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Review article

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Mental health and kidney disease

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Abstract

Multiple long-term conditions, and particularly mental health conditions, are common in adults with chronic kidney disease (CKD). Some mental health conditions increase the risk of developing CKD, contribute to faster disease progression, and complicate care experiences and outcomes. Depression and anxiety are particularly prevalent and are associated with reduced quality of life, unplanned service use and poorer clinical outcomes. The manner in which depression and anxiety are detected and managed as part of routine kidney care can vary widely. Evidence for effective and acceptable treatments is mixed overall, although meta-analyses highlight the benefits of physical activity and cognitive behavioural therapy. Data on the use of antidepressants in people with CKD are also variable, limited by the lack of robust clinical trials. People with particularly complex needs, such as those with severe mental illness and CKD, have markedly shorter lifespans and higher rates of emergency hospitalizations than those without severe mental illness and are also less likely to access specialist nephrology care and to receive a transplantation. Health inequalities are amplified for those contending with wider disadvantages related to social and structural determinants of health. Reducing the burden of mental health in people with CKD is an urgent priority to alleviate personal and health system impacts. Here, we examine current evidence on mental health and CKD to inform policy and research and to support advances in prevention and management approaches.

Sections

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Key points

- People with kidney disease are at higher risk of developing mental health issues. Pre-existing mental health conditions can also worsen the progression and outcomes of kidney disease. The co-occurrence of mental health issues in this context is linked to increased morbidity and mortality.
- Worse outcomes are more likely in patient populations experiencing a greater burden of social and structural determinants of health, who are often also underserved by research. These include disadvantages related to factors such as deprivation, ethnicity, gender, disability and their intersection.
- Kidney health care should be person-centred and inclusive across a spectrum of mental health needs, including severe mental illness. Care should be focused on advancing mental health prevention programmes in populations with chronic kidney disease who are at high risk, with support for adherence and reduced treatment burden, and optimizing overall management to reduce negative impacts.
- Mental health issues are known to compromise kidney care outcomes, but little is known about effective interventions. More high-quality randomized controlled trials and pragmatic real-world studies are needed to establish effective approaches for the management of depression and anxiety in people with kidney disease.
- Currently, kidney and mental health care is fragmented. Health service delivery models that integrate parity in physical and mental health will be beneficial in helping people with kidney disease to live well and in improving overall patient outcomes.

Introduction

The field of psychonephrology has traditionally focused on the interplay between psychiatry, psychosomatic medicine and nephrology[1,2]. Its initial focus on mental health has expanded to include related areas in health psychology and behavioural medicine, including symptom burden[3] (for example, fatigue[4–6]), treatment non-adherence and behaviour change[7,8], and treatment decision-making[9].

Across the kidney care pathway, depression and anxiety are common[10,11] and are associated with adverse outcomes and events[12,13]. Furthermore, mental health conditions, including depression, bipolar disorder and schizophrenia, increase the risk of developing chronic kidney disease (CKD) as well as accelerating the trajectory of disease progression, contributing to poorer clinical outcomes[14,15]. Although the interplay between mental health and CKD is complex, research consistently demonstrates that social, structural and wider determinants of health shape risk, engagement with prevention and early detection, access to care, and outcomes[15]. Yet, evidence to guide effective prevention and management approaches is limited, particularly in relation to addressing the needs and treatment preferences of those traditionally underserved by research.

In this Review, we provide a narrative synthesis of evidence regarding the co-occurrence of CKD and mental health issues, with the broad aim of informing future priorities for disease prevention and integrated models of management. The topic of mental health and CKD is multifaceted, impacting patients across the spectrum of symptom severity. It is beyond the scope of a single review to comprehensively address all aspects. Here, we focus on common mental health conditions, such as depression and anxiety, and some less common severe mental illnesses (SMIs). We acknowledge the significance of neuropsychiatric, neurodevelopmental and neurological conditions associated with CKD, particularly those on the interface between specialities (for example, sleep disorders and dementia); these have been the focus of other specific reviews[16–18]. By prioritizing depression, anxiety and SMI, we address the most substantial and widespread mental health challenges faced by people across the spectrum of CKD, particularly in its advanced stages. First, we will provide a brief overview of mental health and kidney disease through a biopsychosocial perspective. We then summarize evidence regarding the impact of these conditions on clinical outcomes, and the acceptability and efficacy of pharmacological and non-pharmacological interventions. By bringing this body of evidence together, clear recommendations for future research emerge as a lever to influence policy and practice. Examples include addressing mechanisms of prevention and early detection as well as integrated, scalable models of holistic care.

Mental health and CKD: a biopsychosocial perspective

The interplay between mental health and CKD can be understood from a biopsychosocial perspective[19,20]. This approach provides a comprehensive lens through which to view health and illness as arising from the interaction of biological, psychological and social processes. The biopsychological model therefore calls for integrated care[21]. CKD has profound psychological and social implications that are risk factors for worse mental health, greater disease progression and poorer self-management[22,23]. People with CKD experience many challenges related to multiple factors, including the underlying effects of kidney disease, such as uraemia, inflammation and malnutrition, trauma and stigma associated with diagnosis, burden of treatments and side effects (for example, dialysis and multiple medications), and increased multiple long-term conditions, as well as decreased cognitive, physical and social functioning.

Psychological and behavioural factors associated with mental health outcomes in CKD include personality, cognitive appraisal and coping mechanisms[20], illness and treatment perceptions[24–27], body mindsets[28], and health-related behaviours[29]. Psychological factors are often conceptualized within the biopsychosocial model as a cognitive and behavioural framework of the interplay between thoughts and behaviours in relation to biological and social factors[3] (Fig. 1). Such an approach is also applied to understanding the exacerbation and perpetuation of persistent symptoms, including fatigue[4,30]. Importantly, evidence across many settings emphasizes the consistency with which psychological mechanisms contribute to physical health experience, although culture shapes underpinning mechanisms[31,32].

Social factors, such as problematic relationships and lack of support, social and economic oppression, and structural discrimination, further exacerbate mental health challenges and increase health disparities, even in settings with universal access to care services[20,33–36]. As we elaborate later, despite widespread recognition of how context shapes opportunity for good physical and mental health, most kidney research has systematically failed to include and respond to the needs of those who carry a greater risk of physical, mental and combined morbidity. CKD and poor mental health, for example, are individually more prevalent amongst racially minoritized communities, as well as those living in deprivation, with low education levels, or impacted

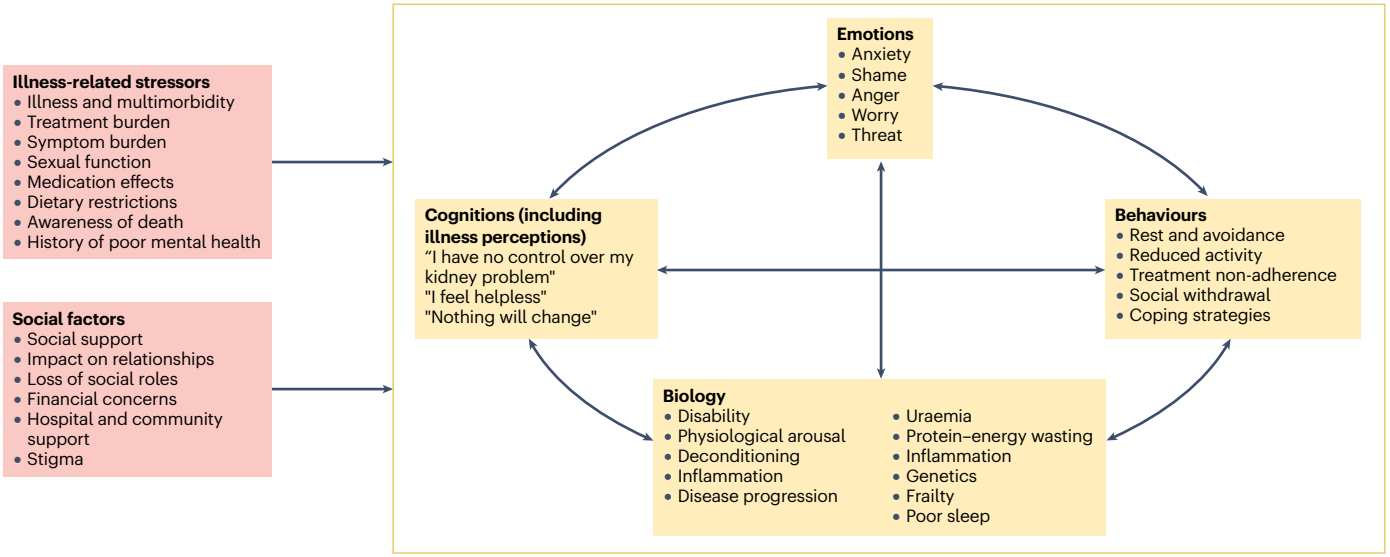

Fig. 1 | A biopsychosocial model of psychological distress in advanced kidney disease. This figure illustrates a biopsychosocial model describing the development and maintenance of psychological distress in people living with chronic kidney disease. Illness-related stressors, including multimorbidity, treatment and symptom burdens, interact with prior mental health history to shape maladaptive cognitions such as perceived lack of control, helplessness and hopelessness. These cognitions give rise to emotional responses, including anxiety, shame, anger, worry and perceived threat, which in turn influence behavioural responses such as rest and avoidance, reduced activity, treatment non-adherence and social withdrawal. Behavioural changes are linked to biological processes, including physiological arousal, deconditioning, inflammation, poor sleep, frailty and disease progression, which may further exacerbate distress. Social factors, such as reduced social support, stigma, financial concerns and limitations in hospital or community support, interact with all the components of the model. Arrows indicate dynamic, bidirectional relationships, highlighting self-reinforcing cycles that sustain psychological distress over time.

by the urban–rural divide[37]. Research examining these complex interactions is sparse.

The biopsychosocial approach to mental health in CKD offers a useful tool to foreground the importance of psychosocial factors in person-centred care, which considers the values, beliefs and preferences of patients through an alliance between patients and health-care professionals[38]. Incorporating person-centredness into a biopsychosocial framework moves researchers and health-care providers beyond the organic pathology of disease to factors that help understand the person so that care is responsive to context, enhances treatment adherence and self-management, reduces emotional distress, and improves quality of life overall[39].

Depression and anxiety in CKD

Definitions and assessment

Major depressive disorder (MDD; sometimes referred to as clinical depression) is a mood disorder classified in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)[40]. The diagnosis of MDD is based on the presence of current or recurrent major depressive episodes. A major depressive episode is defined by the presence of five or more symptoms that persist most of the day, every day, for at least 2 weeks, and that represent a change from previous functioning. The primary symptoms should be depressed mood or loss of pleasure or interest (anhedonia). Additional symptoms might include feelings of guilt or worthlessness, fatigue (or loss of energy), changes to appetite or weight, sleep problems, psychomotor difficulties or agitation, concentration difficulties, and suicidality. The assessment of depression and anxiety in CKD is complicated by overlapping somatic symptoms associated with uraemia (such as fatigue and concentration difficulties)[41,42], with self-reported assessments likely to provide greater false positive cases than diagnostic methods of evaluation[10]. Further, although MDD is a global public health concern, symptom expression is culturally framed[43], which complicates assessment in diverse patient populations[44].

Anxiety refers to experiencing apprehension, worry, fear and uncertainty when anticipating a situation perceived to be threatening. DSM-5 criteria for Generalized Anxiety Disorder include experiencing heightened anxiety and worry about events or activities, occurring more days than not, for at least 6 months, in which the individual finds the worry difficult to control[40,45]. In addition, anxiety and worry are associated with at least three of the following symptoms: restlessness, fatigue, concentration difficulties, irritability, muscle tension and disturbed sleep.

Within research and routine clinical contexts, depression and anxiety symptoms are typically evaluated through self-report screening questionnaires[46–48], including ultra brief instruments, which might be suited to assessments in busy clinical settings[49,50]. The measures most commonly used in studies of people with CKD include, for depression, the Beck Depression Inventory-II (BDI-II)[51], the Patient Health Questionnaire-9 (PHQ-9)[52,53], and the Hospital and Anxiety Depression Scale (HADS)[54], and for anxiety, the Generalized Anxiety Disorder Questionnaire (GAD-7)[55]. Composite measures of depression and anxiety include the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS)[56,57], which measures symptoms of depression and anxiety using the combined scores from the PHQ-9 and GAD-7. Measure-specific symptom cut-off scores are used to indicate

severity (for example, a PHQ-9 score of ≥10); however, these metrics are insufficient for a clinical diagnosis, which requires structured or semi-structured clinical assessment. Evidence regarding the extent to which such tools reliably serve the needs of communities with diverse cultural backgrounds is also mixed[58] and warrants further research to ensure equitable implementation of screening practices. Another commonly used instrument is the distress thermometer[59], which measures psychological distress — a multidimensional term that refers to emotional suffering, including anxiety and depression, as well as other negative emotional and physical states such as stress or panic. Psychological distress itself is not a formal diagnosis but can be an important indicator of the mental health of an individual and might contribute to a clinical diagnosis.

Prevalence of depression and anxiety in CKD

Depression and anxiety are commonly experienced by people with CKD, and often occur concurrently[13]. Prevalence estimates vary, depending on the assessment methods used (diagnostic assessment versus self-reported questionnaires), the stage of kidney disease, the modality of kidney replacement therapy (KRT), and the size and representativeness of the sample population. Data from meta-analyses suggest that ~22–39% and ~19–43% of people with CKD experience depression and anxiety, respectively[10,11]. An analysis conducted in 2024 reported the prevalence of clinical depression to be 26.5%, with estimates significantly higher among people receiving haemodialysis compared with those in pre-dialysis stages (29.9% versus 18.5%, respectively)[60]. Depression was also more prevalent in those receiving haemodialysis compared with those treated with peritoneal dialysis (30.6% versus 20.4%)[60]. Despite the commonality of symptoms, variability exists in how depression and anxiety are identified and treated as part of routine kidney care[46,47]. Longitudinal data showing how symptoms of depression and anxiety change with time are also lacking. Past studies of incident haemodialysis showed that >20% of patients start dialysis experiencing moderate symptoms of depression that worsen with time[24]. A larger study of people with mild-to-moderate CKD found depression symptoms to be mostly stable over time, with approximately a third having persistently moderate depressive symptoms, and just under 10% having persistently high depressive symptoms[61]. Despite prospective studies showing the relative stability of depressive symptoms over time, a study conducted in 2024 that used Ecological Momentary Assessments to investigate symptom burden in people receiving haemodialysis reported diurnal and daily symptom variation. Symptom burden, including experiencing negative mood, was greater on haemodialysis treatment days than on non-haemodialysis days[62].

The impact of depression and anxiety on CKD outcomes

Depression and anxiety negatively impact quality of life[63,64] and are associated with worse clinical outcomes across the kidney care pathway, including faster progression of CKD[65], increased hospitalization[13,66], higher all-cause mortality[12,67,68] and increased risk of graft failure in transplant recipients[69]. The Stockholm CREAtinine Measurements (SCREAM) project found that, in >157,000 people with CKD stages 3–5, depression was associated with a 38% increased risk of disease progression[70]. Moreover, depression increased the risk of major adverse cardiovascular events and all-cause mortality by 22% and 41%, respectively[70]. Depression also represents a risk factor for the development of CKD with national data from China showing a 38% increased risk of CKD in people with depression[71]. Moreover, CKD subsequently increased the risk of incident depression by nearly 50%[71]. These findings suggest that the relationship between depression and CKD outcomes is bidirectional[72].

The mechanisms through which depression and CKD influence each other are complex and likely involve a variety of biopsychosocial pathways. Biological processes include inflammatory pathways and malnutrition[33,73]. A meta-analysis (>9,000 patients with CKD) conducted in 2023 found a significant association between higher levels of pro-inflammatory biomarkers (C-reactive protein, IL-6 and tumour necrosis factor) and the presence of depressive symptoms[74]. Moreover, people with depressive symptoms had significantly lower levels of the anti-inflammatory cytokine IL-10 than those without[74]. A large Mendelian randomization analysis using both summary level and allele-score-based data provided evidence for a potential causal relationship between psychological well-being and kidney function[75]. The findings suggested that a genetic predisposition to positive aspects of well-being is associated with a reduced risk of kidney dysfunction. Conversely, genetically predicted negative psychological states were linked to an increased risk of CKD and lower estimated glomerular filtration rate[75]. Behavioural pathways include factors such as treatment non-adherence[76]. Both anxiety and depressive symptoms are associated with poorer dietary adherence and medication adherence in people with CKD[77]. Depression is also associated with poorer medication adherence in transplant recipients and in people receiving haemodialysis[78]. Social and structural factors have also been implicated in shaping the conditions through which mental health interferes with physical health outcomes in CKD[36], although research applying an intersectional lens is generally lacking. This oversight fails to recognize the dynamics of disease, where disadvantage accumulates over the life course through multiple converging mechanisms[79]. These pathways and processes are important to understand, whereby the biopsychosocial model offers a framework, rather than causal mechanisms to understand and intervene, to disrupt the physical–mental co-occurrence[80].

Suicide and CKD

People with CKD are significantly more likely to die by suicide compared with the general population. Suicidal ideation (that is, thoughts or ruminations about death by suicide) increases proportionally with kidney function decline[81]. A self-report Irish study published in 2023 found that one in four people with CKD had experienced suicidal ideation, and 9.3% had attempted suicide[82]. Of those who had received a mental health diagnosis, 16.1% reported previously attempting suicide. A large case–control study from Taiwan found that CKD was associated with a 25% increase in the risk of suicide compared with controls[83]. Patients receiving haemodialysis had a threefold increase in risk, which was dramatically higher in those who had started haemodialysis within the past 3 months[83]. This finding likely reflects the unique burden of hospital-based haemodialysis compared with other types of KRT. Data from the USA revealed a suicide standardized incidence ratio of 1.84 in people with kidney failure receiving dialysis[84]. Risk factors for suicide included being male or aged 75 years or older, having an alcohol or drug dependency, being white or Asian ethnicity, or a recent hospital admission due to mental illness[84]. People with kidney disease and mental health issues are more likely to die by suicide than those with kidney disease alone or those with kidney disease and cardiovascular complications. Further, females, individuals with Black heritage and those living in certain geographic localities have a greater risk of suicide than demographically matched members of the general population[85], highlighting the need for attention to predisposing factors.

Non-pharmacological management

Growing evidence supports the benefits of non-pharmacological approaches for the management of depression in kidney disease, including moderate-certainty evidence for cognitive behavioural therapy (CBT) and exercise in people receiving dialysis[86]. CBT focuses on identifying and changing unhelpful patterns of thinking and behaviour that contribute to psychological distress by showing how thoughts, emotions and actions connect. CBT approaches often include behavioural activation, which focuses on engaging in meaningful activities to improve mood.

In the context of kidney disease, trials of CBT for depression have predominantly been conducted in people receiving haemodialysis[87–90]. A meta-analysis of randomized controlled trials (RCTs) of CBT in people receiving haemodialysis reported significant improvements in depression (standardized mean difference (SMD) −0.68), anxiety (SMD −0.99) and quality of life (SMD 0.34)[91]. A RCT conducted in 2024 of a therapist-supported CBT digital intervention (COMPASS) in people living with long-term physical health conditions, including kidney disease, showed a significant reduction in psychological distress at 12 weeks post treatment[92]. At follow-up, 88.7% of participants in the COMPASS intervention group reported a clinically significant change in their distress compared with 45.1% in the treatment-as-usual group (standard charity support). CBT, and psychological approaches that include CBT techniques, can also improve treatment adherence in people receiving haemodialysis[88,93,94].

Digital resources can have a pivotal role in facilitating physical activity for individuals with CKD[95,96]. Digital platforms can offer personalized exercise programmes, tailored to a person's health status, fitness level and specific needs, making it easier to incorporate physical activity safely and effectively. Moreover, delivery of these resources does not require high involvement of a specialized workforce. Physical activity can reduce symptoms of depression and anxiety across clinical conditions, including in people with CKD[74]. Given the low physical activity levels and high prevalence of depression and anxiety in kidney disease populations, the potential for improvements from physical activity interventions is high[97].

Kidney BEAM was a multicentre trial conducted in the UK, evaluating a 12-week digital physical activity intervention for people with various stages of CKD, including those receiving KRT. Participants were randomly assigned to the physical activity digital health intervention or a waiting list control group. The trial reported significant improvements in determinants of mental health-related quality of life, observed by the increase in the Kidney Disease Quality of Life Short Form (KDQoL-SF version 1.3) Mental Composite Summary in the intention-to-treat population[96]. This improvement was maintained at 6-month follow-up after a period of self-managed physical activity[95]. Improvements in mental health-related quality of life were accompanied by a reduction of anxiety and depression symptoms in participants who completed the 12-week programme. Mean PHQ-4 scores in the intervention group reduced from a score within the mild category for symptoms of depression and anxiety to a score within the non-clinical range. The Kidney BEAM intervention also had positive effects on anxiety and depression, social interaction, physical function, symptom burden, and patient activation[96]. Subsequently, a polycystic kidney disease-specific version of Kidney BEAM also improved mental health-related quality of life, kidney disease burden and fatigue[98].

Digital approaches might also have a role in preventing poor mental health through behaviour change, particularly given the associations between physical inactivity and smoking with psychological distress[29]. Of note, despite their promise, digital interventions in CKD are biased to evidence drawn from cohorts comprising mostly male participants from European American backgrounds[99]. Effectiveness and acceptability of these interventions across people with CKD remain poorly understood, especially in those impacted by digital determinants of health.

Overall, these RCT findings demonstrate the benefit of non-pharmacological interventions. Such approaches have the potential to improve patient outcomes by reducing the negative consequences of psychological distress, physical inactivity and low self-management. The increasing use of digital delivery demonstrates a potentially scalable implementation model to support psychosocial care in people living with kidney disease, reducing the burden of multiple long-term conditions in this context. However, the needs of those with low digital access and literacy and those affected by wider barriers to digital intervention engagement, for example, cultural barriers or disability, must also be considered. To date, interventions in CKD populations have neglected to systematically operate from a base position of inclusive implementation. Consequently, the needs of those underserved in both mental health and kidney research continue to be overlooked.

Pharmacological management

Selective serotonin reuptake inhibitors (SSRIs) are the antidepressant drug class most commonly used to treat depression in people with CKD[100–102]. However, evidence regarding their efficacy in people with CKD is inconclusive[103,104], with a need for better quality trials. Of note, SSRIs have been associated with adverse short-term outcomes[101] and poor tolerability[105], although a target trial emulation study in CKD stages 3–5, conducted in 2023, found no evidence of long-term adverse outcomes after antidepressant initiation, including all-cause mortality, CKD progression, suicide and major cardiovascular events[101].

To date, the largest SSRI RCT in kidney disease tested the efficacy of sertraline compared with placebo[104]. The double-blinded study screened 14,658 people with non-dialysis-dependent CKD, identifying 997 participants with probable depression. However, a high number (697 of the 977) did not consent to being assessed using a diagnostic interview and were excluded from the study. Following a single-blind, drug run-in period, 201 participants were randomly assigned to receive sertraline ($n = 102$) or placebo ($n = 99$). Over a 12-week follow-up, there was no difference in depression scores between groups and rates of remission were similar. However, participants in the sertraline group reported significantly more side effects than those in the placebo group[104], similar to findings reported in a feasibility trial of sertraline in people receiving haemodialysis[106].

Conversely, an RCT in people receiving haemodialysis in 2024 showed improved symptoms of depression and quality of life after 12 weeks of sertraline, compared with the non-treatment control arm[107]. Furthermore, those in the treatment arm had increased haemoglobin and serum albumin and reduced C-reactive protein. However, the study was limited by a short-term follow-up, pre–post comparisons of outcomes and no placebo control. A comparative RCT of sertraline versus CBT for depression in people receiving haemodialysis demonstrated improvement in depressive symptoms in both groups, with a marginal benefit of sertraline over CBT[108], although this small difference might not be clinically meaningful given the lack of a control group. Adverse events were more common in people on sertraline than in those receiving CBT.

Although pharmacological management has the potential to form part of holistic models of care in CKD, questions remain about

antidepressant efficacy and safety. This uncertainty must be considered as part of shared decision-making on the use of this approach and the choice of antidepressant agent. Moreover, although SSRIs are the antidepressant most frequently prescribed in this setting[100], not all SSRIs are equal. A large retrospective analysis found that people receiving haemodialysis who initiated SSRIs with higher QT-prolonging potential (for example, citalopram or escitalopram) had a significantly increased risk of sudden cardiac death (adjusted hazard ratio 1.18; 95% CI 1.05–1.31) compared with those who initiated SSRIs with lower QT-prolonging potential (fluoxetine, fluvoxamine, paroxetine, sertraline)[109]. Initiating treatment with an SSRI with low QT-prolonging potential, such as sertraline, therefore seems to be a reasonable approach[105]. Sertraline is also free from substantial anticholinergic concerns, which can be problematic with some SSRIs[110], and is considered safe in people with cardiovascular comorbidity, which is highly prevalent in advanced CKD.

Polypharmacy is common in people with CKD and is an important factor in antidepressant choice. For instance, QT interval prolongation occurs in around 30% of people with CKD receiving a combination of two or more drugs with a 'known' risk of Torsades de pointes, with citalopram being an important contributor[111]. Concomitant use of other drugs with anticholinergic activity, such as those used to treat bladder conditions or Parkinson disease, can increase the anticholinergic burden of some SSRIs and therefore enhances the risks of cognitive impairment[112], falls[113] and all-cause mortality[114] in older people. In addition, SSRI use is associated with an increased risk of bleeding, which increases with the concurrent use of NSAIDs, anticoagulants and antiplatelet agents[115].

Whatever agent is chosen, a cautious approach is recommended — initiating medications at a lower dose, monitoring carefully, increasing the dose in the absence of side effects and discontinuing treatment in the absence of improvement[116]. Withdrawal symptoms are common and can be severe and long-lasting, so a gradual reduction is recommended[117].

Although anxiety is common in people with CKD and often comorbid with depressive episodes, less data are available on the use of anxiolytic medications. Hence, the approach to using these agents in this setting needs to be cautiously extrapolated from that in the general population, bearing in mind differences in drug metabolism and propensity for drug interactions. In practice, SSRIs remain the first-line agents, and given its safety profile in CKD, sertraline is a practical option. Benzodiazepines are no longer first-line options given the risks of dependency, withdrawal and cognitive impairment[118]. These drugs are effective for acute anxiety symptoms but long-term use, although not uncommon, is now not generally recommended. Caution is also required when using agents with active metabolites, including chlordiazepoxide, diazepam, flurazepam and clonazepam[119]. Less commonly used agents include β-blockers, gabapentin and pregabalin, the latter two requiring dose adjustments in people with CKD[119].

Severe mental illness and CKD

SMI (including schizophrenia, bipolar disorder, schizoaffective disorder and severe depression) refers to a group of enduring mental health conditions that can present with psychosis and substantially impact the social, occupational and academic functioning of an individual[120] (Table 1). Although SMI is less prevalent than common mental disorders (globally, approximately 1 in 300 people are living with schizophrenia, and 1 in 150 people are living with bipolar disorder)[121,122], these conditions represent a high burden of disease[123], alongside substantial costs to health-care services[124].

The mortality gap — premature mortality in individuals with SMI

People with SMI have shortened life expectancies by an average of 10–20 years[125,126]. Increased rates of suicide and accidents might partly explain this mortality gap but increasing evidence suggests a role for long-term physical health conditions, including cardiovascular and respiratory diseases[125,127–130]. People with SMI often experience multiple long-term physical health conditions, each of which is associated with symptoms and challenges[131]. Although the life expectancy of the general population is increasing, it is not increasing for people with SMI[132]; consequently, the mortality gap is widening[133]. Not only are people with SMI more likely to develop long-term physical health conditions but, once they develop a long-term condition, they have poorer outcomes from these conditions compared to those without SMI[134]. People with SMI also have higher rates of health-damaging behaviours such as smoking, substance misuse, poor diet and physical inactivity[135,136], all of which are risk factors for developing kidney disease. Growing evidence indicates that inequitable access to quality health care also contributes to the premature mortality of people with SMI[128,137], including fewer health screenings[138] and follow-up[139].

Risk of CKD amongst people with SMI

The relationship between SMI and CKD is bidirectional — SMI can affect the risk of developing CKD and CKD can complicate SMI management — and co-occurrence of these conditions is associated with poor clinical outcomes (Fig. 2). As discussed below, SMI can increase the risk of developing CKD through factors including poor health behaviours, limited access to health care, intersectional social determinants of health and the nephrotoxic effects of certain psychotropic medications. Conversely, the presence of CKD can exacerbate psychiatric symptoms and complicate the management of SMI, leading to worse clinical outcomes overall.

Several studies indicate that people with SMI have a higher risk of developing CKD[14]. For example, a large retrospective cohort study found that schizophrenia increased the risk of CKD by ~60%. A cross-sectional study of primary care practices in Scotland found that people with bipolar disorder had a 2.42 higher risk of CKD compared with people without the disorder[140]. Although the prevalence of CKD in the general population is rising rapidly, this increase seems to be notably higher in people with SMI, rising from 0.28% in 2000 to 8.24% in 2012 in the UK[131]. Across the same period, the overall UK prevalence of SMI increased from 0.52% to 0.63%.

The most well-studied driver of CKD in people with SMI is the use of lithium treatment, the mainstay of maintenance treatment for people with bipolar disorders[141]. The kidney side effects of lithium are well documented[142], and lithium toxicity (that is, blood lithium levels of ≥1.5 mmol/l) can result in acute kidney failure[143]. The use of long-term lithium doubles the risk of impaired kidney function, and one in four people receiving long-term lithium will develop CKD[144]. Other psychiatric drugs, including first-generation and second-generation antipsychotics[145,146], as well as anticonvulsants used as mood stabilizers in bipolar disorder[147], have also been associated with a higher risk of CKD.

People with SMI also have higher rates of known risk factors for CKD, although research regarding how these might contribute to rates of CKD in this population is limited. For example, individuals with SMI have higher rates of hypertension and diabetes mellitus, the two most common causes of CKD in the general population[148,149]. Additionally, people with SMI are more likely to smoke[150], to have metabolic syndrome exacerbated by treatment[151] and to exercise less[152], all of which have been associated with a higher risk of developing CKD[153]. These factors are exacerbated by established social risks that also underlie

Table 1 | SMI diagnoses, symptoms and treatment

SMI diagnosis[a]	Symptoms	Medication options[b]	Cautions in CKD[c]
Schizophrenia	Distortions in thinking and perception, including hallucinations and delusions; negative symptoms (for example, poverty of speech, blunting of affect); thought disorder	Antipsychotic drugs Consider clozapine in refractory cases (non-response to two antipsychotic drugs, one of which is a non-clozapine second-generation agent)	Specialist psychiatric input is recommended in most cases First generation — haloperidol generally considered safe but metabolites might accumulate in advanced CKD Second generation — risperidone generally well tolerated although dose reduction is required in advanced CKD Clozapine — specialist psychiatric input mandatory to initiate treatment Caution with use of depot (also known as long-acting injectable) antipsychotic in advanced CKD QT interval prolongation is an issue with many agents
Bipolar disorder	Two or more episodes of elevated mood and increased energy (hypomania or mania)±episodic lowering of mood and energy (depression)	Stop antidepressant monotherapy (if relevant) and initiate antipsychotic medication If antipsychotic medication is ineffective or not tolerated, consider adding lithium If lithium addition is ineffective or not tolerated, consider a change to valproate If medications are ineffective, consider ECT	Specialist psychiatric input recommended in most cases Lithium causes tubulointerstitial damage, leading to CKD Regular monitoring of serum lithium levels and renal function is required with dose adjustment in mild-to-moderate CKD and usually avoidance in advanced CKD Valproate is hepatically cleared so dose reduction is not necessary
Severe depression with psychosis	Episodes of low mood resulting in: reduced energy; reduced activity and fatigue; loss of capacity for enjoyment (anhedonia); intrusive negative thoughts; hallucinations; delusions; stupor and psychomotor retardation (might be severe enough to endanger life)	Pharmacological interventions: antidepressant medication; antipsychotic medication If medications ineffective, consider ECT	Specialist psychiatric input is mandatory to initiate treatment SSRIs (for example, sertraline) are commonly used although with little evidence of efficacy In most cases, dose reduction is not required Caution with SSRIs (for example, citalopram), which prolong QT interval SNRIs (for example, venlafaxine) are alternatives to SSRIs, although many require dose reduction in advanced CKD
Schizoaffective disorder	Symptoms of both schizophrenia and an affective disorder (for example, bipolar disorder) are prominent	Treatment depends on the affective symptoms Options include antipsychotic medication, antidepressant medication and mood stabilizers (for example, lithium and valproate) If medications are ineffective in treating affective symptoms, consider ECT, although it is not generally recommended for treating schizophrenia	Specialist psychiatric input mandatory to initiate treatment Antipsychotics (for example, haloperidol, risperidone or clozapine) Antidepressants (for example, SSRIs) Mood stabilizers (for example, lithium and valproate), as outlined above

CKD, chronic kidney disease; ECT, electroconvulsive therapy; SMI, severe mental illness; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitors. [a]Other conditions, including personality disorder, may be classified as SMI depending on impact on the individual's ability to function in day-to-day life; see also International Classification of Diseases 11th Revision. [b]Pharmacological interventions should be provided alongside psychological interventions; relevant guidelines: NICE Guideline on Bipolar Disorder: Assessment and Management; NICE Guideline on Psychosis and Schizophrenia in Adults: Prevention and Management; NICE Guideline on Depression in Adults: Treatment and Management. [c]Prescription of medications should take into account the drug pharmacokinetics, especially kidney and dialysis clearance; degree of protein binding; and high propensity for drug interactions.

inequities in SMI prevalence across society. In the USA, for example, both CKD and SMI risk are individually higher in individuals of Black ethnic heritage[154,155].

Rates of SMI in CKD

Data from the USA indicates that rates of psychiatric hospitalizations in people with kidney failure are 1.5–3 times higher than those in people with other chronic illnesses[156]. Data from the USA also indicate that 27% of adults with kidney failure enrolled with Medicaid have had hospitalizations with a psychiatric diagnosis[157]. Research indicates that approximately 2–3% of people with CKD have a diagnosis of schizophrenia, schizoaffective disorder, psychosis or bipolar disorder[82,158]. A large Swedish study (>30,000 people with CKD) reported an overall prevalence of SMI of 7.3%, which was 56% higher than that observed in the general population[159].

Clinical outcomes and access to health care for people with CKD and SMI

The overarching physical health inequalities that have been highlighted for people with SMI and co-existing long-term conditions seem to hold in the context of CKD. After developing CKD, people with SMI have worse clinical outcomes and poorer access to health care compared with those without SMI. Individuals with CKD and concurrent SMI have higher rates of mortality[157,160] and die an average of 13 years younger than those without SMI[158]. There is also evidence that people with SMI have more advanced CKD at the time of nephrology referral, and have higher rates of emergency hospitalizations compared with those with CKD without a diagnosis of SMI[157,158,160].

People with SMI who progress to advanced stages of kidney disease might experience inequities in access to KRT. A Swedish cohort study found that people with bipolar disorder and CKD (not on KRT) had an increased risk of disease progression yet a lower rate of KRT initiation[159]. A retrospective cohort study of people with CKD attending a tertiary renal unit in London, UK, found that people with SMI were less than half as likely to receive a kidney transplant, and were also less likely to receive peritoneal dialysis[158]. People with SMI have also been reported to be less likely to receive an evaluation appointment for a kidney transplant, despite evidence that people with SMI have comparable post-transplantation outcomes to those without SMI[14].

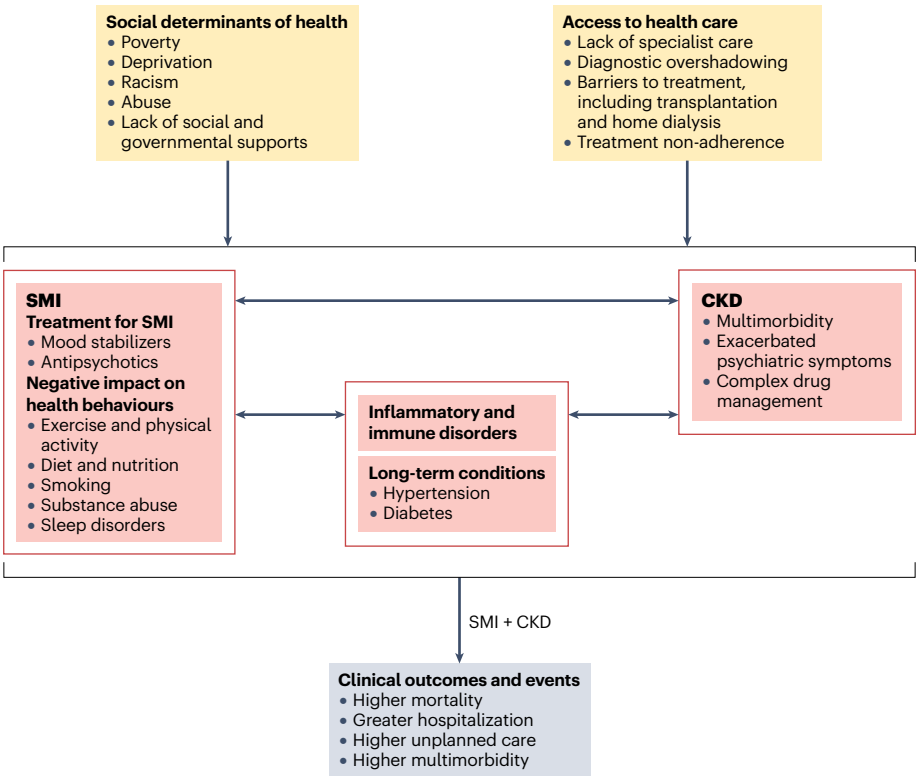

Fig. 2 | Bidirectional pathways between SMI, kidney disease and clinical outcomes. This conceptual framework illustrates the bidirectional and interacting pathways between severe mental illness (SMI) and chronic kidney disease (CKD), and their consequences for clinical outcomes. Social determinants of health, including poverty, deprivation and racism, form a central contextual layer influencing both conditions. SMI is associated with adverse health behaviours, such as reduced physical activity, poor diet and nutrition, and substance misuse, which increase the risk of long-term health conditions, including hypertension and diabetes, which are key contributors to CKD onset and progression. Treatments for SMI, particularly antipsychotics and mood stabilizers, might further exacerbate metabolic and kidney risks. Shared biological mechanisms, including inflammatory and immune dysregulation, can link SMI and CKD directly. The convergence of these pathways contributes to poorer clinical outcomes, including higher mortality, greater hospitalization, increased unplanned care and higher multimorbidity. Arrows indicate complex, reciprocal relationships, emphasizing cumulative disadvantage and reinforcing cycles of risk across the life course.

Another retrospective cohort study found that people with CKD without a schizophrenia diagnosis were 1.7 times more likely to receive dialysis treatment than those with a schizophrenia diagnosis[161]. For those receiving haemodialysis, people with SMI are reported to have more difficulty following dietary, fluid and medication treatment requirements[158].

SMI management and recommendations

Qualitative research indicates that many people with CKD and SMI have greater difficulty accessing quality kidney care owing to difficulties with their mood and mental state, cognitive impairments, and mistrust of the health-care system[162,163]. The separation of mental and physical health care, understaffing and health-care provider stigma were also described as barriers to effective kidney health care for people with SMI. Research indicates that care should be tailored to meet the specific needs of each person with CKD and SMI in order to support adherence, reduce treatment burden, and optimize the management of their concurrent physical and mental health conditions[162,163]. This approach requires a care plan that considers the needs and preferences of the patient as well as the supports available to them.

Research exploring inequalities in health-care access for people with SMI consistently emphasizes the need for more integration of mental and physical health care, with improved communication and collaborative working across specialisms[164]. This integration is particularly crucial in the context of high rates of multimorbidity[165]. Effective and safe treatment for people with CKD and SMI requires integrated physical and mental health care, whereby kidney teams are adequately staffed with mental health professionals, and mental health services are resourced to support the complex health needs of service users with CKD[162,163]. Close communication between kidney and mental health-care services is crucial, particularly regarding the management of psychotropic medication and to support self-management. People with SMI and CKD should also be closely monitored for suicide risk and have timely access to appropriate support when needed[162,163].

To prevent further widening of the inequalities in health-care provision for people with SMI, future research should no longer exclude participants based on having SMI alone[166]. Instead, inclusion in research should be determined by capacity to consent, with appropriately supported and accessible recruitment and consent processes[167] (Box 1).

Mental health in children with CKD

Although a comprehensive review of mental health in children with kidney disease is beyond the scope of this article, it is important, as part of a biopsychosocial life course perspective, to recognize the psychological impact of CKD in children, an under-researched patient community. Paediatric CKD is associated with a considerable health burden that includes poor mental health, behavioural problems and developmental delay[168]. These adverse consequences not only affect health and well-being during childhood but they can also remain risk factors for future mental health conditions in adulthood. Studies have consistently highlighted poorer quality of life and increased risk of depression and anxiety in children with CKD compared with their healthy peers[168–171]. Mental health conditions are also associated with poorer clinical outcomes and increased incidence of associated problems such as medication non-adherence[168]. Tools such as the Paediatric Quality of Life inventory[172] or the Childhood Depression Inventory-2 (ref. 173) have been used to identify those with mental health conditions in clinical and research settings. Discrepancies in studies reporting

the incidence of different conditions, such as depression and anxiety, indicate the need for improved mental health assessment approaches for this patient group[174].

The transition to adult services is a well-recognized period of instability with effects on health outcomes[175,176]. Psychosocial factors, including family cohesion and transition readiness, can be more significant predictors of post-transition health outcomes than disease-related factors[177]. Although tools such as *Ready Steady Go*, which is a transition programme designed to help young people prepare for the move to adult health-care services, are widely used, evidence to inform health and social care providers on how to best support mental health at the time of transition is scarce[178]. This lack of information is compounded by a general shortage of provision of mental health services for children and young people[179]. More research is needed to establish the most appropriate interventions to support children with kidney disease and their families, particularly at key points in the clinical pathway such as dialysis initiation and transition to adult care. Nonetheless, current evidence suggests that preventative mental health strategies implemented early in the paediatric setting might help to maintain well-being and reduce the risk of future mental health episodes[180].

Caregiver burden in CKD

CKD rarely occurs in isolation — it is situated within social contexts, where informal caregivers, such as unpaid family members, provide a wide range of practical and emotional support. Caregiving for individuals with CKD is often complex, including managing medical appointments, dialysis attendance, medication administration, dietary restrictions and financial matters, as well as providing emotional support. Given the demands of caregiving, many caregivers experience chronic stress, reduced quality of life and poor mental health[181]. Caregiving is also associated with poorer physical health outcomes, including dysregulated immune function[182] and increased mortality risk[183]. A study of caregivers of patients receiving dialysis conducted in 2024 found that approximately two in five caregivers reported moderate-to-high caregiver burden[184]. Furthermore, poorer mental health-related quality of life and greater symptom burden in people treated with dialysis were associated with greater levels of perceived caregiver burden and lower mental health-related quality of life in caregivers[184].

Given the bidirectional relationship between patient and caregiver mental health[185], addressing the mental health needs of caregivers is crucial not only for their own well-being but also for the quality of care they provide. Several interventions in caregivers of people with kidney disease have been evaluated, including psychoeducation programmes, family-centred approaches and psychological interventions[186]. For example, an RCT assessing enhanced psychosocial support in caregivers of people receiving palliative kidney care found short-term improvements in caregiver burden and anxiety in those who received the intervention compared with controls who received standard care[187]. Given the essential role caregivers have in the management of kidney disease, more research is needed to establish the most effective approaches to support them, particularly for those from disadvantaged backgrounds. Furthermore, in the paediatric setting, more work is needed to support caregivers dealing with the specific challenges of looking after a child with kidney disease, particularly as their role changes when their children transition to adult kidney care services.

Fragmented psychosocial and mental health care

Broadly speaking, psychosocial care provision in people living with kidney disease is insufficient, varied and fragmented[46,47,188], with care disjointed between primary, secondary and social care settings. One example is the use of depression screening as part of routine kidney care, which is often low, with varied clinical protocols adopted and few systematic pathways available[47,189]. A further example relates to the prescription and monitoring of antidepressant medications, for which, in the context of kidney disease, general practitioners are the predominant prescribers[190], although most data available are from high-income countries. A longitudinal study of people receiving haemodialysis and antidepressants found evidence of low dosing, overprescription and poor drug selection, as well as inadequate follow-up and review, highlighting suboptimal practices and low adherence to national guidelines, at least in settings where they are established[190].

Box 1 | Key policy and practice recommendations regarding care for people with CKD and SMI

1. Kidney care should be tailored to meet the specific needs of each person with severe mental illness (SMI), to support adherence, reduce treatment burden, and optimize management of their concurrent physical and mental health conditions. This approach requires an agreed-upon care plan that considers each of the needs and preferences of the patient as well as the supports available to them. Continuity of care is also highly important.
2. Effective care for people with chronic kidney disease (CKD) and SMI requires integrated physical and mental health care to enable a coordinated 'whole-person' approach to care. Nephrology departments should have comprehensive multidisciplinary team-based care, including psychiatry, psychology, social work and clinical nurse specialists. Frequent and timely communication between kidney and mental health-care services is needed to ensure effective and safe care, particularly when considering changes in psychotropic medication.
3. People with CKD and SMI are at high risk of suicide and self-harm. Therefore, it is vital to ensure access to timely assessment and management of suicidality, safety planning, psychological therapy and pharmacotherapy, where required.
4. Policies that specify which service — mental health service, general practitioner or both — is responsible for monitoring and managing the physical health of people with SMIs are urgently needed.
5. Mental health services require additional resource allocation to adequately support the complex physical health needs of their service users.
6. Interventions are needed to reduce health-care provider stigma and discrimination towards people with SMI. This change is necessary to minimize the risk of diagnostic overshadowing and to improve care for people with CKD and SMI.

Non-pharmacological approaches are also characterized by varied practice patterns given that psychosocial kidney care has generally low provision, accessibility and reach[47]. Although workforce demands are a key consideration, fragmented care ultimately defuses responsibility and management, meaning that people potentially fall through the interface between care settings. Nephrology has an important coordinating role for collaborative mental health care, incorporating general practitioners, local kidney psychosocial teams and general hospital liaison psychiatry[191,192]. Growing evidence highlights the cost–benefit of integrating mental health care into treatment plans for people with long-term conditions, particularly in primary care[193–195] and cancer services[196,197]. To date, examples of mental health pathways embedded within kidney care are limited. A 2025 study from Canada reported a pathway for mental health care for people receiving dialysis[198]. The use of strategies to ensure person-centeredness, which allowed both patients and health professionals to contribute to the development process in meaningful and collaborative ways, was crucial to their approach. Although such integrated collaborative approaches have real potential in CKD, system and structural level issues across health-care settings globally will likely create barriers for implementation, including initial health-care costs, access to psychosocial provision within the kidney team or local hospital, and staff workloads. Indeed, in many countries, the ratio of both nephrology and psychology workforce to the general population is a key limitation to implementing adequate CKD prevention and intervention programmes[199,200]. Despite these limitations, prioritizing holistic care remains an urgent call to action, especially the joining up of multisectoral action.

Conclusions

In conclusion, the intersection of kidney disease and mental health is complex and bidirectional. Although we have focused on depression, anxiety and SMI, acknowledging the importance of various other neuropsychiatric or neurological disorders (for example, cognitive impairment, dementia and delirium) associated with CKD is important given that these conditions can have a substantial impact on patient outcomes, including mental health, and warrant greater focus in future studies regarding their prevalence, aetiology and opportunity for intervention.

People living with kidney disease are at increased risk of mental health issues. Furthermore, pre-existing mental health conditions increase the risk of developing kidney disease, exacerbating kidney disease progression and leading to poorer outcomes. The negative impact of depression and anxiety on morbidity and mortality in people with kidney disease is substantial, highlighting the need for integrated care strategies, including increased support for caregivers. The need to achieve the ambition of psychological framing of health experiences is pressing, particularly for those from vulnerable or underserved populations, including people from lower socioeconomic backgrounds or minority ethnic groups, and for those affected by complex co-occurring conditions such as SMI, who face compounded health inequalities. This framing calls for tailored interventions to address both kidney disease and mental health needs alongside the need for cross-sector working to develop and implement appropriate prevention approaches across the life course.

Kidney care should be personalized, ensuring that treatment plans support adherence, reduce burden and optimize overall management, with equity in relevance and access. Furthermore, there is a clear need for more rigorous, high-quality RCTs to evaluate effective screening protocols and treatments for mental health issues in people with kidney disease, including studies of pharmacological and non-pharmacological management approaches. More emphasis on strategies to prevent mental illness in CKD is also needed. Although research in this area is lacking, psychoeducation, peer-support, self-management and exercise are potentially promising approaches, particularly if implemented in key parts of the kidney care pathway (for example, in the work-up to dialysis). RCTs of primary prevention of mental illness in CKD are needed alongside treatment trials. Involvement of patients and carers as partners in the design of research protocols and treatment pathways will help ensure alignment with their needs and preferences and accelerate adoption of promising approaches. Kidney and mental health care are generally fragmented, even in the most advanced health-care settings such as those offering universal access. Integrating mental health support into routine kidney care has the potential to improve patient outcomes, enhance quality of life and ensure the provision of adequate person-centred health services. Improving outcomes benefits patients, communities and health systems by reducing the overall disease burden.

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Author contributions

All authors researched data for the article. J.C., C.Cogley, C.Carswell, S.A.G., S.S., K.B., K.F. and A.J.L. wrote the manuscript. J.C., C.Cogley, C.Carswell, J.L.H., S.A.G., S.S., K.B. and K.F. made substantial contributions to discussions of the content and reviewed or edited the manuscript before submission.

Competing interests

S.A.G. is a Director of Kidney BEAM Ltd. The other authors declare no competing interests.

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