July 2024

Support tool

MAJOR DEPRESSIVE DISORDER DURING PREGNANCY

This clinical decision tool is intended primarily for front-line healthcare professionals involved in pregnancy follow-up. It is provided for guidance only and does not replace the judgment of the clinician exercising the activities reserved to him or her by law or regulation. These recommendations have been developed using a systematic approach and are supported by the scientific literature and the knowledge and experience of Quebec clinicians with a wide range of expertise. All scientific studies in the present work use gender and not gender identity or expression to describe their participants. Thus, throughout this document, the term "female" includes cisgender, transgender and non-binary people designated at birth as female. For more details, visit **inesss.qc.ca**.

OVERVIEW

Although the recommendations in this guide are aimed at the antenatal period, they should also be applied **before conception** to facilitate management in the event of an unplanned pregnancy.

When planning a pregnancy, optimal stability of mood and functioning should be the aim before conception.

IMPORTANCE OF THE ISSUE

- Approximately 10-15% of women experience a depressive episode during pregnancy.
- A pregnant woman's prenatal mental health is a predictor of her postnatal mental health.
- The presence of a mental health disorder during pregnancy is associated with certain risks for the mother, fetus, or infant, such as:
  - an increased risk of prematurity
  - potential danger to self or others;
  - an increased risk of substance abuse;
  - difficulty taking care of oneself;
  - difficulties with infant attachment, which could have consequences for the child's development;
  - an increased risk of depressive disorder in the life partner.
- Discontinuing treatment for severe depressive disorder during pregnancy is associated with an increased risk of relapse during and after pregnancy.

Tools are available to promote positive mental health in the perinatal period, for example (only in French) : Trousse de soutien Le bien être en période périnatale.

Pregnant women and their families should be referred to an appropriate resource in the health and social services network (e.g. Mental Health Access Desk) or to a community resource in their area, depending on their needs or the presence of risk factors.

The Info-Social service (811, option 2) can be contacted to find out about available resources.

CONSIDER CONSULTING WITH AN EXPERIENCED COLLEAGUE

- Consultation with an experienced colleague should be considered in any situation in which the professional feels less comfortable, particularly if the pregnant woman presents a serious mental health problem (current or past), such as:
  - suicidal ideation
  - bipolar disorder
  - refractory depressive disorder
  - psychosis
  - schizophrenia
  - drug addiction
  - other mood disorders (e.g. dysthymia and severe anxiety disorders)

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If psychotic symptoms or suicidal ideation are present, with serious short-term danger, immediately refer the person to a specialist or to the emergency services.

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CLINICAL OVERVIEW - SPECIFIC FEATURES DURING PREGNANCY

- It's important to be alert for possible depressive signs and symptoms throughout pregnancy, especially for those with one or more risk factors. Depressive symptoms should be identified as part of a discussion with the pregnant woman about her mental health.
  - Use of the Patient Health Questionnaire (PHQ-2) and the Edinburgh Postnatal Depression Scale (EPDS) could be considered to identify depressive symptoms.
  - ! Since anxiety symptoms are common with major depressive disorder, the Generalized Anxiety Disorder Scale (GAD-2) could also be considered to identify anxiety symptoms.
- Diagnosis of an episode of major depressive disorder is based on DSM-5-TR criteria.
  - ! Pregnancy can bring about physiological changes that may resemble some of these criteria. The clinical assessment of major depressive disorder during pregnancy should also consider suboptimal weight gain and disinvestment in pregnancy.
- If depressive symptoms are present, possible physical causes should be ruled out.
  - This assessment can be supported, if necessary, by a recent blood test (including CBC and TSH).
- It is important to ask about the person's consumption of alcohol and psychoactive substances, as well as their lifestyle habits.
- The presence of other concomitant mental health problems and their level of severity should be assessed and considered when planning treatment and monitoring therapeutic response.

TREATMENT PRINCIPLES

Healthy lifestyle habits should be encouraged to promote the person's physical and mental health, particularly regarding sleep hygiene, physical activity, diet, and smoking cessation.
If necessary, the person can be referred to community resources.

- Treatment should be offered to all pregnant women who present with characterized depressive disorder. Treatment options include:
  - psychosocial interventions (e.g. self-care, support groups, and counseling)
  - psychotherapy (e.g. cognitive-behavioural therapy [CBT], interpersonal therapy [IPT])
  - pharmacological treatments.
- A stepped care model, incorporating a range of treatments, considers the severity of the disorder, treatment history, and individual preferences.
  - Psychosocial interventions or psychotherapy should be provided first and foremost.
- Some clinical practice guides refer to the use of complementary approaches (e.g. yoga, acupuncture, light therapy) to support treatment. However, the evidence base for this is often very limited.

ⓘ In the general population:

- In **mild** depression, the efficacy of pharmacological treatments is no greater than that of structured physical activity programs, psychosocial interventions, and psychotherapy, which have a significant effect on depressive symptoms, functioning, quality of life, and remission.
- In **moderate** to **severe** depression, the efficacy of psychotherapy is similar to that of pharmacological treatments in terms of response and remission rates:
  - Treatment response, defined as a 50% reduction in symptoms on the rating scale, occurs in approximately 45-60% of people treated with either intervention.
  - Approximately 30-45% of those treated will go into remission after 6-12 weeks of treatment.
  - Combining psychotherapy with pharmacological treatment may provide additional benefits in terms of symptom improvement, treatment response rate, remission rate, quality of life, and functioning.

DECISION-MAKING PROCESS FOR INITIATING TREATMENT

- Treatment choices for major depressive disorder during pregnancy should be based on a discussion with the pregnant woman about her preferences, the advantages, and disadvantages of each treatment option in relation to the severity of the illness, and the risks associated with untreated or under-treated illness for herself and her unborn child. The Depressive Disorder and Pregnancy - Your Options for an Informed Treatment Choice tool can be used to facilitate this discussion.
- Consider including life partners, families, or significant others in discussions.

An information sheet for people with major depressive disorder during pregnancy is available and can be accessed using this QR code.

DURING PREGNANCY

EVALUATION

How severe is the disease according to DSM-5-TR criteria?

Below diagnostic threshold

Have symptoms persisted (more than 6 months)?

- NO
- YES

Mild

History of severe depression **OR** mild or moderate depression that has not responded to previous treatment?

- NO
- YES

Moderate or Severe

FIRST-LINE TREATMENT

Consider one or more of the following psychosocial interventions:
- Counseling
- Psychological education
- Psychosocial support
- Self-care

Consider psychotherapy alone (CBT or IPT)
OR
one or more of the following psychosocial interventions:

Consider psychotherapy alone (CBT or IPT)
OR
one or more of the following psychosocial interventions:

Consider psychotherapy alone (CBT or IPT)
OR
an antidepressant[1]
OR
a combination of an antidepressant[1] with one of the following psychotherapies or psychosocial interventions:

- Counseling
- Mindfulness meditation
- Psychological education
- Psychosocial support
- Self-care
- Structured physical activity program
- Support groups
- Techniques inspired by CBT or IPT

IN CASE OF REFUSAL

If the person declines all proposed treatment options, discuss their concerns and the risks associated with no treatment, and plan a reassessment of the situation.

If the person declines psychosocial intervention or psychotherapy and wishes to take an antidepressant, discuss the risks and benefits of this option.

If the person declines all proposed treatment options, discuss their concerns and the risks associated with no treatment, and plan a reassessment of the situation within 2 to 4 weeks

[1] For further details, please consult the Decision-making process for the choice of pharmacological agent section.

CBT: cognitive-behavioural therapy; **IPT**: interpersonal therapy.

To make the algorithm easier to read, the proposed interventions are presented in alphabetical order.

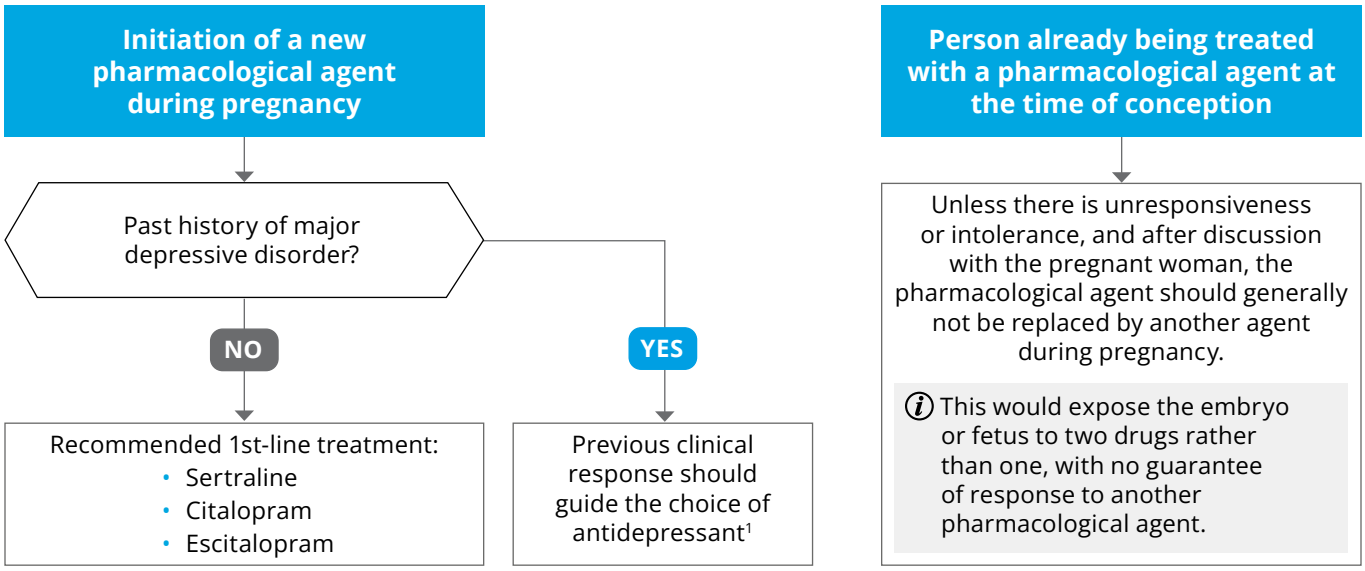
PHARMACOLOGICAL TREATMENT

→ According to studies conducted outside pregnancy, the efficacy of various antidepressants is broadly similar. The choice of pharmacological agent should therefore consider the following factors:

- the individual's previous clinical response;
- risks associated with antidepressants during pregnancy (see Antidepressant safety section);
- the person's comorbidities;
- desirable and undesirable side effects of antidepressants;
- possible drug interactions;
- passage of the drug into breast milk

ⓘ Most antidepressants are present in low concentrations in breast milk and are compatible with breast-feeding.

DECISION-MAKING PROCESS FOR CHOICE OF PHARMACOLOGICAL AGENT



1 In addition to sertraline, citalopram or escitalopram, the use of bupropion, desvenlafaxine, duloxetine, fluoxetine, fluvoxamine, mirtazapine, paroxetine, venlafaxine, tricyclic antidepressants, or quetiapine may be considered in pregnant women who have failed to respond to or tolerate first-line medications in the past, or who have already responded well to one of these medications prior to pregnancy.

Newer drugs (e.g. levomilnacipran, vilazodone, vortioxetine) have generally been less studied in pregnancy and should be reserved for those who do not respond to better-known options.

Important considerations on dosing and polypharmacy

→ Use of the minimum **effective** dose is recommended. A small reduction in dose is not desirable, however, if it risks destabilizing ongoing treatment. Dosage should be reassessed throughout pregnancy and in the postnatal period.

⓪ The minimum **effective** dose may vary during pregnancy.

→ The use of a single drug is recommended whenever possible. In the case of a combination of agents or polypharmacy, the indication, efficacy, and dosage of each drug should be reassessed throughout pregnancy to optimize their efficacy while limiting their adverse effects.

→ In the run-up to childbirth, current data do not justify systematic dose reduction or discontinuation of the drug, when the latter is necessary for the treatment of major depressive disorder.

ANTIDEPRESSANT SAFETY

The information detailed below has several limitations due to the many confounding factors that can influence this type of analysis, including the severity of the underlying disease, polypharmacy, lifestyle habits of the individual, etc. The presence of residual bias cannot therefore be eliminated. **The level of certainty of the evidence is low or very low for the majority of the outcomes cited.**

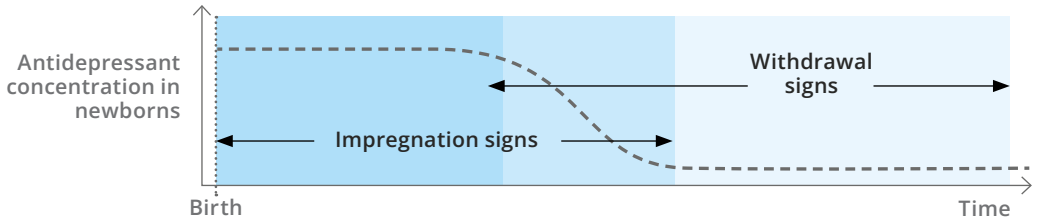
According to the data analyzed, the use of selective serotonin reuptake inhibitors (SSRIs) during pregnancy does not appear to have a significant effect on several outcome parameters, including the risk of preeclampsia, post-partum hemorrhage, spontaneous abortion, major congenital malformations and major cardiac malformations, low birth weight, persistent pulmonary hypertension in the newborn, autism spectrum disorder, attention deficit hyperactivity disorder, major depressive disorder in the child, or problems with the child's psychomotor development.

- An increase in the risk of some specific congenital malformations has been observed with the use of SSRI class molecules. However, the clinical consequences are uncertain and potentially limited, given the very low incidence of these malformations or the small size of the increases.

Every pregnancy carries a basic 3-5% risk of malformation.

However, the use of antidepressants during pregnancy is associated with certain risks, including:

- **Preeclampsia**: the use of serotonin and norepinephrine reuptake inhibitors (**SNRIs**) during pregnancy is associated with an increased risk of preeclampsia, of the order of 3 more events per 100 pregnancies.
- **Premature birth**: the use of **SSRIs**, **venlafaxine** or tricyclic antidepressants (**TCAs**) during pregnancy is associated with an increased risk of premature birth (before 37 weeks' gestation). With exposure to SSRIs, this risk would be of the order of 9 more events per 100 pregnancies. However, some data suggest that SSRI use reduces the average length of gestation by around 3 days, and that the risk of a birth before 32 weeks' gestation is comparable to the baseline risk.
- **Neonatal maladjustment syndrome**: up to 30% of newborns exposed to **antidepressants** may show serotonin-like signs, testifying to the placental passage of these drugs during pregnancy. Although these signs are mild and transient in the majority of cases (usually resolving in 2 to 14 days with appropriate supportive care), they may be more prominent in the presence of certain risk factors. These signs persist for as long as the drug is present in the child's body. As the drug is eliminated, signs of withdrawal may appear.



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Impregnation Signs

- Agitation
- Hyperreflexia
- Myoclonus
- Diarrhea
- Tremors
- Respiratory distress
- Hypoventilation

Withdrawal signs

- Irritability
- Tremors
- Pulses
- Myoclonus
- Increased tone
- Nausea
- Eating difficulties
- Sweating
- Insomnia

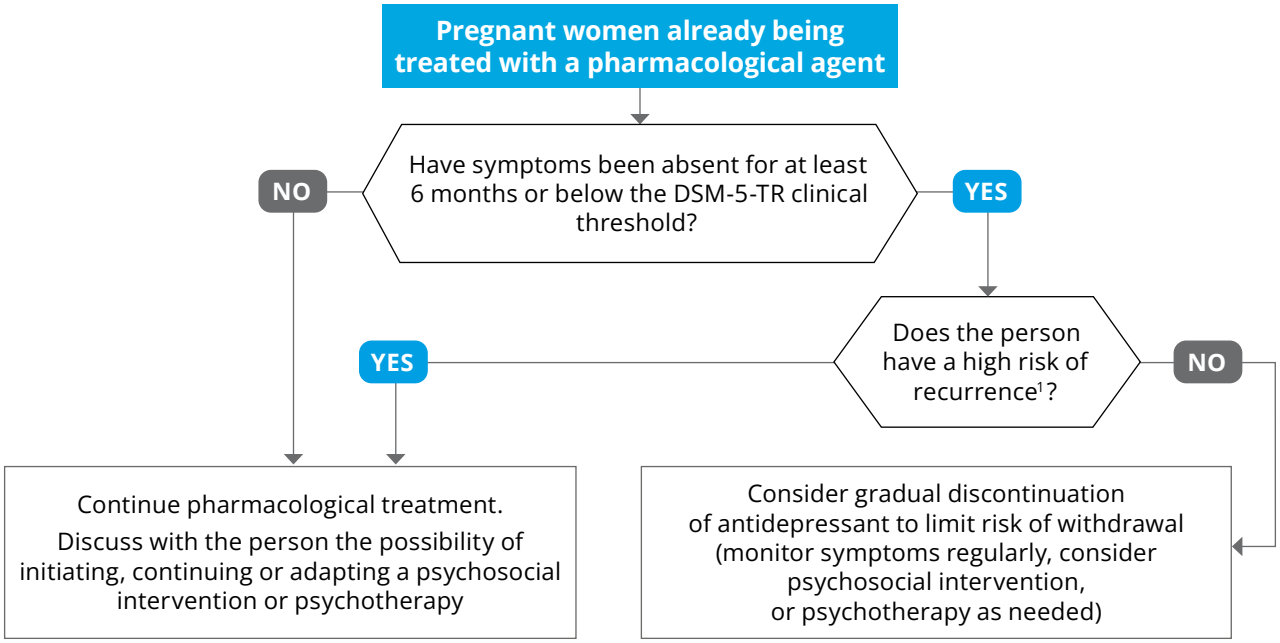
Other data on the use of SNRIs and TCAs, as well as data on bupropion, fluvoxamine, mirtazapine, and quetiapine during pregnancy, are insufficient or associated with a level of certainty of evidence too low to draw conclusions. In addition, data on the use of levomilnacipran, vilazodone, and vortioxetine during pregnancy are very limited and do not allow us to assess their safety profile for the fetus and mother.

Legend: No effects observed | Increased risk | Too little data available or too much uncertainty

MONITORING PHARMACOLOGICAL TREATMENT

DECISION-MAKING PROCESS FOR CONTINUING OR DISCONTINUING PHARMACOLOGICAL TREATMENT

- Treatment choice should be based on a discussion with the pregnant woman about her preferences and the advantages and disadvantages of each treatment option in relation to the severity of the disease.
- Consider including life partners, families, or significant others in discussions.



1 For example, symptoms that are very difficult to treat or stabilize, presence of residual symptoms, history of multiple relapses of major depressive disorder, recurrent or unstable disorder over the past 6 months, presence of psychosocial risk factors

IN PREPARATION FOR CHILDBIRTH AND BREASTFEEDING

- The choice of delivery site should be discussed with the pregnant woman, considering, among other things, information on the safety of antidepressants for mother and newborn.
- The mother's medication list during pregnancy, other exposures (e.g. psychoactive substances), and residual signs and symptoms of psychopathology should be discussed with the interprofessional team to facilitate management of the mother and newborn.
- Taking an antidepressant should not prevent breastfeeding.
  - Several factors should be considered when discussing the advantages and disadvantages of breast-feeding and in the monitoring plan for the infant - e.g. the health status of the baby and mother, the presence of polytherapy, the required use of high doses, the lack of studies on the passage of certain drugs in breast milk).
- Bed-sharing or sleeping with the child should be avoided because of the potential sedative effects of anti-depressants and the risk of crib death.

USEFUL LINKS

- For support or information on all available services and resources: 811, Ma grossesse service
- For more information on perinatal mental health (French only) : SIPPE summary sheet on mental health
- For a better understanding of prenatal depression: Naître et grandir guide
- For more information on the safety of each compound during pregnancy and breastfeeding: Centre IMAGe, LactMed
- For support for family and friends: CAP santé mentale

REFERENCES

- For references, see the accompanying report and appendix.

Institut national d'excellence en santé et en services sociaux
Québec

APPENDIX I

MAIN RISK FACTORS FOR DEPRESSIVE DISORDER (non-exhaustive list)		
Psychiatric history	**Obstetrical and reproductive history**	**Socio-economic factors**
• History of depressive disorder (perinatal or not) • History of antenatal anxiety • Trauma in life history • Family history of mental health disorders	• Excessive preoccupation with pregnancy • Trauma associated with reproduction (e.g. infertility) • Obstetrical complications • Involuntary pregnancy • Bereavement due to obstetrical complication	• Domestic violence • Socio-economic stress • Immigration status • Family difficulties • Lack of social support

Depending on the risk factors present, perinatal support services - e.g. SIPPE (Integrated Perinatal and Early Childhood Services), perinatal resource centers, prenatal classes, etc. - and other community resources should be offered during pregnancy and after childbirth.

There are also protective factors such as a positive co-parenting relationship, positive self-esteem, shared family responsibilities, parents' adaptive abilities, emotional and social support, and the maintenance of healthy lifestyle habits.

APPENDIX II

PHQ-2 (*Patient Health Questionnaire 2 item scale*)

Over the last 2 weeks, have you been bothered by any of the following problems?	Yes	No
Little interest or pleasure in doing things	☐	☐
Feeling down, depressed, or hopeless	☐	☐

If the answer is no to both questions: the presence of a major depressive disorder is unlikely
If the answer is yes to either question: continue investigation using the PHQ-9 or refer the person.

GAD-2 (*Generalized Anxiety Disorder 2 item scale*)

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious or on edge	**0**	**+ 1**	**+ 2**	**+ 3**
Not being able to stop or control worrying	**0**	**+ 1**	**+ 2**	**+ 3**

If the score is 0, 1, or 2, the presence of an anxiety disorder is unlikely
If the score is 3 or more: further investigation using the GAD-7or refer to a specialist.

EPDS Questionnaire (Edinburgh Postnatal Depression Scale)

In the past 7 days:	
1. I have been able to laugh and see the funny side of things 0 As much as I always could 1 Not quite so much now 2 Definitely not so much now 3 Not at all	**6.** Things have been getting on top of me 3 Yes, most of the time I haven't been able to cope 2 Yes, sometimes I haven't been coping as well as usual 1 No, most of the time I have coped quite well 0 No, I have been coping as well as ever
2. I have looked forward with enjoyment to things 0 As much as I ever did 1 Rather less than I used to 2 Definitely less than I used to 3 Hardly at all	**7.** I have been so unhappy that I have had difficulty sleeping 3 Yes, most of the time 2 Yes, sometimes 1 Not very often 0 No, not at all
3. I have blamed myself unnecessarily when things went wrong 3 Yes, most of the time 2 Yes, some of the time 1 Not very often 0 No, never	**8.** I have felt sad or miserable 3 Yes, most of the time 2 Yes, quite often 1 Not very often 0 No, not at all
4. I have been anxious or worried for no good reason 0 No, not at all 1 Hardly ever 2 Yes, sometimes 3 Yes, very often	**9.** I have been so unhappy that I have been crying 3 Yes, most of the time 2 Yes, quite often 1 Only occasionally 0 No, never
5. I have felt scared or panicky for no very good reason 3 Yes, quite a lot 3 Yes, sometimes 1 No, not much 0 No, not at all	**10.** The thought of harming myself has occurred to me 3 Yes, quite often 2 Sometimes 1 Hardly ever 0 Never

Scores can range from 0 to 30.

- A score of 13 or more indicates a probability of major depressive disorder in 80% of cases.
- A positive score on question 10 requires immediate discussion with the person and further assessment by a health professional or emergency resource.

© The Royal College of Psychiatrists 1987. From Cox, JL, Holden JM and Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. British Journal of Psychiatry 1987; 150: 782-6.

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APPENDIX III

GLOSSARY

Self-care
Self-care refers to what a person does for themselves in order to 1) maintain and promote their physical and psychological health and well-being, or 2) prevent or manage symptoms associated with their mental health condition. Self-care can be provided by oneself or with the support of others, such as loved ones, community members or professionals.

Counseling
Intervention or set of interventions such as listening, guidance, support, or education as part of a helping relationship.

Psychological education
The aim of psychological education is to provide information-based learning for the individual. It involves teaching specific knowledge and skills designed to maintain and improve autonomy or health, in particular, by preventing the onset of health or social problems.

Psychosocial interventions
Psychosocial interventions are activities, techniques, or strategies designed to influence the individual's response to treatment by modifying biological, behavioural, cognitive, affective, interpersonal and environmental factors. They may include generic components observed in all interventions, or components associated uniquely with a particular theoretical orientation or approach. Targeted changes affect symptoms related to the person's physical or mental health, functioning and well-being.

Support group
A form of intervention that brings together a limited number of people and focuses on meeting their social and emotional needs.

Mindfulness meditation
CBT or CBT-inspired techniques to develop greater self-awareness by focusing on the present moment and being aware of sensations, feelings, and thoughts.

Physical activity program
Structured program of physical activity (e.g. aerobics) led by an instructor and whose frequency and intensity are determined.

Psychotherapy
Psychological treatment for mental disorders, behavioural disturbances, or any other problem causing psychological suffering or distress, with the aim of promoting significant changes in the person's cognitive, emotional, or behavioural functioning, interpersonal system, personality, or state of health. This treatment is based on recognized theoretical models and goes beyond help in coping with current difficulties, or a counselling or support relationship.

Cognitive Behavioural Therapy (CBT)
Cognitive-behavioural psychotherapy that recognizes thoughts, beliefs, and interpretations and their effects on symptoms. Various skills are developed to replace problematic thoughts, beliefs, and interpretations, and to promote the use of more appropriate coping strategies.

Techniques inspired by CBT or IPT
Interventions based on CBT or IPT principles that are not psychotherapeutic.

Interpersonal therapy (IPT)
Psychotherapy that treats depressive disorder by focusing on the relational context (e.g. role transitions, conflicts, bereavements) and on communication, support, and social functioning.

Psychosocial support
Interventions that provide individual, family, or group help and support to prevent deterioration and reduce the consequences of psychosocial problems.