



PROVINCIAL STANDARDS & GUIDELINES



DEPRESSION AND ANXIETY: THE ROLE OF KIDNEY CARE CLINICS

Effective May 2015

Developed by the Kidney Care Committee




Table of Contents

- 1.0 Scope 3
- 2.0 Depression, Anxiety and Chronic Kidney Disease in *Adults* 3
 - 2.1 Depression and CKD 3
 - 2.2 Anxiety Disorders and CKD 7
 - 2.3 Recommendations and Rationale 10
- 3.0 Depression, Anxiety and Chronic Kidney Disease in *Children and Youth* 15
 - 3.1 Depression, Anxiety and CKD 15
 - 3.2 Recommendations and Rationale 19
- 4.0 Sponsors 21
- 5.0 Effective Date 21
- 6.0 References 21
- Appendix 1: Resources for Depression and/or Anxiety 25
 - Part A: Resources for Adults 25
 - Part B: Resources for Children and their Parents 26
- Appendix 2a: Physician Information Sheet - Common Antidepressants in Chronic Kidney Disease in Adults 28
- Appendix 2b: Physician Information Sheet - Common Antidepressants/Anti-Anxiety Drugs in Chronic Kidney Disease in Children and Adolescents (C & A) 30
- Appendix 3: Depression/Anxiety Working Group Participants 32



BC Provincial Renal Agency
 (BCPRA)
 700-1380 Burrard Street

Phone: 604-875-7340
 Email: bcpra@bcpra.ca
 Web: BCRenalAgency.ca

 [Facebook.com/BCRenalAgency](https://www.facebook.com/BCRenalAgency)
 [@BCRenalAgency](https://twitter.com/BCRenalAgency)
 [Youtube.com/BCRenalAgency](https://www.youtube.com/BCRenalAgency)

Depression and Anxiety: The Role of Kidney Care Clinics

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 dialysis¹, 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?

- Depression is a mood disorder that affects the way a person feels, thinks or behaves, which

may impair social or occupational functioning (Government of Canada, 2006).

- Onset can be triggered by biological, psychosocial or environmental factors, such as traumatic life events (e.g., diagnosis of CKD). Those who have experienced an episode of depression are at increased risk of future episodes (Canadian Task Force on Preventive Health Care, 2013).
- Major Depressive Disorder (MDD) is the most commonly diagnosed mental health disorder. It is characterized by one or more major depressive episodes. MDD is NOT transient unhappiness caused by life experiences or stress, nor is it a normal grief reaction associated with loss.
- MDD is a “spectrum” disorder and can range from mild to severe. A person may have a single episode, recurrent episodes or a chronic illness.

How common is depression?

- Rates vary widely in the published literature. Studies vary in their sample characteristics, measures used to define depression (self report screening tools vs clinical interview; depressive symptoms vs diagnosis of major depression), type of rate reported (point, period and/or lifetime incident/prevalent cases) and sample sizes.
- A large US study (National Co-morbidity Survey Replication) reported prevalence rates of 6.7% for MDD and 9.5% for any mood disorder in the general population. The study used a semi-structured interview format to diagnose a mood disorder (the “gold standard”). See Table 1.

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

Depression and Anxiety: The Role of Kidney Care Clinics

Table 1: Mood Disorder Prevalence Rates (Kesler, RC et al, 2005)

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 2002 Canadian Community Health Survey reported 12-month prevalence rates for MDD of 5% and lifetime prevalence rates of 12.5% (lower than the reported US rates) (Patten, SB and Lee, RC, 2005).
- In people with CKD, the dialysis population has been more studied than the non-dialysis population.

Dialysis population:

- Prevalence rates of 20% - 30%² are commonly reported (Hedayati, SS et al, 2006) (Watnick S et al, 2005) (Lopes AA et al, 2002).
- Rates are generally at the lower end when a semi-structured interview (vs semi-structured questionnaire) format is utilized to diagnose MDD.

Non-dialysis CKD population:

- Reported prevalence rates using self-administered questionnaires range from 7% (Ricardo AC et al, 2010) to 47% (Lee, YJ et al, 2013).
- One study that used a semi-structured interview format reported a 20% prevalence rate (Hedayati, SS et al, 2009).
- Several studies concluded that the stage of CKD did not significantly affect depression rates (Lee, YJ et al, 2013) (Andrade, CP et al, 2010) (Odden, MC et al, 2006).

- While depression rates vary across studies, there is consensus in the literature that rates are significantly higher amongst CKD patients (dialysis and non-dialysis) than in the general population.
- Anxiety disorders frequently co-exist in patients with MDD. The US National Comorbidity Survey Replication estimated that 60% of patients with MDD also suffered from an anxiety disorder during their lifetime (Kessler, RC et al, 2003).

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

- Causes of the higher rates are uncertain.
- Proposed causes include (Novak, M, 2013):
 - Disease-related: co-morbidities, pain, discomfort.
 - Treatment related: possibly medications.
 - Biological: anemia, uremia, neurotransmitters, neurotoxins and possibly inflammation.
 - Psychological: difficulty with adaptation, role changes, life goals, uncertainty, body image.
 - Social: changes in relationships, job, social roles, intimacy-sex
 - Lifestyle: lack of exercise, poor nutrition and difficulty sleeping.

² Rates are based on results of self-administered questionnaires.

Depression and Anxiety: The Role of Kidney Care Clinics

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?

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

How might depression manifest itself 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) (Lee, YJ et al, 2013). Symptoms of depression (and anxiety) often go unrecognized (Preljevic, VT et al, 2012). This is further complicated by cultural differences in the way depression is expressed.

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

- 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).
- Issues with self-care (poor personal hygiene, poor diet, medication adherence issues).
- 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 of feeling “sad” most of the day and a loss of interest in things or relationships that used to be enjoyable.
- Feelings of hopelessness (Asking “Do you have hope for the future?” may help to identify symptoms of depression in patients).
- 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).
- Treatment of depression has the potential to improve depression-related outcomes and quality of life. Several studies have shown

Depression and Anxiety: The Role of Kidney Care Clinics

that this, in turn, can delay the progression and prevent many of the potential complications of CKD and positively impact survival (Anderson, E., 2007) (Cukor D et al, 2006) (Kimmel, PL and Peterson, RA, 2006) (Kimmel, PL, 2002).

- There is substantial evidence that when depression is detected early and is part of a multi-component intervention, depression outcomes are improved (U.S. Preventive Services Task Force, 2009).

What tools are available to help screen for depression?

- If a patient has clinical symptoms suggesting depression, there are several screening tools available, many of which have been validated in CKD populations.
- The PHQ-9 is the depression screening tool most commonly used by family physicians (the mental health module in the BC's Practice Support Program for family physicians recommends and teaches the use of the PHQ-9). 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 enhance the effectiveness of the communication with family physicians.
- The PHQ-9 is a nine-question screening tool for depression. The questionnaire scores each of the nine DSM-V 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.

- PHQ-9 scores of 5, 10, 15 and 20 represent mild, moderate, moderately severe and severe depression (Kroenke, K et al, 2010).
- 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.
- The PHQ-9 is well validated, initially in two large studies (n=6000). The sensitivity and specificity were both 0.88 at a cut point greater than or equal to 10 (Kroenke, K et al, 2010). The tool is valid for patients 16 years and older with grade 4 English comprehension (Anderson, E., 2007). It is available in multiple languages and freely downloadable at www.phqscreeners.com.
- The PHQ-9 has been validated in populations with multiple medical co-morbidities, including patients on dialysis (Drayer RA et al, 2006) (Watnick S et al, 2005). It has also been validated on cognitively impaired residents living in nursing homes (n=3,258) (Kroenke, K et al, 2010). There have been no published validation studies on the use of the tool in the non-dialysis CKD population.

What are the treatment options for depression in CKD patients?

- Limited studies have evaluated treatments for depression in CKD patients (Cohen SD et al, 2007). In the absence of rigorous studies, treatment options offered to CKD patients for depression are similar to those offered to the general population.
- For the treatment of mild to moderate depression in the general population, non-pharmacological treatments have been shown to be as effective as pharmacological treatments. They have also been shown to be

Depression and Anxiety: The Role of Kidney Care Clinics

a useful adjunct to pharmacological treatment for moderate to severe depression and can help with relapse prevention (Anderson, E., 2007).

- Non-pharmacological treatments for the treatment of depression include:
 - Psychotherapies (e.g., cognitive-behavioural 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 (Cuijpers P et al, 2013)
 - Mind-body therapies (e.g., meditation, yoga, relaxation, mindfulness, prayer, biofeedback and creative therapies such as art therapy, music therapy)
 - Exercise therapy

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.
- The National Co-morbidity Survey Replication in the US reported a prevalence rate of 18% for anxiety disorders in the general population using a semi-structured interview format (18% is a compilation of all types of anxiety disorders). See Table 2.

Depression and Anxiety: The Role of Kidney Care Clinics

Table 2: Anxiety Disorder Prevalence Rates (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%

Dialysis population:

- Prevalence rates of 30% (Taskapan, H et al, 2005) to 46% (Cukor, D et al, 2008) have been reported. Taskapan utilized a self-administered questionnaire to diagnose an anxiety disorder while Cukor utilized a semi-structured interview format.

Non-dialysis CKD population:

- Two published studies reported rates of 28% (Lee, YJ et al, 2013) and 54% (Peng, T et al, 2013). Both studies utilized a self-administered screening tool to diagnose an anxiety disorder.
- Lee's study noted that the rates of anxiety disorders did not differ across CKD stages.

Depression often co-exists in patients with anxiety disorders. The US National Co-morbidity Survey reported that 62% of patients with an anxiety disorder also suffered from MDD during their lifetimes (Wittchen, HU et al, 1994).

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 (Cukor, D et al, 2008).
- Reduced quality of life, in turn, has been associated with adverse outcomes, faster progression of CKD and higher rates of mortality (Peng, T et al, 2013) (Tsai, YC et al, 2010).

Depression and Anxiety: The Role of Kidney Care Clinics

What tools are available to help screen for anxiety disorders?

- If a patient has clinical symptoms suggesting an anxiety disorder, there are several screening tools available, many of which have been validated in CKD populations.
- The GAD-7 is the anxiety screening tool most commonly used by family physicians (the mental health module in the BC's Practice Support Program for family physicians recommends and teaches the use of the PHQ-9). Given the importance of close working relationships with family physicians in the management of KCC patients with an anxiety disorder, the GAD-7 is recommended for use in KCCs to enhance the communication with family physicians.
- The GAD-7 is a seven question screening tool. It was originally developed for generalized anxiety disorder (the most common of the anxiety disorders) but it has since proved to have moderately good sensitivity and specificity as a screener for panic, social anxiety and post-traumatic stress disorder (Doctors of BC).
- The GAD-7 scores each of seven questions as "0" (not at all) to "3" (nearly every day) based on frequency of occurrence in the past two weeks. The maximum score is 21.
- GAD-7 scores of 5, 10 and 15 represent mild, moderate and severe levels of anxiety (Spitzer, RL et al, 2006) (Kroenke K et al, 2007).
- The GAD-7 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.
- Unlike the PHQ-9 which can serve both as a screening and severity measure, the GAD-7 is

principally a measure of anxiety severity. The likelihood of an anxiety disorder increases with higher GAD-7 scores, but a clinical interview is required to confirm the presence and type of disorder (Kroenke, K et al, 2010).

- The GAD-7 was initially validated in 2,700 primary care patients. For generalized anxiety disorder, the sensitivity and specificity was 0.89 and 0.82 at a cutpoint greater than or equal to 10 (Spitzer, RL et al, 2006) (Kroenke K et al, 2007). It is available in multiple languages and freely downloadable at www.phqscreeners.com.
- Compared to the PHQ-9, uptake of the GAD-7 is less given its later publication (2006 vs 1999). Lower specificity rates may also be a factor.

What are the treatment options for anxiety in CKD patients?

- The most effective type 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, cognitive-behavioural therapy is the most-studied form of psychotherapy for anxiety and has been shown to be effective (Cuijpers P et al., 2014)
 - Mind-body therapies (e.g., meditation, yoga, relaxation, mindfulness, prayer, biofeedback and creative therapies such as art therapy, music therapy)
 - Exercise therapy

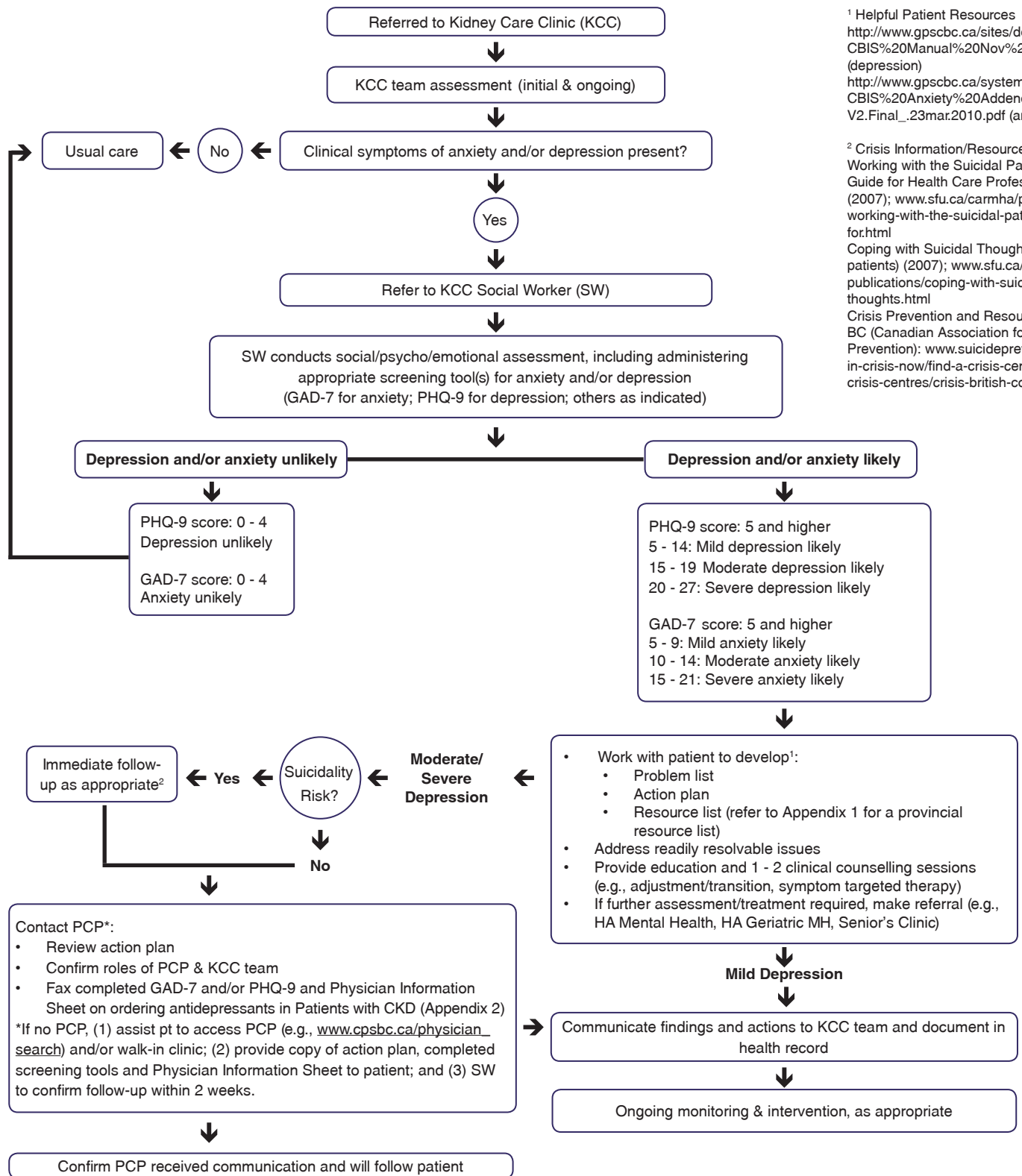
Depression and Anxiety: The Role of Kidney Care Clinics

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 Helpful Patient Resources
<http://www.gpscbc.ca/sites/default/files/CBIS%20Manual%20Nov%202013.pdf> (depression)
http://www.gpscbc.ca/system/files/CBIS%20Anxiety%20Addendum.V2.Final_.23mar.2010.pdf (anxiety)

² Crisis Information/Resources:
 Working with the Suicidal Patient: A Guide for Health Care Professionals (2007); www.sfu.ca/carmha/publications/working-with-the-suicidal-patient-a-guide-for.html
 Coping with Suicidal Thoughts (for patients) (2007); www.sfu.ca/carmha/publications/coping-with-suicidal-thoughts.html
 Crisis Prevention and Resources in BC (Canadian Association for Suicide Prevention); www.suicideprevention.ca/in-crisis-now/find-a-crisis-centre-now/crisis-centres/crisis-british-columbia

Depression and Anxiety: The Role of Kidney Care Clinics

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 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.

Depression and Anxiety: The Role of Kidney Care Clinics

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 tools³:

- Depression: Patient Health Questionnaire-9 (PHQ-9) [http://www.gpsc.bc.ca/sites/default/files/Patient%20Health%20Questionnaire%20for%20Depression%20\(PHQ9\)-BC%20Guidelines.pdf](http://www.gpsc.bc.ca/sites/default/files/Patient%20Health%20Questionnaire%20for%20Depression%20(PHQ9)-BC%20Guidelines.pdf)
- Anxiety: General Anxiety Disorder-7 (GAD-7) <http://www.gpsc.bc.ca/sites/default/files/>

[Generalized%20Anxiety%20Disorder%20Screening%20Questions%20\(GAD7\).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-V 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 <u>only</u> , 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
<ul style="list-style-type: none"> • 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). 	<ul style="list-style-type: none"> • 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). 	<ul style="list-style-type: none"> • 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)

³ There may be specific instances where an alternative or an additional screening tool is utilized which is 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.

Depression and Anxiety: The Role of Kidney Care Clinics

Table 5: Components of a Safety Plan

SAFETY PLAN
<ul style="list-style-type: none">• 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)

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.

Given that KCC patients visit KCCs on a periodic basis only, it is important that they have a PCP to manage non-renal conditions. PCPs play a key role in managing depression (Anderson, E., 2007). For 85% of adult patients with MDD, FPs are the only health care provider (source: BC MSP linked data).

Depression and Anxiety: The Role of Kidney Care Clinics

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 (Pao, M and Bosk, A, 2011) (Pinquart, M and Shen, Y, 2011). There have been limited studies, however, that specifically focus on children with CKD.
- Five studies on depression or anxiety in children with CKD were identified in the published literature between 2004 and 2014. Three of the studies focused on depression/depressive symptoms (Selewski, DT et al, 2014) (Kogon, A et al, 2013) (Hernandez, EG et al, 2011), one on anxiety/anxiety symptoms (Kilis-Pstrusinska K et al, 2013) and one on both types of symptoms (Bakr A et al, 2007). 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) in the three studies where rates

were reported (Bakr A et al, 2007)(Kogon, A et al, 2013) (Hernandez, EG et al, 2011).

- 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 less than 1-2% in school-age children and from 1-7% in adolescents (Costello, EJ et al, 2005). 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.
- 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
- 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.

Depression and Anxiety: The Role of Kidney Care Clinics

Anxiety disorders

- Two studies 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 (Bakr A et al, 2007).
 - 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) (Kilis-Pstrusinska K et al, 2013).
- 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 (Avenevoli, Shelli et. al., 2008).

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 1 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 (Thapar, A et al, 2012) (Bhardwaj, A et al, 2009) (Cook, MN et al, 2009) (Carr, A, 2008) (Menier-Wex, C and Kolch, M, 2008).

Depression and Anxiety: The Role of Kidney Care Clinics

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

AGE GROUP	PRESENTATION
Toddlers	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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.

Depression and Anxiety: The Role of Kidney Care Clinics

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 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 (CDI; Kovacs, 1992) 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 (Orhan et al, 2004), lupus (Louthrenoo et al, 2012), and cancer (Mulhern, 1992). 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 Inc.).
- The Mood and Feelings Questionnaire (MFQ; Angold, et al, 1995) 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: <http://devepi.duhs.duke.edu/mfq.html>. The MFQ has been used to measure depression in a number of pediatric chronic illness populations, including juvenile rheumatoid arthritis (Lal et al, 2011), epilepsy (Stevanovic et al, 2012), and recurrent cardiac arrhythmia (DeMaso et al, 2000).

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 (MASC 2: March et al., 1997): 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 (Kean et al., 2006), lupus (Louthrenoo, et al., 2012) and thalassemia (Mazzone, et al., 2009). The MASC 2 manual includes clinical cut-off scores. The CDI is copyright protected, and can be purchased through the publisher (Multi-Health Systems Inc.).
- The Screen for Child Anxiety-Related Emotional Disorders (SCARED; Birmaher et al, 1997) 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

Depression and Anxiety: The Role of Kidney Care Clinics

measure includes suggested cut-off scores for further assessment for possible Generalized Anxiety Disorder, Separation Anxiety, Social Anxiety Disorder, and school phobia. It is free to download: <http://www.psychiatry.pitt.edu/research/tools-research/assessment-instruments>. The SCARED has been used in studies of children with epilepsy (Stevanovic et al, 2012), chronic pain (Jastrowski Mano et al., 2012), and juvenile rheumatoid arthritis (Stevanovic & Susic, 2013).

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-V 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 to specialized resources as required.
- Within the scope of her role within the BCCH Renal Program, the CKD 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.

Depression and Anxiety: The Role of Kidney Care Clinics

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 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 for support and encouragement to do. 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 behaviour 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.

Depression and Anxiety: The Role of Kidney Care Clinics

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

This provincial guideline was developed to support improvements in the quality of care delivered to patients with chronic kidney disease in BC. Based on the best information available at the time it was published, the guideline relies on evidence and avoids opinion-based statements where possible. When used in conjunction with pertinent clinical data, it is a tool health authorities and health professionals can use to develop local guidelines.

Developed by:

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

Reviewed by:

- BCPRA Kidney Care Committee
- BCPRA Pharmacy & Formulary Committee
- BCPRA Medical Advisory Committee
- BCPRA Executive Committee

5.0 Effective Date

May 2015. This guideline is based on scientific evidence available at the time of the effective date; refer to www.bcrenalagency.ca for most recent version.

6.0 References

Anderson, E. (2007, Oct 12). Depression, Kidney Disease and the Role of Primary Care. *BC Kidney Days Presentation*. Vancouver, BC.

Andrade, CP et al. (2010). Evaluation of depressive symptoms in patients with chronic renal failure. *J Nephrol*, 23(2), pp. 168-174.

Angold, A., Costello, E. J., Messer, S. C., & Pickles, A. (1995). Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. *International Journal of Methods in Psychiatric Research*, 5, 237-249.

Avenevoli, Shelli et. al. (2008). Epidemiology of Depression in Children and Adolescents. In R. Abeta, & B. Hankin (Eds.), *Handbook of Depression in Children and Adolescents* (pp. 6-32). USA: Guildford Publishing.

Bakr A et al. (2007). Psychiatric disorders in children with chronic renal failure. *Pediatr Nephrol*, 22, 128-131. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17048014>.

Bhardwaj, A et al. (2009, Sept). Depression and allied illness in children and adolescents: Basic facts. *Psychoanalytic Psychotherapy*, 23(3), 176-184. Retrieved from <http://www.tandfonline.com/doi/abs/10.1080/02668730903227206#.VEvjrnF8kQ>

Birmaher, B., Khetarpal, S., Brent, D. A., Cully, M., Balach, L., Kaufman, J., et al. (1997). The Screen for Child Anxiety Related Emotional Disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36, 545-553.

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

BC Reproductive Mental Health Program & Perinatal Services BC. (2014). *Best Practices Guidelines for Mental Health Disorders in the Perinatal Period*. Vancouver. Retrieved May 26, 2014, from <http://reproductivementalhealth.ca/resources/best-practice-guidelines-mental-health-disorders-perinatal-period>

Canadian Task Force on Preventive Health Care. (2013). Recommendations on screening for depression in adults. *CMAJ*. Retrieved 11, 2014, from <http://www.cmaj.ca/content/185/9/775.full.pdf+html>

Carr, A. (2008, Jan-Mar). Depression in young people: Description, assessment and evidence-based treatment. *Developmental Neurorehabilitation*, 11(1), 3-15. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17943506>.

Cohen SD et al. (2007). Screening, diagnosis, and treatment of depression in patients with end-stage renal disease. *Clin J Am Soc Nephrol*, 2, pp. 1332-1342.

Depression and Anxiety: The Role of Kidney Care Clinics

Cuijpers P et al. (2013, July). A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *Canadian Journal of Psychiatry*, 58(7), pp. 376 - 385.

Cuijpers P et al. (2014). Psychological treatment of generalized anxiety disorder: a meta-analysis. *Clinical Psychology Review*, 34(2), pp. 130 - 140.

Cukor D et al. (2006). Depression in end-stage renal disease hemodialysis patients. *Nat Clin Pract Nephrol*, 2, pp. 678-687.

Cukor, D et al. (2008). Course of depression and anxiety diagnosis in patients treated with hemodialysis: a 16-month follow-up. *Clin J Am Soc Nephrol*, 3, pp. 1752-1758.

Cook, MN et al. (2009, Sept). Adolescent Depression. *Psychiatry MMC*, 6(9), 17 - 31. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2766285>.

Costello, EJ et al. (2005). The developmental epidemiology of anxiety disorders: Phenomenology, prevalence, and comorbidity. *Child and Adolescent Psychiatric Clinics of North America*, 631-648.

DeMaso, D. R., Spratt, E. G., Vaughan, B. L., D'Angelo, E. J., Van Der Feen, J. R., & Walsh, E. (2000). Psychological functioning in children and adolescents undergoing radiofrequency catheter ablation. *Psychosomatics*, 41, 134-139.

Doctors of BC. (n.d.). *Practice Support Program*. Retrieved May 14, 2014, from General Practice Services Committee: http://www.gpsc.bc.ca/system/files/MH_GAD-7_screening.pdf

Drayer RA et al. (2006). Characteristics of depression in hemodialysis patients: symptoms, quality of life and mortality risk. *General Hospital Psychiatry*, 28, pp. 306 - 312.

Government of Canada. (2006). *The Human Face of Mental Health and Mental Illness in Canada*. Retrieved 11, 2014, from http://www.phac-aspc.gc.ca/publicat/human-humain06/pdf/human_face_e.pdf

Hedayati, SS et al. (2006). The predictive value of self-report scales compared with physician diagnosis of depression in hemodialysis patients. *Kidney Int*, 69, pp. 1662-1668.

Hedayati, SS et al. (2009, Sept). Prevalence of Major Depressive Episode in CKD. *Am J of Kidney Dis*, 54(3), pp. 424 - 432.

Hedayati 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.

Hernandez, EG et al. (2011). Depressive symptomatology in children and adolescents with chronic renal insufficiency undergoing chronic dialysis. *International J of Nephrology*, 1-7. Retrieved from <http://www.hindawi.com/journals/ijn/2011/798692/>

Jastrowski Mano, K. E., Evans, J. R., Tran, S. T., Anderson Khan, K., Weisman, S. R., & Hainsworth, K. R. (2012). The psychometric properties of the Screen for Child Anxiety Related Emotional Disorders in pediatric chronic pain. *Journal of Pediatric Psychology* 37, 999—1011.

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.

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.

Kean, E., M., Kelsay, K., Wamboldt, F., & Wamboldt, M. Z. (2006). Posttraumatic stress in adolescents with asthma and their parents. *Journal of the American Academy of Child & Adolescent Psychiatry*, 45, 78-86.

Kessler, RC et al. (2005, June). Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 62, pp. 593 - 602.

Kessler, RC et al. (2003, June 18). The epidemiology of Major Depressive Disorder: Results from the National Comorbidity Survey Replication (NCS-R). 289, pp. 3095-3105.

Kessler, RC et al. (2005, June). Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 62, pp. 617 - 628.

Kilis-Pstrusinska K et al. (2013). Anxiety in children and adolescents with chronic kidney disease - multicenter national study results. *Kidney & Blood Pressure Research*, 37(6), 579-587. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24356548>.

Kimmel, PL. (2002). Depression in patients with chronic renal disease: What we know and what we need to know. *J Psychosom Res*, 53, pp. 951-956.

Kimmel, PL and Peterson, RA. (2006). Depression in patients with end-stage renal disease treated with dialysis: Has the time to treat arrived? *Clin J Am Soc Nephrol*, 1, pp. 349-352.

Kogon, A et al. (2013, Sept). Depression and its associated factors in pediatric chronic kidney disease. *Pediatric Nephrology*, 28(9), 1855-61. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23700174>.

Kovacs, M. (1992). *Children's depression inventory manual*. North Tonawanda, NY: Multi-Health Systems.

Kroenke K et al. (2007). Anxiety disorders in primary care: Prevalence, impairment, comorbidity, and detection. *Ann Intern Med*, 146, pp. 317 - 325.

Kroenke, K et al. (2010). The Patient Health Questionnaire Somatic,

Depression and Anxiety: The Role of Kidney Care Clinics

Anxiety and Depressive Symptom Scales: a systematic review. *General Hospital Psychiatry*, 32, pp. 345 - 359.

Lal, S., McDonagh, J., Baildam, E., Wedderburn, L. R., Gardner-Medwin, J., Foster, H. E., et al., (2011). Agreement between proxy and adolescent assessment of disability, pain, and well-being in juvenile idiopathic arthritis. *The Journal of Pediatrics*, 158, 307-312.

Lee, YJ et al. (2013, April). Association of depression and anxiety with reduced quality of life in patients with predialysis CKD. *Int J of Clin Pract*, 67(4), pp. 363-368.

Lopes AA et al. (2002). Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe. *Kidney Int*, 62, pp. 199-207.

Louthrenoo, O., Krairojananan, J., Chartapisak, W., & Opastirakul, S. (2012). Psychosocial functioning of children with systemic lupus erythematosus. *Journal of Paediatrics & Child Health*, 48, 1090-1094.

March, J. S., Parker, J. D. A., Sullivan, K., Stallings, P., & Conners, K. (1997). The Multidimensional Anxiety Scale for Children (MASC): Factor structure, reliability, and validity. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36, 554-565.

Mazzone, L., Battaglia, L., Andreozzi, F., Romeo, M. A., Mazzone, D. (2009). *Clinical Practice and Epidemiology in Mental Health*, 5, 5.

Menier-Wex, C and Kolch, M. (2008, Feb). Depression in Children and Adolescents. *Dtsch Arztebl Int*, 105(9), 149-155. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/19633781>

Mulhern, R., Fairclough, D., Smith, B., & Douglas, S. M. (1992). Maternal depression, assessment methods, and physical symptoms affect estimates of depressive symptomatology among children with cancer. *J of Pediatric Psychology*, 17, 313-326.

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.

Novak, M. (2013). Depression in patients with CKD (Presentation). *Psychoneurology: the psychosocial impact of CKD*.

Odden, MC et al. (2006). Depression, stress and quality of life in persons with CKD: the Heart and Soul Study. *Nephron Clin Prac* 2006, 103, pp. c1-7.

Orhan, B., Erdogan, A., Kantarci, O., Akisik, G., Kayaalp, L., & Yalkincaya, C. (2004). Anxiety and depression in children with epilepsy and their mothers. *Epilepsy & Behavior*, 5, 958-964.

Pao, M and Bosk, A. (2011). Anxiety in Medically Ill Children/Adolescents

(Review article). *Depression and Anxiety*, 28, 40-49. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2990785/>

Patten, SB and Lee, RC. (2005). Describing the longitudinal course of major depression using Markov models: data integration across three national surveys. *Popul Health Metr*, 3, p. 11.

Peng, T et al. (2013). Relationship between psychiatric disorders and quality of life in nondialysis patients with CKD. *Am J of Med Sciences*, 345(3), pp. 218 - 221.

Pinquart, M and Shen, Y. (2011, May). Depressive symptoms in children and adolescents with chronic physical illness: an updated meta-analysis. *J Pediatr Psychol*, 36(4), 375-84. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/21088072>

Preljevic, VT et al. (2012). Screening for anxiety and depression in dialysis patients: comparison of the Hospital Anxiety and Depression Scale and the Beck Depression Inventory. *J Psychosom Res*, 139 - 144. doi:10.1016/j.jpsychores.2012.04.015

Ricardo AC et al. (2010). Depressive symptoms and CKD: results from the National Health and Nutrition Examination Survey (NHANES), 2005 - 2006. *Int Urol Nephrol*, 42, pp. 1063-1068.

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

Selewski, DT et al. (2014, June 9). Gaining the Patient Reported Outcomes Measurement Information System (PROMIS) perspective in chronic kidney disease: A Midwest Pediatric Nephrology Consortium study. *Pediatr Nephrol*. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24908324>

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.

Spitzer, RL et al. (2006). A brief measure for assessing generalized anxiety disorder - the GAD-7. *Arch Intern Med*, 166, pp. 1092-1097.

Stevanovic, D., Jancic, J., Topalovic, M., & Tadic, I. (2012). Agreement between

Children and parents when reporting anxiety and depressive symptoms in pediatric epilepsy. *Epilepsy & Behavior*, 25, 141-144.

Stevanovic, D., & Susic, G. (2013). Health-related quality of life and emotional problems in juvenile idiopathic arthritis. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabil*.

Taskapan, H et al. (2005). Psychiatric disorders and large interdialytic weight gain in patients on chronic haemodialysis. *Nephrology*, 10, pp. 15-20.

Depression and Anxiety: The Role of Kidney Care Clinics

Thapar, A et al. (2012, Mar 17). Depression in adolescence. *Lancet*, 379(9820), 1056-1067. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3488279>/Tsai, YC et al. (2010). quality of life predicts risks of end-stage renal disease and mortality in patients with CKD. *Nephrol Dial Transplant*, 25, pp. 1621-1626.

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.

U.S. Preventive Services Task Force. (2009). Screening for depression in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*, 151, pp. 784 - 792.

Watnick S et al. (2005). Validation of 2 depression screening tools in dialysis patients. *Am J Kidney Dis*, 46, pp. 919-924.

Wittchen, HU et al. (1994). DSM-III-R generalised anxiety disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*, 51, pp. 355 - 364

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.

Appendix 1: Resources for Depression and/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. www.healthlinkbc.ca

Crisis Information/Resources:

1. Local Emergency Room
2. Suicide Line at 1-800-784-2433 or 1-800-SUICIDE (24/7). Provides skilled suicide assessment and intervention. www.crisiscentre.bc.ca
3. Coping with Suicidal Thoughts (for patients) (2007) www.sfu.ca/carmha/publications/coping-with-suicidal-thoughts.html
4. Mental Health Support/Crisis Lines. Provide mental health support, information and resources
 - a. Provincial line: 310-6789 (no area code) (24/7).
 - b. Crisis Prevention and Resources in BC (Canadian Association for Suicide Prevention). Provides a list of crisis lines throughout BC: www.suicideprevention.ca/in-crisis-now/find-a-crisis-centre-now/crisis-centres/crisis-british-columbia

Counselling/Support Websites

1. BC Psychological Association. 1-800-730-0522. www.psychologists.bc.ca
2. BC Association of Clinical Counsellors. www.bc-counsellors.org
3. Mood Disorders Association of BC (offers support groups throughout the province). 604 873-0103. www.mdabc.net
4. Anxiety BC (information and brochures about anxiety and self-help strategies; some available in multiple languages and DVD format). www.anxietybc.com/resources/introduction.php
5. Canadian Mental Health Association (provides information, resources and links to CMHA branch offices across BC). www.cmha.bc.ca
6. Canadian Mental Health Association, BC Division (provides information, resources and programs in English and selected other languages). <http://www.cmha.bc.ca/about-us>
7. Bounce Back (telephone coaching and DVD video of practical tips on recognizing and dealing with depression). www.cmha.bc.ca/bounceback
8. Aboriginal Organizations and Services in BC (provincial listing of First Nation, Métis and Aboriginal organizations, communities and community services) www.gov.bc.ca/arr/services/guide.html
9. Kelty Mental Health Resource Centre (mental health and substance use information, resources, and peer support to children, young adults, and their families). www.keltymentalhealth.ca
10. Mind Check (website designed to help youth and young adults in BC connect to mental health resources and support). www.mindcheck.ca

Appendix 1: Resources for Depression and/or Anxiety

Self-help Guides

1. Cognitive Behavioural Interpersonal Skills Manuals (promoted by BC's Practice Support Program for Family Physicians):
 - Depression: [http://www.gpsc.bc.ca/sites/default/files/Patient%20Health%20Questionnaire%20for%20Depression%20\(PHQ9\)-BC%20Guidelines.pdf](http://www.gpsc.bc.ca/sites/default/files/Patient%20Health%20Questionnaire%20for%20Depression%20(PHQ9)-BC%20Guidelines.pdf)
 - Anxiety addendum: [http://www.gpsc.bc.ca/sites/default/files/Generalized%20Anxiety%20Disorder%20Screening%20Questions%20\(GAD7\).pdf](http://www.gpsc.bc.ca/sites/default/files/Generalized%20Anxiety%20Disorder%20Screening%20Questions%20(GAD7).pdf)
2. Antidepressant Skills Workbook (available in multiple languages and as a "talking book"): www.comh.ca/antidepressant-skills/adult/workbook/
3. Positive Coping with Health Conditions, A Self-Care Workbook. (workbook on relaxation, managing worry/depression/anger, solving programs, etc). <http://www.comh.ca/pchc>
4. Here to Help (self-help information website sponsored by BC Partners for Mental Health and Addictions). www.heretohelp.bc.ca. For on-line family mental illness support groups, go to www.reachingfamiliesproject.org/phpBB.
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 tools about suicide prevention in older adults). <http://www.ccsmh.ca/en/projects/suicide.cfm>
2. Link to BC physician guidelines for treating depression and anxiety http://www.bcguidelines.ca/submenu_mental.html

Part B: Resources for Children and their Parents

Community Resources:

1. Family Physician/ Pediatrician / Nurse Practitioner
2. Local Child and Youth Mental Health Teams: CYMH provides a wide range of free community-based specialized mental health services to children & youth up to age 18 years throughout BC. Services are provided through the Ministry of Children and Family Development. Contact information for local offices: http://www.mcf.gov.bc.ca/mental_health/pdf/offices_services.pdf

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.
3. Kids Help Phone: 24-hour toll-free service offering confidential phone or web counseling for ages 20 and under. Available in English and French. Phone: 1-800-668-6868.
4. The Crisis Centre: Provides BC crisis line numbers and related links and resources. Phone: 1-800-784-2433 (1-800-SUICIDE). Online support: www.youthinbc.com.
5. Crisis Line Association of BC's Mental Health Information Line: support and information on a wide range of mental health challenges:

Appendix 1: Resources for Depression and/or Anxiety

Provincial line: 310-6789 (no area code).

6. 24 Hour Helpline for Children: To report suspected cases of child abuse or neglect:
Provincial line: 310-1234 (no area code).

Counselling/Support Websites:

1. Private Practice Registered Psychologists: BC Psychological Association. 1-800-730-0522.
www.psychologists.bc.ca
2. Private Practice Registered Clinical Counsellors: BC Association of Clinical Counsellors. www.bc-counsellors.org
3. Anxiety BC: evidence-based information and brochures about anxiety, including self-help strategies for children, youth, adults, and parents: www.anxietybc.com
4. Kelty Mental Health Resource Centre: Offers help to children, youth, parents, and families on mental health and/or substance use challenges. Includes resources for support and treatment within BC: <http://keltymentalhealth.ca>
5. Mind Check: Helps youth and young adults in BC connect to mental health resources and support: www.mindcheck.ca
6. The F.O.R.C.E. Society for Kids' Mental Health: Supports and empowers families and work collaboratively with professionals and systems in understanding and meeting the mental health needs of families.
<http://www.forcesociety.com>

Self-help Guides:

1. Dealing with Depression: Book that provides teens with accurate information and self-help strategies about depression: http://www.mcf.gov.bc.ca/mental_health/pdf/dwd_writable.pdf
2. Anxiety BC: Self-help strategies for children, youth, adults, and parents: www.anxietybc.com

Website Resources for Parents:

1. Parenting children with health issues, Resources for parents. <http://www.parentingchildrenwithhealthissues.com/index.html>
2. KidsHealth.org, Taking care of you: Support for caregivers http://kidshealth.org/parent/system/ill/caregivers.html?tracking=P_RelatedArticle
3. KidsHealth.org, Caring for a seriously ill child. http://kidshealth.org/parent/system/ill/seriously_ill.html
4. National Kidney Foundation, Parenting children with chronic kidney disease: <https://www.kidney.org/atoz/content/childckdtips>
5. National Kidney and Urologic Diseases Information Clearinghouse, Facing the challenges of chronic kidney disease in children: http://kidney.niddk.nih.gov/kudiseases/pubs/childkidneydiseases/facing_challenges_ckd_children/index.aspx
6. Kidney Foundation of Canada, Your child and chronic kidney disease: <http://www.kidney.ca/document.doc?id=332>

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; ↓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)					
Potential class adverse effects: Increased risk of bleeding, N/V/D, sexual dysfunction, hyponatremia, weight gain (except fluoxetine)					
Citalopram ^{3,4}	No adjustment	No adjustment	No adjustment	No adjustment (HD: not removed)	<ul style="list-style-type: none"> Safe in pts with CV disease but risk of QTc prolongation (max 40 mg/day or 20 mg/day with strong CYP2C19 inhibitors*)
Escitalopram	No adjustment	SD: 10 mg/day, ↑ carefully	SD: 10 mg/day, ↑ carefully	SD: 10 mg/day, ↑ carefully (HD: not removed)	<ul style="list-style-type: none"> Risk of QTc prolongation
Fluoxetine	No adjustment	No adjustment	No adjustment	No adjustment (HD: not removed)	<ul style="list-style-type: none"> Safe in pts with CV disease, but risk of QTc prolongation
Fluvoxamine ⁵	No adjustment	No adjustment	No adjustment	No adjustment (HD: may be removed)	<ul style="list-style-type: none"> Many potential drug interactions Most nauseating and sedating SSRI
Paroxetine ⁶	SD: 10 mg/day, ↑ carefully	SD: 10 mg/day, ↑ carefully	SD: 10 mg/day, ↑ carefully	SD: 10 mg/day, ↑ carefully	<ul style="list-style-type: none"> Most anticholinergic activity among the SSRIs (caution in elderly) Has been used for pruritus management
Sertraline ⁷	No adjustment	SD: 50 mg/day, ↑ carefully	SD: 25 mg/day, consider ↓ max dose	SD: 25 mg/day, consider ↓ max dose (HD: not removed)	<ul style="list-style-type: none"> Safe in pts with CV disease Has been used for treatment of dialysis related hypotension

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 Blumenfeld 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.

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; ↓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)	
Non - 1st line therapies					
Serotonin/Norepinephrine Reuptake Inhibitors (SNRI)					
Potential class adverse effects: N/V/D, sexual dysfunction, increased risk of bleeding, hypertension at higher doses, weight gain (less than SSRIs and mirtazapine)					
Desvenlafaxine	SD: 50 mg Q2days, ↑ carefully	Max: 50 mg Q2days	Max: 50 mg Q2days	Max: 50 mg Q2days	
Duloxetine	No adjustment	SD: 30 mg/day, ↑ carefully	SD: 30 mg/day, ↑ carefully	SD: 30 mg/day, ↑ carefully	<ul style="list-style-type: none"> Consider for concomitant peripheral neuropathy
Venlafaxine	No adjustment	37.5-112.5 mg/day	37.5-112.5 mg/day	37.5-112.5 mg/day	<ul style="list-style-type: none"> Possibly more N/V than SSRIs Consider for concomitant peripheral neuropathy
Serotonin Antagonist/Reuptake Inhibitor (SARI)					
Trazodone	No adjustment	No adjustment	SD: 150 mg/day, ↑ carefully	SD: 150 mg/day, ↑ carefully	<ul style="list-style-type: none"> Good choice for concomitant insomnia (usual dose for this indication: 25-50 mg) Not usually used as monotherapy for depression due to significant sedation at higher doses
Other Antidepressants					
Bupropion ⁸	Max: 150 mg/day	Max: 150 mg/day	Max: 150 mg/day	Max: 150 mg/day	<ul style="list-style-type: none"> Effective for smoking reduction/cessation Non- sedating, may cause insomnia, not associated with weight gain Risk of accumulation of toxic metabolites causing dysrhythmia (wide QRS complex) Caution in seizure disorders Good choice if SSRIs or SNRIs cause sexual dysfunction
Mirtazapine ⁹	No adjustment	15 mg/day, ↑ carefully	15 mg/day, ↑ carefully	15 mg/day, ↑ carefully	<ul style="list-style-type: none"> Has been used for pruritus management May cause sedation, weight gain Good choice for concomitant insomnia (dose: 7.5-15 mg HS) Good choice if SSRIs or SNRIs cause sexual dysfunction

Notes:

- **Tricyclic antidepressants (TCA) and inhibitors of the monoamine oxidase antidepressants (IMAO) are not considered safe options for treating depression in chronic kidney failure patients.**
- **Risk for arrhythmia associated with drug-induced QTc prolongation increased with electrolyte abnormalities (low calcium, magnesium, potassium), diuretic use, females — see <http://circ.ahajournals.org/content/121/8/1047/T2.expansion.html>**

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.

Appendix 2b: Physician Information Sheet - Common Antidepressants 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)					
Potential class adverse effects: Increased risk of bleeding, N/V/D, sexual dysfunction, hyponatremia, weight gain (except fluoxetine)					
Citalopram ^{3,4}	No adjustment	No adjustment	No adjustment	No adjustment (HD: not removed)	<ul style="list-style-type: none"> Safe in pts with CV disease but risk of QTc prolongation (max 40 mg/day or 20 mg/day with 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)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> Safe in pts with CV disease, but risk of QTc prolongation
Fluvoxamine ⁶	No adjustment	No adjustment	No adjustment	No adjustment (HD: partially removed)	<ul style="list-style-type: none"> Many potential drug interactions Most nauseating and sedating SSRI Children: Max 200 mg/day, adolescents: Max 300 mg/day
Sertraline ⁷	No adjustment	SD: 10 mg/day, ↑ carefully	SD: 25 mg/day, ↑ carefully	SD: 25 mg/day, consider ↓ max (HD: not removed)	<ul style="list-style-type: none"> Safe in pts with CV disease Has been used for treatment of dialysis-related hypotension (adults)

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 Hedayati 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 Blumenfeld 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.

Appendix 2b: Physician Information Sheet - Common Antidepressants 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)	
Non - 1st line therapies					
Serotonin/Norepinephrine Reuptake Inhibitors (SNRI)					
Potential class adverse effects: N/V/D, sexual dysfunction, increased risk of bleeding, hypertension at higher doses, weight gain (less than SSRIs and mirtazapine)					
Duloxetine	No adjustment	SD: 30 mg/day, ↑ carefully	SD: 30 mg/day, ↑ carefully	SD: 30 mg/day, ↑ carefully	<ul style="list-style-type: none"> Consider for concomitant peripheral neuropathy 20 mg capsules NOT available in Canada (USA only)
Venlafaxine	No adjustment	37.5-112.5 mg/day	37.5-112.5 mg/day	37.5-112.5 mg/day	<ul style="list-style-type: none"> Consider for concomitant peripheral neuropathy
Serotonin Antagonist/Reuptake Inhibitor (SARI)					
Trazodone	Dose adjustment not required when dosed at 25-50 mg HS for insomnia; higher doses (150-600 mg) <i>virtually never</i> prescribed for depression in C&A				<ul style="list-style-type: none"> 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: 150 mg every third day (HD: not removed)	<ul style="list-style-type: none"> Contraindicated in seizure disorders Effective for smoking reduction/cessation (adults) Non-sedating, may cause insomnia, not associated with weight gain Risk of accumulation of toxic metabolites causing dysrhythmia (wide QRS complex) in renal failure Do not crush or split sustained-release or extended-release tablets A choice if SSRIs or SNRIs cause sexual dysfunction
Mirtazapine ⁹	No adjustment	15 mg/day, ↑ carefully	15 mg/day, ↑ carefully	15 mg/day, ↑ carefully (HD: partially removed)	<ul style="list-style-type: none"> Has been used for pruritus management May cause sedation, weight gain Good choice for concomitant insomnia (dose: 7.5-15 mg HS) Good choice if SSRIs or SNRIs cause sexual dysfunction

Notes:

- **None** of the available antidepressants listed above have formal regulatory approval from Health Canada for treatment of depression or anxiety disorders in children and adolescents. Use for these indications is considered to be on an off-label basis.
- Tricyclic antidepressants (TCA) and monoamine oxidase inhibitor (MAOI) antidepressants are not considered safe treatment options for depression in chronic kidney failure patients. TCAs and MAOIs are also not first or second-line treatment recommendations for depression or other mental disorders in children and adolescents.
- Risk for arrhythmia associated with drug-induced QTc prolongation increased with electrolyte abnormalities (low calcium, magnesium, potassium), diuretic use, females — see <http://circ.ahajournals.org/content/121/8/1047/T2.expansion.html>

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.

Appendix 3: Depression/Anxiety Working Group Participants

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

Child-Specific Section

Name	Discipline	Organizational Affiliation
Erin Moon	Clinical Psychologist	BC Children's Hospital
Tanya Strubin	Social Worker	BC Children's Hospital
Janis Dionne	Nephrologist	BC Children's Hospital
Janet Williams	Project Coordinator	BCPRA

Physician Information Sheet - Antidepressants & CKD (Appendix 2)

Name	Discipline	Organizational Affiliation
Judith Marin	Pharmacist	St. Paul's Hospital
Sue Corrigan	Pharmacist	Surrey Memorial Hospital
Dean Elbe	Pharmacist	BC Children's Hospital