UNIVERSITY OF ALBERTA

Mental Health Assessment and Prescribing by Alberta Pharmacists (MAP-AP)

STUDY PROTOCOL

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Background/Rationale

Mood and anxiety disorders are the most common mental illnesses among Canadians, with approximately 4.0 million individuals living with one of these conditions (including children and adolescents). This number is expected to reach over 4.9 million by 2041 (1).

It has been reported that 7.9-8.6% of Canadians would experience a major depression in their lifetime, characterised by a lack of motivation, loss of ability to enjoy favourite activities, difficulty concentrating, feeling of isolation, and having debilitating effects on daily functioning. Meanwhile, 1.1% of Canadians will be affected by Generalised Anxiety disorder (2).

Mental health also carries a financial burden on the individual and the healthcare system. Annual losses at the workplace are estimated to reach $33 billion, high levels of short-term and long-term disability claims (75% and 79%, respectively) and a very high unemployment rate (70-90%) in individuals with serious mental health (2).

Despite these staggering facts and statistics, stigma is still a barrier to accessing care. In a 2016 survey, 40% of respondents never reached out to healthcare providers, despite experiencing feelings of anxiety or depression (3).

The recent Bloom Program piloted in Nova Scotia revealed the positive patient benefits, when community pharmacists are able to practise to their full scope, in addition to the usual physician care activities that patients with mental health conditions receive (4). These pharmacists were able to demonstrate:

I. Comprehensive consultations reviewing physical and mental health conditions and medications
II. Greater collaboration among health providers
III. Regular patient-centred longitudinal follow-up care and support
IV. Improved resource access and service navigation

In comparison, Alberta pharmacists practise very similarly, but possess unique opportunities using Additional Prescribing Authority (APA) to prescribe Schedule 1 medications independently and in collaboration with physicians, and have the ability to order and interpret lab results to assist in patient management. This places the Alberta Pharmacist in a prime position to enhance the patient experience and improve their accessibility to care (5, 6).

To justify pursuing this unique opportunity, a literature review of existing pharmacist interventions for patients with major depressive disorder (MDD) and generalised anxiety disorder (GAD) was performed to identify clinical monitoring tools, study duration and monitoring intervals, and pharmacist interventions that affected clinical outcomes.

Of the 163 articles screened, the review included 13 articles. Becks Depression Inventory (BDI), Hopkins Symptom Checklist (SCL-20), and Patient Health Questionnaire (PHQ-9)

were the most common clinical monitoring tools used (31, 23, and 15 percent, respectively). A study period of 6 months with a 3-month monitoring interval was most common.

Interventions that produced clinical improvement included:

i) Comprehensive patient education and counselling focused on MDD, antidepressant treatment, adverse effect management, and adherence
ii) Therapy decisions made with the physician
iii) Regular longitudinal follow-up and support
iv) Facilitating access to other services (e.g. counsellors, psychiatrist, etc.).

Evaluations regarding pharmacists prescribing in the community pharmacy setting for depression and anxiety have yet to be explored.

The research group are all registered pharmacists in Alberta with BSc or post-grad PharmD level training. All have additional prescribing authority and PracID for lab ordering and monitoring. Practice backgrounds include hospital, primary care network, and community pharmacy (that operate in close collaboration with physician offices and developed a collaborative clinical practice). In each of these practice settings, we have experience in collaborative management with the patient's primary care providers and/or specialist physicians--ranging from medication education, monitoring, dose adjustments and prescribing actions--for patients with depression and anxiety.

The unique pharmacist prescribing scope in Alberta can build upon and expand beyond medication adherence evaluated by the systematic review and meta-analysis by Reddean et al in 2018--and in addition, directly evaluate pharmacist prescribing, assessment, and monitoring interventions in the community pharmacy setting.

Purpose

This is a clinical trial evaluating the experimental intervention of enhanced pharmacist care by pharmacists with additional prescribing authorization (APA) in Alberta, for patients newly diagnosed with Major Depressive Disorder (MDD) and Generalised Anxiety Disorder (GAD).

Objectives

Primary objective

To evaluate the effect (change in the mean PHQ-9 and GAD-7 score) of enhanced pharmacist care by community pharmacists with APA, in monitoring (lab ordering and interpretation, clinical monitoring of MDD and GAD), counselling (patient education), arranging referrals (in collaboration with prescribing physician), and prescribing (dose adjustment, deprescribing, and the addition of adjunctive medication) interventions for patients who have depression and anxiety and are initiated on pharmacotherapy--in comparison to the usual standard level of care conducted by pharmacist and physician.

Secondary objectives

To evaluate the effect of community pharmacist monitoring, counselling, and prescribing interventions on:

Clinical:

- The rate of achieving remission of MDD and/or GAD compared to usual care (using PHQ-9/GAD-7)
- Cognitive and functional impairment related to MDD and/or GAD
- The occurrence of relapse of depression and/or anxiety
- The proportion of patients receiving appropriate and optimised depression and anxiety medication
- Patient complaints and/or experiences of medication-related side effects during treatment for MDD and/or GAD (i.e. GI intolerance, dizziness, weight gain)

Process:

- Number of patients monitored for MDD and GAD while on treatment by community pharmacist
- The impact of the interventions on patient satisfaction and quality of life.
- Assure sustainability by exploring enabling (i.e. pharmacist reimbursement framework) and potential barrier forces (i.e. pharmacist training in managing patients with MDD and GAD)

Methods

Design:
Multi-centre randomised controlled trial with patients as the unit of randomization.

Setting:
Community pharmacies in Alberta, Canada–with pharmacist partners (practising pharmacists with APA and PracID) involved the dispensing, recruitment, follow-up, interventions, engaging both patients and family physicians

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Patients/Population

Inclusion criteria:

Adults ≥ 18 years of age, newly diagnosed with MDD and/or GAD, including:

- Patients starting on medications for the management of adults with MDD (Appendix 1) (7).
- Patients starting on medications for the management of GAD (Appendix 2) (8).

Exclusion criteria:

- Pregnancy
- Non-Alberta residents
- Unwilling or unable to participate in regular follow-up visits
- Unwilling to participate/sign consent form
- ≥2 suicide attempts per year
- Severe, psychotic, and catatonic depression
- Current substance abuse, intoxication, addiction, or withdrawal requiring acute care management
- Patients diagnosed with comorbid anxiety disorders other than GAD, including: panic disorder, agoraphobia, specific phobia, social anxiety disorder, obsessive-compulsive disorder, posttraumatic stress disorder
- Patients diagnosed with comorbid depressive disorder other than MDD, including: depressive disorder due to another medical condition (e.g. hypothyroidism, MS, OSA, Parkinsons, stroke, TBI, Vitamin B12 insufficiency, Huntington disease, adrenal insufficiency, mononucleosis, systemic lupus erythematosus), adjustment disorder with depressed mood
- Patients diagnosed with concurrent ADHD, bipolar disorder, schizophrenia and schizoaffective disorder

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Recruitment:

Potential participants will be identified and approached by the pharmacist partners (pharmacists with APA and PracID) if they are picking up or dropping off their prescription for a medication listed in Appendix 1 and 2.

Medication indication will be verified with the patient for the treatment of diagnosed MDD and/or GAD (and if additional verification is required--collateral from physician, Netcare consult note, or pharmacy record).

As part of the standard of pharmacist practice (as outlined in the Alberta College of Pharmacist Standards of Practice for Pharmacist and Pharmacy technicians [9]), a patient is clinically assessed for pharmacotherapy appropriateness by the pharmacist partner. This process is performed by the pharmacist partner and is the initial screen to determine if the patient meets any inclusion or exclusion criteria.

Determined by the pharmacist partner, if a patient meets the inclusion criteria for the study and does not meet any exclusion criteria, the patient will be asked if he/she wants to participate in the study and be provided with a formal invite letter to review.

If the patient agrees on participating, he/she will be asked to sign a written informed consent form. After signing the consent form, the patient will be enrolled in the study and randomised as a study participant using the secured electronic study website/database (developed by EPICORE and secured at the University of Alberta research office).

The participant's physician will receive the notification letter for physicians, from the pharmacist partner, to inform him/her that the participant has agreed to participate in the study. Should the physician refuse to have the participant participate in the study, the participant will not be enrolled into the study.

Should the participant decline recruitment into the study, they will continue to receive the same level of pharmacist care as outlined in the Alberta college of pharmacists standards of practice (9).

Randomization

Multiple pharmacies are involved in participant enrollment--therefore, once informed written consent is obtained from the patient, the patients will be randomised by stratified randomization using a blocking factor to assign participants to either intervention or usual care groups.

Each participant will be assigned a unique identifier number and group allocation for the duration of their participation in the study--this unique identifier and allocation will also be communicated to and recorded by the pharmacy partner in the participant's patient profile to ensure consistency of the degree of pharmacist interventions described by the group the participant is allocated to.

The participant will be sent a secured electronic link (to the contact number or email they provided in the written consent form) that will include the participant's unique identifier and group allocation and the electronic version of the PHQ-9/GAD-7 questionnaire tool to complete and submit electronically. If the participant is unable to provide a means for the electronic link to be sent, the questionnaire tool can be completed with the pharmacist partner in person prior to their scheduled in-person/telehealth pharmacist meetings.

The study data (i.e. the participant's submitted electronic questionnaire tool results) will be sent directly to a centralised and secured website/database to ensure allocation concealment for the investigational team.

The participant questionnaire scores are available to the pharmacist partner via a secured electronic website/database prior to their scheduled in-person/telehealth meeting with the pharmacist partner.

Intervention Group (Pharmacist Interventions):

Participants enrolled in the intervention group will receive pharmacist interventions, in addition to standard care outlined in the Alberta College of Pharmacist Standards of Practice for Pharmacist and Pharmacy technicians (9).

Unique pharmacist interventions will include the following (in person) at enrolment (month 0) and at the scheduled month 1, 3, and 6 in-person or telehealth pharmacist meetings:

1) Patient Assessment:
   - Recording participant scores from the combined PHQ-9/GAD-7 questionnaire tool (Appendix 4) completed by the participant, which includes:
     - PHQ-9 (Patient Health Questionnaire 9-item), a multipurpose instrument for screening, diagnosing, monitoring and measuring the severity of depression
     - GAD-7 (Generalised Anxiety Disorder 7-item)

   - If determined clinically relevant by the pharmacist partner will assess:
     - appearance, current mood, sleeping patterns, mental health, medical history, social history, family history, relationships with others, suicidal ideation, previous suicide attempts or hospitalizations, current employment status.

2) Pharmacist-initiated prescribing dose adjustment, medication change to different medication, deprescribing, or prescribing adjunctive add-on medication, to achieve clinical response and/or remission of MDD and/or GAD and establish appropriate cognitive/functional status as per CAMAT guidelines (7, 8).

3) Provide regular communication updates with the patient's family physician after each contact with the patient (via fax or electronic charting).

4) Providing medication counselling and educational support to the participant.

5) Identification of adverse drug effects, drug interactions, or severe deterioration (i.e. suicide attempt)

6) Interim telephone/telehealth follow-up conducted by the pharmacist partner since the last in-person follow-up & a minimum of 1-2 weeks after the last in-person follow-up that involved a dose adjustment, prescribing of adjunctive medication, or discontinuation of therapy. (Note: a telephone follow-up does not replace the scheduled in-person/telehealth follow-up).

7) Collaborate with physician to arrange referral to psychologist, psychiatrist, counsellor or social worker for psychotherapy

Should the participant from the interventional group drop out or complete the 6 month study period, they will be offered to continue with similar interventional care or standard pharmacist care but no data will be collected since their dropout or following study completion.

Control Group (Standard Pharmacist Care):

Patients randomised to the standard pharmacist care groups will receive:

- Standard pharmacist care, as outlined in the Alberta College of Pharmacist Standards of Practice for Pharmacist and Pharmacy technicians (9), and physician care with no specific interventions for the duration of the 6 month study period.

- Should participants from the usual care group drop out or the participant completes the 6 month study period, they will be offered care similar to the interventional group or standard pharmacist care but no data will be collected since their dropout or following study completion.

Both Groups

- Indication of medication (i.e. MDD, GAD, or both) will be recorded by the pharmacist partner in the secured study electronic website/database.
- The electronic PHQ-9/GAD-7 questionnaire (Appendix 4) will be sent securely to and completed by the participant at enrollment (month 0) and prior to the participant's in-person scheduled month 6 (final). The questionnaire results will be available to the study investigator and pharmacist participants but linked only to the participant's study ID.
- Participants will receive a pamphlet copy of Alberta Health Services Access Mental Health resource pamphlet "Know Your Addiction and Mental Health Options" which provides information regarding walk-in services, crisis support, and urgent care (10). An equivalent alternative pamphlet can be developed and provided by the study team if this document becomes obsolete or additional update/information is required.

Continuity of care plan:

- Should participants from either group drop out or complete the 6 month study period, they will be offered care similar to the interventional group or standard pharmacist care as outlined in the Alberta college of pharmacists standards of practice but no data will be collected since their dropout or study completion.

Recording interventions:

Intervention types will be documented by the pharmacist partner using the secured electronic study website/database. This electronic website/database will indicate the participants unique ID, their group assignment, the date of enrollment, current date of interaction. During these interactions (in-person/telehealth), the pharmacist partner will review the participant's PHQ-9/GAD-7 score and select the interventions performed.

The completed interactions will be recorded using the electronic study website/database. All inputs will be encrypted and stored at a central electronic database on University of Alberta servers for the investigational team to analyse at study completion.

Outcomes:

Primary outcomes:

The primary outcome is the mean score difference in PHQ-9 and GAD-7 scores from baseline to end of study participation, between the intervention and standard pharmacist care groups.

- Both PHQ-9 and GAD-7 are validated tools for measuring major depressive disorder and generalised anxiety, respectively, in the primary care setting. They are brief and can be self-administered, with similar results yielded with health care provider administered reports. These are desirable given the time restraints and competing demands we anticipate for community pharmacist partners participating in the study(11, 12).
- PHQ-9 scores reflect depression severity; Ranges from 0-27 (Scores: 0-4 none/minimal, 5-9 mild, 10-14 moderate, 15-19 moderately severe, 20-27 severe) (13).
- GAD-7 scores reflect anxiety severity; Ranges from 0-21 (Scores: 0-4 none/minimal. 5-9 mild, 10-14 moderate, 15-21 severe) (13)

Secondary outcomes:

- Difference in the clinical improvement rates (proportions of participants achieving clinically significant treatment response) between the pharmacist intervention and standard pharmacist care groups from baseline until the end of the study period, using the PHQ-9 and GAD-7 score.
    - For our study, clinically significant treatment response for the PHQ-9 is defined as a reduction in PHQ-9 score by at least 50% from baseline; adequate treatment response for the GAD-7 is defined as a drop in the GAD-7 score by at least 50% from baseline.
- Difference in the proportion of participants with MDD to achieve PHQ-9 score <5 (i.e. remission/no depression) between the pharmacist intervention and standard pharmacist care groups
- Difference in the proportion of participants with GAD to achieve GAD-7 score <5 (i.e. remission/no anxiety) between the pharmacist intervention and standard pharmacist care groups
- Percentage difference in self-reported safety concerns disclosed by participant to pharmacist partner anytime during the study period, between the pharmacist intervention and standard pharmacist care groups:
    - Adverse medication effects (e.g. dizziness, GI intolerance, bleeding, palpitations suggestive of prolonged QTc interval, etc.)

- Suicidal ideation, attempt at suicide
- Causing withdrawal from study

Sample size and analytical plan:

Sample Size Calculation:

Lindell et al (2018), who evaluated the impact of a psychiatric clinical pharmacists intervention on the change in PHQ-9 and/or GAD questionnaire scores (14), reported a baseline PHQ-9 mean of 15.2 (Standard deviation [SD] of 6.9) and GAD mean of 12.0 (Standard deviation [SD] of 5.8).
Using those reported values and the following assumptions of an 80% power and a 2 sided alpha of 0.05, a sample size of:

- 84 patients (42 in each group) is required to detect a 4.3 point difference in the mean reduction in PHQ-9 scores between the intervention and control group
- 80 patients (40 in each group) are required to detect a 8.3 point difference in the mean reduction in GAD scores between the intervention and control group.

We selected the larger sample size of 84 patients and inflated it by 10%(47 in each group) to account for potential losses to follow-up and withdrawal of consent.

A Data Safety monitoring board will be formed to review adverse events, and data will be sent once recruitment reaches 25% (24 participant) recruitment.

Analytical Plan:

All analyses will be conducted on an intention to treat basis. In the case of missing data, a last observation carried forward approach will be used.

Primary outcome will be analysed using ANCOVA, adjusting for all covariates with $p<0.25$ between groups

Secondary outcomes will be analysed using ANCOVA, t-test or chi-square test where appropriate, adjusting for all covariates with $p<0.25$ between groups.

Trial and Data Management will be done by EPICORE Centre

Feasibility:

Remuneration:
Participant Pharmacists will submit to Alberta Health for remuneration of baseline (Comprehensive Annual Care Plan [CACP] or Standard Medication Management Assessment [SMMA]) and follow-up visits, based on eligibility as per Ministerial Order 614/2018 (15, 16). In addition, prescription services that include: initial access prescribing, prescribing to adapt, management of ongoing therapy, and prescribing to renew medication therapy--will also be submitted for remuneration.

Training for Pharmacist Partners:

i) Training and support material:
These will be developed by the research team in close collaboration with psychiatric pharmacist consultants and disseminated via online telehealth platform and/or in person.

- Recordings of these meetings will be made available
- Additional materials will be developed/acquired from major organisations:
    - Canadian Task Force for Preventative Health Care (CTFPHC)
    - Canadian Pharmacist Association (CPHA)
    - Canadian Network for Mood and Anxiety Treatments (CANMAT)
    - Centre for Addiction and Mental Health (CAMH)

Training and support materials will include the following topics:

- Case finding
- Major Depressive Disorder and Generalised Anxiety disorder
    - PHQ9 and GAD7 scoring
    - Clinical assessment and monitoring for patients with depression and anxiety
- Managing Adverse Effects
- Switching medications
- Alberta Health Services Access Mental Health “Know Your Options” brochure
- Preparing CACP and SMMA for remuneration
- CANMAT 2016 guideline for the management of adults with MDD (including treatment, adjustment, and add-on algorithm)
- CANMAT 2014 guideline for the management of anxiety (focusing on GAD treatment)

ii) Competency and adherence:

- Pre and post tests will be administered with corresponding training seminars to ensure minimum competency has been met by pharmacist partners before being able to participate in the study.

- A study coordinator will conduct random audits of data input to ensure that pharmacist partners are adhering to study protocols and identify needs for additional training to be administered by the investigation team.

- Pharmacist partners will be encouraged to collaborate with the participant's physician, psychiatrist, counsellor, social worker, psychologist, or psychiatry pharmacist–to address clinical questions related to the management of the participant's MDD and/or GAD.

- Pharmacist partners will have the ability to contact the study investigators via telephone and/or email to address additional support needs for competency and adherence.

Pharmacy Recruitment:
We will recruit pharmacies through the Alberta College of Pharmacists (ACP) and Alberta Pharmacists Association (RxA), by sending communications to all licensed pharmacists and call for Expressions of Interest.

- Each pharmacy location must have all staff pharmacists (pharmacist partners) with additional prescribing authorization (APA) and PracID authorizations on their current licensure from the Alberta College of Pharmacists.

- Pharmacies and pharmacists will be selected based upon their track record in innovative patient care initiatives, commitment of in-kind resources (e.g., pharmacist and technician time), current APA and PracID status, and service provided to patients with mental health disorders and vulnerable populations (i.e. rural, inner city, elderly, South Asians, Aboriginal, etc.).

What This Study Adds:

This is the first study to evaluate the effectiveness of community pharmacist interventions available to Alberta pharmacists practising at their full scope of practice (which includes the use of additional prescribing authority to adjust or add adjunctive schedule 1 medications, and ordering lab work)--for patients with MDD and/or GAD and who are on pharmacotherapy to manage these conditions.

Demonstrating the ability of prescribing pharmacists to facilitate patient's timely access to psychotherapy (i.e. referral to psychiatrist and/or psychologist) and optimization of pharmacotherapies used in the management of MDD and/or GAD, may highlight the time and cost-saving opportunities available when pharmacists are practising to their full scope of practice.

The data collected will help provide stakeholders (i.e. ACP, RxA, government) and patients the opportunity to evaluate the merits of pharmacists taking an active role in monitoring, counselling, collaborating, and making prescribing interventions (dose adjustments & adding adjunctive medications) to manage patients with MDD and/or GAD. This may also encourage support for community pharmacists to seek additional training and education in mental health management (e.g. pharmacist certification programs focused on mental health

management), and enhance the collaboration between family physicians and community pharmacists in mental health management.

Timelines:

June 2020: Finalise Study Protocol, implementation planning, meeting with partners, agreements signed

June-August 2020: Research Ethics Board Approval

January-June 2020: Recruitment of pharmacy sites

August 2020-December 2022: Development of learning assets, creation of recording database (REDcap), training of pharmacists

December 2022-January 2023: Study Launch meetings

January 2023: Patient recruitment

June 2024: Final follow-up of pharmacist intervention and standard pharmacist care group participants (6 months)

July-September 2024: Data analysis and report writing

October-November 2024: Wrap-up investigators' meeting, discussion re: presentation, media release, etc.

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Appendix:

1)CANMAT 2016 (7)

Table 3. Summary Recommendations for Antidepressants.

Antidepressant (Brand Name(s))	Mechanism	Dose Range
First line (Level 1 Evidence)		
Agomelatine[a] (Valdoxan)	MT_1 and MT_2 agonist; 5-HT_2 antagonist	25-50 mg
Bupropion (Wellbutrin)[b]	NDRI	150-300 mg
Citalopram (Celexa, Cipramil)	SSRI	20-40 mg
Desvenlafaxine (Pristiq)	SNRI	50-100 mg
Duloxetine (Cymbalta)	SNRI	60 mg
Escitalopram (Cipralex, Lexapro)	SSRI	10-20 mg
Fluoxetine (Prozac)	SSRI	20-60 mg
Fluvoxamine (Luvox)	SSRI	100-300 mg
Mianserin[a] (Tolvon)	α_2-Adrenergic agonist; 5-HT_2 antagonist	60-120 mg
Milnacipran[a] (Ixel)	SNRI	100 mg
Mirtazapine (Remeron)[c]	α_2-Adrenergic agonist; 5-HT_2 antagonist	15-45 mg
Paroxetine (Paxil)[d]	SSRI	20-50 mg 25-62.5 mg for CR version
Sertraline (Zoloft)	SSRI	50-200 mg
Venlafaxine (Effexor)[e]	SNRI	75-225 mg
Vortioxetine (Brintellix, Trintellix)[f]	Serotonin reuptake inhibitor; 5-HT_{1A} agonist; 5-HT_{1B} partial agonist; 5-HT_{1D}, 5-HT_{3A}, and 5-HT_7 antagonist	10-20 mg
Second line (Level 1 Evidence)		
Amitriptyline, clomipramine, and others	TCA	Various
Levomilnacipran (Fetzima)[f]	SNRI	40-120 mg
Moclobemide (Manerix)	Reversible inhibitor of MAO-A	300-600 mg
Quetiapine (Seroquel)[e]	Atypical antipsychotic	150-300 mg
Selegiline transdermal[a] (Emsam)	Irreversible MAO-B inhibitor	6-12 mg daily transdermal
Trazodone (Desyrel)	Serotonin reuptake inhibitor; 5-HT_2 antagonist	150-300 mg
Vilazodone (Viibryd)[f]	Serotonin reuptake inhibitor; 5-HT_{1A} partial agonist	20-40 mg (titrate from 10 mg)
Third line (Level 1 Evidence)		
Phenelzine (Nardil)	Irreversible MAO inhibitor	45-90 mg
Tranylcypromine (Parnate)		20-60 mg
Reboxetine[a] (Edronax)	Noradrenaline reuptake inhibitor	8-10 mg

5-HT, 5-hydroxytryptamine (serotonin); MAO, monoamine oxidase; MT, melatonin; NDRI, noradrenaline and dopamine reuptake inhibitor; SNRI, serotonin and noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.
[a]Not available in Canada.
[b]Available as sustained-release (SR) and extended-release (XL) versions.
[c]Available as rapid-dissolving (RD) version.
[d]Available as controlled-release (CR) version
[e]Available as extended-release (XR) version.
[f]Newly approved since the 2009 Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines.

Table 11. Recommendations for Adjunctive Medications for Nonresponse or Partial Response to an Antidepressant.

Recommendation	Adjunctive Agent	Level of Evidence	Dosing
First line	Aripiprazole	Level 1	2-15 mg
	Quetiapine	Level 1	150-300 mg
	Risperidone	Level 1	1-3 mg
Second line	Brexpiprazole[a]	Level 1	1-3 mg
	Bupropion	Level 2	150-300 mg
	Lithium	Level 2	600-1200 mg (therapeutic serum levels)
	Mirtazapine/mianserin	Level 2	30-60 mg
	Modafinil	Level 2	100-400 mg
	Olanzapine	Level 1	2.5-10 mg
	Triiodothyronine	Level 2	25-50 mcg
Third line	Other antidepressants	Level 3	Various
	Other stimulants (methylphenidate, lisdexamfetamine, etc.)	Level 3	Various
	TCAs (e.g., desipramine)	Level 2	Various
	Ziprasidone	Level 3	20-80 mg bid
Experimental	Ketamine	Level 1	0.5 mg/kg, single intravenous dose[b]
Not recommended	Pindolol	Level 1 (lack of efficacy)	Not applicable

TCA, tricyclic antidepressant.
[a]Newly approved since the 2009 Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines.
[b]For acute treatment.

2)CANMAT 2014 (8)

Table 24 Recommendations for pharmacotherapy for GAD

First-line	Agomelatine, duloxetine, escitalopram, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam*, bromazepam*, bupropion XL*, buspirone, diazepam*, hydroxyzine, imipramine, lorazepam*, quetiapine XR*, vortioxetine
Third-line	Citalopram, divalproex chrono, fluoxetine, mirtazapine, trazodone
Adjunctive therapy	**Second-line:** pregabalin **Third-line:** aripiprazole, olanzapine, quetiapine, quetiapine XR, risperidone **Not recommended:** ziprasidone
Not recommended	Beta blockers (propranolol), pexacerfont, tiagabine

CR = controlled release; XL = extended release; XR=extended release.

*Note: These have distinct mechanisms, efficacy and safety profiles. Within these second-line agents, benzodiazepines would be considered first in most cases, except where there is a risk of substance abuse, while bupropion XL would likely be reserved for later. Quetiapine XR remains a good choice in terms of efficacy, but given the metabolic concerns associated with atypical antipsychotic, it should be reserved for patients who cannot be provided antidepressants or benzodiazepines. Please refer to text for further rationale for the recommendations.

3)CACP/SMMA/Follow-Up Eligibility (16)

Resident Eligibility:

3. Is the resident currently registered with the **Alberta Health Care Insurance Plan**?	☐ Yes ☐No

To qualify for a CACP, this resident must have either:
- ☐ Two Chronic Diseases from Column A; or
- ☐ One Chronic Disease from Column A and one Risk Factor from Column B.

To qualify for an SMMA, this resident must have:
- ☐ One chronic disease from Column A and be taking THREE or more different Schedule 1 medications.

To qualify for a Diabetes SMMA, this resident must have:
- ☐ Diabetes Mellitus and be taking
- ☐ Insulin or ONE or more Schedule 1 medications.

A Diabetes SMMA Assessment CANNOT be claimed if the resident has already received A CACP or SMMA.

To qualify for a Tobacco Cessation SMMA, this resident must:
- ☐ Use a tobacco product daily, and
- ☐ Be willing to receive tobacco cessation counseling and support, including pharmacotherapy at this time.

Maximum of four Tobacco Cessation Followups /365 days.

May be claimed in addition to a CACP, SMMA or Diabetes SMMA.

Chronic Diseases (Column A)			Risk Factors (Column B)
☐ **Hypertension**	☐ **COPD**	☐ **Angina Pectoris**	☐ **Obesity** (BMI > or = 30)
☐ **Diabetes Mellitus**	☐ **Asthma**	☐ **Other Chronic Ischemic Heart Disease**	☐ **Addictions**
	☐ **Heart Failure**		☐ **Tobacco**
Mental Disorders*			
☐ Anxiety	☐ Depression	☐ Panic	
☐ ADD/ADHD	☐ Eating Disorders	☐ Paranoia	
☐ Autism	☐ Hallucinations	☐ Personality Disorder	
☐ Bipolar	☐ Insomnia (see exclusions)	☐ PTSD	
☐ Dementia	☐ OCD	☐ Schizophrenia	
☐ Other: _____			

*ICD-9 Codes 290-319, excluding 303, 304, 305.1
* For full listing and exclusions see http://www.health.alberta.ca/documents/Diagnostic-Code-ICD-9.pdf
*Each individual qualifying mental disorder code counts as one chronic disease

Note: A full copy of the CACP/SMMA Care Plan Eligibility Checklist can be viewed on the RxA website, and can be provided to participating pharmacies prior to recruitment phase (unless forms already exist for pharmacy)

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4)PHQ9/GAD7 Questionnaire Tool

Name: _____ Date: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

If you checked off ***any*** problems, how ***difficult*** have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

Over the <u>last 2 weeks</u>, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T____ = ____ + ____ + ____)

5) Summary of Potential Information Gathered from Patients (as Part of Standard Pharmacist Care):

Medical/Social/Psychiatric History

- Age
- Gender
- Demographics
- Hx of suicide attempts in the past year
- Social History - Smoking, substance use, caffeine, EtOH
- Family History of mental health illness
- Diagnosis of Major depressive disorder and/or generalized anxiety disorder
    - Collateral from Netcare consultation notes, discharge summaries
    - Collateral from patient history
    - Collateral from physician notes/fax
- Labs: CBC, electrolytes (Na, K), TSH, Iron Studies (Ferritin, TIBC, serum Fe), serum B12, serum creatinine (to rule out concurrent nutritional or laboratory abnormalities impacting patient psychiatric disposition)
- Current treatments/therapies for major depressive disorder and/or generalized anxiety disorder

Medication History (to anticipate and act on barriers or harms caused by drug interactions, financial, adherence)

- Prescription history on Netcare or pharmacy patient profile
- Collateral from patient history
- Prescription medications
- Non-prescription medications, including: over-the-counter medications, natural health care products, substances
- Drug-insurance information
- Allergies

6) Study team Contributions

Matt Chow has been the main contributor to the research proposal, as a follow-up from his PharmD literature review of pharmacist interventions for mental health in primary care.

Dan Burton has been consultant to Matt Chow re: clinical considerations for inclusion/exclusion criteria, follow-up period.

Randy Howden has been the consultant for the study re: workflow considerations for the community pharmacist that may participate in the study and in the pharmacy recruitment for pharmacist partners.

Yazid Al Hamarneh has been consulted to determine feasibility of developing the electronic database and recording tool to capture participant data.

7) Contact Information

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