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Provincial Health Services Authority

Depression And Anxiety: The Role Of Kidney Care Clinics

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Developed by the Kidney Care Committee

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LAND ACKNOWLEDGEMENT

BC Renal plans and monitors the delivery of kidney care services to a diverse population living in various settings and communities across BC. As a provincial network, we operate on the unceded traditional and ancestral land of many Indigenous peoples, including First Nation, Métis and Inuit people. Our main office is located on the traditional and ancestral territories of the Coast Salish peoples – xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Sel̓ílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations, and the Métis Chartered Community of the Lower Mainland Region.

We acknowledge the health inequities caused by the current and historical colonization of this territory, and we humbly listen and learn from the resilience and strength of Indigenous peoples. We will endeavor to provide culturally safe care and practice throughout our work.

IMPORTANT INFORMATION

This BC Renal guideline/resource was developed to support equitable, best practice care for patients with chronic kidney disease living in BC. The guideline/resource promotes standardized practices and is intended to assist renal programs in providing care that is reflected in quality patient outcome measurements. Based on the best information available at the time of publication, this guideline/resource relies on evidence and avoids opinion-based statements where possible; refer to BCRenal.ca for the most recent version.

For information about the use and referencing of BC Renal provincial guidelines/resources, refer to bcrenal.ca/health-info.

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1.0 Scope

This guideline discusses depression and anxiety in patients with chronic kidney disease (CKD) attending one of BC's Kidney Care Clinics (KCCs). KCC patients are currently not on dialysis,[1] although all live with moderate to severe kidney disease.

The guideline makes recommendations about the role of KCCs with respect to the detection and management of depression and/or anxiety. It focuses on depression and anxiety because these are the most commonly diagnosed mental health disorders. Other mental health disorders may be present or co-exist with depression and/or anxiety.

The guideline assumes that KCC patients have access to a primary care provider (PCP) which may be a family physician (FP) or nurse practitioner (NP). If not, KCC staff will actively assist them in finding appropriate support. PCPs have primary responsibility for the treatment and monitoring of depression/ anxiety.

The guideline is divided into two sections: (1) adults; and (2) children & youth. Many of the concepts in the adult section also apply to children & youth. The children & youth section is intended to highlight child & youth-specific concepts.

2.0 Depression, Anxiety and Chronic Kidney Disease in Adults

2.1 Depression and CKD

What is depression?

- Mood disorders are amongst the most common of the psychiatric disorders. They may involve persistent feelings of sadness, loss of pleasure and interest in nearly all activities, and a host of other symptoms. They affect the way a person feels, thinks, and behaves, and significantly impair functioning.[1,2]
- Onset may be triggered by interactions between biological, psychosocial, and environmental factors, such as traumatic life events (e.g., diagnosis of CKD).[3]
- Mood disorders can range from mild to serious. A person may have a single episode, recurrent episodes, or a chronic illness. The most common type of mood disorder is called major depressive disorder (MDD).

How common is depression?

- Rates vary widely in the published literature due to differences in study methodology and sample characteristics.
- General population:
  - The National (US) Co-morbidity Survey Replication (NCS-R, carried out in 2001 - 2003) reported a 12-month prevalence rate of 7% for MDD and 10% for any mood disorder (interview format).[4] See Table 1. Lifetime prevalence rates were reported at 17% and 21% respectively.[5]

[1] Less than 50% of KCC patients will ever go on dialysis or receive a kidney transplant.

Table 1: 12-Month Mood Disorder Prevalence Rates[4]

DSM-IV CATEGORY	12-MONTH PREVALENCE	SEVERITY OF ILLNESS			LIFETIME PREVALENCE
		SERIOUS	MODERATE	MILD	
MDD	6.7%	30%	50%	20%	16.6%
Any mood disorder	9.5%	45%	40%	15%	20.8%

- The Canadian Community Health Survey (carried out in 2019) estimated that 14% of Canadians aged 12 and older reported having a diagnosed mood and/or anxiety disorder. The incidence was higher in females than males (17% vs 11%) and higher among Indigenous people (27%).[6]
- The Mental Health Commission of Canada study (carried out in 2010) estimated that 11.7% of people aged 9 and older were reported to have a mood and/or anxiety disorder.[7]
- Data from the World Mental Health Survey Initiative was analyzed from 18 countries (n=18,037). Reported rates of MDD for high-income countries were above those for low and middle-income countries: 12-month prevalence rates were 5.9% vs 5.5% respectively and lifetime prevalence rates were 14.6% and 11.1% respectively.[8]
- Kidney-specific studies:
  - Patients with CKD who are not on dialysis have rates of depression up to 3 times higher than those in the general population.[9,10]
  - A systematic review and meta-analysis by Palmer et al examined the prevalence of depression in patients with CKD. (216 studies, 55,982 patients, up to Jan 2012):[9]
    - Not on dialysis: 26.5% when evaluated by screening questionnaire and 21.4% when evaluated by clinical interview.
    - On dialysis: 39.3% when evaluated by screening questionnaire and 22.8% when evaluated by clinical interview.
  - Studies published since Palmer's meta-analysis using screening questionnaires have reported prevalence rates between 20% and 50% (varying combinations of patients not on dialysis and on dialysis).[11-15]
  - Several studies concluded that the stage of CKD did not significantly affect depression rates when evaluated by clinical interview (vs questionnaire)[10,12,16]
  - Coexistence of anxiety disorders with MDD:
    - A worldwide survey reported that 45.7% of people with lifetime MDDs had a lifetime history of one or more anxiety disorder.[17] 41.6% of people with 12-month MDD had one or more anxiety disorder over the same 12-month period (i.e., both disorders existed at the same time).[17]
    - Data from the Sequenced Treatment Alternatives to Relive Depression (STAR*D) study reported that 53% of patients with MDD had significant anxiety and were considered to have an anxious depression.[18]

Why is the rate of depression higher for CKD patients than the general population?

Causes of the higher rates are uncertain.
Proposed causes include:[10,19]

- Disease-related: co-morbidities (e.g., sleep apnea, heart failure), discomfort, pain.
- Treatment related: medications.
- Biological: anemia, uremia,

neurotransmitters, neurotoxins and possibly inflammation.
- Psychological: difficulty with adaptation, role changes, life goals, uncertainty, body image.
- Behavioural: frequent clinic and hospital visits, dietary restrictions, increased pill burden, home monitoring of glucose, blood pressure and weight.
- Socio-economic: changes in relationships, job, social roles, intimacy-sex.
- Lifestyle: lack of exercise, poor nutrition and difficulty sleeping.

What are the risk factors for depression?

- Personal or family history of mood or anxiety disorder
- Multiple medical co-morbidities (e.g., diabetes)
- Acute cardiovascular events (myocardial infarction, stroke)
- Chronic pain or fatigue
- Multiple or complex life/financial stressors
- Traumatic experience(s)
- Poor social support – social isolation, recent move, poverty, cultural or language issues
- Recent adverse life event (e.g., loss of close relative or friend, job loss, divorce).

What are some common indicators of depression?

- Persistent feelings of sadness, emptiness, or hopelessness
- Lack of motivation, loss of interest in activities or hobbies once enjoyed
- Difficulty concentrating, remembering details, and making decisions
- Fatigue and decreased energy
- Complaints of physical aches and pains (headaches, indigestion, etc)
- Feelings of worthlessness, low self-esteem
- Difficulty sleeping, early-morning wakefulness or excessive sleeping
- Weight gain or loss
- Suicidal ideation

How might depression manifest in our KCC patients?

Identifying depression in patients with CKD is challenging because many of the symptoms overlap with the symptoms of CKD (e.g., loss of appetite, sleep disturbances, fatigue, and pain).[10,12] Symptoms of depression (and anxiety) often go unrecognized[20] and under or untreated.[10,21]

Examples of ways that depression might manifest in our KCC patients include:

- Reports of feeling “sad” most of the day and withdrawing from activities that were previously enjoyable.
- Issues with self-care (poor personal hygiene, poor diet, medication adherence issues).
- Feelings of hopelessness (asking “Do you have hope for the future?” may help to identify symptoms of depression in patients).
- Reluctance to book appointments, frequent cancellations and/or no shows.
- Lack of eye contact during appointments and/or apparent difficulty in understanding/ concentrating on information provided (and/or signs of being overwhelmed).
- Multiple complaints of aches and pains (e.g., headaches, stomach pain, joint pain).
- Weight gain or loss.
- Sleep disturbances.
- Dismissing or contradicting concerns raised by healthcare providers or family; steering the

conversation to safer topics (e.g., diet rather than treatment options); focusing on only one aspect of CKD (e.g., GFR or diet restrictions).
- Passively defers to family member(s) for responses, increased reliance on caregiver and/or signs of caregiver exhaustion.
- Reports by patient or family of memory concerns and/or of withdrawal, becoming less social, less motivated.
- Increased irritability with spouse/family members/KCC staff.
- Frustration amongst KCC team with patient or tendency of team to "blame" patient for lack of follow-through with treatment plan(s).

Refer to: BC Renal website, Sadness and Depression

Why is it important to recognize and treat depression?

The presence of depression in the CKD population is associated with increased risk of progression to dialysis, reduced quality of life, adverse medical outcomes, hospitalization, and death.[12,15,22-24]

In the general population and in patients with chronic illness, treatment with antidepressants or psychotherapy can significantly improve depressive symptoms and psychosocial outcomes,[25-27] and treatment with a combination of both has been shown to be more effective than either alone.[28] Studies specific to the CKD population are few in number.

What tools are available to help screen for depression?

- The PHQ-9 is one of the most commonly used depression screening tools and was initially validated in two large studies (n=6000). The sensitivity and specificity were both 0.88 at a cut point >10.[29] The tool is valid for patients 16 years and older with grade 4 English comprehension. It is available in multiple languages and freely downloadable at Phqscreeners.com.
- A systematic review (2020) of depression screening tools for patients with kidney failure concluded that there is limited research evaluating the diagnostic accuracy of most depression screening tools for patients with kidney failure. Studies suffer from limitations related to methodology quality and/or reporting. The authors recommended that future research target widely used, free tools such as the Patient Health Questionnaire 2 (PHQ-2) and PHQ-9 given the success of these tools with the general population.[30]
- The PHQ-9 is a depression screening tool commonly used by family physicians in BC (and is included in the Family Physician Guide for Depression, Anxiety Disorders, Early Psychosis and Substance Use Disorder[31] and on the Ministry of Health website (Gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/depression_patient_health_questionnaire.pdf). Given the importance of close working relationships with family physicians in the management of KCC patients with depression, the PHQ-9 is

recommended for use in KCCs to facilitate communication with family physicians.

- The PHQ-9 is a nine-question tool for screening or monitoring levels of depressive symptoms. The questionnaire scores each of the nine DSM-5 criteria as "0" (not at all) to "3" (nearly every day) based on frequency of occurrence in the past two weeks. The maximum score is 27. Question 9 screens for the presence and duration of suicide ideation. A follow-up, non-scored question 10 assigns weight to the degree to which depressive problems have affected the patient's level of function.
- Of the 9 items, 5 or more are checked off PHQ-9 scores on the first 9 questions of 5, 10, 15 and 20 represent mild, moderate, moderately severe, and severe depression.[29] A patient response of "very difficult" or "extremely difficult" on the 10th non scored question suggests that the patient's functionality is impaired.
- The PHQ-9 can be self-administered or administered in a face-to-face interview or by telephone. It can be administered repeatedly, which can reflect improvement or worsening of symptoms in response to treatment.

What are the treatment options for depression in CKD patients?

- For the treatment of mild to moderate depression in the general population, non-pharmacological interventions have been shown to be as effective as pharmacological treatments. They have also been shown to be a useful adjunct to pharmacological treatment for moderate to severe depression and can help with relapse prevention.
- Non-pharmacological treatments for the treatment of depression include:
  - Psychotherapies (e.g., cognitive-behavioural therapy, mindfulness-based cognitive therapy, interpersonal therapy, psychodynamic or insight therapy, brief problem-solving therapy). To date, cognitive-behavioural therapy has the greatest weight of research evidence to support its effectiveness.[21,32]
  - Adjunct therapies include mind-body therapies (e.g., meditation, yoga, relaxation, mindfulness, prayer, biofeedback, and creative therapies such as art therapy, music therapy), and exercise.
- Patients with moderate to advanced CKD have generally been excluded from large antidepressant trials because of concerns for adverse events and limitations in the availability of data on the safety of antidepressants in this population.[21] Thus the literature on the use of antidepressants among CKD patients remains controversial. Most suggest using non-pharmacological interventions first and if pharmacological treatment is needed, consider selective serotonin reuptake inhibitors (SSRIs), the most studied class of antidepressants in CKD patients.[21,33] Tricyclics (TCAs) and selective serotonin reuptake inhibitors (SSRIs) may also be considered.[10]

- Patients receiving hemodialysis:
  - Nagler et al[34] (1 RCT) and Palmer et al[35] (3 RCTs) completed systematic reviews of antidepressant use on dialysis patients. While one 1 RCT showed no benefit, 3 showed benefit in treating with antidepressants (SSRIs) over placebos. Similar reviews have not been done on the non-dialysis population.
  - An RCT concerning the use of sertraline vs CBT was conducted on patients receiving hemodialysis (n=120, 2019). When comparing both groups, sertraline appeared to be modestly better than CBT. However, adverse events were more frequent in the sertraline than the CBT group.[36]
- CKD patients not on hemodialysis:
  - The CAST Randomized Clinical Trial (n=201, 2017, 12-week follow-up) studied the effectiveness of sertraline (SSRI antidepressant) in patients with stage 3, 4 or 5 non-dialysis dependent CKD. Interestingly, treatment did not improve depressive symptoms or quality of life and resulted in increased adverse effects (nausea, vomiting and diarrhea being the most common) compared with placebo.[37] The study concluded that sertraline may not be an effective treatment for MDD in this patient population.

2.2 Anxiety Disorders and CKD

What is anxiety? What is an anxiety disorder?

- Anxiety is a natural and necessary adaptive response in humans. It can, however, become a disorder when it becomes excessive and uncontrollable, requires no specific external stimulus, and manifests with a wide range of physical and affective symptoms and changes in behavior and cognition.
- Anxiety is not a single disorder but is a group of related disorders. The most common anxiety disorders are: Phobias, Post-Traumatic Stress Disorder, Generalized Anxiety Disorder (GAD) and Panic disorders.
- Anxiety disorders have been much less studied than depression, both in the general population and the CKD population, despite their relatively common occurrence.

How common are anxiety disorders?

- Rates for anxiety disorders vary widely in the published literature for reasons similar to those discussed for depression.
- General population: The National Co-morbidity Survey Replication (NCS-R) in the US reported a 12-month prevalence rate of 18% for an anxiety disorder (interview format).[4] See Table 2. Lifetime prevalence rates were reported at 29%.[5]

Table 2: Anxiety Disorder Prevalence Rate (Kesler, RC et al, 2005)

DSM-IV CATEGORY	12-MONTH PPREVALENCE	SEVERITY OF ILLNESS			LIFETIME PREVALENCE
		SERIOUS	MODERATE	MILD	
Specific phobia	8.7%	22%	30%	48%	12.5%
Social phobia	6.8%	30%	39%	31%	12.1%
Post-traumatic stress syndrome	3.5%	37%	33%	30%	6.8%
GAD	3.0%	32%	45%	23%	5.7%
Panic disorder	2.7%	45%	29%	26%	4.7%
Any anxiety disorder	18.1%	23%	34%	43%	28.8%

- Hemodialysis population: Two studies of hemodialysis patients reported prevalence rates (at a point in time) of 30%[38] and 46%[39] (any anxiety disorder).
- Non-dialysis CKD population: Two studies reported prevalence rates (at a point in time) of 28% [40] and 54%.[41] Lee's study[40] noted that the rates did not differ across CKD stages.
- Depression often co-exists in patients with anxiety disorders.
  - A World Health Organization (WHO) World Mental Health Survey of the general population reported that 46% of people with lifetime major depressive disorder also had a lifetime history of one or more anxiety disorder. 42% of people with 12-month major depression also had one or more anxiety disorder of the same 12-month period.[17]
  - The lifetime comorbidity of depression for people with an anxiety disorder in other studies was estimated at 20% - 70%, depending on the type of anxiety disorder.[42]

What are the risk factors for anxiety?

- Risk factors are similar to that for depression. See earlier section "What are the risk factors for depression?"

How might anxiety manifest itself in our KCC patients?

- Anxiety may manifest in similar ways to

depression (and often co-exists with depression). See earlier section "How might depression manifest itself in our KCC patients?"

- Anxiety has been reported to negatively impact on quality of life. This association is over and above that associated with depression.[39,41]
- Reduced quality of life, in turn, has been associated with adverse outcomes, faster progression of CKD and higher rates of mortality.[41,43]

What tools are available to help screen for anxiety disorders?

- Screening tools for anxiety disorders are less commonly used than depression screening tools. The multiple classes of anxiety disorders and lower specificity rates are likely factors.
- A systematic review of anxiety screening tools (2020) identified the Generalized Anxiety Disorder-7 (GAD-7) as one of the most commonly used tools to screen for generalized anxiety disorder (validated in 6 studies). Using a cut-off >10, the sensitivity = 76% and specificity = 64% for the GAD-7 (meta-analysis of two studies). The GAD-7 is available in multiple languages and freely downloadable at Phqscreeners.com.[44]
- Other common tools are the Hospital Anxiety and Depression Scale (HADS) and Beck's Anxiety Inventory (BAI).[45]

What are the treatment options for anxiety in CKD patients?

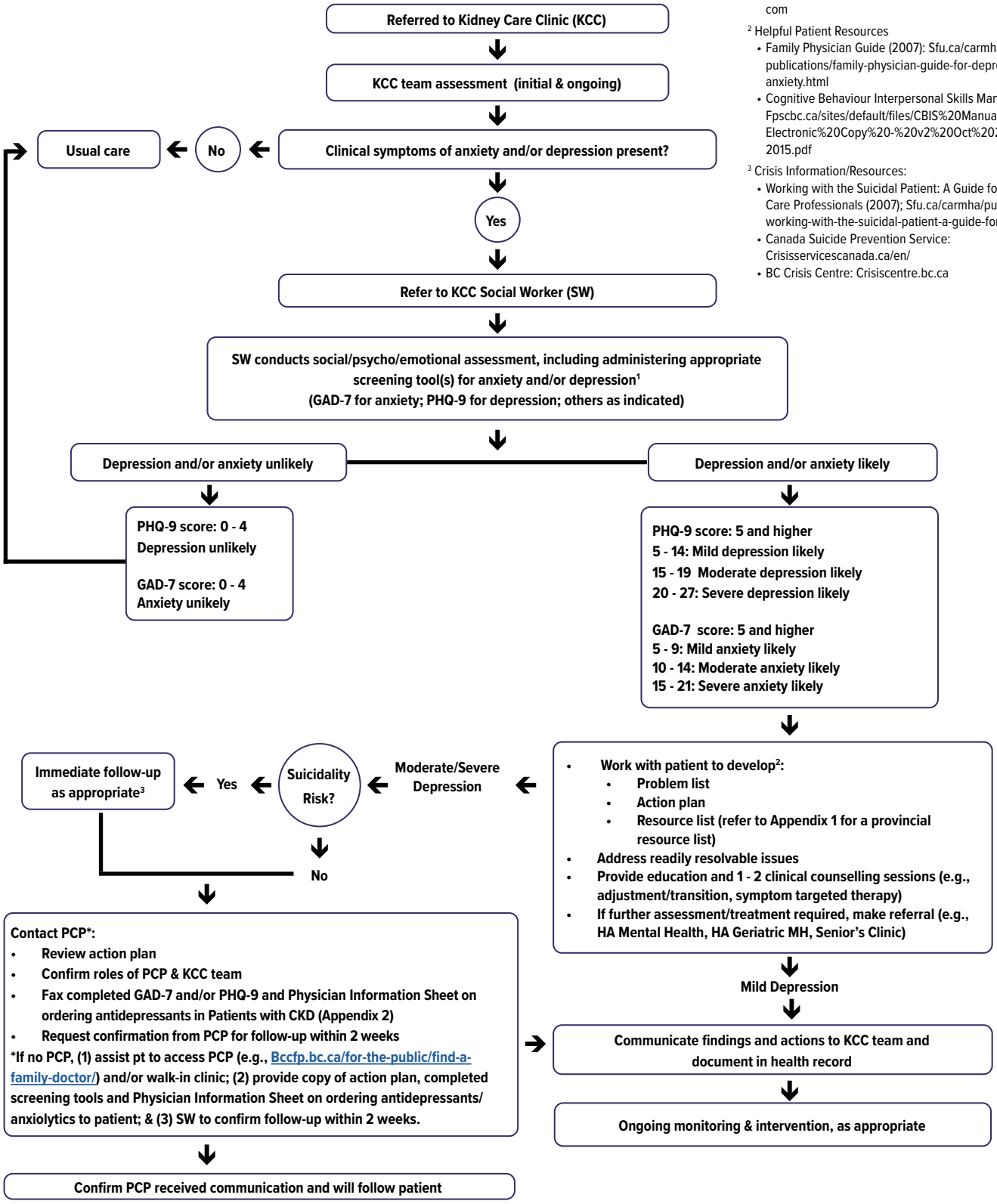
- The most effective type of treatment for anxiety depends on the specific disorder and severity.
- Similar to depression, non-pharmacological treatment is typically preferred for mild to moderate anxiety. For severe anxiety, a combined pharmacological and non-pharmacological approach is often used.
- Non-pharmacological treatments used in the treatment of anxiety include:
  - Psychotherapies. Similar to research on the treatment of depression, CBT is the most-studied form of psychotherapy for anxiety and has been shown to be effective.[46]
  - Adjunctive therapies include mind-body therapies (e.g., meditation, yoga, relaxation, mindfulness, prayer, biofeedback, and creative therapies such as art therapy, music therapy), and exercise.

2.3 Recommendations & Rationale

The recommendations in this guideline are based on reviews of the literature, the experience of staff and physicians working at BC's Kidney Care Centres (KCCs) and expert mental health clinicians.

Recommendations in this guideline are based on the algorithm in Table 3.

Table 3: Depression/Anxiety Algorithm for KCC Patients



[1] Screening Tools
- PHQ-9 (Depression) & GAD-7 (anxiety): phqscreeners.com

[2] Helpful Patient Resources
- Family Physician Guide (2007): Sfu.ca/carmha/publications/family-physician-guide-for-depression-anxiety.html
- Cognitive Behaviour Interpersonal Skills Manual: Fpscbc.ca/sites/default/files/CBIS%20Manual-Electronic%20Copy%20-%20v2%20Oct%2022,%202015.pdf

[3] Crisis Information/Resources:
- Working with the Suicidal Patient: A Guide for Health Care Professionals (2007); Sfu.ca/carmha/publications/working-with-the-suicidal-patient-a-guide-for.html
- Canada Suicide Prevention Service: Crisisservicescanada.ca/en/
- BC Crisis Centre: Crisiscentre.bc.ca

Recommendation #1: Be alert to clinical symptoms to identify patients who may be experiencing depression and/or an anxiety disorder (universal screening of all KCC patients is not recommended). If symptoms are identified, refer to KCC Social Worker for further assessment.

For clinical symptoms, refer to sections 2.1 and 2.2 (Depression and Anxiety Disorders and CKD).

Universal screening of CKD patients for depression and/or an anxiety disorder:

- The most recent Canadian group of experts to systematically study the literature on depression screening was the Canadian Task Force on Preventive Health Care (2013). They recommended against routine screening even in subgroups of the population who may be at increased risk for depression (including people with chronic diseases such as CKD).
- While there has not been a similar review published for anxiety screening, it is likely the findings would be similar (especially given there is even less published about anxiety screening than depression screening).

Recommendation #2: Incorporate into the orientation of all new KCC staff and physicians:

1. Clinical symptoms of depression and/or an anxiety disorder in KCC patients;
2. Successful approaches in working with KCC patients/families experiencing depression and/or an anxiety disorder.

Successful approaches in working with KCC patients experiencing depression and/or an anxiety disorder include:

- Educate the patient and their family about depression and anxiety, its presentation in people with chronic disease and the reasons that it is important to address.
- Explain that having a chronic disease affects people differently depending on their past experiences and current circumstances.
- Be aware of how the patient's symptoms of depression and/or anxiety may be interfering with efforts to communicate with and educate the patient.
- Clarify the patient's understanding of health information and address their perceptions/ emotions prior to proceeding.
- Suggest that the patient bring someone with them to their appointments to provide an additional set of eyes and ears and to help them process the information provided.
- Tell patients that it is normal to have trouble understanding some of the information provided and that it is fine to ask for information to be repeated.
- Encourage the patient to contact their KCC if they become confused or worried about information that they have received.
- Normalize that there are social and psycho emotional aspects to CKD and explain that the role of social work in KCC is to assess and help them with these aspects.

Recommendation #3: If clinical symptoms of depression and/or anxiety are present, KCC Social Worker conducts a social/psycho/emotional assessment interview, including administering appropriate screening tool(s) for anxiety and/ or depression. symptoms. Suggested screening tools[2]:

- Depression: Patient Health Questionnaire-9 (PHQ-9) Gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/depression_patient_health_questionnaire.pdf
- Anxiety: General Anxiety Disorder-7 (GAD-7) Camh.ca/-/media/files/formgad7-pdf.pdf

Screening tools are not diagnostic tools. The "gold standard" for diagnosing depression and/or anxiety disorders (or other mental health disorders) is an assessment interview and comparison of the responses to the DSM- criteria.

Recommendation #4: Assess suicide risk at the time of the assessment interview and periodically thereafter. If present, take immediate follow-up action. See Table 4.

Table 4: General Responses to Identified Suicide Risk

ASK Suicidal Thoughts • Plan • Lethality • Means		
↓	↓	↓
Suicidal ideation or thoughts only, without a plan	**Suicidal ideation with a plan or history of suicide attempt, without immediate intent**	**Suicidal ideation with an imminent plan**
↓	↓	↓
Low Risk	**Medium Risk**	**High Risk**
• Refer to primary care provider (PCP) as soon as possible for further assessment &/or mental health referral • Provide information about crisis/urgent telephone lines e.g., 1-800-SUICIDE (1-800-784- 2433) • Develop a Safety Plan with the patient (see Table 5).	• Refer to primary care provider (PCP) as soon as possible for further assessment &/or mental health referral • Provide information about crisis/urgent telephone lines e.g., 1 800-SUICIDE (1-800-784- 2433) • Develop a Safety Plan with the patient (see Table 5).	• Refer &/or take immediately to local Emergency Room. If off-site, call 911 (or other immediate response such as "car 87" in Vancouver).

Adapted from (BC Reproductive Mental Health Program & Perinatal Services BC, 2014) [47]

Clinician resources on Suicide Risk assessments:
1. Compass Toolkit
2. Suicide Risk Assessment Guide (Ontario Hospital Association)

Table 5: Components of a Safety Plan

SAFETY PLAN
• Warning signs of the risk of imminent suicide (e.g., feeling trapped, worthless, hopeless, talking about death, writing a will, hoarding medications). • Coping strategies that decrease the patient's level of risk (activities that calm or comfort the patient such as deep breathing, meditation, taking a bath, a walk, etc). • People within the patient's network who can assist in times of need (friends/family). • Health professionals, agencies and crisis lines that can be contacted for help.

Adapted from (BC Reproductive Mental Health Program & Perinatal Services BC, 2014) [47]

Safety plan templates:
1. Suicide Prevention Toolkit (Centre for Suicide Prevention) (page 6)
2. EMentalHealth.ca

[2] There may be specific instances where an alternative or an additional screening tool is utilized which his more appropriate or specific for a particular group. The Geriatric Depression Scale (GDS) is an example of a tool which has been tested and utilized extensively in the older population to screen for depression.

Recommendation #5: If, after the assessment interview, mild depression and/or an anxiety disorder is confirmed:

- Address readily resolvable issues.
- Provide education & resources and one or two clinical counselling sessions (e.g., adjustment/ transition, symptom targeted therapy).
- If further assessment/treatment required, make referral.
- Refer to applicable community-based resources (see Appendix 1).

Recommendation #6: If, after the assessment interview, moderate or severe depression and/or an anxiety disorder is confirmed:

1. Work with the patient to develop a problem list, action plan and resource list (see Resources List in Appendix 1).
2. Contact the patient's PCP to review the action plan and confirm the respective roles of the PCP and KCC team. Send copy of completed screening tool(s) and the Physician Information Sheet on Ordering Antidepressants/Anxiolytics in Patients with CKD (Appendix 2a). If medications are required, the PCP is responsible for ordering and monitoring.
3. Communicate actions to KCC team. Put completed screening tool and document assessment findings and follow-up actions in patient's health record.
4. Confirm PCP received communication and will follow patient.

3.0 Depression, Anxiety and CKD in Children & Youth

Many of the concepts in the adult section (section 2.0) also apply to children & youth. Child & youth-specific concepts are discussed in this section.

3.1 Depression, Anxiety and CKD

How common is depression and/or anxiety in children & youth?

- There is considerable literature to suggest that children with chronic medical conditions have higher rates of depression and anxiety when compared to their healthy counterparts.[48,49] There have been limited studies, however, that specifically focus on children with CKD.
- Eight studies on depression or anxiety in children with CKD were identified in the published literature between 2004 and 2021. Five of the studies focused on depression/ depressive symptoms,[50-54] one on anxiety/ anxiety symptoms[55] and two on both types of symptoms.[56,57] The studies included children with CKD stages 1 - 5 and children on dialysis, post-transplant and receiving conservative care.

Depression/depressive symptoms

- Prevalence rates of depression/depressive symptoms were higher in children & youth with CKD than in children & youth in the general population.
- Rates ranged from 10% (n=38) to 30% (n=44) to 53% (n=67) to 64% (n=47) in the studies where rates were reported.[50-52,56]
- Rates in the general child and youth population are difficult to ascertain due to methodological differences in the studies (screening methods, cut-off points, etc). Point prevalence rates of major depressive disorders range from <1% - 2% in school-age children and from 1 - 7% in adolescents.[47] These rates underestimate the rates of children/adolescents with depression/ depressive symptoms.
- Age was considered a factor in one study (much

higher rates of depression in adolescents than children), was ruled out in two studies and was not mentioned in the others.
- Older age at time of CKD diagnosis was associated with higher depression scores in one study,[52] but not mentioned in others.
- Gender was considered a factor in one study (higher rates for girls), was ruled out in one study and was not mentioned in the others.
- Lower weekly Kt/V values were associated with higher rates of depressive symptoms in one study but not mentioned in the others.
- Obesity was associated with her rates of depression in one study.[54]
- Stage 4 and 5 CKD were associated with a slightly lower risk for depression than stage 3 CKD in one study, stage of disease was ruled out in another and not mentioned in the others.
- Recent hospitalizations (within the past 6 months), the presence of co-existing medical conditions and the presence of edema were associated with higher depression and anxiety scores on a self-reported survey in one study.

Anxiety disorders

- Two studies that focused on rates of anxiety disorders in children & youth with CKD.
  - One study reported a 5% prevalence rate (n=38) with no difference in the rate for children who were pre-dialysis vs on hemodialysis.[56]
  - A second study did not report a prevalence rate but did report there was no increase in anxiety levels amongst children on peritoneal dialysis (n=20) or receiving conservative treatment (n=95) when compared to a control group. Levels for children on hemodialysis, however, were increased (n=22)[55].
- Rates in the general child and youth population vary significantly depending upon study methodologies, the ages of children studied, studies of specific anxiety disorders vs any anxiety disorder, etc. Rates range from 6.1% - 9.5% for pre-school children and 2.8% - 25% for school-age children and adolescents.[58]

How might depression and/or anxiety manifest itself in children & youth?

- Children & youth may present with many of the same symptoms as adults (refer to section 2.0 of this guideline), although some may be expressed differently depending upon developmental age. Neurobiological and psychosocial factors also influence the presentation of anxiety and depression in children & youth.
- The literature describing the differences in the ways depression and anxiety manifests in children, youth and adults is based on studies of the general population. No studies specific to those with chronic medical conditions (including CKD) were identified.
- In children & youth, depression and/or anxiety often occurs in conjunction with other disorders such as attention deficit disorder, learning disorders and substance use disorders.
- See Table 6 for generalizations about the presentation of anxiety and/or depression in children and adolescents by age group. The table was compiled from a review of 5 articles.[59-63]

Table 6: Generalizations about the Presentation of Anxiety and Depression in Children & Youth

AGE GROUP	PRESENTATION
Toddlers	• Typically present with somatic symptoms such as loss of appetite, sleeping problems, failure to thrive and developmental disorders or stomach pain and no organic cause can be established. • After an initial period of increased distress (e.g., crying), these children become increasingly more passive and apathetic.
Pre-school	• Typically present with symptoms such as reduced psychomotor activity (slow movements, speech and reaction time), low energy, irritability and mood swings. • May show signs of aggression (e.g., grabbing toys or hitting or kicking other children).
School-age	• Typically report sadness (or sometimes boredom), guilt or fear of failure and withdraw from social contacts. • Somatic complaints are more common in school-age children than adolescents. Their mood is often more reactive and improves with positive experiences. • May experience separation anxiety and/or phobias. • Psychotic symptoms are rare, and when present they usually have hallucinations (auditory are the most common), rather than delusions. • Sometimes, suicidal ideation can occur.
Adolescents	• Presentation is more similar to adults. Typically present with loss of drive and interests, problems with self-esteem and self-confidence and social withdrawal. May report issues with concentration and performance at school. • Adolescents are more likely than adults to present with irritability, mood swings, a low frustration tolerance, violent temper and disruptive behaviour. • Phobias and compulsive activities may co-occur with the depression or become more pronounced. • If the depression and/or anxiety takes a chronic course, substance misuse and suicidality may result. • Depression is more often missed in adolescents than adults, probably because symptoms such as irritability and mood swings are perceived as “normal” adolescent behaviour. It may also be missed if it is masked by other presenting problems such as unexplained physical symptoms, eating disorders, anxiety, refusal to attend school, substance use or behavioural problems.

What tools are available to help screen for depression and anxiety in children & youth?

Depression

- A number of tools are available to screen for depression in children and adolescents. Two widely used tools with good evidence for their psychometric properties and a psychosocial interview mnemonic tool are summarized below. Generally, screening tools are most appropriate for use with children aged 8 years and older. To date, screening tools for depression have not been validated with pediatric CKD populations.
- The Children's Depression Inventory[64] is the most widely used screening tool for depression in children and adolescents. The age range of the CDI is 7-17 years. It is made up of 27 items that cover a broad range of symptoms of depression. The CDI takes approximately 10-20 minutes to complete. The manual includes suggested clinical cut-off scores. Although the CDI has not been validated for use with pediatric CKD, it has been used successfully in studies of children with other chronic medical conditions such as epilepsy,[65] lupus,[66] and cancer.[67] A revised version of this measure, the CDI 2, was published in 2011. The CDI 2 is copyright protected and can be purchased through the publisher — Multi-Health Systems (mhs.com).
- The Mood and Feelings Questionnaire[68] is designed to assess symptoms of depression in children & youth aged 8-18 years. It consists of 32 items and takes approximately 10 minutes to complete. There is no single clinical cut-off score for the MFQ, but a number of published articles are available to help users choose the most appropriate cut-off for various circumstances. The MFQ is free to download. The MFQ has been used to measure depression in a number of pediatric chronic illness populations, including juvenile rheumatoid arthritis,[69] epilepsy,[70] and recurrent cardiac arrhythmia.[71]
- The HEADSS/HEEADSSS mnemonic is a comprehensive psychosocial assessment tool for health care providers to facilitate risk identification in children, adolescents and young adults (10 years and older) in domains including sexuality, suicidality, depression and mood. [72,73]

Anxiety

- Two widely used tools for screening symptoms of anxiety in children and adolescents with good evidence for their psychometric properties are outlined below. Similar to screening tools for depression, there has been little research published to date on the validity of these tools in pediatric CKD populations.
- The Multidimensional Anxiety Scale for Children, Second Edition.[74] The MASC 2 is a 50-item scale that measures symptoms of anxiety disorders. It takes approximately 15 minutes to complete. The age range for the MASC-2 is 8-19 years. The MASC has been used in studies of children with asthma,[75] lupus[66] and thalassemia.[76] The MASC 2 manual includes clinical cut-off scores. The CDI is copyright protected and can be purchased through the publisher — Multi-Health Systems (mhs.com).
- The Screen for Child Anxiety-Related Emotional Disorders[77] is a 38-item scale designed to assess symptoms of anxiety in children aged 8-18

years old. The SCARED takes approximately 10 minutes to complete. The measure includes suggested cut-off scores for further assessment for possible Generalized Anxiety Disorder, Separation Anxiety, Social Anxiety Disorder, and school refusal. It is free to download. The SCARED has been used in studies of children with epilepsy,[70] chronic pain,[78] and juvenile rheumatoid arthritis.[79]

3.2 Recommendations and rationale

Screening, identification and management of depression and/or anxiety disorders in children & youth

- Recommendations are similar to those outlined in section 2.3.
- Universal screening for depression and/or anxiety in children with CKD is not recommended. It is recommended that all members of the renal team be educated and alert to clinical symptoms and, when identified, refer the child to the KCC Social Worker.
- The KCC Social Worker utilizes a psychosocial interview and/or structured screening tool(s) (see section above for a description of the tools) to further assess the child/family. Note: Screening tools are not diagnostic instruments. The gold standard for assessment of depression and anxiety disorders is a detailed diagnostic interview that covers DSM-5 criteria.
- If symptoms of mild depression and/or anxiety are identified, the KCC Social Worker educates the child/family, provides resources and psychotherapy and refers to relevant community resources.
- If moderate or severe depression and/or anxiety are identified, the child/family is referred to the KCC Psychologist for a diagnostic assessment and treatment. For acute/high risk children and those requiring medication therapies, a referral may also be made to a Child and Adolescent Psychiatrist. Fax the Physician Information Sheet on Common Antidepressants/Anti-anxiety Drugs in CKD in Children & Adolescents (Appendix 2b) to the Psychiatrist.
- Although a detailed discussion is beyond the scope of this guideline, it should be noted that the renal team often identifies other mental health and developmental conditions in pediatric CKD patients (e.g., ADHD, Autism, Intellectual Disabilities, Learning Disabilities). These children are referred by the KCC Social Worker and/or Psychologist for specialized resources as required.
- Within the scope of their role within the BCCH Renal Program, the KCC Psychologist accepts referrals if one or both of the following are indicated: 1) the child has a psychological problem that is having a significant negative impact on the treatment of his/her medical condition, 2) the child's medical condition and/or treatment is having a significant negative impact on his/her psychological well-being. In cases where children present with mental health concerns that are not clearly linked with their medical condition, the KCC Psychologist facilitates referrals to appropriate hospital and/or community resources.

Supporting parents/caregivers of pediatric CKD patients experiencing depression and/or anxiety

- Parents and caregivers of children diagnosed with CKD may experience symptoms of anxiety and depression. In some cases, parents have pre-existing symptoms or diagnoses, and other parents may develop symptoms following their child's medical diagnosis.
- The KCC Social Worker meets with parents during their child's initial presentation and obtains a psycho-social-emotional assessment of the family. Families are seen during subsequent clinic visits (every 1 - 6 months depending on disease progression) for on-going assessment and intervention as needed. The KCC Social Worker may see parents multiple times per year, and speak on the phone between clinic visits, which aids in developing long-term therapeutic relationships. Additionally, other members of the KCC team share concerns regarding parents' mood, behaviour, or difficulty coping with the KCC Social Worker.
- Parents and caregivers demonstrating symptoms of anxiety or depression will be supported by the KCC Social Worker to access appropriate services. It is recognized that caring for a child with chronic illness is emotionally, financially, and practically demanding for parents. It may be difficult for parents to care for their own mental health needs; social work provides support and encouragement to do so. Parents may be screened via a screening tool in clinic or referred to an outside professional for screening. Parenting strategies, resources, and counseling on the topic of coping with a child with chronic illness and parent self-care will be provided in the clinic. When more intensive assessment or services are required, social work assists in facilitating referrals to:
  - Family physician
  - Reproductive Mental Health for new mothers
  - Community psychologist, Employee Assistance Program or a community-based counseling programs (with sliding fee scale for low-income families)
  - Community based family support workers and/or group parenting classes
- In instances where significant mental health issues are impacting parents' ability to care for a child with chronic illness, the KCC Social Worker will consider referral to Ministry for Children and Family Development for intensive in-home support programs and monitoring.
- For parents of children with significant developmental delays, the KCC Social Worker will liaise with Child and Youth with Special Needs to advocate for services such as respite and behavioural therapists to aid parents in coping with the challenges of caring for their child.
- Where anxiety and depression preclude a parent from maintaining employment, the KCC Social Worker will assist in navigating sick leave benefits, employment insurance and disability benefits.
- For children with CKD admitted to hospital, the Social Worker may request provision of additional support to parents by Spiritual Care and Child Life Specialists.

Resources for children with depression and/or anxiety disorders & their parents/caregivers

- Refer to Appendix 1, part B.

Physician information sheet: Common antidepressants & CKD

- Refer to Appendix 2b.

4.0 Sponsors

Developed by:

- Working Group of KCC multidisciplinary care providers from across BC (see Appendix 3 for a list of participants) (2015, 2024).

Reviewed by:

- BC Kidney Care Clinic Committee (2015); KCC Leadership Group (2024)
- BC Renal Pharmacy & Formulary Committee (2015).
- BC Renal Medical Advisory Committee (2015).

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Appendix 1: Resources for Depression &/or Anxiety

Social Workers at each KCC maintain a list of resources available locally for adults and children experiencing depression and/or anxiety. If resources are required outside the local catchment area, the KCC Social Worker contacts a Social Worker at the appropriate KCC or a known local resource.

Part A: Resources for Adults

Community Resources:

1. Family Physician/ Nurse Practitioner
2. Local Adult Mental Health and/or Older Adult Mental Health Team
3. HealthLink BC at 811 (24/7). Provides non-emergency health information and information about local resource. Healthlinkbc.ca

Crisis Information/Resources:

1. Local Emergency Room
2. Crisis Lines/On-line Support:
   a. 1-800-SUICIDE (1-800-784-2433). (BC, 24/7). 140 languages. For people who are or know someone who is having thoughts of suicide. Crisiscentre.bc.ca
   b. 310-Mental Health (310-6789 – no need to dial area code) (BC, 24/7). For people looking for emotional support, information, and resources. Crisiscentre.bc.ca
   c. Online chat service (BC, noon- 1 AM), Crisiscentrechat.ca
3. KUU US Crisis Line Society: First Nations and Indigenous-specific crisis services through education, prevention, and intervention programs. Includes 24/7 crisis line (adults, elders and youth). 1-800-588-8717. Kuu-uscrisisline.com

Counselling/Support Websites

1. BC Psychological Association. 1-800-730-0522. Psychologists.bc.ca
2. BC Association of Clinical Counsellors. BC-counsellors.org
3. Mood Disorders Association of BC (offers support groups throughout the province). 604 873-0103. Mdabc.net
4. Anxiety Canada (information and brochures about anxiety and self-help strategies). Anxietycanada.com
5. Canadian Mental Health Association, BC Division (provides mental health promotion and mental illness recovery-focused programs and services for people of all ages and their families). CMHA.bc.ca
6. Bounce Back (free skill-building program designed to help adults and youth 15+ manage low mood, mild to moderate depression, anxiety, stress or worry. Delivered online or over the phone with a coach). Bouncebackbc.ca
7. Aboriginal Organizations and Services in BC (provincial listing of First Nation, Métis and Aboriginal organizations, communities, and community services) Gov.bc.ca/arr/services/guide.html
8. Kelty Mental Health Resource Centre (mental health and substance use information, resources, and peer support to families across BC). 1-800-665-1822 or Keltymentalhealth.ca
9. Foundry BC (offers young people ages 12 – 24 health and wellness resources, services and supports – online and through integrated service centres in communities across BC).

Foundrybc.ca
Foundrybc.ca/info-tools/mental-health-substance-use

Self-help Guides

1. Cognitive Behavioural Interpersonal Skills Manuals (promoted by BC's Practice Support Program for Family Physicians):
   - Depression: Gpscbc.ca/sites/default/files/CBIS%20Manual-Electronic%20Copy%20-%20v2%20Oct%2022,%202015.pdf
   - Anxiety addendum: Yumpu.com/en/document/read/28521592/anxiety-addendum-gpsc
2. Antidepressant Skills Workbook (available in multiple languages and as a "talking book"): Sfu.ca/carmha/publications/antidepressant-skills-workbook.html/
3. Positive Coping with Health Conditions, A Self-Care Workbook. (workbook on relaxation, managing worry/depression/anger, solving programs, etc). Sfu.ca/carmha/publications/positive-coping-with-health-conditions.html
4. Here to Help (self-help information website sponsored by BC Partners for Mental Health and Addictions). Heretohelp.bc.ca.
5. Ten Days to Self-Esteem (Burns, D, 1998) and PTSD Workbook (Williams, MB et al, 2002) (available through multiple sources - on-line or bookstores).

Website for Health Care Professionals

1. Canadian Coalition for Seniors' Mental Health Late Life Suicide Prevention Toolkit (educational program about suicide prevention in older adults). Ccsmh.ca/projects/suicide
2. Link to BC physician guidelines for treating depression and anxiety
   - Depression, Adults: Gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/depression-in-adults
   - Anxiety and Depression in children & Youth: Gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/anxiety-and-depression-in-children-and-youth

Part B: Resources for Children and their Parents

Community Resources:

1. Family Physician/ Pediatrician / Nurse Practitioner
2. Child & Youth Mental Health Intake Clinics (specialized services provided through the Ministry of Children and Family Development by Child and Youth Mental Health Teams in BC, by geographic area). Gov.bc.ca/gov/content/health/managing-your-health/mental-health-substance-use/child-teen-mental-health/mental-health-intake-clinics
3. Foundry BC (offers young people ages 12 – 24 health and wellness resources, services and supports – online and through integrated service centres in communities across BC). Foundrybc.ca; Foundrybc.ca/get-support/find-community-services
4. HealthLink BC at 811 (24/7). Provides non-emergency health information and information about local resource. Healthlinkbc.ca

Crisis Information/Resources:

1. Local Emergency Room.
2. Child and Adolescent Response Team (CART): Provides urgent response (within 72 hours), short-term mental health service to school-aged children & youth in Vancouver experiencing acute psychiatric or emotional crises. Services include urgent assessment and consultation, clinical intervention, and coordination with community resources: 604-874-2300. Vch.ca/en/location-service/child-adolescent-response-team-cart-west-broadway
3. Kids Help Phone (24/7): National support service offering professional counselling, information and referrals and volunteer-led text-based support. English and French. Phone: 1-800-668-6868. Kidshelpphone.ca
4. Crisis Lines/On-line Support:
    a. 1-800-SUICIDE (1-800-784-2433). (BC, 24/7). 140 languages. For people who are or know someone who is having thoughts of suicide. Crisiscentre.bc.ca
    b. 310-Mental Health (310-6789 – no need to dial area code) (BC, 24/7). For people looking for emotional support, information, and resources. Crisiscentre.bc.ca
    c. Online chat service (BC, noon- 1 AM), Crisiscentrechat.ca
5. Helpline for Children: To report suspected cases of child abuse or neglect in BC (24/7): 1-800-663-9122. 310-1234 (no area code).
6. KUU US Crisis Line Society: First Nations and Indigenous-specific crisis services through education, prevention, and intervention programs. Includes 24/7 crisis line (adults, elders and youth). 1-800-588-8717. Kuu-uscrisisline.com

Counselling/Support Websites:

1. BC Psychological Association. 1-800-730-0522. Psychologists.bc.ca
2. BC Association of Clinical Counsellors. BC-counsellors.org
3. Anxiety Canada (information and brochures about anxiety and self-help strategies). Anxietycanada.com
4. Canadian Mental Health Association, BC Division (provides mental health promotion and mental illness recovery-focused programs and services for people of all ages and their families). CMHA.bc.ca
5. Bounce Back (free skill-building program designed to help adults and youth 15+ manage low mood, mild to moderate depression, anxiety, stress or worry. Delivered online or over the phone with a coach). Bouncebackbc.ca
6. Aboriginal Organizations and Services in BC (provincial listing of First Nation, Métis and Aboriginal organizations, communities, and community services) Gov.bc.ca/arr/services/guide.html
7. Kelty Mental Health Resource Centre (mental health and substance use information, resources, and peer support to families across BC). 1-800-665-1822 or keltycentre@cw.bc.ca; Keltymentalhealth.ca

8. Foundry BC (offers young people ages 12 – 24 health and wellness resources, services and supports – online and through integrated service centres in communities across BC). Foundrybc.ca; Foundrybc.ca/info-tools/mental-health-substance-use
9. Drug Cocktails (facts about mixing medicine, booze and street drugs for youth and professionals). Drugcocktails.ca

Self-help Guides:

1. Dealing with Depression: Antidepressant Skills for Teens: Gov.bc.ca/assets/gov/health/managing-your-health/mental-health-substance-use/child-teen-mental-health/dealing_with_teen_depression_writable.pdf
2. Anxiety Canada (information and brochures about anxiety and self-help strategies). Anxietycanada.com; MindShift CBT (includes app): Anxietycanada.com/resources/mindshift-cbt

Website Resources for Parents:

1. Parenting children with health issues, Resources for parents. Parentingchildrenwithhealthissues.com/index.html
2. KidsHealth.org, Support for caregivers
3. National Kidney Foundation, Parenting children with chronic kidney disease: Kidney.org/kidney-topics/children-chronic-kidney-disease-tips-parents
4. FamilySmart: Support for families of children and young people, including Parent Peer Support. Familysmart.ca

Clinician Resources:

1. BC Children's Hospital Compass Program (telephone consultation support to community providers and prescribers to care for children and youth with mental health or substance use concerns). Compassbc.ca; 1-855-702-7272.

Appendix 2a: Physician Information Sheet - Common Antidepressants in Chronic Kidney Disease in Adults[1,2]

Abbreviations: CV: cardiovascular; eGFR: estimated Glomerular Filtration Rate; HD: hemodialysis; HS: at bedtime; Max: maximum dose, N/V/D: nausea/vomiting/diarrhea; PD: peritoneal dialysis; **SD: starting dose, increase carefully from this dose;** ↑ increase; ↓ decrease

Medications	Dosing adjustment in renal failure				Comments
	eGFR 30-60 mL/min	eGFR 15-30 mL/min	eGFR less than 15 mL/min	Dialysis (PD or HD)	
1st line therapies					
Selective Serotonin Reuptake Inhibitors (SSRI)					
Citalopram[3,4]	No adjustment	No adjustment	No adjustment	No adjustment (HD: not removed)	• Risk of QTc prolongation (max 40 mg/day or 20 mg/day if strong CYP2C19 inhibitors concurrently prescribed*)
Escitalopram	No adjustment	SD: 10 mg/day	SD:10 mg/day	SD:10 mg/day, (HD: not removed)	• Risk of QTc prolongation
Fluoxetine[5]	No adjustment	No adjustment	No adjustment	No adjustment	• Risk of QTc prolongation
Fluvoxamine[6]	No adjustment	No adjustment	No adjustment	No adjustment	• Many potential drug interactions • Most nauseating and sedating SSRI
Paroxetine	SD: 10 mg/day	SD: 10 mg/day	SD: 10 mg/day	SD: 10 mg/day	• Most anticholinergic activity among the SSRIs (caution in elderly)
Sertraline[7, 8]	No adjustment	SD: 50 mg/day	SD: 25 mg/day	SD: 25 mg/day	• Can been used for pruritus • Used in CAST study (SD: 50 mg/d, max dose: 200 mg/d, median dose: 150 mg/d)[8]
Vortioxetine[9]	No adjustment	No adjustment	No adjustment	No adjustment	• CYP 2D6 is primarily metabolic pathway

continued...

[1] Nagler EV, Webster AC, Vanholder R, et al. Antidepressants for depression in Stage 3-5 chronic kidney disease: a systemic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP). Nephrol Dial Transplant 2012; 27:3736-45.

[2] Hedeyati SS, Yalamanchili V and Finkelstein FO. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. Kidney Int 2012; 81: 247-55.

[3] Joffe P, Larsen FS, Pedersen V and Ring-Larsen H. Single-dose pharmacokinetics of citalopram in patients with moderate renal insufficiency or hepatic cirrhosis compared with healthy subjects. Eur J Clin Pharmacol 1998; 54: 237-42.

[4] Spigset O, Hagg S, Stegmayr B and Dahlqvist R. Citalopram pharmacokinetics in patients with chronic renal failure and the effect of hemodialysis. Eur J Clin Pharmacol 2000; 56: 699-703.

[5] Blumenfield M, Levy NB, Spinowitz B et al. Fluoxetine in depressed patients on dialysis. Int J Psychiatry Med 1997; 27: 71-80.

[6] Kamo T, Horikawa N, Tsuruta Y et al. Efficacy and pharmacokinetics of fluvoxamine maleate in patients with mild depression undergoing hemodialysis. Psychiatry Clin Neurosci 2004; 58: 133-7.

[7] Schwenk MH, Verga MA, Wagner JD. Hemodialyzability of sertraline. Clin Nephrol 1995; 44: 121-4.

[8] Hedeyati SS, Gregg LP, Carmody T, Jain N, et al. Effect of Sertraline on Depressive Symptoms in Patients in Chronic Kidney Disease Without Dialysis Dependence: The CAST Randomized Clinical Trial. JAMA 2017; 318(19): 1876-90.

[9] Vortioxetine. Lexi-Drugs. UpToDate Lexidrug. UpToDate Inc. https://online.lexi.com. Accessed August 9, 2024.

Medications	Dosing adjustment in renal failure				Comments
	eGFR 30-60 mL/min	eGFR 15-30 mL/min	eGFR less than 15 mL/min	Dialysis (PD or HD)	
Non - 1st line therapies					
Serotonin/Norepinephrine Reuptake Inhibitors (SNRI)					
Desvenlafaxine	SD: 50 mg Q2days	Max: 50 mg Q2days	Max: 50 mg Q2days	Max: 50 mg Q2days	
Duloxetine[10]	No adjustment	SD: 30 mg/day	SD: 30 mg/day and increase carefully; max: 60 mg/day	SD: 30 mg/day and increase carefully; max: 60 mg/day	• Also used for peripheral neuropathy (has indication for pain associated with diabetic peripheral neuropathy)
Venlafaxine	No adjustment	SD: 37.5 mg/day and increase carefully; typical max: 112.5 mg/day. If needed, dose can be increased to 150 mg/day with very close monitoring	SD: 37.5 mg/day and increase carefully; typical max: 112.5 mg/day. If needed, dose can be increased to 150 mg/day with very close monitoring	SD: 37.5 mg/day and increase carefully; typical max: 112.5 mg/day. If needed, dose can be increased to 150 mg/day with very close monitoring	• Possibly more N/V than SSRIs • Also used off-label for peripheral neuropathy • "Typical max" listed here is consistent with monograph that recommends max 225 mg/day and 50% dose reduction for eGFR < 30 mL/min. Suggestion for increasing dose as needed to 150 mg/day is based on clinical experience with using up to 300 mg/day in patients with normal renal function
Serotonin Antagonist/Reuptake Inhibitor (SARI)					
Trazodone	No adjustment	No adjustment	SD: 150 mg/day	SD: 150 mg/day	• Good choice for concomitant insomnia (usual dose for this indication: 25-50 mg)
Other Antidepressants					
Bupropion[11, 12]	Consider max dose 150 mg/day	Max dose 150 mg/day	SD: 100 mg PO q48h or 150 mg PO q72h. Increase carefully; max 150 mg/day	SD: 100 mg PO q48h or 150 mg PO q72h. Increase carefully; max 150 mg/day	• Risk of accumulation of toxic metabolites causing dysrhythmia (wide QRS complex) • Caution in seizure disorders
Mirtazapine[13]	No adjustment	SD:7.5-15 mg/d	SD:7.5-15 mg/d	SD: 7.5-15 mg/d	• Also used off-label for pruritus • Good choice for concomitant insomnia and appetite stimulation

continued...

[10] Duloxetine. Lexi-Drugs. UpToDate Lexidrug. UpToDate Inc. https://online.lexi.com. Accessed August 9, 2024.
[11] Worrall SP, Almond MK, Dhillon S. Pharmacokinetics of bupropion and its metabolites in haemodialysis patients who smoke. A single dose study. Nephron Clin Prac 2004; 97) :c83-9.
[12] Bupropion. Lexi-Drugs. UpToDate Lexidrug. UpToDate Inc. https://online.lexi.com. Accessed August 9, 2024.
[13] Mirtazapine. Lexi-Drugs. UpToDate Lexidrug. UpToDate Inc. https://online.lexi.com. Accessed August 9, 2024.

Medications	Dosing adjustment in renal failure				Comments
	eGFR 30-60 mL/min	eGFR 15-30 mL/min	eGFR less than 15 mL/min	Dialysis (PD or HD)	
Tricyclic antidepressants (TCAs)					
Not preferred agents. Use with caution; dialysis patients have demonstrated increased sensitivity to the anticholinergic side effects of TCAs, possibly due to glucuronide metabolite accumulation.[14]					
Amitriptyline	No dose adjustment required. However, use with caution and monitor closely with dose increases.				• Also used off-label for peripheral neuropathy • Among TCAs, one of the agents associated with more sedation, anticholinergic side effects, and weight gain[15] • The TCA that has been most commonly associated with Torsade de pointes in case reports[16]
Clomipramine	No dose adjustment required. However, use with caution and monitor closely with dose increases.	SD: 10 mg/day. Use with caution and monitor closely with dose increases.	SD: 10 mg/day. Use with caution and monitor closely with dose increases.	SD: 10 mg/day. Use with caution and monitor closely with dose increases.	• Also used for peripheral neuropathy (has indication for pain associated with diabetic peripheral neuropathy)
Desipramine	No dose adjustment required. However, use with caution and monitor closely with dose increases.	No dose adjustment required. However, use with caution and monitor closely with dose increases.	SD: 25 mg/day. Use with caution and monitor closely with dose increases.	SD: 25 mg/day. Use with caution and monitor closely with dose increases.	• Also used off-label for peripheral neuropathy • Relatively well tolerated TCA (fewer anticholinergic side effects and less sedating) [15]
Doxepin	No dose adjustment required. However, use with caution and monitor closely with dose increases.				• Also used for insomnia (usual dose 3-6 mg) and pruritus (off-label) • Highly sedating and associated with weight gain[15] • Among TCAs, one of the agents associated with more QTc prolongation[16]
Imipramine	No dose adjustment required. However, use with caution and monitor closely with dose increases.	SD: 10 mg/day. Use with caution and monitor closely with dose increases.	SD: 10 mg/day. Use with caution and monitor closely with dose increases.	SD: 10 mg/day. Use with caution and monitor closely with dose increases.	• Also used off-label for peripheral neuropathy • Associated with more orthostatic hypotension than other TCAs[15] • Among TCAs, one of the agents associated with more QTc prolongation[16]
Nortriptyline	No dose adjustment required. However, use with caution and monitor closely with dose increases.				• Also used off-label for peripheral neuropathy • Relatively well tolerated TCA (fewer anticholinergic side effects and less sedating) [15]

Notes:
- Risk for arrhythmia associated with drug-induced QTc prolongation increased with electrolyte abnormalities (low calcium, magnesium, potassium), diuretic use, females – see[16] Ncbi.nlm.nih.gov/pmc/articles/PMC8237186/pdf/postgradmedj-2020-138661.pdf.
- List of strong CYP2C19 inhibitors: omeprazole, esomeprazole, lansoprazole, rabeprazole, clopidogrel, voriconazole, fluoxetine, fluvoxamine.[17]

[14] Lieberman JA, Cooper TB, Suckow RF, Steinberg H, Borenstein M, Brenner R, Kane JM. Tricyclic antidepressant and metabolite levels in chronic renal failure. Clin Pharmacol Ther. 1985; 37(3):301-7.
[15] Hirsch M, Birnbaum RJ. Tricyclic and tetracyclic drugs: Pharmacology, administration, and side effects [cited 09 Aug 2024]. Available from: UpToDate [subscription required to view].
[16] Funk M, Beach S, Bostwick J, et al. APA resource document on QTc prolongation and psychotropic medications. AM J Psychiatry 2020; 177(3):273-4.
[17] Verstuyft C, Simon T, Kim RB. Personalized medicine and antiplatelet therapy: ready for prime time? Eur Heart J 2009; 30: 1943-63.

A special thank you to Dr. Andrea Wan, clinical pharmacy specialist in psychiatry at St. Paul's Hospital for reviewing this summary table.

Appendix 2b: Physician Information Sheet - Common Antidepressants/ Anti-Anxiety Drugs in Chronic Kidney Disease in Children & Adolescents (C&A)[1,2]

Abbreviations: CV: cardiovascular; eGFR: estimated Glomerular Filtration Rate; HD: hemodialysis; HS: at bedtime; Max: maximum dose, N/V/D: nausea/vomiting/diarrhea; PD: peritoneal dialysis; SD: starting dose; ↑ increase; ↓ decrease

Medications	Dosing adjustment in renal failure				Comments
	eGFR 30-60 mL/min	eGFR 15-30 mL/min	eGFR less than 15 mL/min	Dialysis (PD or HD)	
1st line therapies					
Selective Serotonin Reuptake Inhibitors (SSRI)					
Citalopram[3,4]	No adjustment	No adjustment	No adjustment	No adjustment (HD: not removed)	• Safe in pts with CV disease, but risk of QTc prolongation (Max 40 mg/day or 20 mg/day w/ strong CYP2C19 inhibitors) • Half as potent as escitalopram, therefore NOT interchangeable
Escitalopram	No adjustment	SD: 10 mg/day, ↑ carefully	SD:10 mg/day, ↑ carefully	SD:10 mg/day, ↑ carefully (HD: not removed)	• Safe in pts with CV disease, but risk of QTc prolongation (Max 20 mg/day) • Twice as potent as citalopram, therefore NOT interchangeable
Fluoxetine[5]	No adjustment	No adjustment	No adjustment	No adjustment (HD: not removed)	• Risk of QTc prolongation
Fluvoxamine[6]	No adjustment	No adjustment	No adjustment	No adjustment HD: partially removed)	• Children: Max 200 mg/day, Adolescents: Max 300 mg/day
Sertraline[7]	No adjustment	SD: 25-50 mg/day ↑ carefully	SD: 25-50 mg/day consider ↓ max dose	SD: 25 mg/day, consider ↓ max dose (HD: not removed)	• Safe in pts with CV disease

continued...

[1] Nagler EV, Webster AC, Vanholder R, et al. Antidepressants for depression in Stage 3-5 chronic kidney disease: a systemic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP). Nephrol Dial Transplant 2012; 27:3736-45.
[2] Hedeyati SS, Yalamanchili V and Finkelstein FO. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. Kidney Int 2012; 81: 247-55.
[3] Joffe P, Larsen FS, Pedersen V and Ring-Larsen H. Single-dose pharmacokinetics of citalopram in patients with moderate renal insufficiency or hepatic cirrhosis compared with healthy subjects. Eur J Clin Pharmacol 1998; 54: 237-42.
[4] Spigset O, Hagg S, Stegmayr B and Dahlqvist R. Citalopram pharmacokinetics in patients with chronic renal failure and the effect of hemodialysis. Eur J Clin Pharmacol 2000; 56: 699-703.
[5] Blumenfield M, Levy NB, Spinowitz B et al. Fluoxetine in depressed patients on dialysis. Int J Psychiatry Med 1997; 27: 71-80.
[6] Kamo T, Horikawa N, Tsuruta Y et al. Efficacy and pharmacokinetics of fluvoxamine maleate in patients with mild depression undergoing hemodialysis. Psychiatry Clin Neurosci 2004; 58: 133-7.
[7] Schwenk MH, Verga MA, Wagner JD. Hemodialyzability of sertraline. Clin Nephrol 1995; 44: 121-4.

Medications	Dosing adjustment in renal failure				Comments
	eGFR 30-60 mL/min	eGFR 15-30 mL/min	eGFR less than 15 mL/min	Dialysis (PD or HD)	
Non - 1st line therapies					
Serotonin/Norepinephrine Reuptake Inhibitors (SNRI)					
Duloxetine	No adjustment	SD: 30 mg/day, ↑ carefully	SD: 30 mg/day, ↑ carefully	SD: 30 mg/day, ↑ carefully	• Consider for concomitant peripheral neuropathy (no data in C&A)
Venlafaxine	No adjustment	37.5-112.5 mg/day	37.5-112.5 mg/day	37.5-112.5 mg/day	• Consider for concomitant peripheral neuropathy (no data in C&A)
Serotonin Antagonist/Reuptake Inhibitor (SARI)					
Trazodone	Dose adjustment not required when dosed at 25-50 mg HS for insomnia; higher doses (150-600 mg) *virtually never* prescribed for depression in C&A				• Theoretical risk for serotonin syndrome when combined with SSRI/SNRIs but clinically of little concern at dose of 25-50 mg HS
Other Antidepressants					
Bupropion[8]	Max: 150 mg/day	Max: 150 mg/day	Max: 150 mg/day	Max: 100mg every 48 hours or 150 mg every 72 hours (HD: not removed)	• Non-sedating, may cause insomnia, not associated with weight gain • Risk of accumulation of toxic metabolites causing dysrhythmia in renal failure
Mirtazapine[9]	No adjustment	15 mg/day, ↑ carefully	15 mg/day, ↑ carefully	15 mg/day, ↑ carefully (HD: partially removed)	• May cause sedation, weight gain • A choice for concomitant insomnia (dose: 7.5-15 mg HS) and appetite stimulation

Additional Notes:

- Very few available antidepressants have formal regulatory approval from Health Canada for treatment of depression or anxiety in children and adolescents.
- Tricyclic antidepressants (TCA) are not first or second-line treatment options for depression in children and adolescents, though they may be used for non-depression indications. As TCAs are predominantly renally eliminated and have significant propensity for anticholinergic adverse effects, they are not typically recommended in children or adolescents with kidney impairment. [1,10]

[1] Nagler EV, Webster AC, Vanholder R, et al. Antidepressants for depression in Stage 3-5 chronic kidney disease: a systemic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP). Nephrol Dial Transplant 2012; 27:3736-45. [8] Worrall SP, Almond MK, Dhillon S. Pharmacokinetics of bupropion and its metabolites in haemodialysis patients who smoke. A single dose study. Nephron Clin Prac 2004; 97) :c83-9.
[9] Unterecker S, Müller P, Jacob C, Riederer P, Pfuhlmann B. Therapeutic drug monitoring of antidepressants in haemodialysis patients. Clin Drug Investig 2012; 32: 539-45.
[10] Eyler RF, Unruh ML, Quinn DK, Mary Vilay A, editors. Psychotherapeutic Agents in End- Stage Renal Disease. Seminars in dialysis; 2015: Wiley Online Library.

A special thank you to Dr. Dean Elbe, clinical pharmacy specialist in child & adolescent mental health at BC Children's and Women's Hospital, for reviewing this summary table.

Appendix 3: Depression/Anxiety Working Group Participants

Name	Discipline	Organizational Affiliation
Monica Beaulieu (2015)	Nephrologist	St. Paul's Hospital/BC Renal
Mike Bevilacqua (2021)	Nephrologist	Fraser Health/BC Renal
Erin Moon (2015)	Clinical Psychologist	BC Children's Hospital
Carole Richford (2015)	Psychiatrist	St. Paul's Hospital
Annemarie Falk (2015)	Family Physician	Vancouver
Angela Guan (2015)	Family Physician	Vancouver
Joslyn Conley (2015)	Nephrologist	Royal Inland Hospital, Kamloops
Bobbi Preston (2015)	Renal SW	Abbotsford Regional Hospital and Cancer Centre
Esther Krahn (2015)	Social Work Practice Leader	Interior Health, South Okanagan
Sue Saunders (2015)	RN	Interior Health
Nadia Zalunardo (2015)	Nephrologist	Vancouver General Hospital
Maureen Paciejewski (2015)	RN	University Hospital of Northern BC
Janet Williams (2015, 2024)	Project Coordinator	BC Renal

Child-Specific Section

Name	Discipline	Organizational Affiliation
Erin Moon (2015)	Clinical Psychologist	BC Children's Hospital
Anisha Varghese (2021)	Clinical Psychologist	BC Children's Hospital
Tanya Strubin (2015)	Social Worker	BC Children's Hospital
Janis Dionne (2015)	Nephrologist	BC Children's Hospital
Katie Haubrich (2015, 2021)	Pharmacist	BC Children's Hospital
Janet Williams (2015, 2024)	Project Coordinator	BC Renal

Physician Information Sheet - Antidepressants & CKD (Appendix 2)

Name	Discipline	Organizational Affiliation
Andrea Wan (2021, 2024)	Pharmacist	St. Paul's Hospital
Dean Elbe (2015, 2021, 2024)	Pharmacist	BC Children's Hospital
Hilary Wu (2024)	Pharmacist	Vancouver General Hospital
Judith Marin (2015, 2021, 2024)	Pharmacist	St. Paul's Hospital
Katie Haubrich (2015, 2021, 2024)	Pharmacist	BC Children's Hospital
Sue Corrigan (2015)	Pharmacist	Surrey Memorial Hospital