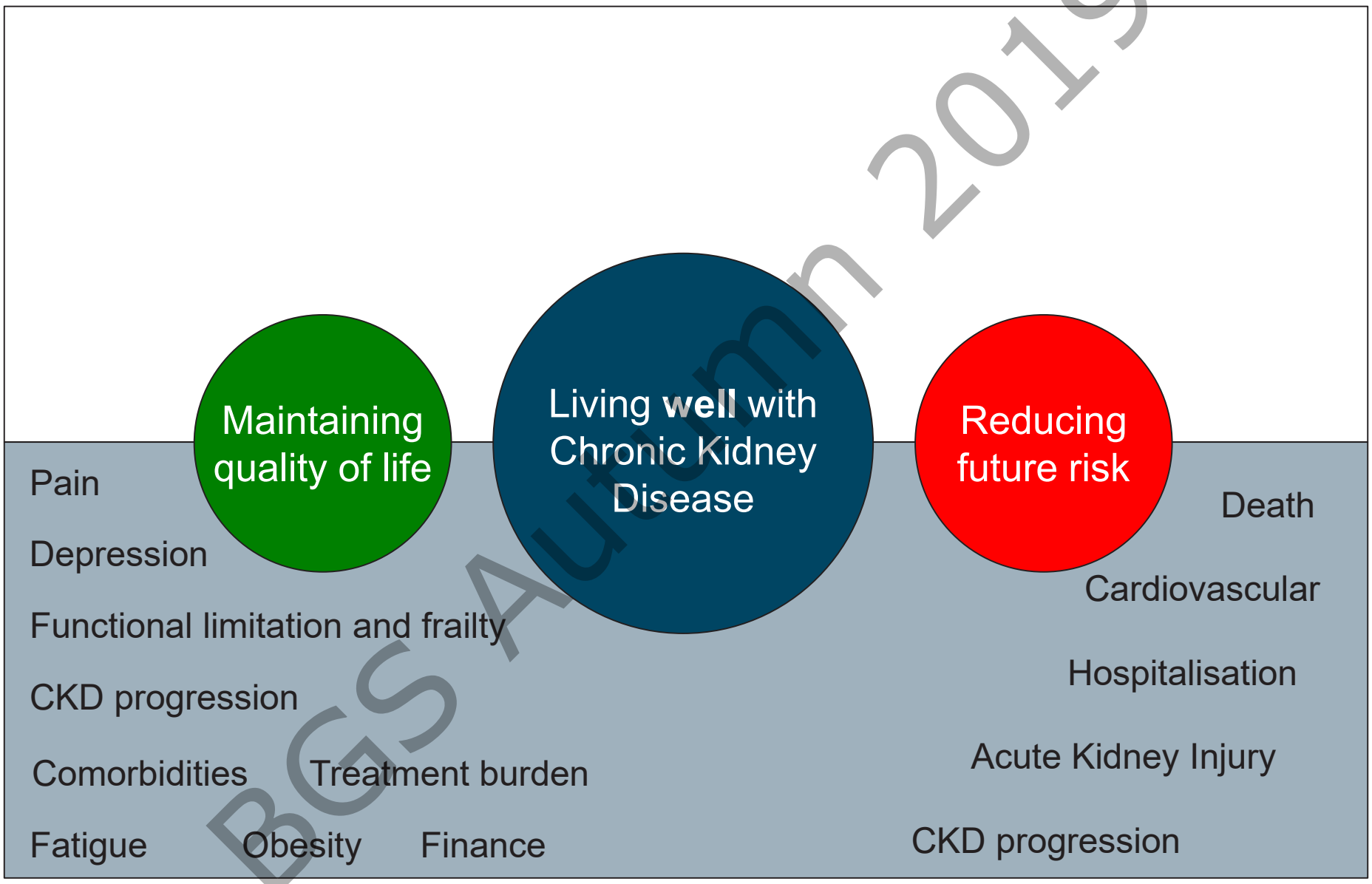

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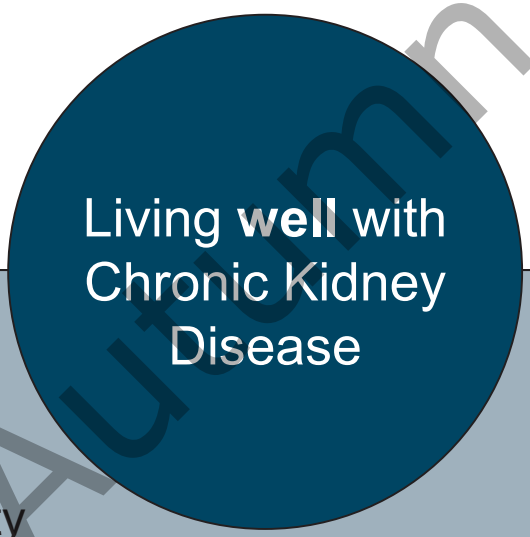
So what can we do?



Pain

Depression

Functional limitation and frailty

CKD progression

Comorbidities

Treatment burden

Fatigue

Obesity

Finance

Death

Cardiovascular

Hospitalisation

Acute Kidney Injury

CKD progression

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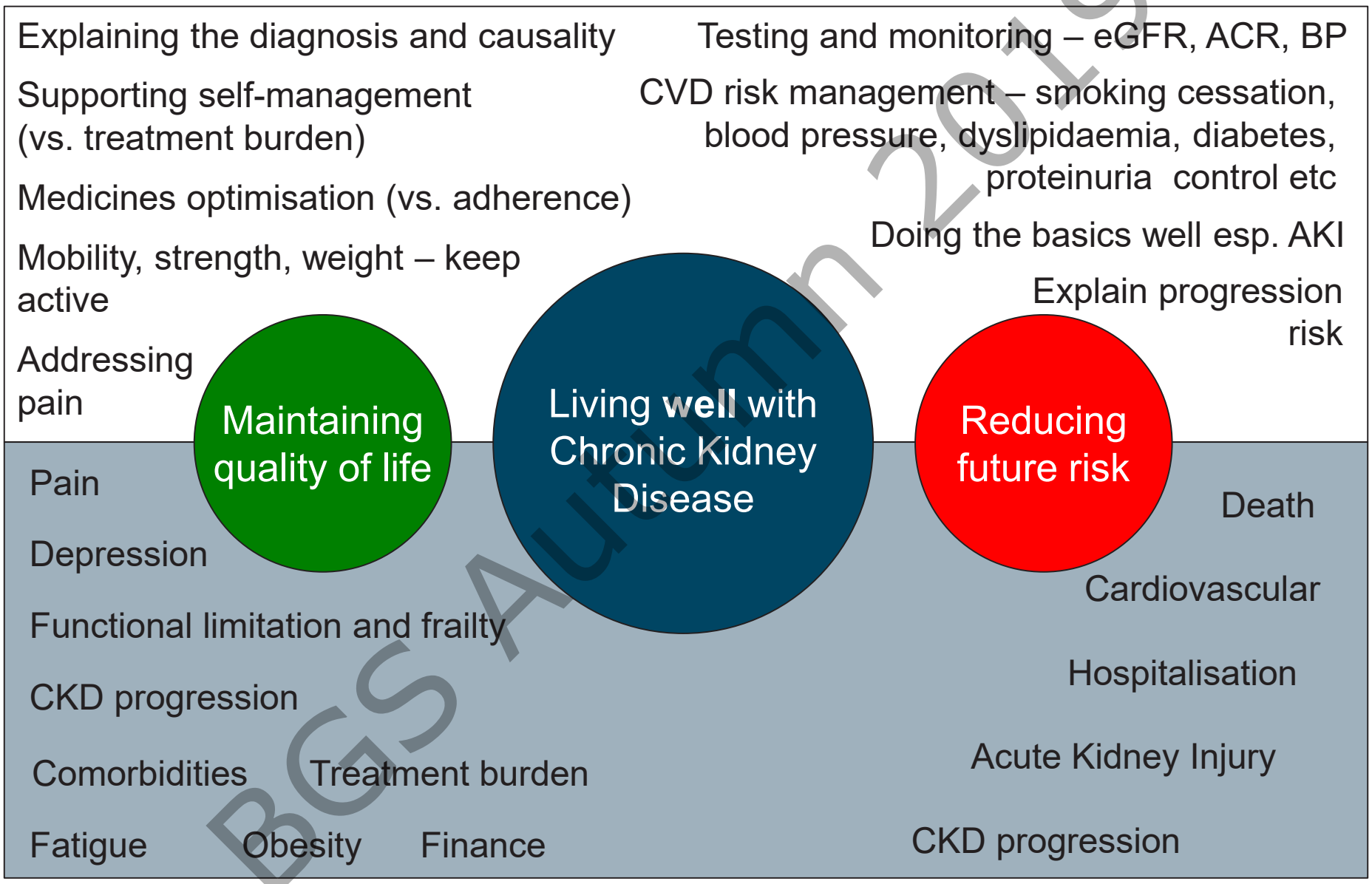

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CKD – key risk management issues

- Albuminuria testing
- Blood pressure management
- Checking CKD diagnosis and stage

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Proposed management pathway for older patients with advanced CKD.

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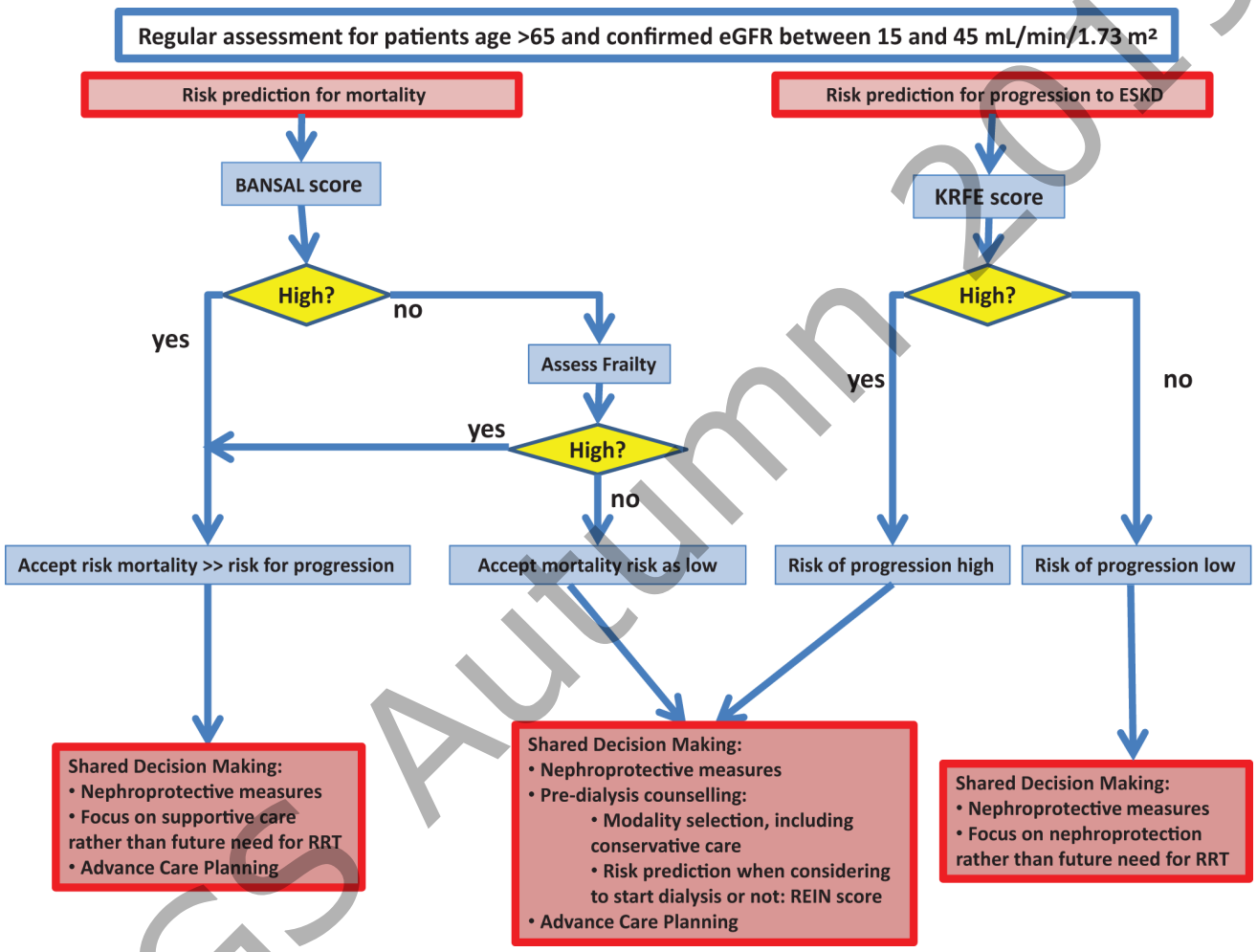

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Farrington K, Covic A, Nistor I et al. Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR<45 mL/min/1.73 m2): a summary document from the European Renal Best Practice Group. Nephrol Dial Transplant. 2017; 1;32(1):9-16.

Tangri NStevens LAGriffith J et al. A predictive model for progression of chronic kidney disease to kidney failure. JAMA 2011; 305: 1553–1559

Bansal NKatz RDe Boer IH et al. Development and validation of a model to predict 5-year risk of death without ESRD among older adults with CKD. Clin J Am Soc Nephrol 2015; 10: 363–371

Couchoud CGBeuscart JBAldigier JC et al. Development of a risk stratification algorithm to improve patient-centered care and decision making for incident elderly patients with end-stage renal disease. Kidney Int 2015; 88: 1178–1186

CKD – key quality of life issues

- Addressing pain safely
- Burden of treatment vs medicines optimisation
- Clarity in Communicating diagnosis and prognosis

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Pain management in CKD

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Helpful stepwise approach in this review

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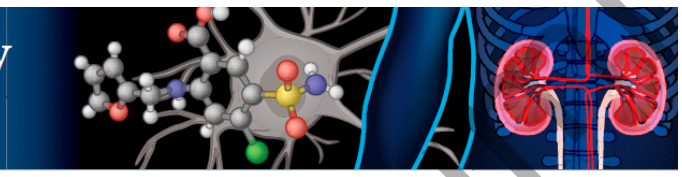
Nephropharmacology for the Clinician



Clinical Pharmacology Considerations in Pain Management in Patients with Advanced Kidney Failure

Sara N. Davison

Abstract

Pain is common and poorly managed in patients with advanced CKD, likely due to both under and over prescription of appropriate analgesics. Poorly managed pain contributes to patients' poor quality of life and excessive health care use. There is tremendous variability within and between countries in prescribing patterns of analgesics, suggesting that factors other than patient characteristics account for these differences. This article discusses the pharmacologic management of acute and chronic pain in patients with advanced CKD, and the role analgesics, including opioids, play in the overall approach to pain management.

CJASN 14: 917–931, 2019. doi: https://doi.org/10.2215/CJN.05180418

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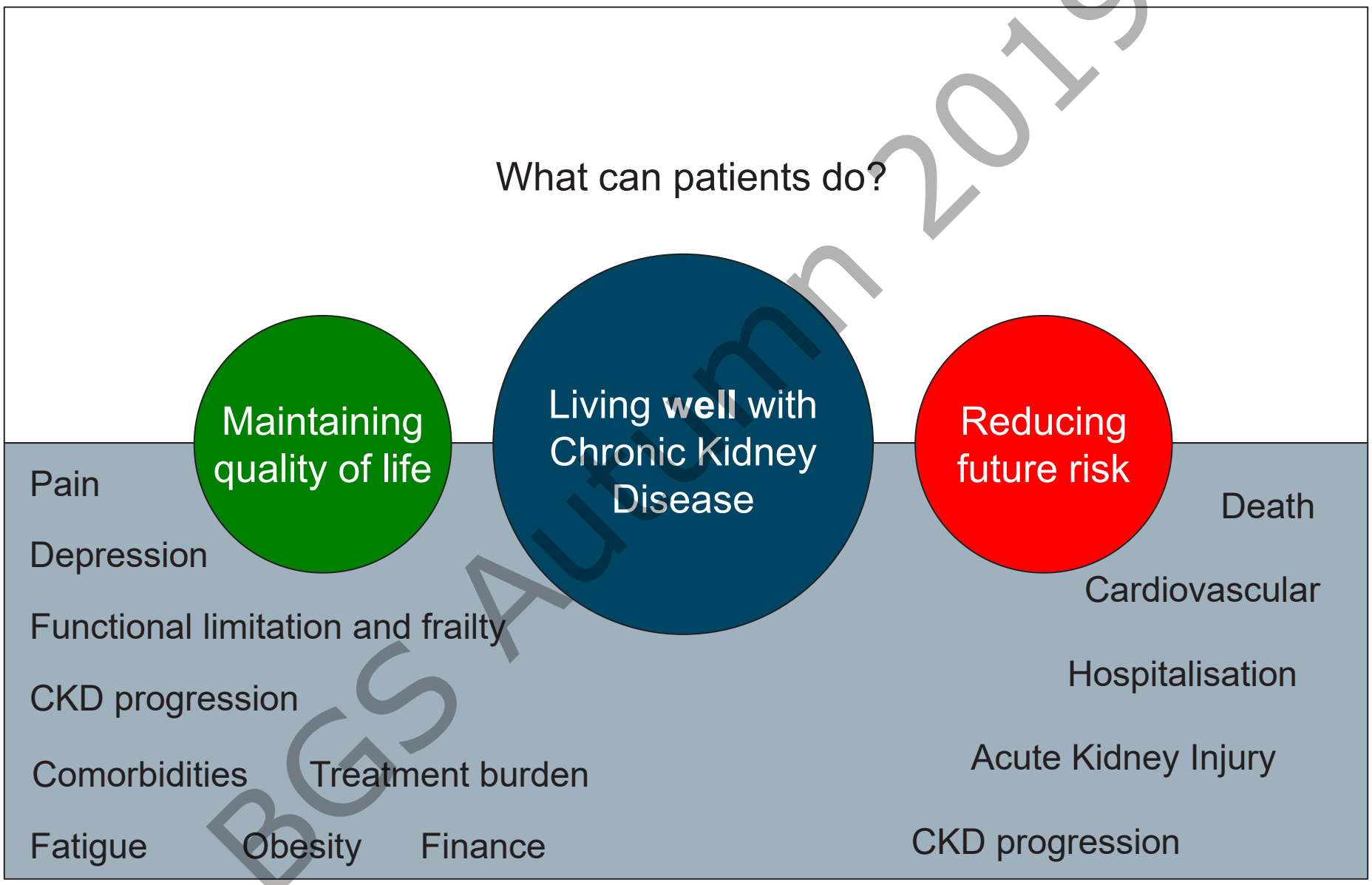
Introduction

Pain is common in patients with advanced CKD. Over 58% of patients experience pain and approximately 49% of patients report moderate or severe pain, whether they are treated with dialysis or managed conservatively (1). It is widely recognized that pain, in particular chronic pain, is associated with psychologic distress; depressive disorders; limitations in work, family, and social life; decreased life satisfaction and quality of life (QOL); and increased hospitalizations and emergency department visits (2–5). For patients receiving hemodialysis (HD), with advanced CKD, including patients with ESKD treated with dialysis or conservative kidney management. The role analgesics play in the overall approach to pain management will be discussed, with the understanding that analgesics should not be the sole focus of treatment and should only be used when needed, in conjunction with other treatment modalities, to meet patient-specific treatment goals.

Key Considerations in the Evaluation of Pain to Guide Pharmacologic Management

Davison SN. Clinical Pharmacology Considerations in Pain Management in Patients with Advanced Kidney Failure. Clin J Am Soc Nephrol. 2019;14(6):917-931.

What can patients do?



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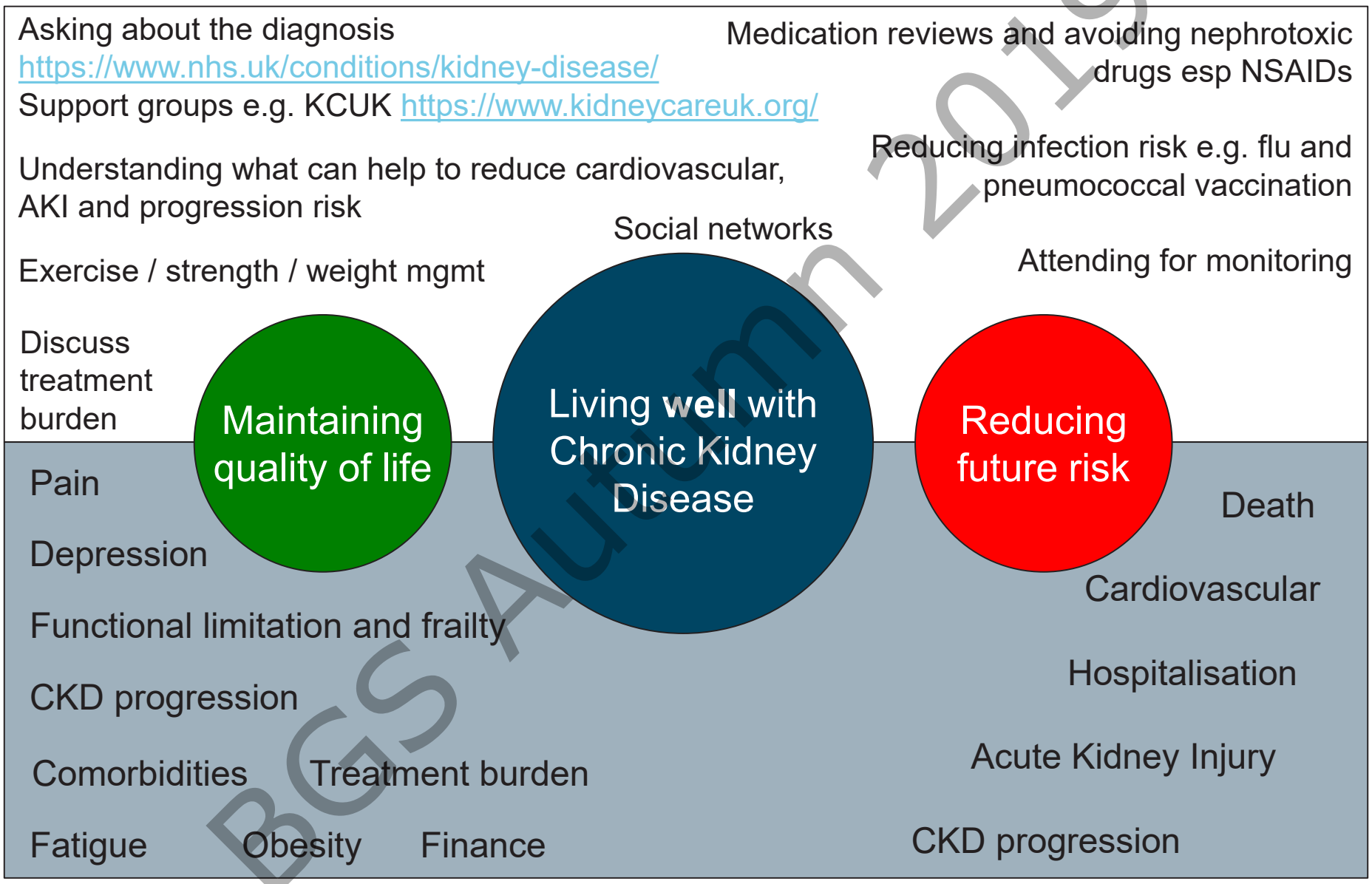

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Thank you

Dr Simon Fraser
Associate Professor of Public Health

British Geriatrics Society Autumn Meeting
November 2019

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