

Towards Better Mental and Physical Health: Preventing and Managing Concurrent Mental and Physical Conditions

A Scoping and Rapid Realist Review

Acknowledgements

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Glossary

Chronic condition self-management:	A self-management program is a structured program applied at the individual or group level that explicitly aims to improve the way individuals self-manage their chronic conditions, optimize their health, and live well. They may be delivered in a number of ways including face-to-face, by telephone or on a computer. ¹
Collaborative care:	Multi-professional approaches, that employ structured management, scheduled follow-up, and enhance inter-professional communication. ^{2,3,4}
Comorbidity:	Refers to the co-occurrence of at least one mental health problem or illness and at least one physical disease or disorder in the same person, regardless of the chronological order in which they occurred or the causal pathway linking them. ⁵
Frailty:	The Canadian Frailty Network defines frailty as a medical condition of reduced function and health in older individuals. It often includes several features such as inactivity, poor nutrition, social isolation or loneliness, and the use of multiple medications.
Mental health problems or illnesses:	Mental health problems or illnesses include a broad range of conditions that affect one's mood, thinking, and/or behaviour. This report includes information about NCDs that are comorbid with depressive and anxiety disorders, bipolar and related disorders, schizophrenia spectrum and other psychotic disorders, obsessive-compulsive and related disorders, trauma- and stressor-related disorders, substance use and addictive disorders (see separate definition), or feeding and eating disorders. In addition, common mental health symptoms that are comorbid with NCDs, such as depression and anxiety, are discussed. These terms are used interchangeably with mental health conditions throughout the report.
Metabolic Syndrome (MetS):	MetS is a health disorder that, if left untreated, increases the risk of many chronic conditions such as type 2 diabetes and cardiovascular disease. MetS is diagnosed when a person has three of the following conditions: high blood pressure, high blood glucose levels, high triglycerides, low HDL-cholesterol, or large waist circumference. ⁶
Non-communicable diseases (NCDs):	NCDs, also often referred to as chronic diseases, last for at least 3 months, are not passed between people, and are progressive. Some of conditions, such as Huntington's disease, may be inherited. In this report, the NCDs and related conditions included are arthritis (rheumatoid and osteoarthritis), cancer, cardiovascular disease, chronic respiratory diseases, dementia, diabetes mellitus, epilepsy, frailty, Huntington's disease, inflammatory bowel disorders (ulcerative

colitis and Crohn's disease), kidney disease, metabolic syndrome, obesity, and Parkinson's disease.

Priority and equity-seeking populations:

These are diverse populations that the Mental Health Commission of Canada (MHCC) seeks to improve mental health services, supports and policies for. They include immigrant, refugee, ethnocultural and racialized (IRER) communities, First Nations, Inuit and Métis, the 2SLGBTQ+ community, people in minority language situations, individuals living in rural or remote communities, those earning low income, and seniors.

Substance misuse and substance use disorders:

Substance misuse is defined as the use of a substance for a purpose not consistent with legal or medical guidelines.⁷ The criteria for substance-use disorders are defined in the DSM-5, and may be generally defined as symptom patterns that result from the use of a substance that one continues to take, despite experiencing problems as a result.⁸

Summary

Background

Physical and mental health co-morbidities are common, however, little is known about their prevalence, incidence, associated healthcare-related costs, shared etiology, prevention and management. A better understanding of how to prevent, screen, diagnose, and treat common physical and mental health co-morbidities can lead to the development of improved and sustainable health system approaches for diverse populations.

This report provides a synthesis of current international knowledge about physical and mental health co-morbidities, including information, where available, about how they intersect with sex/gender and how their characteristics may vary across priority and equity-seeking populations such as immigrant, refugee, ethnocultural and racialized (IRER) communities, First Nations, Inuit and Métis, the 2SLGBTQ+ community, and linguistic minorities. The non-communicable diseases (NCDs) discussed in this report include arthritis, cancer, cardiovascular disease, chronic respiratory diseases, dementia, diabetes mellitus, epilepsy, frailty, Huntington's disease, inflammatory bowel disorders, kidney disease, metabolic syndrome, obesity, and Parkinson's disease. The mental health comorbidities discussed with these NCDs include depressive and anxiety disorders, bipolar and related disorders, schizophrenia spectrum and other psychotic disorders, obsessive-compulsive and related disorders, trauma- and stressor-related disorders, substance use and addictive disorders, or feeding and eating disorders. In addition, common mental health symptoms that are comorbid with NCDs, such as depression and anxiety, are discussed. Finally, a rapid realist review that drew upon selected interventions from the literature was conducted to better understand what strategies are considered for different people and the mechanisms to explain why they were effective.

Highlights and Recommendations

Based on the synthesis of more than 800 research documents, a number of conclusions and recommendations arise from this review that are aimed at practitioners, policy-makers, decision-makers, and researchers.

Policies

- All of the physical and mental health comorbidities highlighted have shared biological, psychosocial, and environmental etiological pathways. Policies and preventive programming that target these pathways, particularly psychosocial and environmental targets, are recommended. These should aim to address resource allocation to mental health promotion, screening and monitoring practices, and interventions.
- Policies aimed at life course, population health, and mental health promotion have the potential to prevent or delay the development of physical and mental health conditions. Policy targets should include food environments, healthy eating, food security, physical activity, affordable childcare, affordable housing, social assistance, employment, as well as health and income equity.

Programs, Education, and Services

- Interventions that are comprehensive, integrated, tailored, and based on shared decision-making will help to address the multiple underlying factors contributing to physical and mental health comorbidities. These practices can reduce health system costs by shifting resources towards health promotion and prevention, reducing reliance on acute care, facilitating health care continuum transitions, and fostering health system sustainability.
- As part of integrated health services, stepped-care models show potential to further optimize care for those with physical and mental health comorbidities and reducing health care costs. Stepped care refers to the delivery of care intensity that is matched to the complexity of the health issue. To facilitate the delivery of these approaches, supportive administrative and reimbursement structures are needed that are inclusive of allied health professionals who can work collaboratively with other practitioners to best support the end-user's physical and mental health needs.
- Collaborative care models need to target human capacity and technology to optimize service provision. These approaches need to be inclusive of all health disciplines, including substance use disorder experts.
- Public health campaigns which help to dispel myths and stigma associated with having chronic conditions could minimize potential of mental health impacts. Exemplars of positive messaging and images could include showing individuals with health conditions leading healthy productive lives and working effectively with their health care team.
- While primary care provides the foundation for physical and mental health care services, there is a need to better integrate these approaches with social services to address the multi-faceted complex needs of those with mental and physical health comorbidities. These services need to be accessible to all, particularly groups which face barriers to access such as those residing in rural and remote communities.

Research

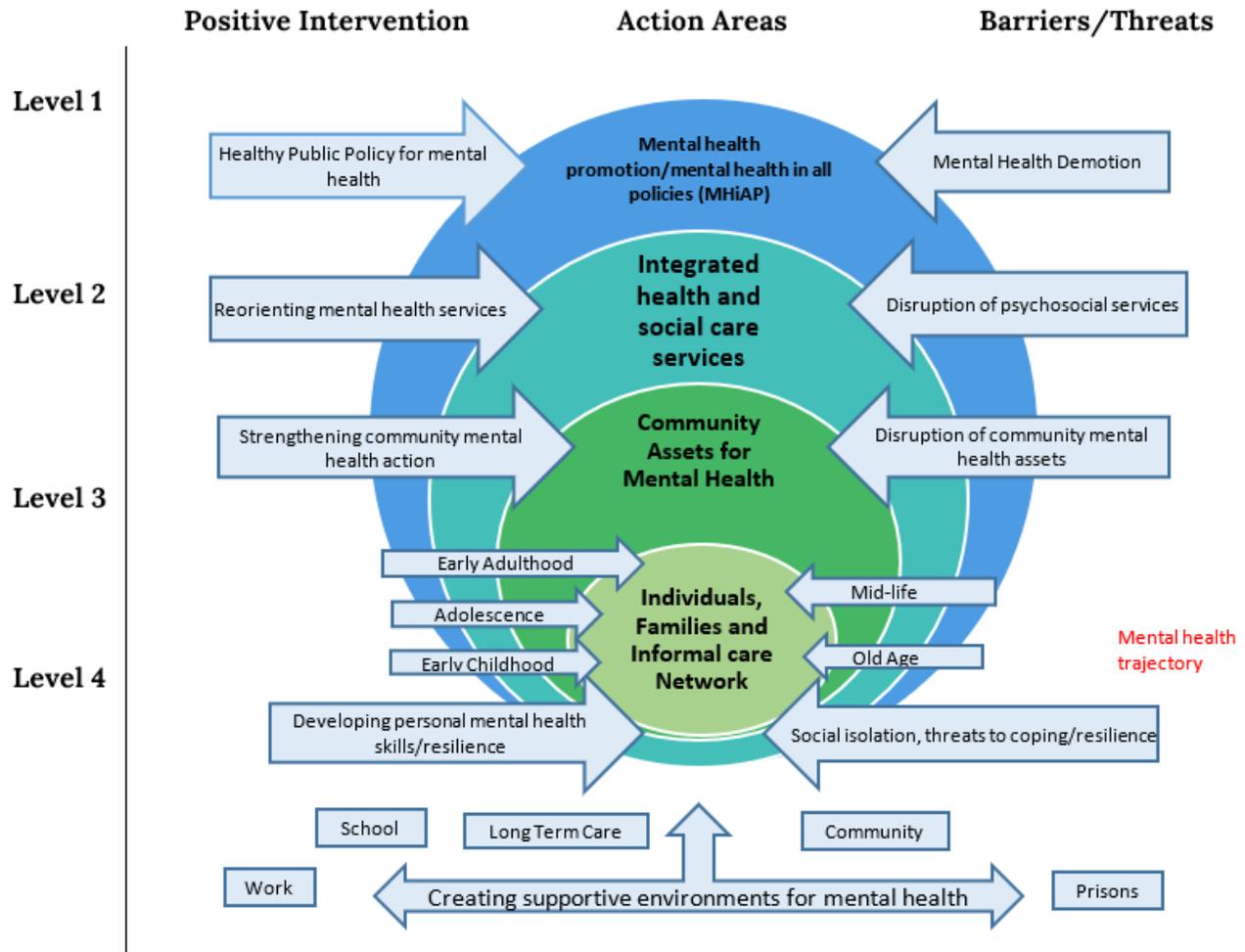
- Health research that can better inform practice, programming, and policy includes ongoing exploration of the determinants of health condition comorbidities, optimal delivery and integration of health and social services, and examining policy alternatives to optimize population mental health interventions, or a co-intervention (pulmonary rehabilitation).
- Future research should include individuals with lived experiences of physical and mental health comorbidities, their families, and carers.

Rapid Realist Findings and Outcomes

Further exploration of the literature using a rapid realist approach was conducted to understand how, for whom, and under what circumstances interventions function in different environments. Using an approach called context-mechanism-outcome (CMO) configuration, the rapid realist synthesis aimed to generate new ideas for programming and policy beyond that which is achieved in reviews providing a summary of aggregated evidence. Further

analysis of key interventions located from the literature search within a socio-ecological framework for mental health promotion (see diagram) lead to four broad guideline recommendations to better direct efforts at the prevention and management of physical and mental health comorbidities. These are highlighted in the following:

A Socio-ecological Model of Mental Health Promotion Interventions



Level 1: Healthy Public Policy for Mental Health: Mental Health Promotion/Mental Health in All Policies (MHiAP)

Individuals living with mental and physical illnesses have the potential to live a flourishing, joyful life. We must also try to promote and strengthen health assets, including structurally (social, economic, cultural) supportive environments, community resilience, and life coping skills.

A Program Theory for Mental Health in All Policies (MHiAP)

A MHiAP strategy → Intersectoral governance for mental health → Changes in policies (usually signaled by some sort of strategic document/plan) → Policy actions (legislative, regulatory, budgetary/investment tools) to promote mental health → Impact on social determinants of mental health → Improved mental health outcomes (e.g. increased well-being, happiness, improved coping and resilience, reduced mental stress, reduced incidence of mental illness, reduced harms from substance misuse, reduced incidence of suicide).

Agenda Setting for a MHiAP Strategy

A 'Health in All Policies' (HiAP) approach to intersectoral collaboration has been gaining ground globally as a policy-level agenda aimed at addressing the wider social determinants of health. Advocates of HiAP highlight the importance of mental health promotion as central to successful HiAP approaches, and as a means to contribute to addressing health equity and inequality;^{9,10} conversely, advocates of mental health promotion have identified HiAP as a key policy framework for advancing mental health and physical health.^{11,12}

Based on a review of the literature on HiAP adoption and implementation, we propose five simple rules for successful HiAP initiation:

- 1) Developing a shared language and fluency around a broader understanding of 'health' to include well-being and happiness, and general welfare;
- 2) Linking evidence for how HiAP initiatives are able to contribute to sustainable economies and sustainable health systems (both theoretical and empirical);
- 3) Having an 'entry point' to initiate an HiAP agenda;
- 4) Developing 'win-win' scenarios, goals and objectives across sectors;¹³
- 5) Building and fostering long-term collaborative partnerships and engagement with intersectoral stakeholders.

In the Canadian context, not only is mental health well placed to be included in any HiAP policy agenda, it may in fact be the key entry point for raising the awareness and urgency of an HiAP approach at the federal and provincial levels. First, with the help of key policy elites, such as Senators Kirby and Wilson, and with the establishment of the Mental Health Commission of Canada (MHCC), much of the foundational work in boosting awareness has already taken place. In this collective work, Canadian researchers, practitioners, policy-makers and people with lived experience have worked on developing a more inclusive, shared language around mental health, that by its nature tends to be less 'deficit-focused' and more positive and strengths-based.

Level 2: Reorienting Mental Health Services: Integrated Health and Social Services

Beyond the HiAP approach, a key role for public policy is to provide the regulatory, legislative, and financial context for the transformation of health and social services more broadly in society. For Canadians, 'health reform'¹⁴ is an ongoing reality that is complex and multi-faceted, with varying objectives across provinces, and widely differing governance strategies

and outcomes. However, a common recurrent theme is the need to develop *integrated, collaborative systems of health and social care* to address the increasingly complex needs of an aging population, with the concomitant multimorbidity of chronic diseases, both physical and mental, being the driving force of this complexity. While these efforts require many transformational changes at the health and social service/organizational level, there is a strong role for high-level policy in successfully moving towards the ideal system. It is generally acknowledged, based on decades of research evidence,¹⁵ that comprehensive primary health care, as originally outlined in the Alma Ata Declaration,¹⁶ is the overarching framework for efficiently, effectively, and equitably organizing health and social services in order to produce optimum health in populations.

The **program theory** at this level is: by providing *universal financial coverage, under government control and regulation, with equitable distribution of services, comprehensive coverage, and with low or no co-payments*, then you attain “*greater first contact access and use, more person-focused care over time, greater range of services available and provided when needed, and coordination of care.*” (Starfield, 2012, p. 20).

Integrating care via simple rules allows relatively autonomous actors to use their contextual knowledge to come up with creative implementation solutions. At the integrated care level, there are some important contextual factors to consider. In order for clients to have a voice in decision-making (e.g., priority physical and social/mental needs), power differentials need to be ‘smoothed.’ Differential power dynamics impede effective collaborative practice among different service providers,¹⁷ but they also relegate clients to a marginalized role with respect to decisions around their care needs. Physicians are considered the top of the healthcare hierarchy, and this conceptual approach can break the success of any reform program or change initiative.

Level 3: Strengthening Community Mental Health Action: Community Assets for Mental Health

At this systems level, community “assets” for mental health are the chosen foci, as they bring together three important theoretical approaches to mental health: mental health promotion,¹⁸ the two-continuum approach;¹⁹ and, the Canadian Mental Health Association’s framework for support approach.^{20,21}

The **program theory** at the community level is: by helping to *co-create, strengthen and sustain community mental health assets*, people can be supported to live happy, joyful, flourishing lives, whether or not they are living with mental or physical illness *and* they can be empowered to help co-produce and shape the mental health services they receive in community through context-appropriate co-produced mental health service planning.

We propose a series of context-mechanism-outcome configurations (CMOCs). Many of the CMOCs are similar to those derived through community-based participatory action

research.²² Based on our review of literature at the other systems levels, there is evidence that these “collaboration” CMOCs are relevant to each systems levels and our simple rules approach and are outlined as follows.

Context-Mechanism-Outcome (CMO) Configurations to Complement Simple Rules	
Factor	CMO
Trust	High trust (context) creates partnership synergy (mechanism) leading to successful outcomes at all systems levels (e.g., mental health services delivery).
Formalization	Formalization through policy (context) creates greater initial trust (mechanism) leading to greater uptake of mental health inclusion, mental health awareness at all systems levels.
Shared Vision	Having a shared vision (context) reduces the potential for conflict (mechanism) leading to improved trust/high trust (outcome) at all systems levels.
Commitment/ Accountability	Evidence of preparedness and accountability (context) results in reduced conflict (mechanism) leading to greater trust (outcome) among partners at each systems level.
Power	Power imbalances among partners (context) creates partner domination (mechanism) leading to reduced trust, blocked mental health services delivery at each systems level.
Faith	High faith (context) creates partnership synergy (mechanism) leading to enhanced mental health services delivery at each systems level.
Authenticity	Authentic collaboration (context) increases faith (mechanism) leading to increased agreement over common goals, such as mental health services delivery (at each systems level).
Leadership	Positive, authentic leaders (context) create more effective integration of different partners/cultures (mechanism) leading to greater trust among partners at each systems level (outcome).
Culture	Cultural closeness or coherence (context) decreases conflict (mechanism) leading to greater trust among partners at each systems level.
Flexibility	Greater flexibility in directives/guidelines (context) increases the likelihood of goal achievement (mechanism) leading to more efficient, effective mental health services delivery (outcome) at each systems level.
Entry Point	Designated entry points (context) provide clarity (mechanism) leading to more confidence (e.g., consistent model for mental health services delivery) (outcome) at every systems level.

Level 4: Developing Personal Health Skills/Resilience: Individuals, Families and Informal Supports

This level examines the personal resources individuals utilize to help them develop resilience, hope, confidence and well-being. There are many resources and interventions that aim at strengthening individual coping skills and resilience to bolster mental health and prevent the worst impacts of mental illness (e.g., self-aid, mutual aid, peer support networks).

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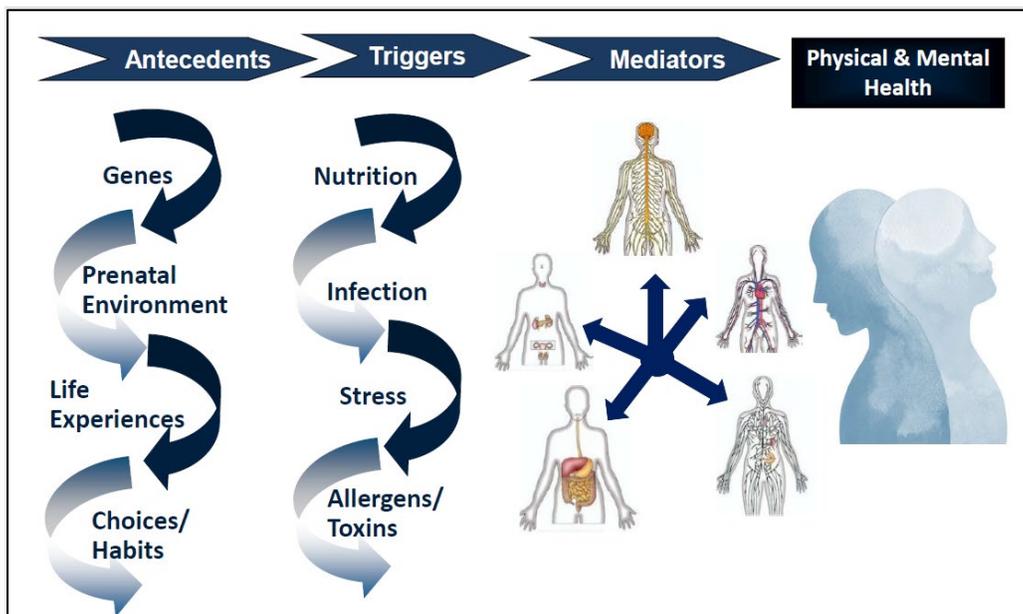
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1. Introduction

1.1 Background

Non-communicable diseases (NCDs) and their behavioural and metabolic risks are a leading global cause of mortality and morbidity that contribute to an escalating economic, public health, and societal burden.^{23,24,25} NCDs often co-occur with poor mental health as the interplay of biology, illness experience, behavioural risk factors (e.g., poor diet, physical inactivity, substance use) and the determinants of health (e.g., income, housing) can increase the likelihood of someone living with a physical health condition developing mental health symptoms or a co-existing mental health condition or vice versa.^{26,27, 28} (Figure 1.1) Mental health conditions, such as major depression, schizophrenia spectrum conditions, psychosis, anxiety disorders, bipolar affective disorders, and eating disorders, are commonly linked with diabetes, cancer, cardiovascular disease, chronic respiratory diseases, arthritis, and inflammatory bowel disorders.^{29,30,31,32,33,34,35,36,37,38,39} For example, some studies estimate that the prevalence of depression and anxiety is at least double amongst those being treated for cancer.^{40,41}

Figure 1.1: Overview of Shared Etiology Between Physical and Mental Health^{42,43,44}



Current knowledge about the shared etiology of physical and mental health comorbidities draws on unifying theories of neurobehaviour. Health is heterogeneous and culminates from many factors that include an interplay of antecedents, such as prenatal environment, life experiences, choices and habits, genetic background; triggers that may include “pro-inflammatory factors” such as exposures to infection, stress, allergens, or toxins. These factors interact with various mediators in different body systems that lead to specific physical and/or mental health outcomes.

Although there are many biological, behavioural, social, and environmental intersections between NCDs and mental health-related conditions (e.g., major depressive disorder, schizophrenia spectrum disorders), several knowledge gaps currently exist related to prevalence and incidence in Canada, healthcare-related cost estimates, shared mechanisms and effective targets for primary prevention, screening, assessment, management, and policy.⁴⁵ Better understanding, screening, diagnosis, and treatment of mental health conditions and NCDs can have a positive global impact on formulating integrated approaches and fostering health system sustainability.^{30,31}

To better address the prevention or treatment of physical and mental health co-morbidities, an integrated scoping and rapid realist review was conducted to help address knowledge gaps related to their prevalence/incidence, shared etiology, prevention, and management.

1.2 Rationale and Scope

The project objectives of this evidence synthesis were to synthesize and appraise international knowledge about common physical and mental health comorbidities related to:

- i. Their prevalence, incidence, and healthcare-related cost estimates across the lifespan and as they intersect with sex/gender and among priority and equity-seeking populations including immigrant, refugee, ethnocultural and racialized (IRER) communities, First Nations, Inuit and Métis, the 2SLGBTQ+ community, and linguistic minorities;
- ii. Biological, behavioural, and social pathways that contribute to their shared etiology;
- iii. Efficacious models for screening, primary prevention, care, and treatment of comorbidities for priority and equity-seeking populations; and
- iv. Gaps and biases in knowledge related to prevalence and incidence, healthcare-related cost estimates, causal pathways, screening, prevention and management of physical and mental health co-morbidities, including priority and equity-seeking populations.

2. Approach

2.1 Questions of Interest

The questions guiding this report include:

1. What is the prevalence, incidence, and healthcare-related cost estimates of common physical and mental health comorbidities? How do these differ by sex/gender and across the lifespan and among priority and equity-seeking populations including immigrant, refugee, ethnocultural and racialized (IRER) communities, First Nations, Inuit and Métis, the 2SLGBTQ+ community, and linguistic minorities?
2. What are biological, behavioural, social, and environmental pathways that contribute to both common physical and mental health co-morbidities?
3. What models for screening, primary prevention, care, and treatment of common physical and mental health co-morbidities work for what populations, in what contexts, and why? What enables or constrains the implementation of screening, primary prevention, care, and treatment of common physical and mental health co-morbidities?

2.2 Approach

2.2.1 Evidence Searches

A comprehensive literature search of standard bibliographic databases that cover a range of health and related disciplines (i.e., MEDLINE, CINAHL, PsycInfo, Sociological Abstracts) and grey literature sources (e.g., theses, dissertations, conference proceedings, digital publications repositories of relevant government, non-profit, and health care provider organizations) was undertaken (see Appendix A for full search strategy). In addition, cited reference checking and consultation with relevant knowledge users was undertaken. All types of literature were considered ranging from systematic reviews with meta-analyses to opinion papers. In topic areas where extensive literature was located, the scope of documents included in this knowledge synthesis focused on highest level evidence sources.

Abstracts located from the academic literature searches were screened by two reviewers. Full text articles of the abstracts which met the criteria were subsequently reviewed by two reviewers. The final set of selected documents were assessed for quality using various standard assessment tools. Data extraction was undertaken using an extraction template developed by the team.

2.2.2 Evidence Synthesis

Scoping Review

For all NCDs, information from the evidence searches was summarized in relation to mental health-related comorbidities. For each comorbidity, evidence was highlighted about prevalence and incidence estimates of the physical and mental health comorbidity, shared etiology, mental health screening of individuals who have the indicated NCD, prevention strategies, as well as management and interventions.

Rapid Realist Review

For literature sources which provided in-depth information about how interventions interact with contexts and mechanisms to influence the effectiveness of strategies aimed at managing symptoms of physical and mental health comorbidities, rapid realist review methods⁴⁶ were applied. The rapid realist review was guided by a Mental Health Promotion Framework co-constructed by the project team and in consultation with the MHCC (see Figure 4.1). The framework provided guidance about which interventions work, for whom, how, to what extent and in which contexts. The framework and review focused on applications in health and social services provided at macro, meso, and micro intervention levels (e.g. policy, design, implementation, delivery of services). The review addressed the following questions:

1. What are guiding principles by which interventions can be implemented successfully?
2. What are the mechanisms by which these principles operate? What are the contextual factors influencing the principles?
3. What impact do the interactions between contextual factors and mechanisms have on intervention outcomes?

For the rapid realist review, data was extracted regarding the interventions' strategies, activities and resources, and the context, mechanisms and outcomes directly stipulated in the documents. To aid the project team during the extraction process and to ensure consistency and transparency, specified definitions of important realist concepts (Table 3.1) were used as realist methods are still developing and realist evaluators continue to unpack and operationalise terms like 'context', 'mechanisms', and 'interventions' and how these interrelate.⁴⁷

Intervention:	interventions' implemented activities, strategies, and resources ⁴⁷ (e.g., health behaviour module)
Mechanism:	what 'triggers' participants to want to participate, or not, in an intervention. Mechanisms usually pertain to cognitive, emotional, or behavioural responses to intervention resources and strategies (e.g., participant feels enabled from skills development)
Context:	an intervention's background or setting. Context includes the pre-existing organizational structures, the cultural norms, history of the community, the nature and scope of pre-existing networks, and geographic location

	effects ^{48,49} (e.g., previous experience of organization co-conducting interventions with community partners)
Outcome:	intervention outcomes that can be either intended or unexpected ⁴⁸ (e.g. macro-level: well integrated services; meso-level: participants' engagement in health and social services; or micro-level: participants' health outcomes)

Using completed extractions, Context-Mechanism-Outcome configurations (CMOs) were constructed to better understand and explain why interventions work, or not, and to generate guiding principles. For this review, the project team only created CMOs if the contexts, mechanisms and outcomes were explicitly correlated in the papers themselves. The CMOs were clustered intervention types to ensure that the guiding principles were supported by mechanisms located across different interventions and contexts. Mechanisms were thematically clustered and from these, guiding principles were developed. Each guiding principle was cross-referenced to mechanisms from different documents to verify they were transferable across different interventions and contexts.

3. Evidence Highlights: Physical and Mental Health Comorbidities

In this section, the results of the scoping review are highlighted by physical health condition (alphabetical). Each section highlights the prevalence, incidence, associated healthcare-related costs, shared etiology, and management interventions to support mental health.

3.1 Mental Health Characteristics by Physical Health Condition

3.1.1 Arthritis

A. OSTEOARTHRITIS (OA)

OA involves the degeneration of cartilage in the joints that leads to joint pain, stiffness and limitations of motion, and can cause significant disability. The hand, knee, and hip are the commonest sites of the body to be affected. OA is prevalent in mid-age to older adults. Women over the age of 50 years are more likely to have the condition.⁵⁰

Prevalence and Incidence of OA with Mental Health Problems or Illnesses

- Based on studies of modest samples, 58–66% of people with OA have some type of mental health concern including depression, anxiety, psychosis, and obsession/compulsion. Results can vary by the affected joint⁵¹
- Measures of depression among people with OA at the hand, knee, hip, back/neck or other indicated that having multi-site OA (i.e., OA \geq 2 sites; OR=1.48, 95% CI 1.07–2.05) and the specific presence of hip (OR=1.72; 95% CI 1.08–2.73) or knee OA (OR=1.43; 95% CI 1.03–1.98) were associated with greater odds of developing depressive symptoms compared to people without OA⁵²
- A longitudinal study of 74,393 individuals with mental health conditions reported that affective psychoses, neurotic illnesses or personality disorders, as well as alcohol and drug dependence or abuse were risk factors for OA. Individuals with schizophrenia were not at risk of OA⁵³
- A longitudinal study of adults (n = 3,662) aged \geq 45 years reported an increased risk of arthritis for those with depressive symptoms (Men: Hazard Ratio (HR)¹ =3.51, 95% CI 2.32–5.29; women: HR=2.03, 95% CI 1.45–2.85) compared to those who did not develop depressive symptoms⁵⁴

¹Hazard ratio (HR) is a measure of how different factors or an intervention are associated with an outcome of interest over time

Mental Health Screening

- A cost-utility analysis of routine anxiety and depression screening in people with OA suggests routine screening by general practitioners appears to not be cost-effective⁵⁵

Regular screening for depression in people with OA is recommended by the National Institute for Health and Care Excellence⁵⁰

- A cluster randomized trial conducted in primary care that assessed point-of-care electronic template to prompt routine anxiety and depression screening in people with OA showed no beneficial outcome for self-reported pain reduction or functional outcomes⁵⁶
- It is recognized that screening could identify subthreshold anxiety and depression symptoms which are more common and facilitate dialogue with clinicians to identify unmet needs contributing to distress⁵⁷

Common Pathways

- Pain and inflammation are underlying shared pathways of OA and mental health (Figure 3.1)
- OA and poor mental health may be mediated by abnormal regulation of the hypothalamic–pituitary–adrenal (HPA) axis and inflammatory cytokines, such as interleukin-6 (IL-6) and tumour necrosis factor- α (TNF- α)⁵⁸
- Alterations in the autonomic nervous system combined with sleep disturbances can worsen joint pain. This can lead to a vicious cycle with declining mental health by boosting sympathetic nervous system activity.⁵⁹ Abnormal HPA axis regulation can amplify centralized pain and lower mood⁵⁸
- Mechanical burden on joints, reactive oxidative stress, and low-grade cartilage cell (chondrocyte) inflammation worsen OA.⁶⁰ Altered neurotransmitter transmission followed by pro-inflammatory reactions can increase production of neurotoxic catabolites and impact mental health⁶¹
- For women, estrogen deficiency after menopause could contribute to the development of OA, depression, and anxiety disorders⁶²
- For men, aging-related decline of testosterone levels might cause metabolic imbalance leading to sarcopenic obesity, which in turn can contribute to the risk of OA^{63,64} and depression⁶⁵

Management of OA and Mental Health

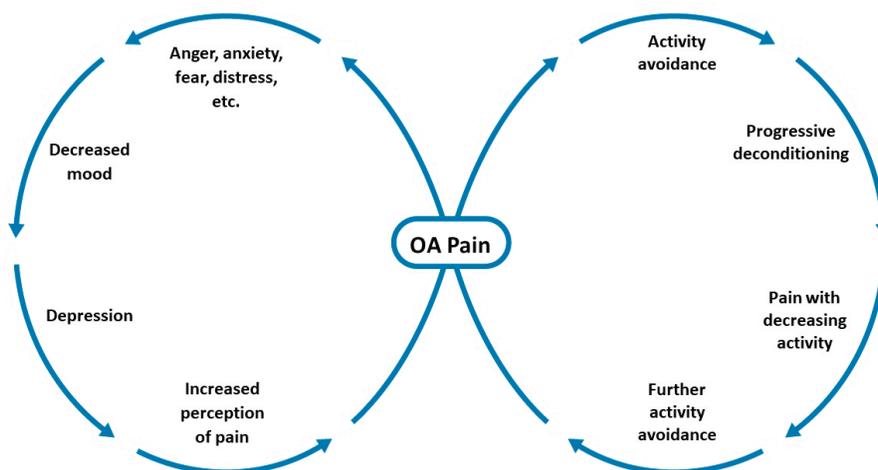
- Mental health, particularly depression, and OA pain appear to be interlinked. Studies which have focused on pain reduction or coping have shown to simultaneously improve both physical and mental health symptoms⁶⁶
- The results of studies about the benefits of exercise interventions and concurrent reductions in mental and physical symptoms are mixed. Further research needs to clarify the importance of exercise programmes in terms of duration, intensity, and frequency⁶⁶

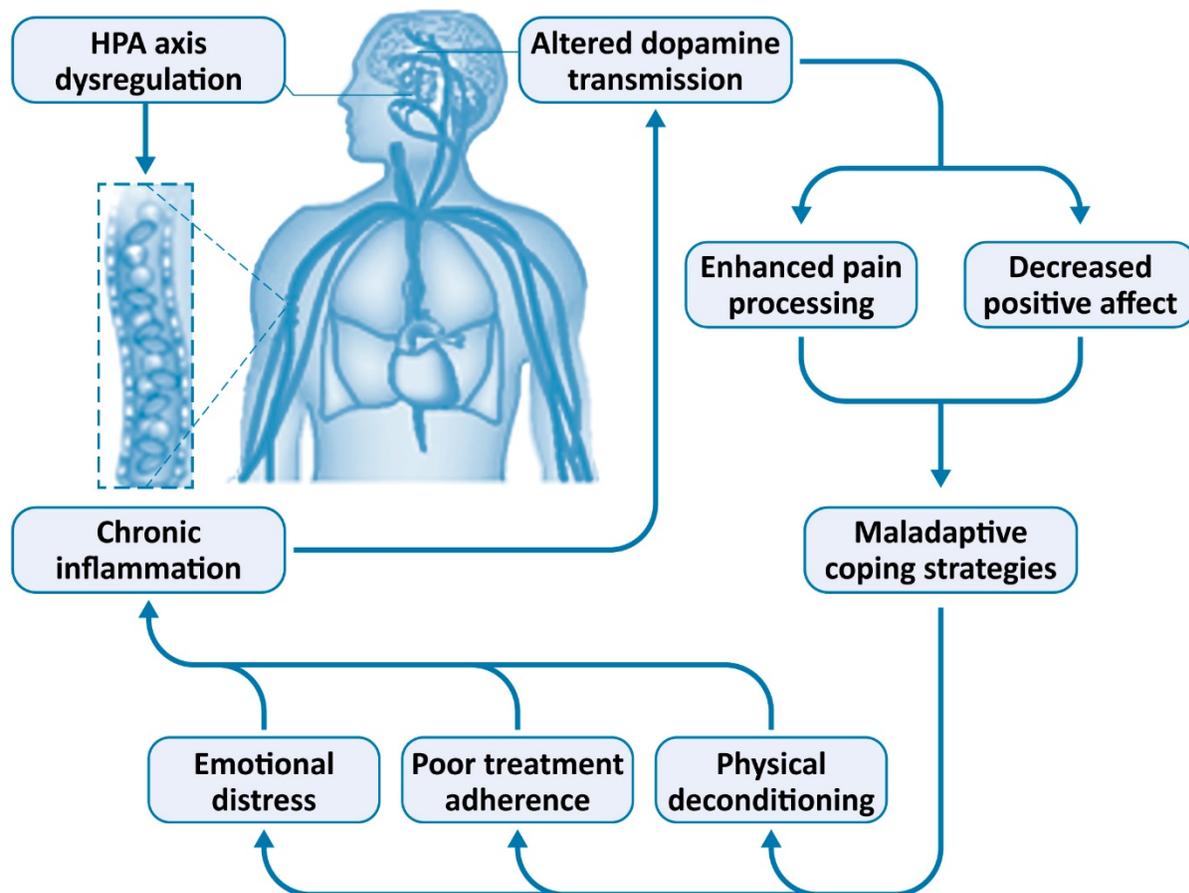
- A review of complementary therapies to treat musculoskeletal conditions and mental health found moderate to good quality evidence for acupuncture and tai chi⁶⁷
- Results of a meta-analysis reported that psychotherapeutic counselling and psychoeducational interventions improve pain and pain coping. Anxiety and depression also improved but were not significant. More rigorous studies are needed⁶⁸

Interventions provided under a collaborative care model may significantly reduce healthcare costs associated with comorbid depression and anxiety that occurs in individuals with OA⁷¹

- To optimize psychosocial well-being, strategies such as maintaining function, using positive language to describe the condition, increasing social participation, and maintaining employment are recommended. For example, a person's harmful attitudes towards pain and damage may be reduced through education that addresses negative mistaken language and mistaken beliefs
- Beliefs about the health condition may be formed from external sources of information, such as the media, and prior to diagnosis.⁶⁹ Public health campaigns can help to dispel myths about OA more broadly and help to minimize mental health impacts post-diagnosis
- Cognitive behaviour therapy, neuroscience education, and centrally-acting drugs could be alternative treatment modalities for relieving OA-related pain and poor mental health⁷⁰
- Researchers suggest combined intervention approaches for depression and pain, for example, aerobic exercise with psychological support may be effective⁶⁶
- Among individuals with coexisting OA and depression, excess healthcare expenditures associated with depression were mainly due to comorbid anxiety⁷¹

Figure 3.1: Shared etiology between OA and mental health⁷²





OA contributes to inflammation through HPA axis dysregulation, which leads to altered responses to stress, such as muscle tone that is maintained predominantly by impulses from the sympathetic nervous system. Chronic inflammatory states can alter neurotransmission in the brain which can enhance pain processing and dampen positive affective responses. This can manifest as depression, potentially affect disease-relevant behaviour, such as exercise, treatment adherence, and social withdrawal, and lead to further adverse effects on both physical and mental health.

B. RHEUMATOID ARTHRITIS (RA)

RA is a chronic, inflammatory autoimmune disease that initially affects small joints, progressing to larger joints, and eventually the skin, eyes, heart, kidneys, and lungs. Often, the bone and cartilage of joints are destroyed, and tendons and ligaments weaken. Damage to the joints causes deformities, bone erosion, and pain. Common symptoms include morning stiffness of the affected joints, weight loss, and joints that are tender, swollen, and warm. The onset of RA is usually between 35-60 years.⁷³

Prevalence and Incidence of RA with Mental Health Problems or Illnesses

Depression and Anxiety

- Estimates of depression and anxiety in individuals with RA are reported to range from 10–42%⁷⁴
- Anxiety is reported to occur in 22–31% of those with RA;⁷⁵ lifetime prevalence rates of anxiety disorders have been reported at 16%.⁷⁶ Anxiety is associated with higher RA disease activity⁷⁷
- A systematic review reported the incidence of anxiety for those with RA to be 1.2 (95% CI OR 1.03–1.39)⁷⁸
- A meta-analysis about depression and RA comorbidity found a prevalence of 17% for major depressive disorder⁷⁹

Bipolar Disorder, Schizophrenia, and Post-Traumatic Stress Disorder

- An analysis of population-based administrative health data from Manitoba, Canada of 10,206 incident cases of RA and 50,960 sex-, age-, and geographically matched controls reported that the incidence rate ratio (IRR) of bipolar disorder was 1.21 (95% CI 1.00–1.47); the incidence of schizophrenia did not differ between groups (IRR 0.96, 95% CI 0.61–1.50)⁸⁰
- Post-traumatic stress disorder (PTSD) may be a risk factor for developing RA in adulthood.⁸¹ Only a few studies, most based on veteran samples, have demonstrated this relationship^{81,82}
- Individuals with RA seem to show decreased rates of schizophrenia compared to the general population⁸³

Mental Health Problems and Illnesses

- The co-occurrence of RA with psycho-social problems is reported to be 46%⁸⁴
- For community-based adults (<45 years), arthritis is a risk factor for the development of a mental health condition in later life; conversely, having a mental health condition does not reliably predict the later development of arthritis⁸⁵

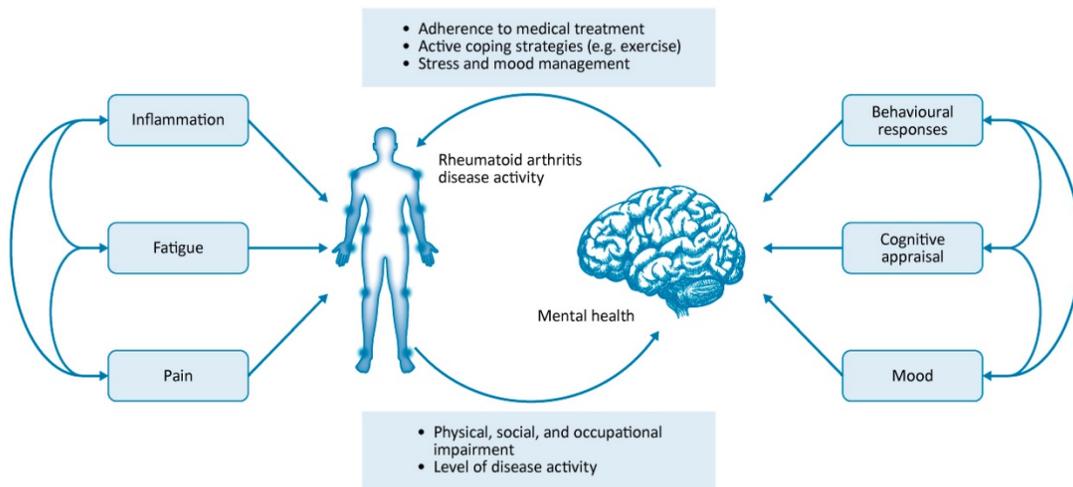
Mental Health Screening

- Clinicians recommend use of the Hospital Anxiety and Depression Scale (HADS) for screening,⁸⁶ however its validity and reliability in this population has not been assessed

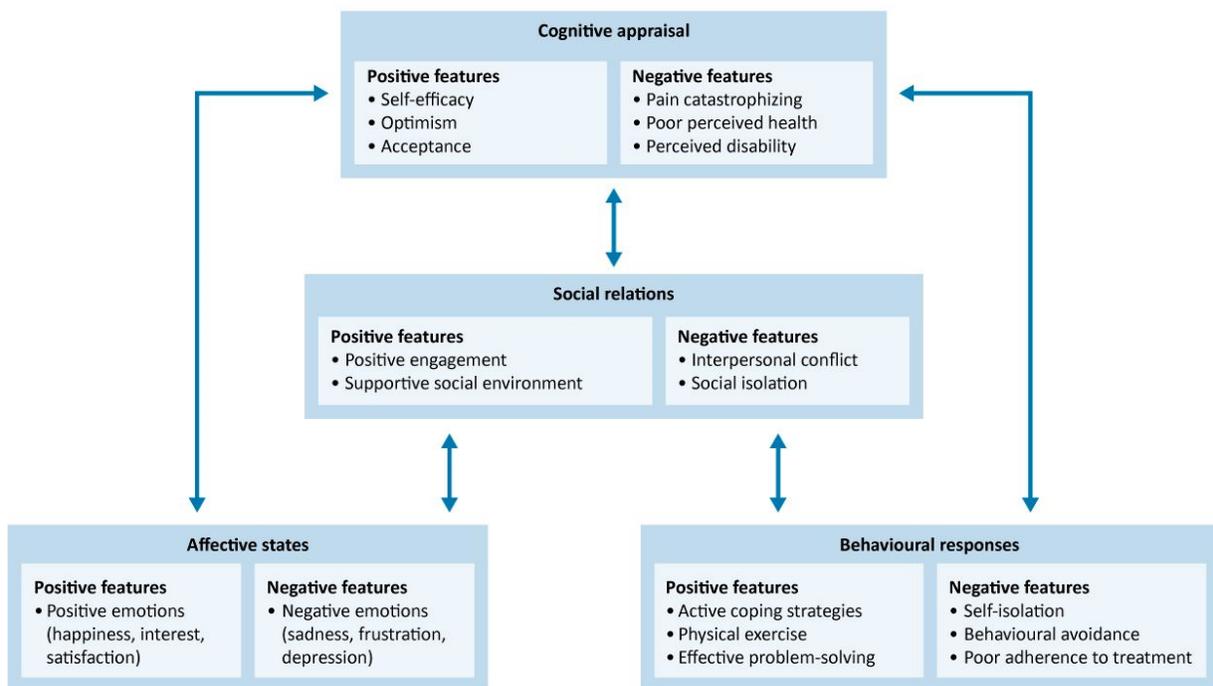
Common Pathways

- Mental health and RA comorbidity interactions include dysregulation of inflammatory responses, difficulties with pain and fatigue, and the development of cognitive and behavioural responses that could exacerbate physical and psychological difficulties (Figure 3.2)⁸⁷
- Social contexts can affect coping strategies, psychological responses, and impair responses to treatment due to disruption of therapeutic alliance and treatment adherence (Figure 3.2)⁸⁷

Figure 3.2: Shared etiology between RA and mental health⁸⁷



Interactions of social and psychological factors



RA manifestations, such as pain, fatigue, and inflammation, act as stressors and influence mental health by influencing changes in one's interpretation or appraisal of disease status, affective states, and coping responses. Cognitive, affective, and behavioural factors interact with one's self-efficacy. The extent to which one uses healthy coping responses impacts their ability to self-manage. How a person responds to their RA psychologically is also dependent on the broader social environment and this relationship is bi-directional. Supportive social environments foster an individual's resilience to declines in physical and psychological function. Conversely, individual level responses, such as self-imposed isolation, can adversely influence their immediate social environments.

- Reciprocal relations between mood and RA may be due to factors such as reduced medication and physical activity adherence, leading to deconditioning and increased pain. Psychological factors may impact disease activity by altering immune response, increasing pro-inflammatory cytokines (e.g., TNF and IL-6)², and lead to inflammation^{88, 89}
- For individuals with schizophrenia, rates of RA are lower due to high blood concentrations of IL-1 receptor antagonist, an anti-inflammatory cytokine that may be protective to RA⁹⁰

Management of RA and Mental Health

- Psychological evaluation and care are recommended to be among the therapeutic objectives for those with RA and mental health illnesses or problems⁸⁶
- Broad positive social messaging about RA should be employed to mitigate affective responses post-diagnosis⁸⁶
- The goals of care should aim to engage and motivate the person toward goal-setting, attend to psychological needs of caregivers, generate trust and empathy, negotiate treatment options, and promote self-efficacy⁸⁶
- For individuals not achieving joint remission, it is recommended that increased emphasis be placed on depression and anxiety being considered as part of a treat-to-target³ strategy.⁹¹ Alternative targets may be considered in the shared decision making between the individual and practitioner⁴
- Support by psychologists and patient associations can foster mental health by offering support and empathy relation⁸⁶

A systematic review concluded that better physical and mental health outcomes for those with RA are likely to result from integrated mental health care provided within routine clinical practice⁵⁶⁷

²A proinflammatory or inflammatory cytokine is a signaling molecule secreted from immune and other types of cells that promote inflammation. Examples include interleukin-1 (IL-1), IL-12, and IL-18, and tumor necrosis factor alpha (TNF- α). Excess chronic production of inflammatory cytokines contribute to inflammatory physical and mental health conditions⁵⁷³

³Treat-to-target (TTT) strategy is a therapeutic approach which specifies that the therapeutic target in RA should be a state of remission, or an alternative goal could be a low disease activity. TTT should be based on shared decision making and aim to maximize long-term health-related quality of life through control of symptoms, prevention of structural damage, and normalization of function, and social participation⁹¹

⁴This is in reference to recommendation #5 and #6 of the “Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force” which indicates that the choice of the measure of disease activity and the target value should be influenced by comorbidities (e.g., depression, anxiety), individual factors, and drug-related risks. Furthermore, disease activity measures must be obtained and documented regularly. This should be done monthly for those with high/moderate disease activity or less frequently (such as every six months) for those in sustained low-disease activity or remission⁹¹

C. PSORIATIC ARTHRITIS (PSA)

PsA is a chronic inflammatory arthritis, associated with psoriasis. People with PsA may present with musculoskeletal involvement (peripheral arthritis, inflammation at the sites where tendons or ligaments insert into the bone, spine inflammation, skin and nail disease or extra-articular manifestations, e.g. inflammatory bowel disease). PsA is a distinctive disease because it sums up the effect of both arthritis and skin psoriasis.⁹²

Prevalence and Incidence of PsA with Mental Health Problems or Illnesses

- Prevalence estimates based on self-report of diagnosis according to International Classification of Disease Codes indicate that one in three people with PsA have at least mild anxiety, while 1 in 5 report at least mild depression. These conditions tend to occur with greater disease activity⁹³
- It has been reported that depression and anxiety in individuals with PsA ranges between 9 to 37%⁹⁴
- One study suggested a higher incidence rate of “any suicidality” in people with PsA than the general population.⁹⁵ More research is needed about suicide/self-harm and substance misuse

Mental Health Screening

- Screening tools that were reported in the literature as being used in practice include the Hospital Anxiety and Depression Scale (HADS), General Anxiety Disorder-7 (GAD-7), and Patient Health Questionnaire-9 (PHQ-9). However, there is a need to validate these tools in populations with inflammatory rheumatic diseases⁹³

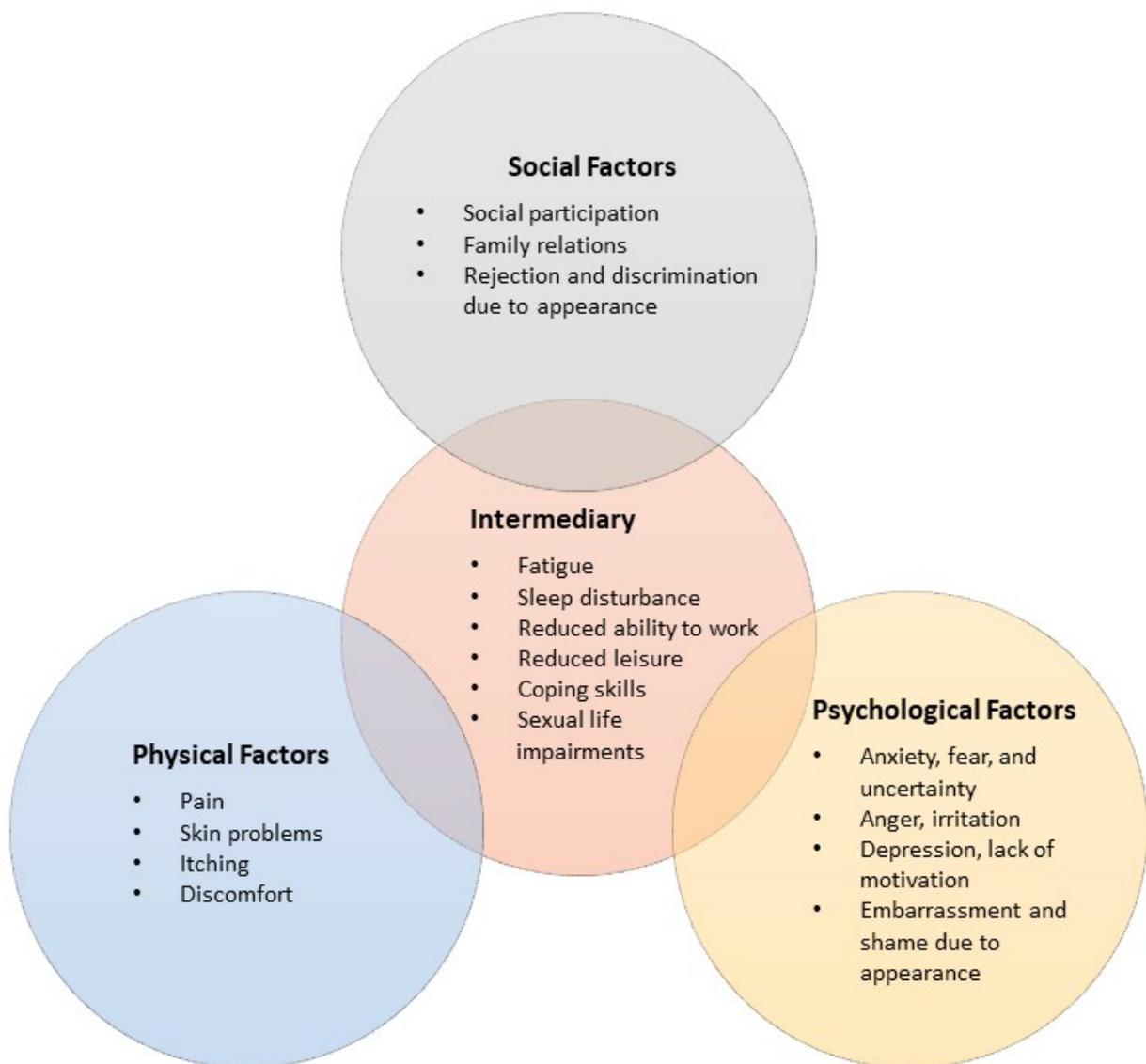
Common Pathways

- Several physical, social, and environmental factors interact and impact the individual with PsA (Figure 3.3)⁹²
- Poor mental health is a predictor for developing fibromyalgia for those with PsA. This, in turn, is associated with worse physical health outcomes⁹⁶
- Composite treatment targets, such as the Disease Activity Score 28 (DAS 28) or minimal disease activity⁹⁷, include components such as pain and patient global visual analogue scales that may be influenced by comorbid mental health conditions
- Treatment escalation driven by non-inflammatory symptoms may increase adverse events and appears to provide modest improvements in mental health-related areas (e.g., quality of life)⁹⁸
- Inflammation may influence neurocognitive functions;⁹⁹ studies have found significantly higher disease activity and pain in those with comorbid anxiety or depression⁹³

Management of PsA and Mental Health

- Based on joint guidelines of care, people with psoriasis should be informed about the association of psoriasis and anxiety and depression and asked about signs and symptoms by their health provider¹⁰⁰
- If positive signs or symptoms of anxiety, depression, or suicidal ideation are indicated, referral should be made to an appropriate health care professional¹⁰⁰
- Psoriasis-specific therapy is recommended to improve psoriasis-associated anxiety and depression in individuals with psoriasis¹⁰⁰

Figure 3.3: Shared etiology between PsA and mental health⁹²



3.1.2 Cancer

Cancer is a collection of diseases that can start almost anywhere in the body. Cancer develops when the instructions from genes get mixed up, causing our cells to grow and divide out of control or not die when they should. Many cancers form solid tumours. Cancers of the blood (e.g., leukemias) generally do not form solid tumours. Cancerous tumours are malignant, which means they can spread into, or invade, nearby tissues. As these tumours grow, some cancer cells can break off and travel in the body through the blood or the lymph system and form new tumours at other sites.^{101,102}

Prevalence and Incidence of Cancer with Mental Health Problems or Illnesses

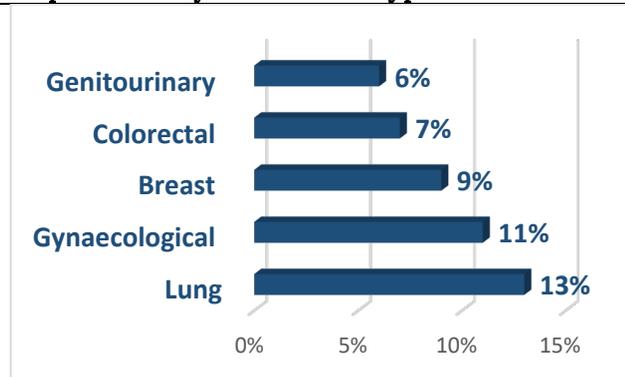
A. DEPRESSION AND ANXIETY

- A meta-analysis of incidence studies indicated a small and positive association between depression and cancer (RR=1.15, 95% CI: 1.09-1.22)¹⁰³
- A systematic review and meta-analysis reported the prevalence of major depression (15%), minor depression (20%), and anxiety (10%) in people treated for cancer was at least double that of general population estimates^{40,41}
- Meta-analyses indicate that approximately one-third of persons with cancer in acute care hospitals are affected by common mental health conditions, particularly anxiety and depression^{104,40}
- A history of anxiety or trauma¹⁰⁵ and metastatic disease (for some cancers) appear to be stronger predictors of depression¹⁰⁶
- A systematic review focused on those undergoing chemotherapy reported that lower social support, higher anxiety, higher perceived stress, and lower self-efficacy were consistently associated with depression¹⁰⁷
- Limitations of incidence estimates include the variability in depression indicators used, lack of account for important confounding factors (e.g., substance use), and omission of relevant factors for specific cancer subtypes (e.g., no account of menopausal status in relation to breast cancer)¹⁰³
- Risk factors identified for depression in cancer include younger age and social deprivation, which is broadly defined as having reduced access to aspects of one's culture and society due to many factors (e.g., poverty, family intervention)¹⁰⁸
- A systematic review examining depression in cancer survivors indicated a pooled prevalence of 21% for depression and anxiety and these do not differ from the general population¹⁰⁹
- A Canadian survey of 12,929 adult cancer survivors found that 78% experienced at least one emotional concern one to three years post cancer treatment; 42% experiencing 3 or more³⁹

Estimates of Depression or Anxiety by Cancer Subtypes

- Among cancer subtypes, significant overall risks were found for liver (RR = 1.20, 95% CI: 1.01-1.43) and lung cancer (RR = 1.33, 95% CI: 1.04-1.72). For breast, prostate, and colorectal/colon cancer, no significant associations with depression were found¹⁰³
- Estimates of depression vary by cancer type with highest estimates among those which impact the reproductive systems (e.g., 17% for gynecological and genitourinary cancers) (Figure 3.4)¹⁰⁸
- The highest levels of anxiety are reported in lung, gynecological, and haematological (affect blood, bone marrow and lymph nodes) cancers⁴¹

Figure 3.4: Prevalence Estimates of Depression by Cancer Subtypes¹⁰⁸



Genitourinary cancers occur in the male reproductive system and adrenal glands. They include prostate cancer, kidney cancer, bladder cancer, testicular cancer and cancers of the penis; Gynaecological cancers occur in the female reproductive system and include ovarian, endometrial/uterine, cervical, vulvar and vaginal cancer.

Estimates of Depression or Anxiety by Subpopulations

- The prevalence of depression, using the GADS screening tool, in older African Americans with cancer was reported to be 27%¹¹⁰
- For colorectal and lung cancers, female gender is an identified risk factor¹⁰⁸
- Among Latino and Afro-Caribbean immigrants diagnosed with cancer and living in New York City, the prevalence of depression was reported to be 10%; slightly more Latino immigrants (12%) showed depression symptoms compared to those who were Afro-Caribbean (7%)¹¹¹
- A mediation analysis that compared US Hispanic and non-Hispanic cancer survivors, that included tumour characteristics and treatment factors, reported that most of the ethnic differences of heightened anxiety or depression among Hispanic cancer survivors were explained by younger diagnosis age, lower education level, lower proportions of employment, less likely of being born in the USA, less insurance, and less social support¹¹²

B. OBSESSIVE-COMPULSIVE DISORDER (OCD)

- A national population retrospective cohort study that examined 22 cancer types among people with OCD found overall cancer rates were not elevated among people with OCD. A slight association was found only within the first year of OCD diagnosis (standardized incidence ratio (SIR)=1.21, 95% CI 1.01-1.43)¹¹³

C. POST-TRAUMATIC STRESS DISORDER (PTSD)

- A random effects meta-analysis estimated an odds of 1.66 (95% CI 1.09-2.53) for PTSD in cancer survivors compared to controls. The prevalence of PTSD diagnosis in breast cancer was higher than that in colorectal, head and neck, and prostate cancers, but lower than that in brain, gynecological, and hematological cancers¹¹⁴
- Factors associated with PTSD include measurement type (clinical interview vs. self-report instrument), type of cancer, type of treatment, geographic region, prior trauma, age, and time since diagnosis¹¹⁴

D. SCHIZOPHRENIA

- Mortality risk from cancer diagnosis is reported to be 90% higher in individuals with schizophrenia and 20% higher in patients with prior depression with concurrent cancer diagnosis¹¹⁵

E. SUBSTANCE USE

Alcohol Use

- Alcohol use has been reported to contribute to approximately 3.5% of all cancer deaths and approximately 18 years of potential life lost for each alcohol-related cancer death; it is estimated 30% of alcohol-related cancer deaths are attributed to heavy drinking¹¹⁶
- The Canadian Population Attributable Risk of Cancer (ComPARE) study indicates that alcohol is attributable to 5.1% of all alcohol-related cancer cases in Canada¹¹⁷
- Based on analysis of data from 193,197 individuals, including 16,504 cancer survivors, with age ≥ 18 years old in the 2012–2017 National Health Interview Survey, the prevalence of heavy drinking was identical for cancer and non-cancer individuals at 5.2%.; for frequent binge drinking, the prevalence was lower in cancer survivors (2.8% vs. 4.9% in non-cancer survivors)¹¹⁸
- Compared with cancer survivors with a short cancer history (2–4 years), survivors with a cancer history of 5–9 years were more likely to be current drinkers after adjusting for the selected factors. Cancer status, alcohol-related cancer type, and length of cancer history had no impact on excessive alcohol intake¹¹⁸

Drug Use

- Among 169,162 respondents of the National Survey on Drug Use and Health (2015–2018), 5.2% were cancer survivors, with 1.2% and 4.0% reporting having more recent and less recent cancer histories, respectively. Rates of prescription opioid misuse were similar among more recent (3.5%; 95% CI 2.4%–5.2%; OR, 1.27; 95% CI 0.82–1.96; $P = .36$) and less recent (3.0%; 95% CI 2.4%–3.6%; OR 1.03; 95% CI 0.83–1.28; $P = .76$) survivors compared with respondents without cancer (4.3%, reference group)¹¹⁹
- Among 169 162 respondents of the National Survey on Drug Use and Health from (2015–2018), factors associated with prescription opioid misuse among cancer survivors included younger age (18–34 vs ≥ 65 years: OR 7.06; 95% CI 3.03–16.41;

P < .001), alcohol use disorder (OR 3.22; 95% CI 1.45-7.14; P = .005), and nonopioid drug use disorder (OR 14.76; 95% CI 7.40-29.44; P < .001)

Tobacco Use

- In 2018, 11.8% of cancer survivors aged 18 and older in the United States were current cigarette smokers¹²⁰
- Compared with non-smoking-related cancer survivors, smoking-related cancer survivors have a higher risk of being cigarette smokers and of continuing smoking (10.63% vs 19.78%)¹²¹
- Cancer survivors that were younger, had lower education levels, were any marital status other than married or widowed, were uninsured, or survived cervical cancer were more likely to be smokers than other survivors¹²²
- National data indicate that between 44% and 48% of cervical cancer survivors are current smokers,^{123,124} nearly 3 times as high as the smoking rate of survivors of all cancers combined^{123,125}

Various Substances

- In a large study of US veterans with cancer diagnoses (n=482,688), 6.6% had a comorbid substance use disorder diagnosis¹²⁶
- A retrospective longitudinal cohort study of young-old (66-74 years) and old-old (≥ 75 years) men who were fee-for-service Medicare enrollees with advanced prostate cancer reported prevalence of substance use as 12.4% in the young-old and 7.4% in the old-old group¹²⁷
- The young-old men whose substance use were in the 'drug psychoses and related' category had higher inpatient, outpatient, and ER usage as well as mortality (HR=2.2; CI=1.5, 3.1) compared to those without substance use. For the old-old men, the 'drug psychoses and related' category was associated with highest inpatient and outpatient use; and 'Non-dependent use of drugs' was associated with highest ER use, compared to those without substance use¹²⁷

Estimates of Substance Use by Subpopulation

- Three studies show that sexual minority cancer survivors are more likely to be current smokers as compared to heterosexual cancer survivors^{128,129,130}
- Compared to heterosexual cancer survivors, sexual minority male cancer survivors consume alcohol more days/week, more drinks/day, and more drinks/30 days¹²⁹
- Of the 602 cancer survivors who participated in the National Health and Nutrition Examination Survey (NHANES) from 2001-2010, sexual minorities were 2.6 times more likely to report a history of illicit drug use (aOR=2.4, 95% CI 1.04, 5.35)¹³¹

F. SUICIDE

- A retrospective, population-based study of program data collected between 1973-2014 reported that the rate of suicide was 28.58/100,000-person years, and the standardized mortality ratio (SMR) of suicide was 4.44 (95% CI 4.33-4.55)¹³²

- Suicide is reported to be more common in men (83%) and in those who are white (92%)¹³²
- Cancers of the lung, head and neck, testes, bladder, and Hodgkin lymphoma had the highest SMRs (> 5-10). Compared to others with cancer, elderly, white, unmarried males with localized disease are at highest risk¹³²
- A systematic review examining association between suicide ideation and physical illness in older adults found suicidal behaviour was associated with malignant diseases¹³³

G. OTHER MENTAL HEALTH ILLNESSES AND PROBLEMS

- Nearly one-third of cancer survivors are diagnosed with mental health conditions⁴⁰
- The most common occurring mental health illnesses among cancer survivors, including those in active treatment and long-term survivors, are major depression, generalized anxiety disorder, adjustment disorder, panic disorder, and post-traumatic stress disorder¹³⁴
- For people with severe mental illnesses and substance use disorders, significantly worse survival after cancer diagnosis is reported. This is independent of cancer stage at diagnosis and other potential confounders¹¹⁵

Mental Health Screening

It is recommended screening be done at different stages of cancer (e.g., pre-treatment, periodic follow-ups post-treatment, and survivorship periods)⁵⁷⁶

- Many different screening tools are used such as the Center for Epidemiologic Studies Depression Scale (CES-D) and Hamilton Depression Scale (HAM-D); there is no clear consensus about the use of one specific screening tool
- The challenges in screening tool selection are that symptoms can differ by cancer type and they can overlap with features of the health condition (e.g., fatigue)
- A prospective longitudinal study of adults newly diagnosed with a first occurrence of primary head and neck cancers, indicated that anxiety was a precursor to post-treatment Major Depressive Disorder (MDD). Identification and prophylactic treatment of anxiety upon diagnosis of head and neck cancer may prevent or delay MDD diagnosis¹³⁵

Common Pathways

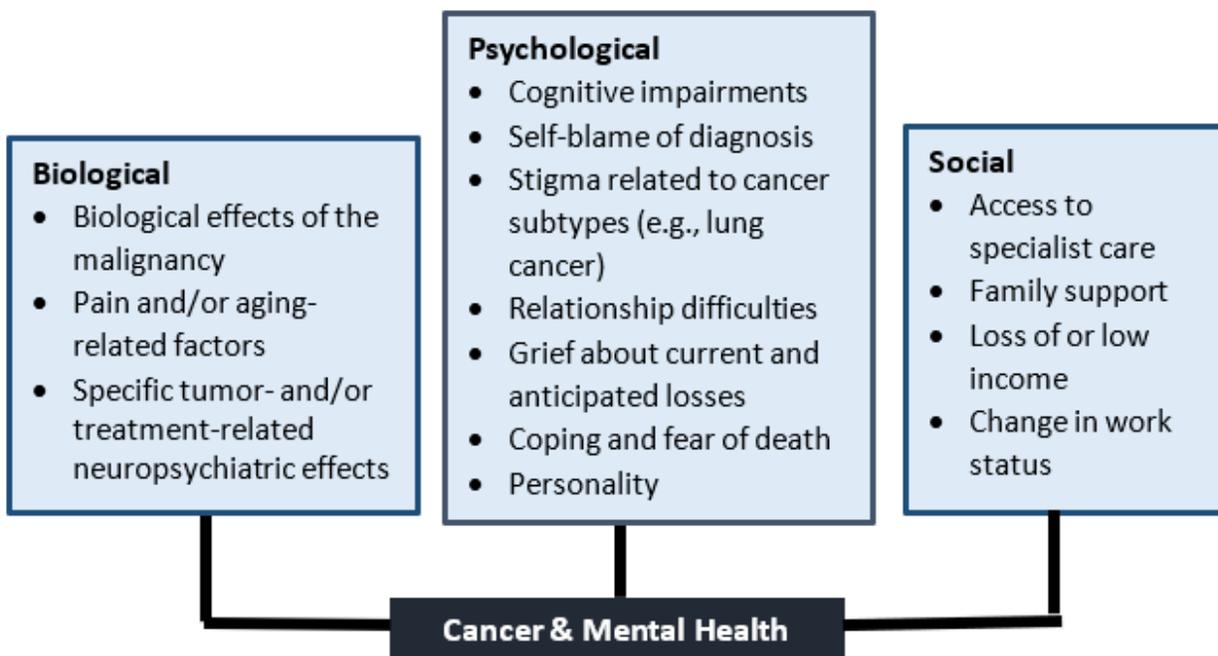
Common Factors Contributing to Mental Health Illnesses or Responses

- Psychological reactions, such as depression and anxiety, tend to occur in response to diagnosis, treatment, relapse, end of life care, or survivorship
- Common shared biological pathways include dysfunctional immune responses, including increased concentrations of inflammatory cytokines such as TNF- α and IL-6
- Psychological, biological, and social factors intersect to impact mental health in those with cancer (Figure 3.5)¹³⁶

Factors Contributing to Mental Health Problems or Illnesses by Cancer Subtypes

- Depression and anxiety may occur secondary to or in response to cancer treatments (Figure 3.6). The most common include tumours of the pancreas (severe cytokine-mediated depression) and lung (depression and anxiety due to endocrine paraneoplastic syndromes⁵)
- Among individuals with small cell lung cancer (SCLC), 15% develop the syndrome of inappropriate antidiuretic hormone secretion (SIADH) which can lead to mood changes due to hyponatremia (low sodium concentration in blood)¹³⁶
- Depression secondary to hypercalcemia can be driven by ectopic parathormone-related peptide production in non-small cell lung cancer (NSCLC), myeloma, sarcoma, breast, renal, gynecological, head and neck cancers, and bone metastases¹³⁷
- For individuals diagnosed with lung cancer that are current or former smokers, stigma can lead to negative psychosocial impact¹³⁸

Figure 3.5: Shared etiology between cancer and mental health



⁵Paraneoplastic syndromes occur due to the production of chemical signalling molecules (such as hormones or cytokines) by tumour cells or by an immune response against the tumour.

Figure 3.6: Examples of shared depression and anxiety etiology related to specific tumours and cancer treatments¹³⁶

Cancer Treatments	Tumours
<p>Cancer Surgery</p> <ul style="list-style-type: none"> • gastrectomy or ileal resection → vitamin B₁₂ deficiency • oophorectomy → estrogen depletion • frontal lobe neurosurgery → apathy and/or emotional lability 	<p>Brain</p> <ul style="list-style-type: none"> • meningiomas, gliomas, or metastases → frontal &/or temporal lobe changes → apathy, emotional lability, hallucinations, executive function deficits, motor behavioral disturbance • pituitary tumours → altered secretions (e.g., adrenocorticotrophic hormone, prolactin)
<p>Radiotherapy</p> <ul style="list-style-type: none"> • head and neck → hypothyroidism • pelvic → Vitamin B₁₂ deficiency • brain → melatonin deficiency & insomnia, thyroid stimulating hormone, growth hormone, &/or gonadotropin deficiency 	<p>Parathyroid</p> <ul style="list-style-type: none"> • overproduction of parathyroid hormone → cognitive impairment
<p>Chemotherapy (e.g., mitotic spindle toxins, anti-metabolites) → mood disturbance & instability</p>	<p>Lung</p> <ul style="list-style-type: none"> • bronchus carcinoid tumours → carcinoid syndrome, paraneoplastic endocrine syndrome, &/or pellagra → aggression, cognitive impairment, Cushing's syndrome, irritability • non small cell lung cancer → paraneoplastic endocrine syndrome → hypercalcemia • small cell lung cancer → paraneoplastic Cushing's syndrome or SIADH → Cushing's syndrome, encephalopathy, delirium
<p>Monoclonal antibodies (e.g., checkpoint inhibitors, EGFR inhibitors)</p>	<p>Pancreas: interleukin-6 release</p>
<p>Hormone Treatments</p> <ul style="list-style-type: none"> • corticosteroids → agitation, psychosis, euphoria, mania, suicidal ideation 	<p>Ovary</p> <ul style="list-style-type: none"> • onconeural (anti-NMDA receptor) antibody-mediated limbic encephalitis → psychosis

<ul style="list-style-type: none"> • androgen deprivation → irritability 	
	Adrenal <ul style="list-style-type: none"> • cortical → Cushing's syndrome • pheochromocytoma → mood swings, psychosis, irritability
	Testicular <ul style="list-style-type: none"> • paraneoplastic endocrine syndrome → hyperthyroidism • onconeural (anti Ma2) paraneoplastic syndrome → disorientation, hallucinations
	Other Tumour Types Examples: myeloma, breast, renal, gynecological, sarcoma, breast, head, neck → hypercalcemia

Management of Cancer and Mental Health

Cancer and Mental Health Considerations in Management

- Some components of cancer care may contribute to re-traumatization.¹³⁹
 - Pelvic, breast, or rectal examinations may exacerbate pre-existing posttraumatic stress disorder
 - Relapses of a depressive disorder may occur after mastectomy
 - Relapse of manic or depressive episodes in bipolar affective disorder may occur secondary to essential treatment with corticosteroids
- Individuals treated with some chemotherapeutic agents, hormone deprivation treatment, immunotherapies and targeted agents, radiotherapy, and cancer surgery may experience neuropsychiatric effects, such as depression, anxiety, and/or suicidal ideation:¹³⁹
 - About 10% of individuals who receive radiotherapy for head and neck cancer develop clinical hypothyroidism; of these, about 66% may develop depressive symptoms
 - After pelvic irradiation, about 14% of individuals acquire vitamin B₁₂ deficiency due to disrupted gut absorption; depression is a common presenting symptom
 - Bilateral oophorectomy in premenopausal women is associated with a long-term increased risk of depressive disorder and of anxiety symptoms
- Addressing underlying factors such as vitamin B₁₂ deficiency, hypothyroidism, SIADH, hypercalcemia, and pain can improve mental health¹³⁹

Management Approaches

Mental Health

Medications and Complementary Therapies

- A Cochrane review of antidepressants for depression in people with cancer reported overall low quality evidence. The authors recommended antidepressants be prescribed on an individual basis; selective serotonin reuptake inhibitors (SSRIs) are suggested to have a positive safety profile¹⁴⁰
- Complementary therapy use, such as herbs for symptom relief, is common. A systematic review that examined 100 single-herb RCTs that were considered safe for use in cancer treatments found that lavender, passionflower, and saffron produced benefits comparable to standard anxiety and antidepressant medications; 45% of the studies reported fewer adverse effects than conventional medications. Results need to be confirmed with larger RCTs¹⁴¹
- A systematic review of music therapy for individuals receiving cancer treatment reported no positive effect on anxiety; several methodological limitations were noted among the trials included¹⁴²
- Results of a systematic review that examined yoga for improving mental health and cancer-related symptoms in women diagnosed with breast cancer indicated moderate-quality evidence for yoga as a supportive intervention for reducing depression and anxiety when compared with psychosocial/educational interventions¹⁴³

Models of Care

- In a meta-analysis that examined collaborative care, pharmacological, and psychological treatments, collaborative care interventions were significantly more effective than usual care and depression reduction was maintained after 12 months¹⁴⁴
- Results of a systematic review of 9 studies indicated that life review programs benefited individuals with cancer by reducing depression and anxiety, as well as improving self-esteem and quality of life¹⁴⁵
- Stepped care is a system of delivering and monitoring treatments, such that effective, yet least resource-intensive, treatment is delivered to individuals first. It is recommended that stepped care approaches for mental health interventions in cancer should include the following considerations:¹⁴⁶
 - i. Medication: psychotropic medications should be guided by clinical parameters, particularly interactions with chemotherapies, to identify specific contraindications;
 - ii. Psychological therapies: Cognitive-behavioural interventions can help to understand the thoughts, feelings, and behaviours that can cause or maintain symptoms of depression or anxiety (e.g., treatment refusal, avoidance behaviour, excessive reassurance seeking);
 - iii. Availability of specialist psychological therapy varies geographically and by expertise. Therapeutic expertise needs include complex illness beliefs, challenging side effects (e.g., psychosexual), physical disfigurement, and end-of-life issues.

- Integrated mental and physical cancer care approaches are also recommended. One reported model of the UK NHS Cancer Strategy includes:¹⁴⁷
 - i. Collaborative screening and treatment;
 - ii. Cancer clinical nurse specialist delivery of supervised cognitive-behavioural interventions for depression; and
 - iii. Guidance to general practitioners by liaison psychiatrists to optimize the prescribing of antidepressant medication
- In Canada, examples of integrated mental and physical cancer care approaches exist. For example, The Tom Baker Cancer Centre and the Odette Cancer Centre at Sunnybrook Health Sciences Centre.
- Better integration between primary and tertiary cancer care is understood to lead to improved coordination, continuity and quality of care.

Peer, Self-Care, and Education Approaches

- A randomized longitudinal study of 50 women with breast cancer, 21 years+ who were randomly assigned to moderated or peer-led groups found no significant differences in depressive symptoms by group or by extent of group participation¹⁴⁸
- A clinical trial that compared an intervention where women with breast cancer received training sessions (three 25- to 30-minute sessions) based on the Orem's model,⁶ on a weekly basis with the control group that received only routine care, reported significantly different pre- and post-anxiety levels in the intervention group when compared to the control group ($P < 0.001$)¹⁴⁹
- An RCT compared comprehensive education and care (CEC) program versus basic health education and rehabilitation over 12 months and the effects on anxiety, depression, quality of life, and survival in patients with hepatocellular carcinoma who underwent surgical resection. The CEC group received health education, psychological nursing, caring activity, and telephone condolence. The results showed greater improvements in HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D) scores as well as better survival¹⁵⁰
- A systematic review examining supportive care interventions (psychoeducation, psychoeducation alone, exercise program) for individuals diagnosed with lung cancer reported that psychotherapy plus psychoeducation and exercise significantly improved depressive symptoms. Psychoeducation alone did not yield significant effects¹⁵¹

Substance Use

- Quitting smoking prior to cancer treatment may improve survival, as continuing to smoke after a cancer diagnosis is associated with higher risk of cancer recurrence,

⁶Dorothea Orem's Self-Care Model⁵⁷⁴ focuses on an individual's "ability to perform self-care, defined as 'the practice of activities that individuals initiate and perform on their own behalf in maintaining life, health, and well-being.'" Orem's self-care deficit theory focuses on scenarios needing the attention of nurses, and ways to help such as acting for and doing for others, guiding others, supporting another, providing an environment promoting personal development in relation to meeting future demands, and teaching another.

second primary cancers, and development and progression of other smoking-related morbidities, such as cardiovascular and respiratory diseases¹⁵²

Multi-level approaches to reduce stigma barriers in the context of lung cancer help to improve quality of care. Examples include patient-focused stigma-reduction interventions to facilitate timely diagnosis and treatment adherence, and training focused on clinician empathy and communication with lung cancer patients¹³⁸

- Cervical cancer survivors should be provided with a survivorship care plan that addresses the dangers of continued tobacco use and the risk of subsequent malignancy that persists throughout the survivor’s lifetime¹⁵³

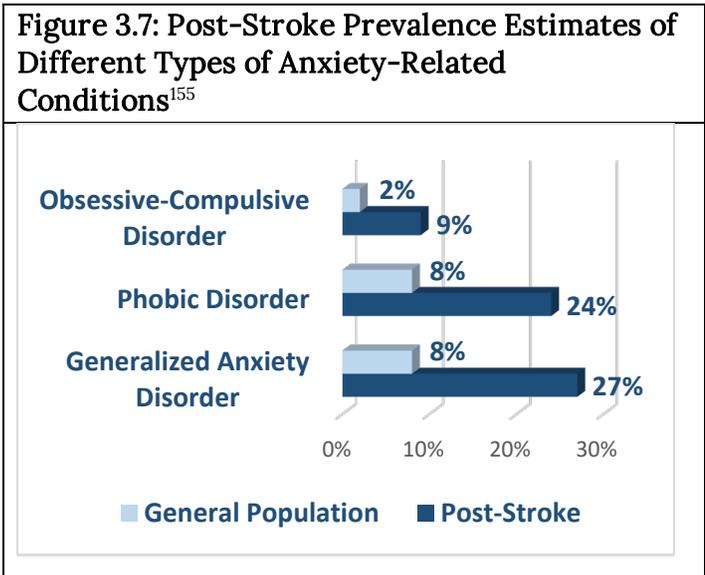
3.1.3 Cardiovascular Disease (CVD)

CVD refers to a group of conditions that affect the structure and functions of the heart. These conditions can include hypertension, coronary artery disease (CAD) which can lead to coronary heart disease (CHD) and myocardial infarction (MI), cerebrovascular disease (stroke), peripheral vascular disease, and heart failure (HF).¹⁵⁴

Prevalence and Incidence of CVD with Mental Health Problems or Illnesses

A. ANXIETY

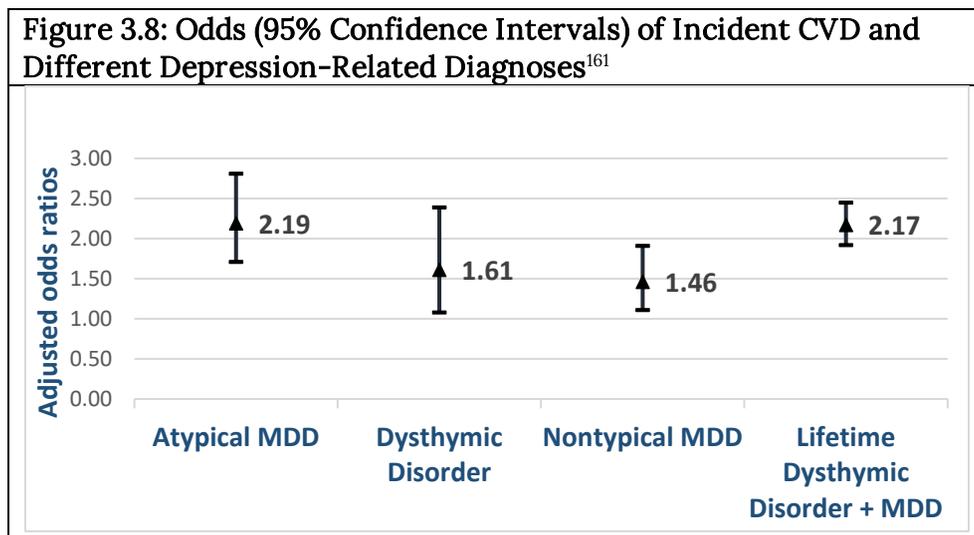
- A meta-analysis examining anxiety and new onset of CVD combined 37 studies (n = 1,565,699) with follow-up ranges of 1 to 24 years. Anxiety was associated with a 52% increased incidence of CVD (HR = 1.52, 95% CI 1.36–1.71) suggesting it is a causal factor¹⁵⁶
- There is high prevalence of different types of anxiety after stroke (Figure 3.7) with the biggest difference in estimates between generalized anxiety disorder versus the general population
- Female sex and having depression were significant predictors of anxiety disorder in those with who experienced a stroke¹⁵⁵



B. DEPRESSION

- Depression can occur with CVD in two forms: precardiac and postcardiac:

- *Precardiac depression* is more common, persistent, and chronic and has been linked to additional risk of reoccurrences of depressive symptoms and relapses. Those with precardiac depression experienced major depression on average 17 years prior to the CVD onset¹⁵⁷
- *Postcardiac depression* is transient and can remit after the stress of an acute exacerbation subsides¹⁵⁸
- Prevalence of depression varies by type of heart disease and severity with estimates between 15-20%; at the high end of this range is depression which occurs in relation to CAD, peripheral artery disease, and HF¹⁵⁹
- Depression has been reported to be more than three times that which occurs in general populations. Higher reports of depression in CVD may be due to changes in quality of life¹⁵⁹
- Higher prevalence of depression occurs among those who have had a stroke (34%, 95% CI 29%–38%) or myocardial infarction (MI) (24%, 95% CI 20%–28%)¹⁶⁰
- Prospective data from 28,726 adults reported those with different forms of depression had higher odds of incident CVD than no depression history (Figure 3.8)¹⁶¹



- Based on a systematic review, the prevalence of depression in those with stroke was reported as 29% (95% CI 25–32) and remained stable for 10 years, with a cumulative incidence of 39–52% within 5 years of stroke. Major predictors of depression were disability, depression pre-stroke, cognitive impairment, stroke severity, anxiety, lower quality of life, mortality, and disability¹⁶²
- A meta-analysis with meta-regression reported that depression can occur from 2 days to 7 years after stroke (mean 6.87 months, N=33 in acute, N=43 in rehabilitation and N=69 in the community/outpatients). The point prevalence of depression was 17.7% (95% CI=15.6% to 20.0%). Dysthymia was present in 3.1% (95% CI=2.1% to 5.3%). Any depressive disorder was present in 33.5% (95% CI=30.3% to 36.8%)¹⁶³

- Relative risk of any depressive disorder was reported to be higher following left (dominant) hemisphere stroke, aphasia, and among people with a family history and past history of mood disorders¹⁶³

C. BIPOLAR DISORDER

- In an analysis of two waves of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the 3-year incidence of CVD for bipolar I disorder (n = 1,047), bipolar II disorder (n=392), MDD (n=4,396), and among controls (n=26,266) was 6.30%, 5.74%, 3.98%, and 3.70%, respectively. Adjustments were made for age, sex, race, cigarette smoking, hypertension, obesity, and alcohol and drug use disorders¹⁶⁴

D. OBSESSIVE-COMPULSIVE DISORDERS

- In a longitudinal analysis of individuals diagnosed with OCD (n=25,415) from a cohort of 12,497,002 individuals, those with OCD had a higher risk of any metabolic or cardiovascular complications compared with the general population (adjusted HR=1.45, 95% CI 1.42-1.49) and their unaffected full siblings (adjusted HR=1.47, 95% CI 1.40-1.54)¹⁶⁵

E. PATHOLOGICAL GAMBLING

- A prospective study about at-risk/problem/pathological gambling (ARPG) and incident medical conditions among older adults reported that the odds of arteriosclerosis was 2.3 times that of those who identified as having no APRG (p=0.0035) after adjustment for socio-demographic characteristics, psychiatric comorbidity, substance use, and BMI¹⁶⁶

F. POST-TRAUMATIC STRESS DISORDER

- A cohort study of 6,481 first responders nested within the World Trade Center Health Program in New York City reported, even after controlling for depression, an elevated risk (HR=2.22, 95% 1.30–3.82) for MI and stroke (HR=2.51, 95% CI 1.39–4.57) among those with PTSD. There were no significant differences between men and women¹⁶⁷

G. SCHIZOPHRENIA

- A study comparing effects of schizophrenia on major adverse cardiac events, length of hospital stay, and prevalence of somatic comorbidities following acute coronary syndrome reported heightened risk for major adverse cardiac events (HR=1.62, 95% CI 1.45–1.81) and stroke (HR= 1.51, 95% CI 1.15–1.99)¹⁶⁸

H. SUBSTANCE USE

- A study that examined primary heart failure hospitalizations in the 2014 National Inpatient Sample reported that of 989,080 heart failure hospitalizations, 15.5% (n =

152,965) had documented tobacco (n = 119,285, 12.1%) or substance (n = 61,510, 6.2%) use disorder¹⁶⁹

- After accounting for demographic factors in the above-indicated study, female sex was associated with lower rates of tobacco (OR=0.72; 95% CI 0.70–0.74) and substance (OR=0.37; 95% CI 0.36–0.39) use disorder. Native American race was associated with increased risk of alcohol use disorder (OR=1.67; 95% CI 1.27–2.20); Black race was associated with alcohol (OR=1.09; 95% CI 1.02–1.16) or drug (OR=1.63; 95% CI 1.53–1.74) use disorder. Medicaid insurance or income in the lowest quartile were associated with increased risk of tobacco and substance use disorders¹⁶⁹

I. SUICIDE IDEATION

- A systematic review examining association between suicide ideation and CVD in older adults found mixed results among 7 studies¹³³

J. ESTIMATES OF MENTAL HEALTH COMORBIDITIES BY SUBPOPULATIONS

Depression and Anxiety

- Among women with CHD, prevalence estimates of depression range between 36–40%; higher prevalence occurs both at baseline (hospitalization [36% vs 23%]) and over 24 months (23% vs 20%) when compared to men¹⁷⁰
- Studies of gender differences regarding anxiety after acute myocardial infarction indicate that women tend to have higher anxiety than men. This appears to be consistent across the western and eastern cultures¹⁷¹
- A meta-analysis examining depression in older adults reported that among the pooled sample of 47,625 older people (mean 74, SD ± 7.4 years), over a median follow-up of 8.8 years, participants with depressive symptoms had a comparably higher risk of stroke (HR 1.36, 95% CI 1.18–1.56) and all-cause mortality (HR 1.44, 95% CI 1.35–1.53), but not of MI (HR 1.08, 95% CI 0.91–1.29)¹⁷²
- In a cross-sectional study which compared stroke survivors who were Latino, Black, and white, Those who were Latino were three times the odds of depression (95% CI 1.18–6.35) in compared to those who were white; People who were Black and white had similar odds of depression¹⁷³
- Logistic regression results from analysis of National Survey of American Life (NSAL) data indicated that African American women with MDD were 1.59 times more likely to have CVD compared to those without MDD and these results were similar among those living in and not living in poverty¹⁷⁴
- A prospective, descriptive-correlational repeated-measures study involving individuals living in rural settings admitted to hospital for ACS suggested that persistent anxious state occurs in individuals up to 8 hours later. The development and testing of protocols for anxiety reduction may be needed¹⁷⁵

PTSD

- Using data from the Collaborative Psychiatric Epidemiology Surveys (CPES), the National Latino and Asian American Study (NLAAS) and the National Comorbidity

Survey Replication (NCS-R), an increased likelihood of cardiovascular events was reported for those with a diagnosis of PTSD (OR = 2.10, 95% CI 1.32-3.33) when compared to those who had not experienced trauma¹⁷⁶

- Among subgroups studied in the above-indicated study, the likelihood of having a cardiovascular event in those with PTSD was significant for non-Latino Whites (OR=1.86, 95%CI, 1.08-3.11), Latinos (OR = 1.94 95% CI 1.04-3.62) and non-Latino Blacks (OR=3.73, 95%CI 1.76-7.91, but not for Asian respondents¹⁷⁶

Mental Health Screening

Mental Health

- Various studies recommend that all people diagnosed with CVD be screened for depression and anxiety, particularly at key periods such as post myocardial infarction or major surgical interventions
- A systematic review of studies about heart failure and coronary artery disease concluded that screening and treating of depression did not improve heart failure management or reduce rates of heart attacks or death¹⁷⁷
- Although there is currently no direct evidence that screening for depression leads to improved outcomes in cardiovascular populations, depression has been linked with increased morbidity and mortality, poorer risk-factor modification, lower rates of cardiac rehabilitation, and reduced quality of life¹⁵⁷
- Screening tools to assess cardiac and mental health comorbidity should screen for symptoms, stress, quality of life, risk factors, and protective factors¹⁷⁸
- Self-report questionnaires used for screening of depression in CVD include the Patient Health Questionnaire (PHQ), Beck Depression Inventory (BDI), Hospital Anxiety Depression Scale (HADS), Cardiac Depression Scale (CDS), and the Center for Epidemiologic Studies Depression Scale-10 (CES-D). Many of these have been validated in many different languages. An American Heart Association Science Advisory suggested the PHQ is most useful¹⁷⁹
- The two-item PHQ for identifying individuals with depression may be used in outpatient settings, and added to questionnaires that are completed at registration¹⁷⁸
- The CDS measures the range of depressive symptoms in CVD and is reported to have excellent psychometric properties (e.g., high sensitivity and specificity) for the diagnosis of MDD¹⁸⁰
- The European Guidelines on CVD prevention suggest two core questions that cover mandatory criteria for MDD diagnosis: ‘Do you feel down, depressed, or hopeless?’ and ‘Have you lost interest and pleasure in life?’¹⁸¹
- For people thought to have Type D personality,⁷ which is characterized by enduring features of depression, it is recommend asking: ‘In general, do you often feel

⁷Type D personality is described as one where the person has the tendency to experience increased negative emotions across time and situations and tend not to share these emotions with others, because of fear of rejection or disapproval¹⁵⁷⁵

anxious, irritable, or depressed?’ and ‘Do you avoid sharing your thoughts and feelings with other people?’¹⁸¹

- For people that have had an acute coronary syndrome, depression screening is recommended while in hospital and rescreening should occur two months after the acute event¹⁸²

Substance Use

- Tobacco¹⁸³ and cocaine¹⁸⁴ use are associated with increased readmission risk in heart failure patients
- Screening for tobacco and substance use disorders has historically been deficient in primary care, emergency department, and hospital settings¹⁸⁵

Screening for tobacco and substance use disorders is recommended in those hospitalized for heart failure¹⁶⁹

- A Danish longitudinal record linkage study of consecutive drug use disorder (DUD) treatment admissions (2000 and 2006) reported that of 17,642 patients seeking treatment for DUD, 4.5% had a history of CVD at treatment entry; 1,535 new incident cases of CVD were observed during a mean follow-up time of 7.5 years¹⁸⁶
- CVD incidence in the above indicated study was associated with intravenous drug use [sub hazard ratio (SHR)=1.41, p<0.001], not responding to injection question (SHR=1.23, p=0.005), older age (SHR=1.04 per year, p=0.000), use of prescription methadone (SHR=1.32, p<0.001), use of benzodiazepines (SHR=1.21, p=0.005), and being referred to methadone treatment (SHR=1.15, p=0.022). The use of amphetamines was negatively associated with CVD risk (SHR=0.75, p=0.001)¹⁸⁶

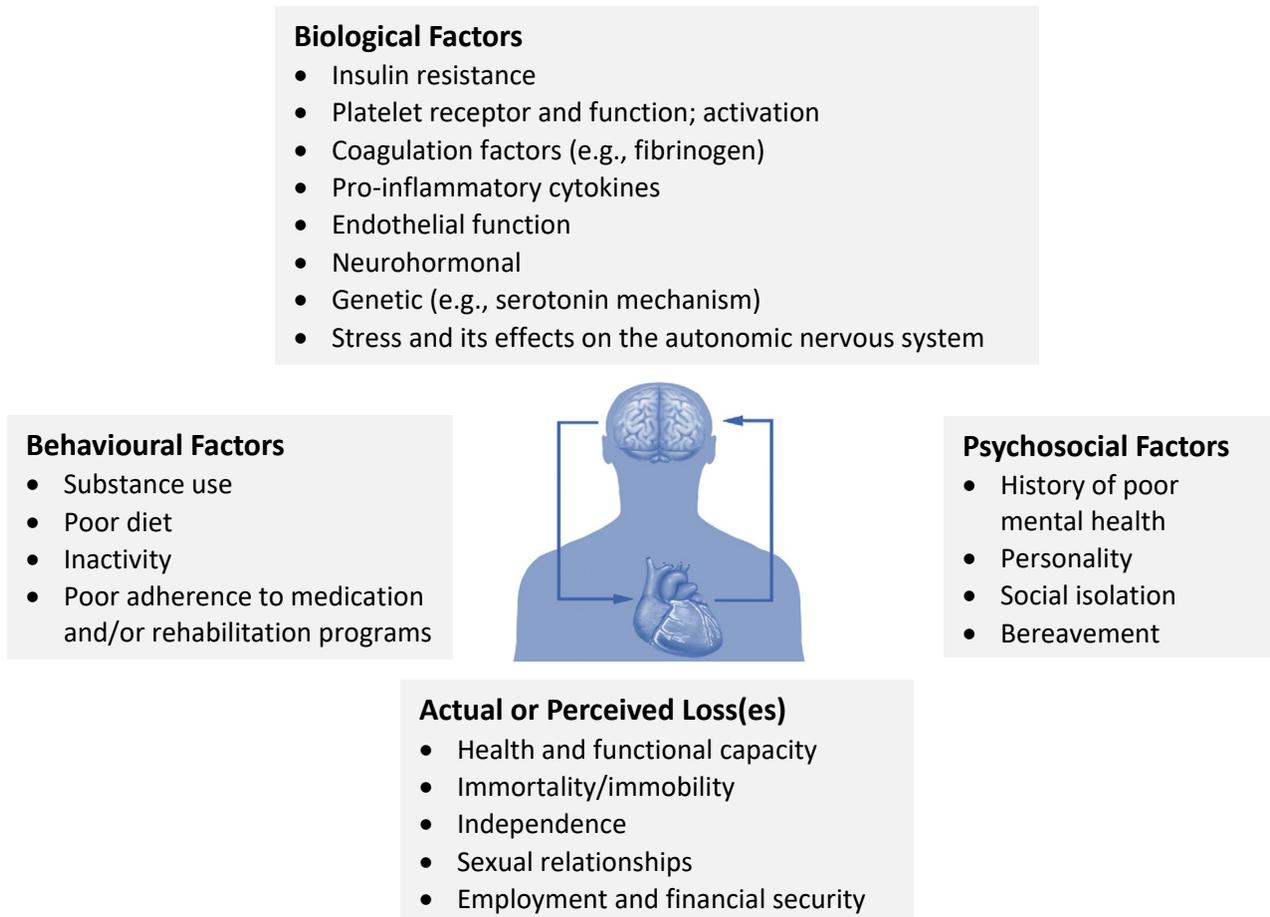
Common Pathways

Mental Health

- Biological and behavioural pathways that include insulin resistance and high circulating levels of stress hormones interact in a vicious cycle with health behaviours (Figure 3.9)
- MDD can cause deregulation in the sympathetic nervous system and HPA axis which can lead to effects such as hypertension, left ventricular hypertrophy, coronary vasoconstriction, endothelial dysfunction, platelet activation, and the production of proinflammatory cytokines. Potential consequences include an elevated risk of ventricular arrhythmias and MI¹⁸⁷ (Figure 3.9)
- Inflammatory markers that include C-reactive protein (CRP), and proinflammatory cytokines, such as interleukin 1, 2, 6, and TNF may also be part of the shared etiology¹⁸⁷
- A large prospective study reported that the presence of a major depressive episode is a risk factor for stroke, especially in those who smoke¹⁸⁸
- A meta-analysis examining the magnitude of cardiovascular responses (heart rate, diastolic and systolic blood pressure) to sadness and angry rumination (43 studies;

3,348 participants) found association between rumination and cardiovascular reactivity; angry rumination may have larger cardiovascular effects than sadness rumination. Autonomic dysregulation due to long-term rumination may be linked to depression and hostility to CVD¹⁸⁹

Figure 3.9: Shared etiology between CVD and mental health^{190,191,192}

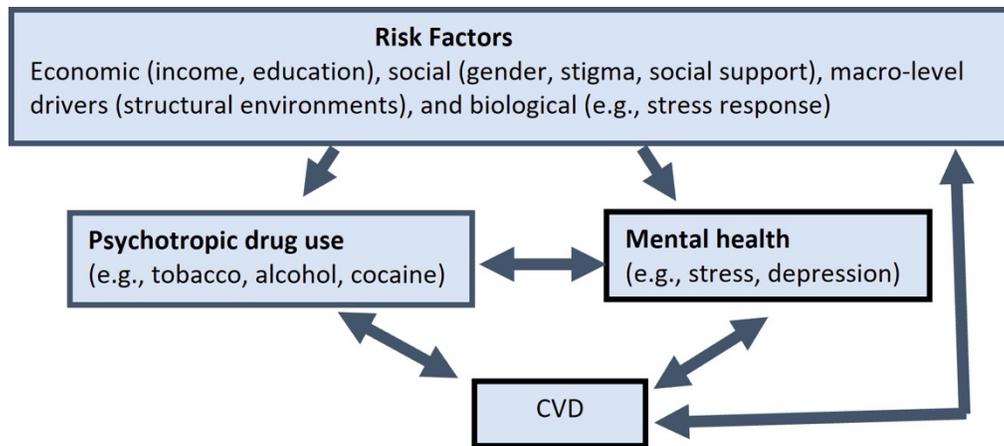


Substance Use

- A number of mechanisms related to economic, social, macro-level drivers, and biological pathways explain potential inter-relations between substance use and CVD (Figure 3.10)
- Injection use may lead to venous disease,¹⁹³ and thrombosis, septicaemia or endocarditis¹⁹⁴
- Opioid exposure is associated with increased arterial stiffness and vascular age¹⁹⁵ in a dose-dependent fashion¹⁹⁶
- High doses of methadone may worsen CVD by causing QT interval prolongation^{197,198}
- High doses of cocaine and amphetamine are associated with acute vascular events, such as arrhythmias and elevated blood pressure^{199,200}
- Benzodiazepines are associated with risk of CVD among patients with depression or anxiety;²⁰¹ this association is difficult to disentangle from the severity of mood and anxiety disorders²⁰²

- Case reports have indicated that cannabis use may be associated with acute myocardial infarction²⁰³

Figure 3.10: Examples of shared etiology between CVD and substance use



A number of mechanisms related to economic, social, macro-level drivers, and biological pathways explain potential inter-relations among substance use, mental health, and CVD. It is well established that poor mental health and substance use frequently co-occur.²⁰⁴ Substance use may be a cause or consequence of mental ill health or share a common origin with mental ill health. An alternative explanation is that mental ill health and substance use interact and maintain each other.

Management of CVD and Mental Health

- Lower treatment rates for depression occur among those who have had a stroke (24%, 95% CI 20%–27%) when compared to those who have had an MI (14%, 95% CI 8%–19%).¹⁶⁰ Frequent assessments with needed treatment plan adjustments are recommended

A. CARDIAC REHABILITATION AND EXERCISE

- Cardiac rehabilitation, based on exercise training in a group setting, results in less depression²⁰⁵
- For those with CHD, aerobic exercise in a group setting reduces depression to levels similar to antidepressant medication; improved cardiovascular function (VO₂ peak) was also found²⁰⁶
- Based on clinical trial data, exercise training reduces depression in people with heart failure, even up to 12 months after the intervention²⁰⁷
- An RCT that compared supervised exercise vs home-based exercise vs antidepressant medication (sertraline, 50–200 mg daily) vs a placebo in individuals with CHD risk factors (brachial artery flow-mediated dilation, carotid intima-media thickness, serum lipids, and 10-year atherosclerotic cardiovascular disease (ASCVD)

risk), indicated that compared with the placebo, both exercise groups and sertraline therapy were associated with an improvement in CHD risk factors²⁰⁸

B. PSYCHOLOGICAL INTERVENTIONS, INCLUDING COMBINED TREATMENTS

- An RCT that compared internet based CBT with treatment as usual in people with recent MI reported lowered HADS scores over time (mean delta=-5.1, P<.001) but no difference between the study groups at follow-up (beta=-0.47, 95% CI -1.95-1.00). Treatment adherence was low with only 46% of the intervention group completing the introductory module.²⁰⁹ Internet-based CBT has also been indicated to be unsuitable for moderate-to-severe depression or anxiety²¹⁰
- A meta-analytic review concluded that CBT and problem solving showed some benefit for those with CVD.²¹¹ CBT may also reduce subsequent cardiovascular events²¹²
- A 3-group, parallel, RCT where individuals with stroke were randomized within 1 month of hospital admission to problem-solving therapy or non-specific support given by volunteers or treatment as usual indicated, at 6- and 12-month follow-ups, psychological and activity measures favoured problem-solving therapy. The authors concluded that the results suggest it is possible to prevent mood disorder in stroke patients using a psychological intervention²¹³
- A study of CBT in reducing depression in this population found CBT in combination with exercise was effective²¹¹
- In a controlled, randomized study that examined uncertainty management intervention delivered over 10 months to outpatients with COPD, the intervention group showed significant improvement in uncertainty, coping strategy, anxiety, depression, and the mental health domains of quality of life compared to controls²¹⁴

C. PHARMACOLOGICAL TREATMENTS

- Anti-depressant medications are reported to improve depression in individuals with CVD, however, efficacy vs. potential risks need to be considered.²¹⁵ For example, tricyclic anti-depressants have been shown to alter cardiac muscle cell activity (e.g., lengthen cardiac muscle cell action potentials)²¹⁵

D. STEPPED-CARE

- Combination therapies appear to reduce depression after acute coronary syndrome (ACS). In a multi-centre RCT of people with some depression 2-6 months after an ACS, a combined therapeutic approach of 'stepped' care resulted in significantly less depression after 6 months compared with usual care²¹⁶

E. TARGETED EDUCATION

- A systematic review of heart failure (HF) disease management reported that anxiety and depression were better in programs offering CBT plus an HF disease

management education program when compared to usual care plus an HF education program only; improvement was sustained over time²¹⁷

- A single-blind RCT that involved distributing four text messages/week for 6 months that provided education, motivation and support for diet, physical activity, general cardiac education and smoking, reported lower depression at 6 months compared with the control group. The frequency of mild or greater depressive symptoms at 6 months were significantly lower in the intervention group (6.3% vs 24.6%) and lowered risk (relative risk (RR) 0.26, 95% CI 0.16-0.40)²¹⁸

F. HOME-BASED INTERVENTIONS

- A systematic review and meta-analysis of a small number of RCTs that examined the effects of home-based interventions on anxiety reduction in people with CAD reported that compared with usual care or center-based cardiac rehabilitation, home-based interventions had a small but significant effect in reducing anxiety (effect size: 0.13; 95% CI 0.20-0.06)²¹⁹
- A multi-site RCT examined the effects of home-based robot-assisted rehabilitation coupled with a home exercise program compared with a home exercise program (control) on depression and quality of life in people after stroke and reported significant changes in all but one domain on the Stroke Impact Scale and the CES-Depression Scale for both groups²²⁰
- An RCT comparing a web-based distance education remote training program for individuals post MI vs standard care found significantly reduced depression and anxiety symptoms in the intervention group. The program covered seven topics including structure of the heart, myocardial infarction, risk factors, and daily life activities such as nutrition and physical activity²²¹

G. INTERVENTIONS FOR SUBPOPULATIONS

Gender-Specific

Results of a clinical trial indicated that gender-tailored cardiac rehabilitation programs were more effective at reducing depressive symptoms in women when compared to traditional programs⁵⁷⁷

- Qualitative work examining psychosocial issues affecting underserved individuals' ability to manage CVD that compared textual data by gender reports that:²²²
 - Interventions for women should include peer-led support groups rather than an emphasis on family inclusion in self-management plans and self-management training that focuses on self-efficacy and empowerment as women report greater vulnerability to illness (internal effects of disease) than men
 - Interventions for men may need to include help with anger management, as well as social services support to help them deal with the external effects of CVD, such as financial impacts

Older Adults

- A meta-analysis of selected cardiac rehabilitation programs for CAD and congestive heart failure for older adults (64 years+) offered in their home reported significant reduction in depression. It was concluded that tailored interventions combined with psychosocial interventions are likely to be more effective in decreasing depression in older adults with heart disease than usual care²²³

3.1.4 Dementia

Dementia is a term used to describe loss of memory, language, problem-solving and other thinking abilities that are severe enough to interfere with daily life. Alzheimer's disease (AD) is the most common cause of dementia.²²⁴

Prevalence and Incidence of Dementia with Mental Health Problems or Illnesses

Depression and Anxiety

- Prevalence estimates of depression and AD/dementia range between 12-42% based on defined diagnostic criteria for both depression and dementia from the American Psychiatric Association²²⁵
- Prevalence estimates of comorbid depression and dementia are reported to be higher among women (57%, 95% CI 50-64%) versus men (43%, 95% CI 37-50%)²²⁶ and among those receiving home care (34%) versus those in long-term care (18%)²²⁷
- A systematic review reported that late-life depression was associated with a significant risk of all-cause dementia (1.85, 95% CI 1.67-2.04) and AD (1.65, 95% CI 1.42-1.92)²²⁸

Psychosis and Schizophrenia

- Psychotic symptoms, defined as the occurrence of delusions or hallucinations, are frequent in AD, and are reported to affect about 40%-60%²²⁹ of people with AD
- It is reported that dementia is twice as common among people living with schizophrenia, compared to those without the illness; the most common type of dementia in people living with schizophrenia differs from Alzheimer's in its clinical features²³⁰

PTSD

- In a longitudinal study examining medical records, it was reported that PTSD was associated with increased risk of dementia over an average of 8 years of follow-up (Females: HR= 1.59, 95% CI 1.30-1.95; Males: HR= 1.96, 95% CI 1.51-2.55)²³¹
- A two-fold risk of dementia has been reported in those with both PTSD and depression (Females: HR= 2.08; 95% CI 1.66-2.59; Males: HR= 2.06; 95% CI 1.47-2.91) compared to those without²³¹

Mental Health Screening

- There is no strong consensus about what criteria should be used to diagnose depression in AD as symptoms, such as apathy and anxiety, occur in both conditions
- Screening tools for subtypes of depression, such as dysthymia, need to be validated for use with AD. For example, increased awareness of function deficits is significantly associated with dysthymia but not with major depression, suggesting there are different depressive syndromes²³²
- Most existing depression self-report scales used for older adults (e.g., Beck Depression Inventory-II, CES-D, Zung Self-Rating Depression Scale) do not consider the level of cognitive impairment and visual deficits²³³

Common Pathways

Dementia and Depression

- There may be a common event underlying both the occurrence of major depressive disorder (MDD) and AD. For example, with a diagnosis of MDD the brain may be sensitized to a second event ('hit') that precipitates AD (Figure 3.11)
- Having an MDD may accelerate brain aging, by pathways involving DNA and increased stress hormones, such as cortisol
- Based on studies reported to date, common genetic predisposition for MDD and AD appears unlikely. Genes predicting risk for AD (e.g., variants of ApoE4) are not risk factors for MDD. Other genes, implicated in MDD development (e.g., variants of SLC6A4 gene) are not risks for AD²³⁴
- There is no strong indication that an environment/gene event occurs during some forms of MDD that predisposes individuals to later AD, though the evidence is limited²³⁴
- Glucocorticoids have been shown to be altered in some cases of MDD and in AD which may have degenerative actions on the brain regions such as the hippocampus, affect new cell development, and brain plasticity
- Reported risk factors for the development of depression in people with AD include ApoE4 positivity²³⁵ and the use of medications such as beta-blockers, corticosteroids, benzodiazepines, dopamine agonists, stimulants, anticonvulsants, hormone-altering drugs, proton pump inhibitors and H2 blockers, statins or lipid-lowering drugs, and anticholinergics²³⁶

Dementia and Psychosis

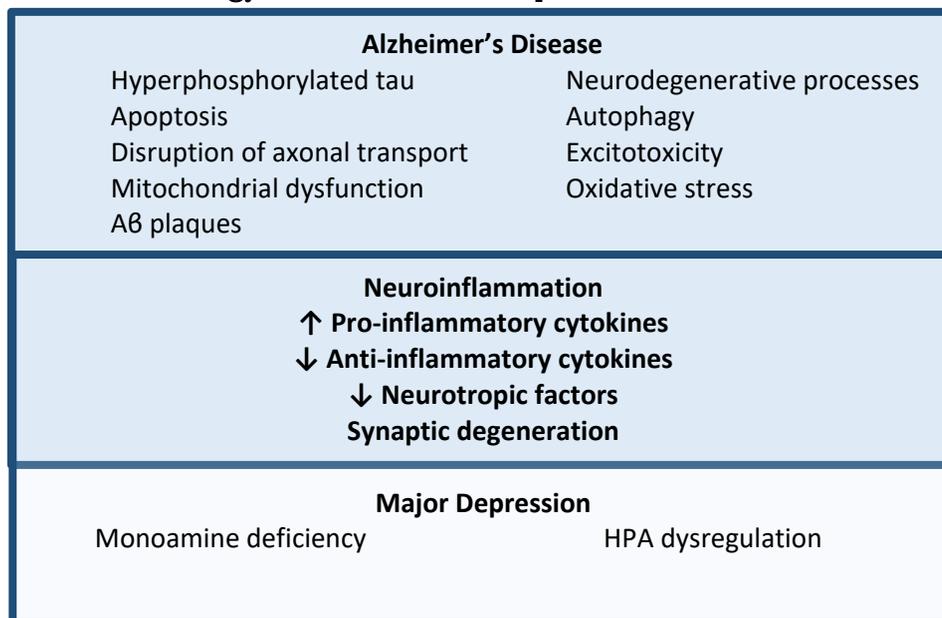
- AD and psychosis are associated with polygenic risk for a set of novel loci and inversely associated with polygenic risk for schizophrenia. Biologic pathways identified by the associations of schizophrenia with AD and psychosis are endosomal trafficking, autophagy, and calcium channel signalling²³⁷

Dementia, MDD, and PTSD

- There are proposed shared links among MDD, PTSD, and dementia.²³⁸

- i. Increased activation of the HPA axis and increases in cortisol^{239,240} impact cognitive ability and lead to later life cognitive impairment.²⁴⁰ Prolonged exposure to high cortisol levels results in neurodegeneration.^{239,240} Increased levels of inflammatory cytokines may also be released and this is seen in both MDD and PTSD and may increase risk of dementia^{241,242}
- ii. Increase in amyloid beta (A β) plaques. The A β plaques, a diagnostic feature of AD, are also present in MDD. People with both AD and MDD show an increased rate of A β deposition compared to those with AD alone.²⁴² PTSD may also cause alterations of hormones involved in the production and deposition of A β plaques²⁴³
- iii. Cognitive reserve. PTSD and MDD may diminish cognitive reserve, which may increase the risk of or speed up dementia development.^{239,244} Factors such as higher SES may be protective against this²⁴⁵
- iv. Inflammatory neurodegeneration. Related to the above-indicated mechanisms (i to iii). Exposure to stress, acute or prolonged, increases inflammation and can result in neurodegeneration.²⁴⁶ The inflammatory response involves an increase in pro-inflammatory cytokines, which in turn activate microglia²⁴⁶ which leads to an increase in the release of inflammasomes that induce inflammation and inhibition of brain-derived neurotrophic factor (BDNF), and result in neurodegeneration.²⁴⁶ Dementia is characterised by lower levels of BDNF and higher levels of the inflammasome NLRP3, stimulated by increased levels of A β plaques.²⁴⁶ Inflammatory markers may mediate MDD/PTSD and dementia²⁴⁶
- v. Reduced brain reserve. Shared mechanisms of MDD/PTSD may increase levels of reduction in brain reserve and increase risk of dementia²⁴⁷

Figure 3.11: Shared etiology between AD and depression



AD is characterized by A β plaques and neurofibrillary tangles which results in neurodegeneration via mechanisms including excitotoxicity and mitochondrial dysfunction. Depression is characterized by monoamine deficiency and HPA-axis dysregulation. Common factors include inflammation and reduction in neurotrophic support.

Management of Dementia and Mental Health

Exercise

- A systematic review found that exercise programmes may significantly improve cognitive functioning and improve the ability of people with dementia to perform daily activities²⁴⁸
- A systematic review of 13 RCTs of physical activity interventions in people with dementia reported there is some evidence that physical activity interventions improve physical function in older people with dementia, however, evidence for an effect on depression is limited²⁴⁹

Peer Approaches

- In an evaluation conducted by the Mental Health Foundation about peer support groups for people with dementia living in extra care housing, those with early stage dementia who participated in the groups showed improvements in wellbeing, social support, and practical coping strategies²⁵⁰

Pharmacological Interventions

- Based on a systematic review that examined the anti-depressants sertraline, sertraline combined with mirtazapine, imipramine, fluoxetine, and clomipramine, seven studies met inclusion criteria and reported no statistically significant difference between these and a placebo²⁵¹
- Few RCTs are available on the efficacy of antidepressants to treat depression in AD, limiting clear conclusions of their potential role
- Current National Institute for Health and Care Excellence (NICE) guidelines for dementia indicate that antidepressants should not be offered to manage mild to moderate depression in people living with mild to moderate dementia, unless they are indicated for a pre-existing severe mental health problem²⁵²

Psychological Treatments

- Emotion-oriented therapies aim to provide therapy to the emotional needs of people with AD by utilizing approaches such as validation, reminiscence, reality, and simulated-presence therapy. There is insufficient research providing data on their effects on depression²³⁶
- Brief psychotherapeutic interventions have also been shown to be particularly effective in this population.²⁵³ Behavioural therapies are more commonly applied in

the later stages of dementia, while modified cognitive-behavioural strategies appear to be more successful with those in the earlier stages of cognitive decline²⁵⁴

National Institute for Health and Care Excellence (NICE) guidelines suggest psychological treatments for people with mild-to-moderate dementia who have mild-to-moderate depression⁵⁶⁸

- Most CBT programs for persons with dementia involve their caregivers, both as CBT coaches for the care recipient and as treatment partners. The strongest evidence is for short-term CBT and problem-solving therapy²⁵⁵
- Based on research that compared social engagement, medication use, and depressive symptoms of older adults, including African Americans, with incident dementia, it was found that size of social network and lower perceived social isolation were associated with lower depression. This suggests depression management at the time of dementia diagnosis should include interventions to increase social engagement²⁵⁶

Sensory Therapies

- A RCT that compared the effects of bright light vs low intensity light exposure on depression and agitation in persons with dementia residing in long-term care reported significant improvements in depression (3 measures) and agitation (4 measures) in those exposed to bright light therapy²⁵⁷
- Sensory stimulation therapies, such as music therapy, art therapy, pet therapy, aromatherapy, activity therapies, and multisensory approaches (e.g., Snoezelen), have the potential for benefit in depressed patients with cognitive impairment. However, few rigorous studies have been performed, and efficacies are mixed

3.1.5 Diabetes Mellitus (DM)

DM is a metabolic disease that results from impairments of insulin. Type 2 DM (T2DM), which accounts for 90–95% of cases of DM, is thought to be due to insulin resistance. Conversely, type 1 DM is due to absolute insulin deficiency. Apart from genetic disposition, the factors associated with risk of T2DM appear to be diet, inactivity, and excess body weight. T2DM often goes undiagnosed in its early stages because of lack of symptoms. DM, if undetected or poorly controlled, can result in health problems such as diabetic neuropathy, retinopathy, peripheral vascular disease, renal failure, heart disease and stroke.²⁵⁸

Prevalence and Incidence of DM with Mental Health Problems or Illnesses

A. ANXIETY AND DEPRESSION

- A systematic review of 248 studies reported 28% (95% CI 27-29%) of individuals with T2DM live with different severity levels of depressive disorders²⁵⁹

- Prevalence estimates are higher among females (34%, 95% CI 31-38) compared to males (23%, 95% CI 20-26), those who are younger than 65 compared to older adults (31% vs. 21%), and in those with prediabetes and undiagnosed DM compared to those diagnosed with DM²⁵⁹
- Estimates are three-times higher in those with T2DM compared to T1DM; estimates are twice as high in people with T2DM compared with the general population worldwide²⁵⁹
- A meta-analysis of longitudinal data reported no increased risk for depressive symptoms in individuals with prediabetes or newly developed diabetes, whereas there was an increased risk for individuals with clinically identified DM²⁶⁰
- Based on findings of a cohort study of 30 to 75 year olds, depression with comorbid anxiety may be a subgroup that is at risk of T2DM²⁶¹

B. EATING DISORDERS AND IMPULSE CONTROL DISORDERS

- A systematic review examining eating disorders and DM reported that both binge eating disorder (OR 3.69, 95% CI 1.12-12.12) and bulimia nervosa (OR 3.45 1.92-6.1) were associated with T2DM, while anorexia nervosa was not. Cohort studies showed increased risk of T2DM with bulimia nervosa (RR 1.7, 95% CI 1.2-2.5), and decreased risk with anorexia nervosa (RR 0.71, 95% CI 0.52-0.98). For binge eating disorder the association was not significant²⁶²
- A series of cross-sectional face-to-face household surveys of community-dwelling adults (n=52,095) in 19 countries assessed associations between 16 DSM-IV mental disorders and type 2 DM. Based on multivariable analysis, associations were found for intermittent explosive disorder (OR 1.6; 95% CI 1.1, 2.1), binge eating disorder (OR 2.6; 95% CI 1.7, 4.0) and bulimia nervosa (OR 2.1; 95% CI 1.3, 3.4)²⁶³

C. PTSD

- The prevalence of PTSD among Indigenous people in the USA with T2DM is reported as 22%²⁶⁴

D. SUBSTANCE USE

- An analysis of electronic health record data on 170,853 unique adults aged ≥18 years reported that prevalent diagnoses among adults with T2DM were substance use disorders (SUD) (17.02%: tobacco 13.25%, alcohol 4.00%, drugs 4.22%). SUD was positively associated with mood, anxiety, personality, somatic, and schizophrenia diagnoses.

E. ESTIMATES OF MENTAL HEALTH COMORBIDITIES BY SUBPOPULATIONS

- The prevalence of depression among individuals with DM living in rural settings is estimated as 17%. Associated factors include lack of sleep and frequent inactivity²⁶⁵
- Secondary analysis of a national electronic database that examined PTSD in asylum seekers and the relationship to DM indicated age-adjusted prevalence ratios (APR)

of 1.40 (95% CI 1.12–1.76) in men and 1.22 (95% C, 0.95–1.56) in women compared with individuals without PTSD. Individuals with PTSD had a higher prevalence of T2DM compared with those without PTSD (APR=1.47, 95% CI, 1.15–1.87 in men and APR=1.27, 95% CI, 0.97–1.66 in women). Among the depressed individuals, however, there was no association between PTSD and T2DM (APR=0.87, 95% CI 0.43–1.76 in men and APR=1.00, 95% CI, 0.54–1.83 in women]²⁶⁶

- A Canadian study that examined a cohort of new anti-diabetic (AD) medication users from administrative claims data identified 114,366 new oral AD users (18 years+) and an overall incidence rate of depression of 10.72/1,000 person years (PYs) for women and 8.27/1,000 PYs for men. The results suggested that among new anti-diabetic medication users, women, individuals of younger age, those with a low SES, and a history of anxiety or depression may need to have their physical and mental health tracked closely²⁶⁷

Mental Health Screening

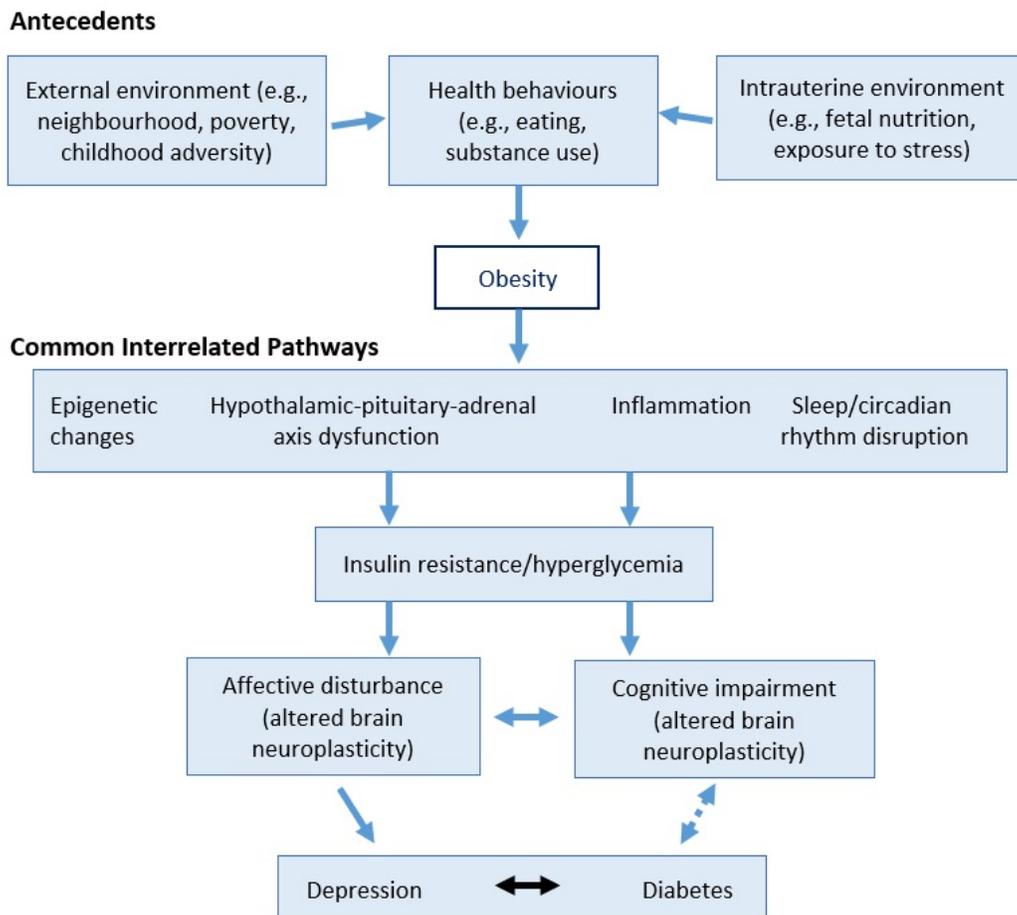
- The BDI and CES-D Scale are popular screening tools (used in ~45% of studies)
- The cultural applicability of screening tools has not been thoroughly assessed. Most studies only include details of the language translation process, few reported reliability data, and most showed moderate-good sensitivity and specificity but a high rate of false positives
- In longitudinal studies, people with both diabetes and depression were found to have a higher risk of developing microvascular and macrovascular complications of diabetes and mortality compared with people without depression;²⁶⁸ screening may help to reduce or delay these risks
- Screening individuals using home healthcare services for mental health comorbidity with the PHQ-2 (and PHQ-9 if applicable) is required by the Centers for Medicare and Medicaid Services Outcomes and Assessment Information Set (OASIS-C) used to collect baseline information at the start of care and at each time point²⁶⁹

Common Pathways

- Various pathways link DM and mental health such as inborn immunity, inflammation, the HPA axis, insulin resistance, and circadian rhythms. A pathway that is often overlooked is in-utero and early childhood experiences, which can be particularly relevant to T2DM and mental health²⁷⁰
- The relationships between DM and mental health appear to be bidirectional²⁷¹ (Figure 3.12)
- Three inter-related major pathophysiologic pathways are often discussed as common mechanisms for the development of depression in T2DM:
 1. **Hyperglycaemia and T2DM**
 - The brain is vulnerable to fluctuating plasma glucose levels because neurons do not have an active glucose transporter
 - High intracellular glucose levels can induce oxidative stress and the formation of advanced glycation end products (AGEs). Both processes may lead to neuronal damage and depression^{272,273}

- Hyperglycaemia also leads to increased levels of cortisol, a known pathway that is also involved in the development of depression²⁷⁴
- 2. Small blood vessel (Microvascular) dysfunction**
- In DM, blood vessel damage in certain brain regions may impact mood regulation²⁷⁵
 - A meta-analysis of longitudinal studies identified that brain scans which show small vessel disease are associated with a higher risk of depressive symptoms^{276,277}
 - Studies of pathways related to small blood vessel dysfunction and artery stiffening that are involved in the development of cerebrovascular damage are strongly related to diabetes^{278,279,280}
- 3. Low-grade inflammation, diabetes, and depression**
- T2DM is accompanied by systemic low-grade inflammation,²⁸¹ which is a mechanism that is involved both in the development of its cardiovascular complications and depression^{282,283}
 - A meta-analysis reported that treatment resistance to antidepressants is associated with higher low-grade inflammation²⁸⁴ suggesting that treatment-resistant depression differs from other types of depression

Figure 3.12: Common etiological pathways of DM and mental health²⁷¹



- Risk factors for depression in DM include living alone, poor social support, low SES, persistent poor glycaemic control, insulin therapy in T2DM, lower literacy, rural domicile, marriage and duration of DM of >2 years, and presence of DM-related complications²⁸⁵
- Sedentary life without adequate physical activities and lack of self-care are often the factors that precipitate depression in a T2DM patient and vice versa
- Schizophrenia is associated with an at-risk allele for T2DM located in the TCF7L2 gene, suggesting that DM and schizophrenia may share familial risk factors or common genetic predisposition²⁸⁶

Management of Diabetes and Mental Health

A. DIGITAL HEALTH APPLICATIONS

- There are many digital health applications available as complementary to care but evidence to support their use is preliminary. Trials of eHealth and mobile technology-based health (mHealth) interventions suggest these are less effective than face-to-face psychotherapeutic treatments²⁸⁷

B. PHARMACOLOGICAL INTERVENTIONS

- A Cochrane review reported that antidepressants had a moderate effect on depression severity and improved glycemic control with a mean difference for glycosylated hemoglobin (HbA1c) of 0.4% (95% CI -0.6 to -0.1)²⁸⁸

C. PSYCHOLOGICAL INTERVENTIONS

- An RCT of adults with T2DM that compared usual care plus psychotherapy for depression via home telehealth (home monitor that captured clinical measures) and usual care reported significant reductions of HbA1c and healthcare costs (mean \$3,781 vs. \$4,662; $p < 0.001$) in the intervention group compared with usual care. Depression outcomes were not specifically evaluated²⁸⁹

D. MODELS OF CARE

- Holistic, preventive services focusing on healthy diet, physical activity, and healthy weight management to promote both physical and mental health is recommended
- A Cochrane review examining self-management programs for individuals with severe mental health conditions indicated there was insufficient evidence demonstrating efficacy in reducing physical or mental health outcomes²⁹⁰
- Although there are mixed effects on glycemic control, interventions that include diabetes self-management education reported benefits for glycemic control²⁹¹
- Depression in T2DM varies among ethnic groups, which suggests the need to address stressors unique to racial/ethnic minorities to improve diabetes-related outcomes²⁹²
- An RCT comparing pharmacist-led group shared medical appointment visits versus standard care found that the intervention was efficacious in attainment of glycemic

control in people with T2DM and depression without change in depression symptoms²⁹³

Collaborative care presents good results for treatment of depression and anxiety in diabetes. Delivery of collaborative care, which provided a stepped care intervention with a choice of starting with psychotherapy or pharmacotherapy, to a primary care population, yielded an effect size of -0.29 (95% CI -0.43 to -0.16)⁵⁶⁹

- A pilot trial of an integrated intervention that included behavioural activation and motivational interviewing techniques, co-developed with end-users (Latino immigrants), their family members, and provider stakeholders, had a positive impact on both diabetes and depression-related outcomes²⁹⁴
- A pilot trial comparing a basic integrated intervention to an integrated intervention that used patient prioritized planning (incorporated financial, social and emotional needs for primary care patients with T2DM and depression) was reported to be effective in improving HbA1c and depression symptoms (CES-D)²⁹⁵
- Collaborative care models should be expanded to also address SUD and related psychiatric comorbidity for people with diabetes²⁹⁶

3.1.6 Epilepsy

Epilepsy is a brain disease that is characterized by abnormal electrical activity which can cause seizures or unusual behaviour, sensations and sometimes loss of awareness. It is one of the most common neurological diseases. Mental health issues such as depression and anxiety, make seizures worse and reduce quality of life.²⁹⁷

Prevalence and Incidence of Epilepsy with Mental Health Problems or Illnesses

A. ANXIETY

- Prevalence estimates of anxiety disorders were reported as 17% in a small study of individuals with epilepsy (n=96);²⁹⁸ anxiety symptom estimates are 46%²⁹⁹

B. DEPRESSION

- Depression rates appear to increase as one moves from primary to secondary and tertiary care³⁰⁰
- Based on a systematic review the overall prevalence of active (current or past-year) depression in people with epilepsy was 23% (95% CI 21%–28%).³⁰⁰ A subset of the studies (5/14 total studies) reported that the overall odds of active depression were 2.77 (95% CI 2.09–3.67). For lifetime depression, 4 studies reported overall prevalence of 13% (95% CI 5–33%), and 3 studies reported overall odds of 2.20 (95% CI 1.07–4.51)³⁰⁰

C. PTSD

- In a large national longitudinal study, it was reported that individuals with PTSD had an elevated risk of developing epilepsy (HR=3.72, 95% CI 2.27–6.11) after adjustment for demographic data and medical and psychiatric comorbidities³⁰¹
- A study of 120 individuals with difficult-to-treat epilepsies that completed the Posttraumatic Stress Diagnostic Scale as part of an interview indicated that 50 participants identified a seizure that fulfilled the criteria for a traumatic event and 6 fulfilled all PTSD criteria caused by a traumatic seizure (three had PTSD)³⁰²

D. SUICIDE IDEATION

- A meta-analysis reported the pooled prevalence for suicide ideation in people with epilepsy (24 studies) and suicide attempts (18 studies) was 23.2% (95% CI 18-30%) and 7% (95% CI 3-17) respectively. The pooled rate of death due to suicide (10 studies) was 0.5% (95% CI 0.2-2%)³⁰³

E. ESTIMATES OF MENTAL HEALTH COMORBIDITIES BY SUBPOPULATIONS

- A study of 38 Spanish-speaking immigrants with epilepsy and 47 US-born persons with epilepsy reported that depression was significantly higher in the immigrant population (21.65±14.6 vs 14.50±10.2; p=.025)³⁰⁴

Mental Health Screening

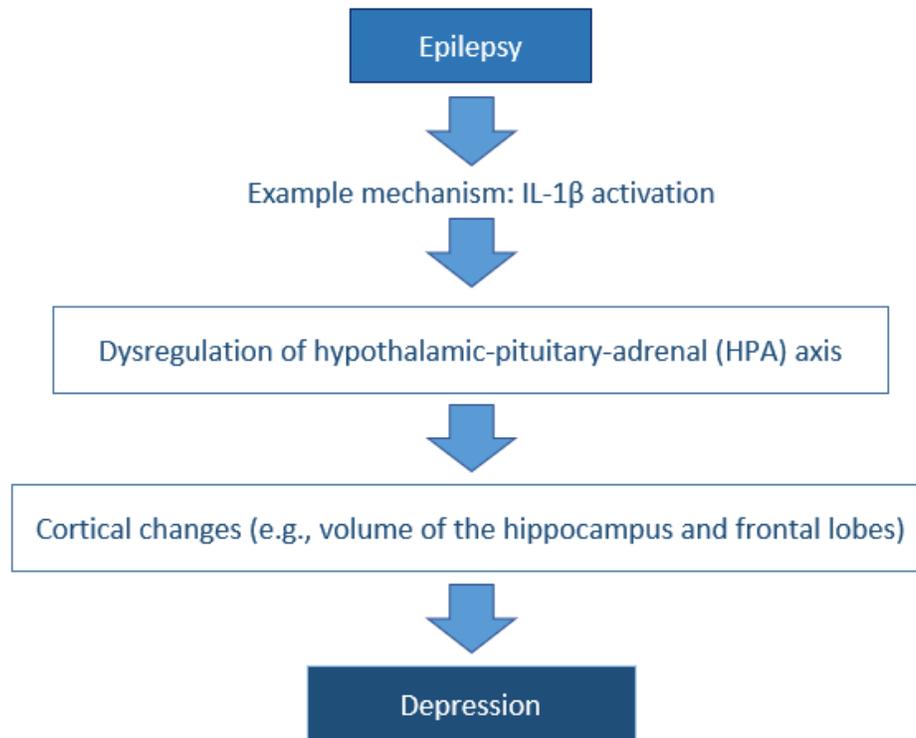
- The Beck Depression Inventory (BDI) I and II have been well-validated as a depression screening tool in epilepsy³⁰⁵
- Depression in people with epilepsy is categorized into four types suggesting screening tools and management may need to be adapted:³⁰⁶
 - i. Peri-ictal: Dysphoric, depressive symptoms or anxiety that precedes the seizure and subsides with the ictus
 - ii. Ictal: described in temporal lobe epilepsy, has an incidence of about 10%
 - iii. Post-ictal: second most common form, seen with unilateral frontal or temporal foci, and thought to be due to inhibitory mechanisms that result in cessation of seizure activity
 - iv. Inter-ictal: the most common form and includes episodes of major depression, dysthymia or affective mood disorder

Common Pathways

- The relationships between epilepsy and depression are believed to be bidirectional³⁰⁷
- Depression may develop through chronic stress exposure and inherent vulnerability.³⁰⁸ The unpredictability of seizures may induce learned helplessness³⁰⁹
- Depression may facilitate the epileptic activity through hyperactivity of the HPA axis and disturbances of glutamate and γ -aminobutyric acid (GABA) neurotransmitters,³⁰⁷ and cortical changes (Figure 3.13)

- A systematic review examining risk factors for depression in epilepsy living in community found that sociodemographic, disease-related, psychological, treatment-related, and genetic risk factors are consistently associated with depression³⁰⁰

Figure 3.13: Example of a common etiological pathway of epilepsy and depression³¹⁰



Chronic epilepsy leads to the dysregulation of the HPA axis³¹¹ via several mechanisms, one of those being activation of IL-1 β signalling in the hippocampus³¹² resulting in compromised hippocampal serotonergic transmission and behavioural symptoms of depression³¹²

Management of Epilepsy and Mental Health

- A systematic review of treatments for individuals with epilepsy and comorbid depression did not provide strong evidence. Oxcarbazepine, venlafaxine, and lamotrigine may improve mood, CBT improves both depression and epilepsy outcomes, and quality of life improves with treatment of depression among those with epilepsy³¹³
- A systematic review of self-management interventions for epilepsy indicated limited evidence for the effectiveness of interventions to improve quality of life in people with epilepsy. Two intervention types, the specialist epilepsy nurse and self-management education, have some evidence of benefit. At present it is not possible to advocate any single model of service provision for self-management in epilepsy³¹⁴

3.1.7 Frailty

There are many ways in which frailty is defined. Frailty is a medical condition of reduced function and health in older individuals. It often includes several dimensions or features, such as inactivity, poor nutrition, social isolation or loneliness, and the use of multiple medications.³¹⁵

Prevalence and Incidence of Frailty with Mental Health Conditions

- Reports about the prevalence of frailty and depression are highly variable; reported ranges are 2.5%–21.1% (cross-sectional studies) and 6.5%–25.3% (longitudinal studies at baseline) for frailty and depressive symptomatology³¹⁶
- The high variability is due to differences in the classification and nature of depressive symptomatology and liberal inclusion criteria (e.g., include dementia or stroke)

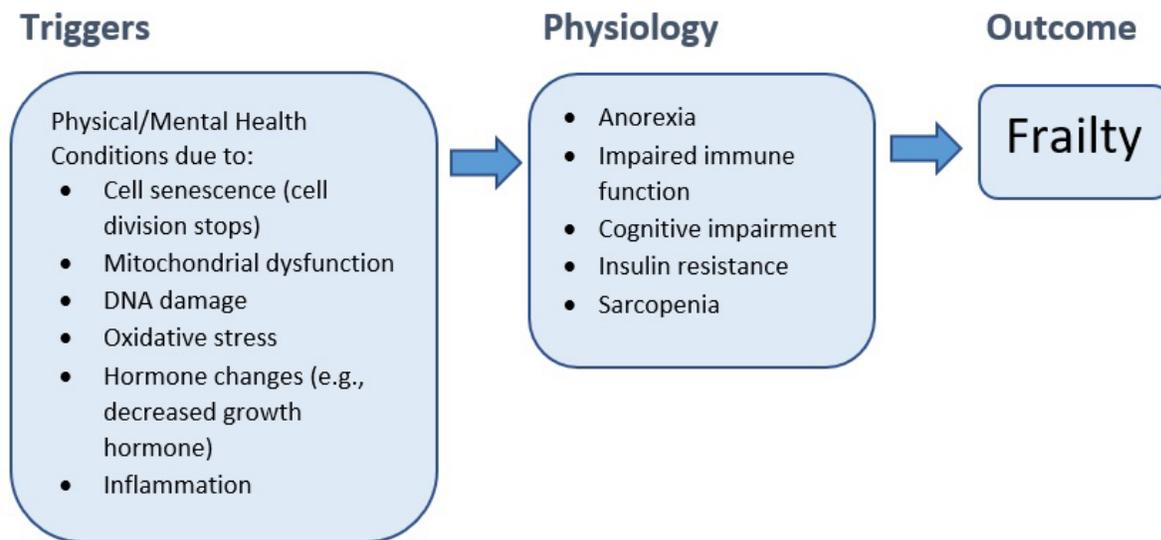
Mental Health Screening

- The frailty phenotype is a topic of debate. Experts agree frailty should include the assessment of mental health.³¹⁷ For this report, frailty is defined as a geriatric syndrome distinct from multimorbidity, characterized by increasing vulnerability and decreasing physical reserve due to accumulating multisystem deficits³¹⁸
- Screening of mental health in frailty is complicated as mental health may be considered part of the condition's definition
- Of the screening tools used to assess depression in frailty, the most common are the Geriatric Depression Scale, HADS, Yesavage Depression scale, and the CES-D. None have been specifically evaluated in these populations for reliability and validity

Common Pathways

- Although similar biological mechanisms such as subclinical CVD and inflammation are part of physical and mental health manifestations,³¹⁹ it is unlikely that one mechanism is largely responsible for either or both syndromes in all individuals
- Figure 3.14 illustrates the different biological pathways of frailty; many are shared with depression
- Frailty and depression have been associated with higher serum CRP and IL-6 levels. High circulating levels of neutrophil gelatinase-associated lipocalin (NGAL), an acute phase protein, may also be a factor³²⁰

Figure 3.14: Example of etiological pathways between frailty and depression^{321,322,323,324}



Management of Frailty and Mental Health

- When targeting frailty in disability prevention or intervention, identifying subgroups in which the largest effect is likely to result may be the most pragmatic approach in real-world settings with limited resources
- Group and individual sessions with a geriatrician may impact risk of depression with frailty^{325,326}
- The task force of the International Conference of Frailty and Sarcopenia Research (ICFSR) recommend the following guidelines for managing frailty:³²⁷
 - i. Address polypharmacy, the management of sarcopenia, the treatable causes of weight loss, and the causes of exhaustion (depression, anaemia, hypotension, hypothyroidism, and vitamin B₁₂ deficiency)
 - ii. All persons with frailty should receive social support as needed to address unmet needs and encourage adherence to a comprehensive care plan
 - iii. Include a multi-component physical activity programme with resistance-based training
 - iv. Provide protein/caloric supplementation when weight loss or undernutrition are present
- At this time, there is insufficient evidence to support therapies such as cognitive therapy, problem-solving therapy, vitamin D supplementation, and hormone-based treatment³²⁷

3.1.8 Huntington's Disease (HD)

HD is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of cognition. Adult-onset HD usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, depression, small involuntary movements, poor coordination, and trouble learning new information or making decisions. Affected individuals may have trouble walking, speaking, and swallowing. People with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. Individuals with the adult-onset form usually live about 15 to 20 years after signs and symptoms begin.³²⁸

Prevalence and Incidence of HD with Mental Health Problems or Illnesses

- Prevalence estimates of mental health-related concerns in HD include ranges between 15–69% for depression, with no significant differences in the estimates between men and women,³²⁹ 28–62% for apathy,^{330,331} 13% for irritability and aggression,³³¹ 1% for psychotic symptoms, and 2–20% for suicidal ideation or attempts³³²
- Reports of depression are most prevalent during stage 2 (~45%), where the individual is functioning at work, but at a lower capacity³³³
- Behavioural symptoms are common during the illness period before manifestation of motor symptoms (prodrome) and can lead to family disruption, social isolation, and withdrawal³³⁴
- Obsessive/compulsive behaviours are estimated at 13%.³³¹ Perseveration, or the repetition of a thought, behaviour, or emotion beyond the psychological context, is most common³³⁵

Mental Health Screening

- Mental health-related comorbidities reported in HD have included depression, irritability, anxiety, apathy, hallucinations, and perseveration³³⁶
- An assessment of the quality of behavioural rating scales commissioned by The Movement Disorder Society concluded that of 27 behavioural rating scales examined, the Irritability Scale was recommended for irritability; the Beck Depression Inventory-II and the Hospital Anxiety and Depression Scale were recommended for depression³³⁶
- Challenges associated with mental health screening are the co-occurrence of multiple behavioural symptoms, features of behavioural symptoms in HD, and the need to address stage- and disease-specific features, including cognitive impairment and insight³³⁶

Common Pathways

- Current evidence supports a model in which biological risk factors interacting with life stresses/events lead to the development of mental ill-health (Figure 3.15)³³⁷

- Irritability and impulsivity symptoms can be caused by the frustrations of loss of capacities, difficulties in expressing oneself, and related neurological/psychological fatigue
- Anxiety correlates with loss of essential functions, family, social and economic issues, depression, suicide, irritability, quality of life, pain, illness beliefs, and coping³³⁴

Figure 3.15: Common Etiological Pathways of Huntington’s Disease and Mental Health³³⁷



Management of HD and Mental Health

- Mental health management should be based on the identification of underlying environmental or somatic (e.g., pain, side effects of medications) triggers causing changes in mood or behaviour
- International Guidelines for the Treatment of Huntington’s disease suggest mindfulness-based cognitive therapy and Acceptance and Commitment Therapy, personalized cognitive stimulation, establishing routines, a structured programme of activities, and psycho-education for the family regarding diversion strategies to mitigate confrontations³³⁴
- There has been limited study of the effectiveness and risk/benefits of psychotropic medications. Current recommendations include SSRIs or serotonin noradrenaline reuptake inhibitors (SNRIs), or Mianserin or Mirtazapine in case of sleep disruption. Neuroleptics have been prescribed for symptoms such as agitation³³⁴
- For depression that is resistant to medications, electroconvulsive therapy (ECT) may be indicated³³⁴
- Suicide risk should be assessed regularly, including at diagnosis and when the disease starts to impact on daily activities. Individuals with active suicidal ideation and a plan require immediate psychiatric evaluation³³⁴
- Over the course of HD, symptoms of repetitive thoughts may replace obsessive-compulsive disorder. The distinction between obsessive-compulsive phenomena and perseverations will lead to differential approaches³³⁴

3.1.9 Inflammatory Bowel Diseases (IBDs)

HD is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of cognition. Adult-onset HD usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, depression, small involuntary movements, poor coordination, and trouble learning new information or making decisions. Affected individuals may have trouble walking, speaking, and swallowing. People with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. Individuals with the adult-onset form usually live about 15 to 20 years after signs and symptoms begin.³²⁸

Prevalence and Incidence of IBDs with Mental Health Problems or Illnesses

- Prevalence estimates of depression and anxiety within the IBD literature have most commonly been based upon anxiety and/or depression-specific questionnaires, such as the HADS and PHQ9, with reported ranges of 26-42% for depression, 20-28% for presence of at least one anxiety condition, and 11% for depressive disorder^{339, 340,341,342}
- Analysis of data from the 2012 Canadian Community Health Survey-Mental Health examined presence of generalized anxiety disorder using the WHO-CIDI lifetime criteria and self-reported IBD. The likelihood of individuals with IBD having anxiety was about twice that of those without IBD (OR=2.18; 95% CI 1.50-3.16) and this was similar among those with Crohn's disease and ulcerative colitis. The factors most closely linked with anxiety were childhood sexual abuse, female gender, and chronic pain³⁴³
- One survey suggested that 21% currently sought help for mental health issues while 12% reported having at least one psychological condition but not seeking treatment³⁴⁰
- The prevalence of mental health issues may be as high as 80% during flare-ups³⁴⁴
- Analysis of data from the National Health Insurance Research Database (3,590 people with IBD and 14,360 propensity score-matched individuals without IBD) reported low prevalence of bipolar disorder (BD) (0.72%). Regression modelling results reported heightened odds of BD among those with IBD (OR=2.10, 95% CI 1.30-3.38) compared to the comparison group. Those with ulcerative colitis had slightly higher likelihood (OR=2.23, 95% CI: 1.31-3.82) compared to the comparison group³⁴⁵

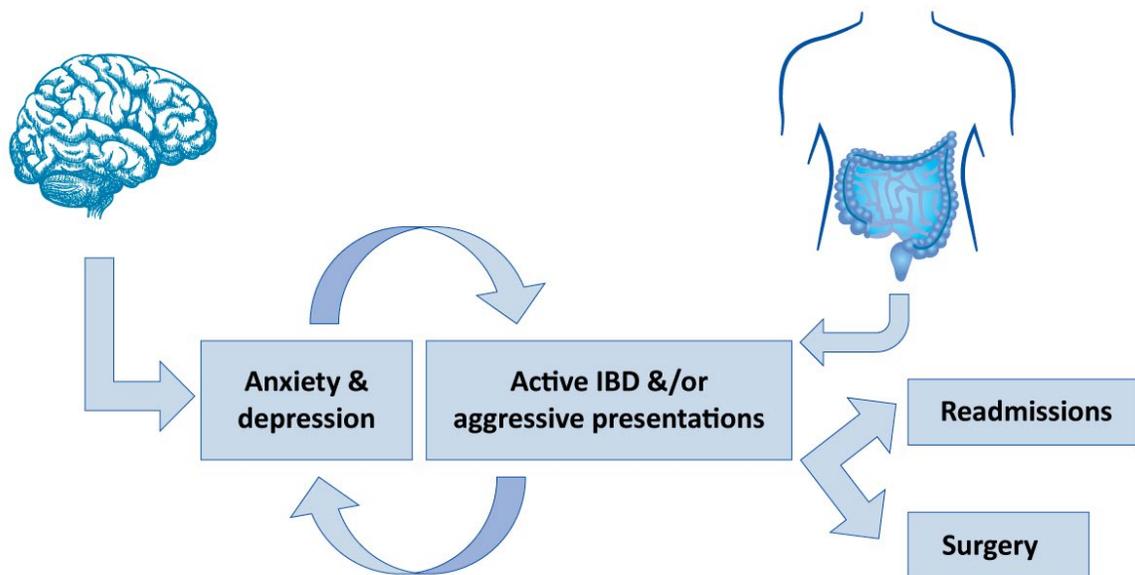
Mental Health Screening

- Anxiety and depression symptoms are commonly identified to be associated with increased IBD activity and reduced quality of life³⁴⁶
- Ongoing psychological distress can exacerbate disease activity, and increase the risk of flare-ups and health care costs³³⁹

Common Pathways

- Anxiety, depression, and relapse appear to be concomitant in a self-perpetuating cycle with devastating effects for IBD patients³⁴⁷
- Interactions between the digestive tract, and its microbiome, and the central nervous system are bidirectional and form the gut-brain-microbiota axis (GBA)^{348,349} that can influence central neurochemistry and behaviour³⁵⁰
- The aggravation of GI symptoms can be attributed to the worsening of co-morbid psychological disorders^{33,351}
- Figure 3.16 outlines how the use of anti-depressants can help reduce mental and physical health symptoms

Figure 3.16: Shared links between mental health and IBD³⁵²



Management of IBD and Mental Health

- Research suggests that the management of IBDs can be improved by reducing stress with support from psychological interventions, which in turn improves health-related quality of life³⁵³

The British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults suggest psychological interventions (psychotherapy, patient education and relaxation techniques) for anxiety, pain, and stress levels improve mood⁵⁷⁰

- The availability of psychotherapy is limited for GI conditions due to limited psychological resources available to these populations.³⁵⁴ Online approaches have been proposed, however, a systematic review of online psychological interventions found limited research and insufficient evidence to demonstrate the effectiveness of online CBT to manage mental and physical outcomes in gastrointestinal diseases³⁵⁵

- A Cochrane Review reported no benefit of psychological interventions for adults with IBD³⁵⁶
- The evidence for benefits of CBT is mixed^{357,358,359}
- Mindfulness as an adjunct to pharmacological therapy may improve psychological symptoms in IBD and facilitate coping with symptoms during a disease flare^{360,361,362}
- Gut directed hypnotherapy has an established evidence base for the control of IBS symptoms, however more research is needed to determine if there are mental health benefits in those with IBD^{363,364}

3.1.10 Kidney Disease (Chronic) or CKD

HD is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of cognition. Adult-onset HD usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, depression, small involuntary movements, poor coordination, and trouble learning new information or making decisions. Affected individuals may have trouble walking, speaking, and swallowing. People with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. Individuals with the adult-onset form usually live about 15 to 20 years after signs and symptoms begin.³²⁸

Prevalence and Incidence of Chronic Kidney Disease with Mental Health Problems or Illnesses

- Diagnosis of major depression in individuals with CKD is challenging as the symptoms of uraemia (increased blood levels of urea) can mimic those of clinical depression³⁶⁶
- The overall prevalence estimate of depression is reported at 27%; estimates vary according to disease stage ranging from 27% for those with kidney transplant to 39% for those in the end stages of the disease^{367,368}
- Incidence of self-reported depressive symptoms is reported to be higher in individuals with chronic graft failure compared with those with well-functioning grafts or dialysis patients awaiting transplantation
- Results of a nationwide population study of people diagnosed with schizophrenia (n = 27,516), and matched by age and sex controls, indicated higher odds of CKD in those with schizophrenia (adjusted OR = 1.62, 95% CI 1.45–1.82)³⁶⁹
- Among those receiving hemodialysis, higher levels of depression are found among those who are younger and of Chinese ethnicity³⁷⁰

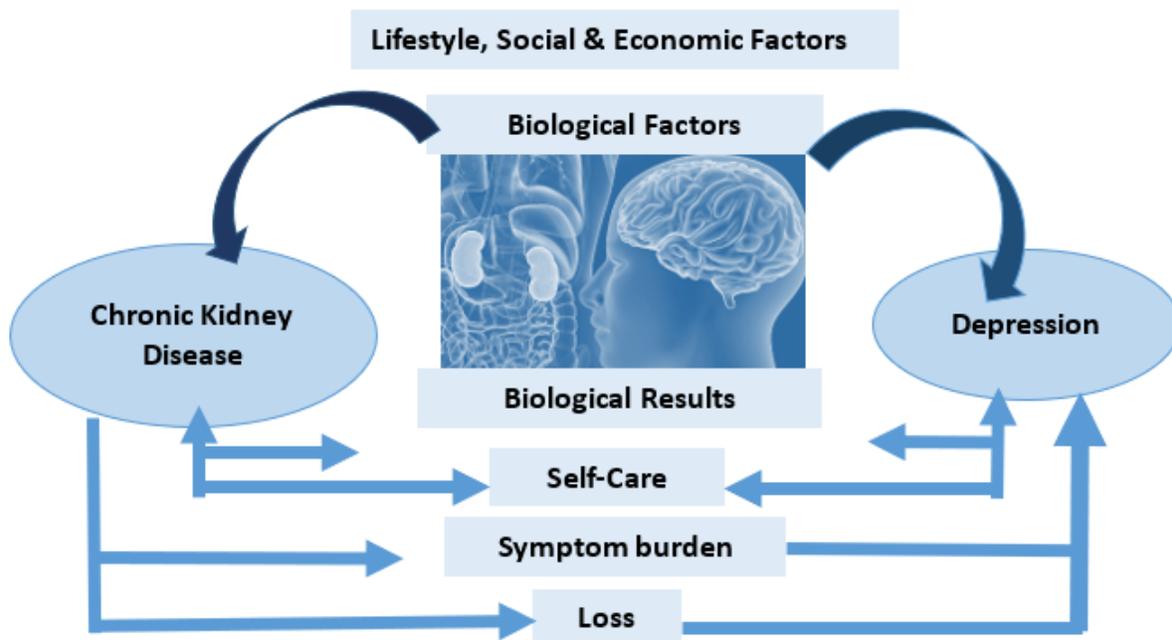
Mental Health Screening

- Some research suggests there is insufficient high-quality data to show that screening for, or treatment of, depression in CKD populations improves clinical symptoms and quality of life³⁶⁶
- Other studies support screening programs and suggest screening for depression should take place at key transition points such as at the initial evaluation, dialysis initiation, and regular intervals thereafter³⁶⁶

Common Pathways

- Health related, socio-economic, and biological factors contribute to CKD and comorbid mental ill health (Figure 3.17) ^{337,371}
- The relationships among kidney function tests, self-care factors, and mental health are bidirectional; one-directional pathways are reported between associated symptom burden and loss in relation to depression in CKD ^{337,371}
- Inflammatory cytokines, deregulation of the HPA axis, disturbance in glucose-insulin homeostasis, and oxidative stress are thought to be involved in the etiology of depression and CKD ³⁷¹
- Chronic pain, a frequent symptom in CKD, can induce clinical depression through chronic, stress-mediated activation of the HPA axis
- Psychosocial factors such as changed identity, symptom burden, fear of dialysis, uncertainty of the disease outcome, negative experiences with the healthcare system, lifestyle disruption, financial struggles, changes in self-concept and self-esteem, guilt feelings for the perceived burden on family members, and side effects of medications may contribute to depression ³⁷¹
- Donor transplant recipients may mourn the death of the unknown deceased donor and may feel guilty for having their lives saved at the cost of another life. Live donor recipients may struggle with handling their indebtedness to the donors or feel guilty and fear graft failure ³⁷¹

Figure 3.17: Common Etiological Pathways of Chronic Kidney Disease and Mental Health ^{337,371}



Biological Factors	Psychosocial Factors
<ul style="list-style-type: none"> • Uremic toxins • Chronic inflammation • Disturbance of glucose-insulin homeostasis • HPA axis dysregulation • Chronic pain leading to stress-mediated activation of the HPA axis • Side effects of medications 	<ul style="list-style-type: none"> • Changes in lifestyle, social role, self-concept, and self-esteem • Decreased autonomy and control • Limited capacity for self-expression, productivity, and social involvement • Body image concerns • Low self-esteem • Symptom burden; fear of dialysis, fear of uncertain future, ill health, death and dying; existential questions, meaning of life • Negative experiences with healthcare system • Guilt feelings for the perceived burden on family members • Low perceived social support • Unemployment
	
<p>Changes in neuro-hormonal activity</p>	
	
<p>Somatic symptoms</p>	
<ul style="list-style-type: none"> • Sleep disturbance, pain, fatigue • Reduced appetite • Decreased sexual drive 	

Management of Chronic Kidney Disease and Mental Health

A. PHARMACOLOGICAL INTERVENTIONS

- The benefits and harms of anti-depressants need to be weighed. The medications are broken down by the liver and end products may not be removed significantly by the kidneys or through dialysis. Further concerns are increased risk of drug interactions and accumulation of toxic metabolites. The evidence about the effectiveness of antidepressants versus placebo in patients with CKD3-5 and depression is insufficient and well-designed RCTs are needed³⁶⁶

B. PSYCHOLOGICAL INTERVENTIONS

- CBT may be beneficial during changes in dialysis regimen³⁶⁶

A potential target for management is illness perceptions;³⁶⁶ a person's cognitive appraisal and understanding of their health condition.⁵⁷⁸ These perceptions may include both positive and negative illness beliefs that can influence the ability to cope with the disease and to perceive it as manageable or threatening⁵⁷⁹

- Positive illness perceptions are associated with higher autonomy and self-esteem levels which can support mental health³⁶⁶

C. SELF-MANAGEMENT INTERVENTIONS

- An RCT of a nurse-led, in-center breathing training program for individuals on maintenance hemodialysis reported significantly greater improvements in depression (Beck Depression Inventory-II scores) compared to controls³⁷²
- Chronic disease self-management programming that includes activities such as exercise therapy may foster mental health³⁶⁶

3.1.11 Metabolic Syndrome (MetS)

MetS is a health condition that, if left untreated, increases the risk of many chronic conditions such as type 2 diabetes and cardiovascular disease. MetS is diagnosed when a person has three of the following conditions: high blood pressure, high blood glucose levels, high triglycerides, low HDL-cholesterol, or large waist circumference.⁶

Prevalence and Incidence of MetS with Mental Health Problems or Illnesses

- Approximately 40% of those with a serious mental illness meet National Cholesterol Education Panel-Adult Treatment Panel III (NCEP-ATP-III) guidelines for MetS^{373,374}
- A meta-analysis reported that the prevalence of MetS is 58% higher in people with mental health conditions than in the general population³⁷⁵ and the risk was similar in those with schizophrenia, bipolar disorder (BD), and major depressive disorder (MDD)
- A meta-analysis reported that in individuals with BD, using antipsychotic medication contributed to 1.72 times greater risk of MetS compared to those not taking antipsychotic medication³⁷⁶
- A meta-analysis reported that individuals with schizophrenia have a significantly higher risk of MetS (OR=2.35);³⁷⁷ metabolic disturbances increase with illness duration³⁷⁸ and age.³⁷⁹ Individuals with schizoaffective disorder have slightly higher rates of MetS compared to those with schizophrenia³⁸⁰
- In a cross-sectional study of individuals with verified diagnosis of MDD and MetS, effect modifications were observed by sex and age; younger females (20-49 years) with MDD were more often affected by MetS than younger females without MDD (OR=2.21, 95% CI 1.39-3.50). This association was not observed in older participants (50-82 years)³⁸¹
- Among individuals with alcohol dependence syndrome, the prevalence of MetS was found to be 21% and 10% according to revised National Cholesterol Education Programme Adult Treatment Panel (NCEP ATP-III) criteria and International Diabetes Federation (IDF) criteria, respectively.
- Among individuals with opiate dependence syndrome, the prevalence of MetS was found to be 20% and 5% according to revised NCEP ATP III criteria and IDF criteria, respectively³⁸²

Mental Health Screening

- Screening for metabolic syndrome in individuals with mental health conditions, particularly those taking anti-psychotic medications, is part of standard care
- Based on a validation study, the HADS is considered to be a reliable screening tool for current major depressive episode and generalized anxiety disorder in middle aged and elderly population with and without MetS. Optimal thresholds of the HADS-Depression subscale for current MDD is ≥ 9 for individuals with MetS. Optimal threshold of the HADS-Anxiety subscale is ≥ 9 for current GAD in individuals with and without MetS³⁸³

Common Pathways

- Antidepressant medications, especially tricyclic antidepressants (TCAs) and serotonin and norepinephrine reuptake inhibitors (SNRIs), change heart-related regulation,^{384,385} which contributes to hypertension among medication users³⁸⁶
- A meta-analysis of treatment trials that evaluated short-term weight change after antidepressant treatment found that amitriptyline, mirtazapine, and paroxetine were associated with a greater risk of weight gain³⁸⁷ which can lead to MetS
- Recent studies point to MetS abnormalities in depressed persons with many atypical, neurovegetative symptoms, including hyperphagia, hypersomnia, lack of energy, and leaden paralysis^{384,388,389}

There are several shared etiological pathways between mental health and MetS (Figure 3.18) summarized as follows:

A. LIFESTYLE AND MEDICAL CARE

- Health behaviours such as poor quality diet, smoking, and lack of physical activity may be part of the shared etiology of MetS and serious mental illness^{390,391}
- Long-term treatment with first and second-generation antipsychotic medication can increase the risk of diabetes, hypertension, and hyperlipidaemia³⁹²
- The reduced likelihood of people with mental health conditions receiving standard (optimal) levels of medical care likely contributes to an unhealthier metabolic profile³⁹³

B. CENTRAL AND PERIPHERAL IMMUNE, METABOLIC, AND ENDOCRINE DYSREGULATIONS

- Different groups with mental health conditions share inherent features of deregulated homeostasis systems, including the HPA-axis and inflammatory responses linked to MetS development
- Disturbances of glucocorticoid sensitivity³⁹⁴ accompanied with hypercortisolemia induces lipolysis, the release of fatty acids, and synthesis of very-low-density lipoprotein (VLDL), resulting in hypertriglyceridemia³⁹⁵
- White adipose tissue produces inflammatory cytokines and hormones (e.g., leptin) and contributes to pathogenic immune- and metabolic-related responses in the central nervous system and peripherally

- Inflammatory cytokines can enter the brain and lead to decreased nerve cell development (neurogenesis) in emotion-regulating brain structures.³⁹⁶ They also reduce synthesis of serotonin and increase synthesis of tryptophan breakdown products (catabolites), which alter neurotransmission and lead to neuronal damage³⁹⁷
- Proinflammatory response stimulates the release of lipids in the bloodstream, resulting in a reduction in HDL-C and an increase in triglycerides. The sustained HPA-axis and inflammatory activation may affect insulin sensitivity³⁹⁷
- Higher levels of oxidative and nitrosative stress (overproduction of nitric oxide) may be involved in both the development of mental health issues or problems and metabolic dysregulations³⁹⁸

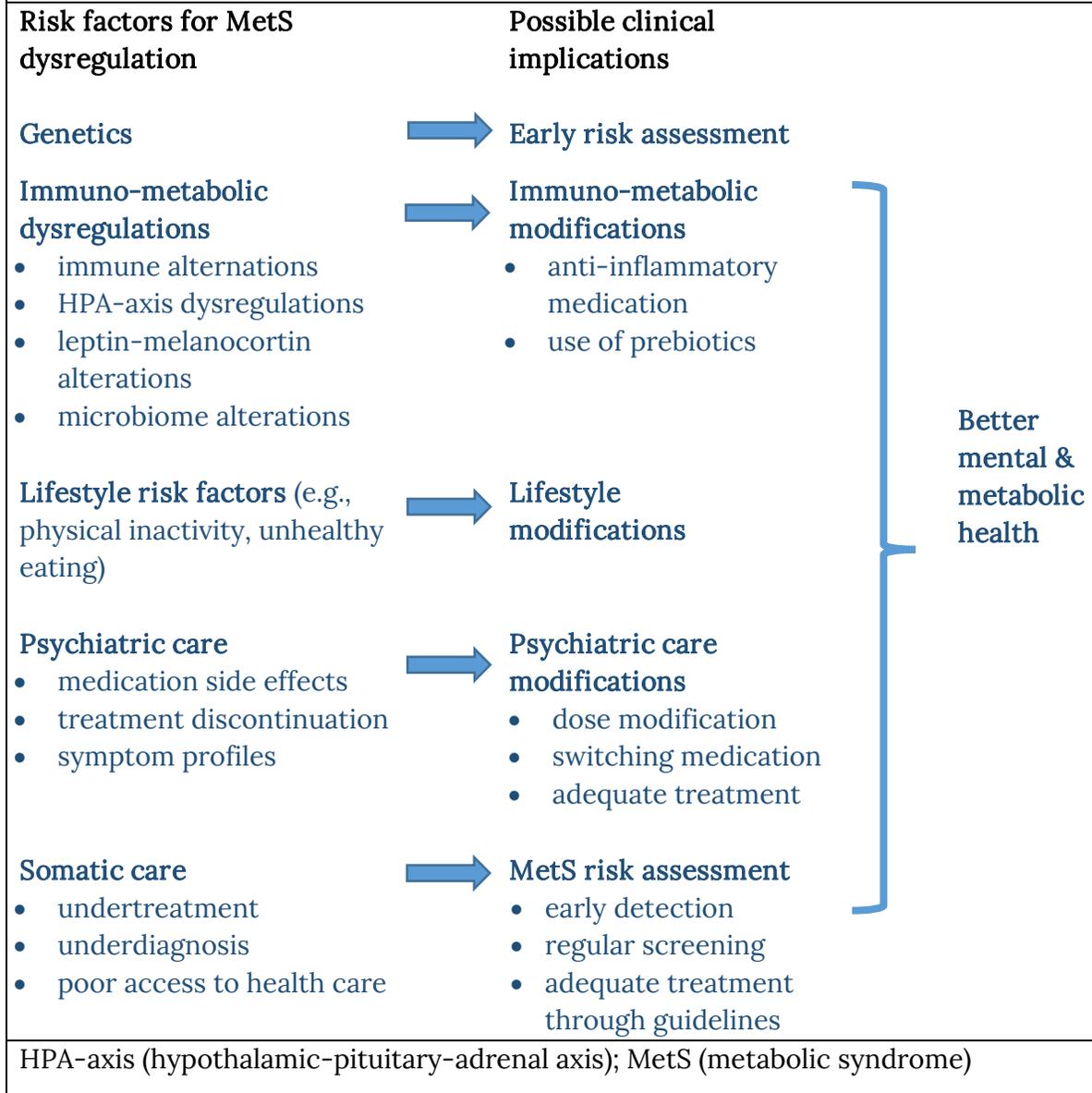
C. SHARED GENETIC VULNERABILITY

- There appears to be pharmacogenetic risk for metabolic syndrome and poor mental health^{374,399}
- Certain genes seem to be shared between mood disorders and cardiometabolic conditions,⁴⁰⁰ including CACNA1D (encoding calcium voltage-gated channel subunit $\alpha 1 D$), FTO (encoding fat mass and obesity-associated protein), BDNF (encoding brain-derived neurotrophic factor), POMC (encoding proopiomelanocortin), and IGF1 (encoding insulin-like growth factor 1)
- Shared genetic pathways include corticotropin-releasing hormone, axonal guidance, serotonin and dopamine receptors, circadian rhythm, and leptin signaling
- Leptin genes, MTHFR (encoding methylenetetrahydrofolate reductase), and serotonin receptor 2C genes may be involved in the pathogenesis of both MetS and schizophrenia⁴⁰¹

D. GUT MICROBIOME ALTERATIONS

- Commensal bacteria, which act on the host's immune system to induce protective responses that prevent colonization and invasion by pathogens, are a connecting factor to both metabolic and mental health. The penetration of bacteria across the gut epithelium may modulate a range of proteins involved in brain development and plasticity, resulting in chronic low grade inflammation, which further induces MetS⁴⁰²

Figure 3.18: Factors underlying shared etiology of MetS and mental health with clinical implications³⁹⁵



Management of MetS and Mental Health

A. ANTIPSYCHOTIC MEDICATIONS AND METABOLIC MONITORING

- Baseline metabolic screening should be part of standard care for all individuals with a regular prescription of any antipsychotic medication⁴⁰³
- Reports of routine metabolic screening practices in high-income countries (USA, UK, Australia, Canada and Spain) have shown that metabolic testing was inconsistent despite widespread dissemination of the guidelines^{404, 405}
- A systematic review reported there was some indication of a possible protective effect by antipsychotics in preventing diabetes and high blood cholesterol levels (e.g., hyperlipidaemias). Long-term prospective studies are required for accurate

appraisal of risk for diabetes, hypertension, and hyperlipidaemia in those exposed to antipsychotic polypharmacy⁴⁰⁶

- A study of mental health based primary care of individuals accessing services of a community mental health center that assessed quality indicators related to outpatient medical visits, diabetes HbA1c⁸ monitoring, and metabolic monitoring of antipsychotic treatment reported that the program improved metabolic monitoring for individuals taking antipsychotics, but did not impact other quality indicators⁴⁰⁷

B. PHARMACOLOGICAL INTERVENTIONS

- A meta-analysis of 22 studies reported that antidepressants, mainly SSRIs, reduced cytokine levels during treatment,⁴⁰⁸ and may be protective against MetS

3.1.12 Obesity

Obesity (BMI > 30) is characterized by excess or abnormal body fat that can impair one's health. Many organizations, including Obesity Canada, the Canadian Medical Association, the American Medical Association, and the World Health Organization, consider obesity to be a chronic disease because it is a lifelong process to manage it.⁴⁰⁹

Prevalence and Incidence of Obesity with Mental Health Problems or Illnesses

A. ANXIETY AND DEPRESSION

- Mental health concerns, particularly depression, are common in obesity (>50% screen positive)
- Studies of patients seeking bariatric surgery report prevalence rates of 21 – 56% for any current Axis I disorder, 22–32% for mood disorders, and 15–24% for anxiety disorders⁴¹⁰

B. BIPOLAR DISORDER

- A meta-analysis of nine cross-sectional epidemiological studies reported that obesity is associated with an increased prevalence of bipolar disorder (BD) (OR=1.77, 95% CI 1.40–2.23).⁴¹¹ The rate of obesity in women with BD has been found to be higher than in men with BD⁴¹²

C. EATING DISORDERS

- Studies of patients seeking bariatric surgery report prevalence rates of 3–23% for binge eating disorders (BED)⁴¹⁰

⁸Glycated hemoglobin refers to the attachment of glucose (a type of sugar) molecules in the blood to hemoglobin molecules. Hemoglobin A1c, or HbA1c is a test that can be done to detect how much glucose has attached to hemoglobin in a given time period and is an indicator of blood glucose control

D. SUBSTANCE USE

- Among candidates for bariatric surgery, the prevalence of being a former or recent tobacco user is 55%; history of a substance use disorder is 13%⁴¹³

E. ESTIMATES OF MENTAL HEALTH COMORBIDITIES BY SUBPOPULATIONS

- In two longitudinal studies of African Americans (17-29 years), 23%–27% showed increasing substance use over time, 18%–27% showed increasing obesity over time, and 9%–11% showed increases in both¹²⁶
- Depression in obesity varies by race and income. Among white women, obesity is positively associated with depressive symptoms across income levels, while obesity was not associated with depression for African American women at any income level. Obesity was only associated with depressive symptoms among middle-income white men (OR=1.44, 95% CI 1.02–2.03) and among high-income African American men (OR=4.65, 95% CI 1.48–14.59)⁴¹⁴

Mental Health Screening

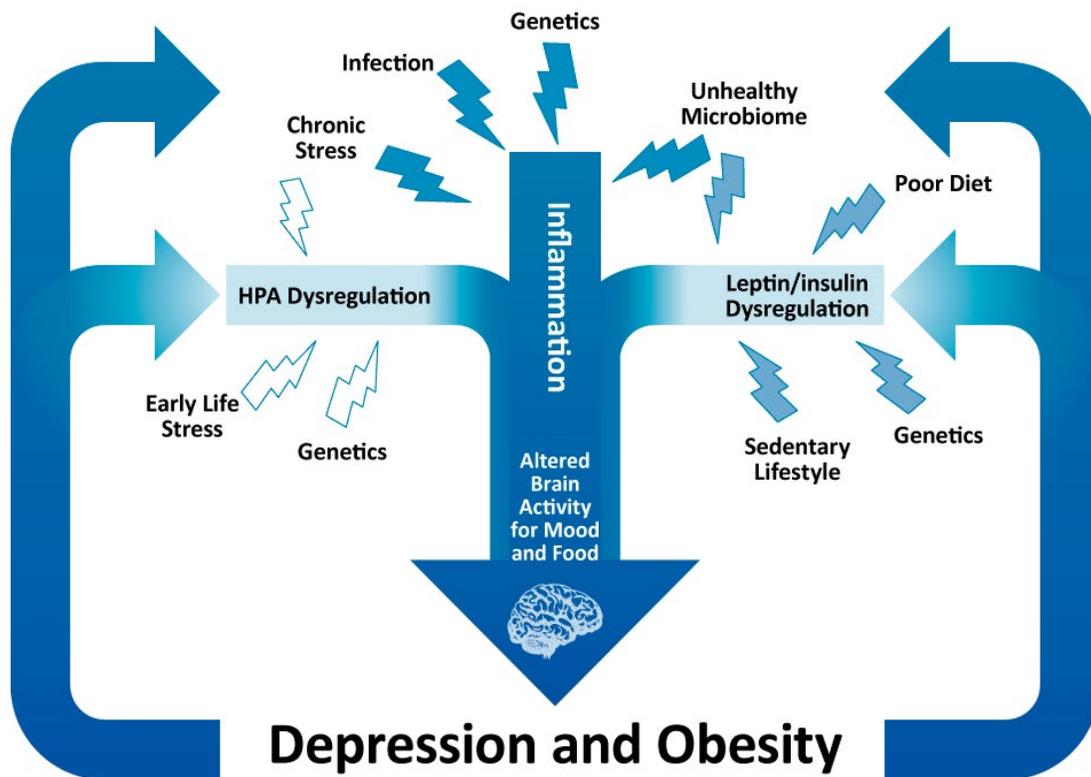
- A typical tool used for mental health screening is the Patient Health Questionnaire-9 or PHQ-9
- Screening is particularly recommended in sarcopenic obesity, defined as the presence of loss of muscle and obesity typically related to aging

Common Pathways

A. DEPRESSION

- Shared biological pathways of depression-obesity include genetics, alterations in systems involved in homeostatic adjustments (HPA axis, immuno-inflammatory activation, neuroendocrine regulators of energy metabolism including leptin and insulin, and microbiome) and brain circuitries integrating homeostatic and mood regulatory responses (Figure 3.19)^{415, 416, 417}
- Factors that can induce inflammation and depressive symptoms include psychological stress and obesity.⁴⁴ Central adiposity in obesity is a source of inflammatory cytokines that can promote neuroinflammation. Metabolic disturbances in obesity can lead to increases in cortisol, leptin, and insulin levels resulting in HPA axis dysregulation and insulin resistance, with subsequent inflammation and worsened depression⁴¹⁸
- Obesity and the co-morbid chronic conditions associated with it are closely associated with multiple mental health concerns.⁴¹⁹ Factors such as prejudice, stigmatization, and employment discrimination may contribute to both obesity and poor mental health⁴²⁰
- A systematic review examining whether obesity and depression relationships are bi-directional reported that the association between overweight and depression was not found to be significant in either direction. The strength of the association is greater for the direction leading from depression to obesity and more pronounced for young and middle-aged women⁴²¹

Figure 3.19: Shared etiology of obesity and depression⁴¹⁵



B. BIPOLAR DISORDER (BD)

- BD and obesity also share common pathogenic pathways:
 - i. Similar phenotypic expression of the brain reward system is observed in both overeating behaviour and hypomania, which is related to self-stimulating behaviours such as food seeking and hypomanic symptoms⁴²²
 - ii. Regulatory pathways, especially mediated by serotonin and dopamine, are involved with energy balance and mood modulation⁴²³
 - iii. Obesity and BD are associated with cognitive dysfunction and body mass index, and depressive and manic episodes are negatively correlated with memory and executive function.⁴²⁴
 - iv. The HPA axis may be disrupted by increased leptin released by adipose tissue, which affects normal mood modulation, and leads to extreme and/or rapid mood fluctuations such as depression, mania, or the cycle of both
 - v. Adipose tissue in obese individuals can release increased amounts of inflammatory cytokines, such as IL-6 and TNF- α , leading to HPA axis abnormalities and are linked with BD⁴²⁵
 - vi. Mood stabilizing drugs like lithium, valproate, and certain antipsychotics (e.g., olanzapine) are related to increased food intake and weight gain. The obesity-BD link may mutually increase the occurrence of both obesity and BD⁴¹¹

C. SCHIZOPHRENIA

- The links between obesity and schizophrenia are also multifactorial and include dietary intake, treatment with second-generation antipsychotics, particularly clozapine and olanzapine, and psychosocial factors such as social isolation, negative discrimination, stigma, and low SES.⁴²⁶ Factors such as deficits in executive function and memory, residual psychotic symptoms, self-management skills, and substance misuse can be barriers to management of the conditions⁴²⁷

Management of Obesity and Mental Health

A. BEHAVIOURAL AND LIFESTYLE INTERVENTIONS

- A meta-analysis that examined psychosocial effects of exercise in individuals with obesity did not show that exercise was better than control conditions for quality of life or depression⁴²⁸
- Behavioural interventions that involve treatments that modify behaviour, emotions, and cognition can improve both psychological and physical well-being⁴¹⁹
- Current work is being done to investigate tools which can engage self-regulation and behaviour change targets to improve mood and weight outcomes that include microbiome-gut-brain and immune pathways in integrated behavioural treatment⁴²⁹

B. DIGITAL HEALTH APPLICATIONS

- Mobile health (mHealth), a health practice supported by mobile devices, such as mobile phones, monitoring devices, personal digital assistants (PDAs), and other wireless devices, may have potential in managing obesity and mental health. They can be used in everyday lives (i.e., in real time) and in natural settings (i.e., real world) and may facilitate remote access to health services
- Apps that monitor weight, physical activity, psychological wellness, cognitions, and emotions separately generally show favourable outcomes. No mobile app was found that integrated all of these features to enable simultaneous management of overweight/obesity and depression/anxiety⁴³⁰

C. METABOLIC MONITORING

- Current guidelines related to management of overweight and obesity in adults align with risk profiles for CVD⁴³¹ and integrate guidelines for cardiometabolic monitoring for those with weight gain related to anti-psychotic use (Figure 3.20)

Figure 3.20: Cardiometabolic monitoring of individuals receiving anti-psychotics as mental health treatment

a) Suggested algorithm for cardiometabolic monitoring of patients treated with antipsychotics.

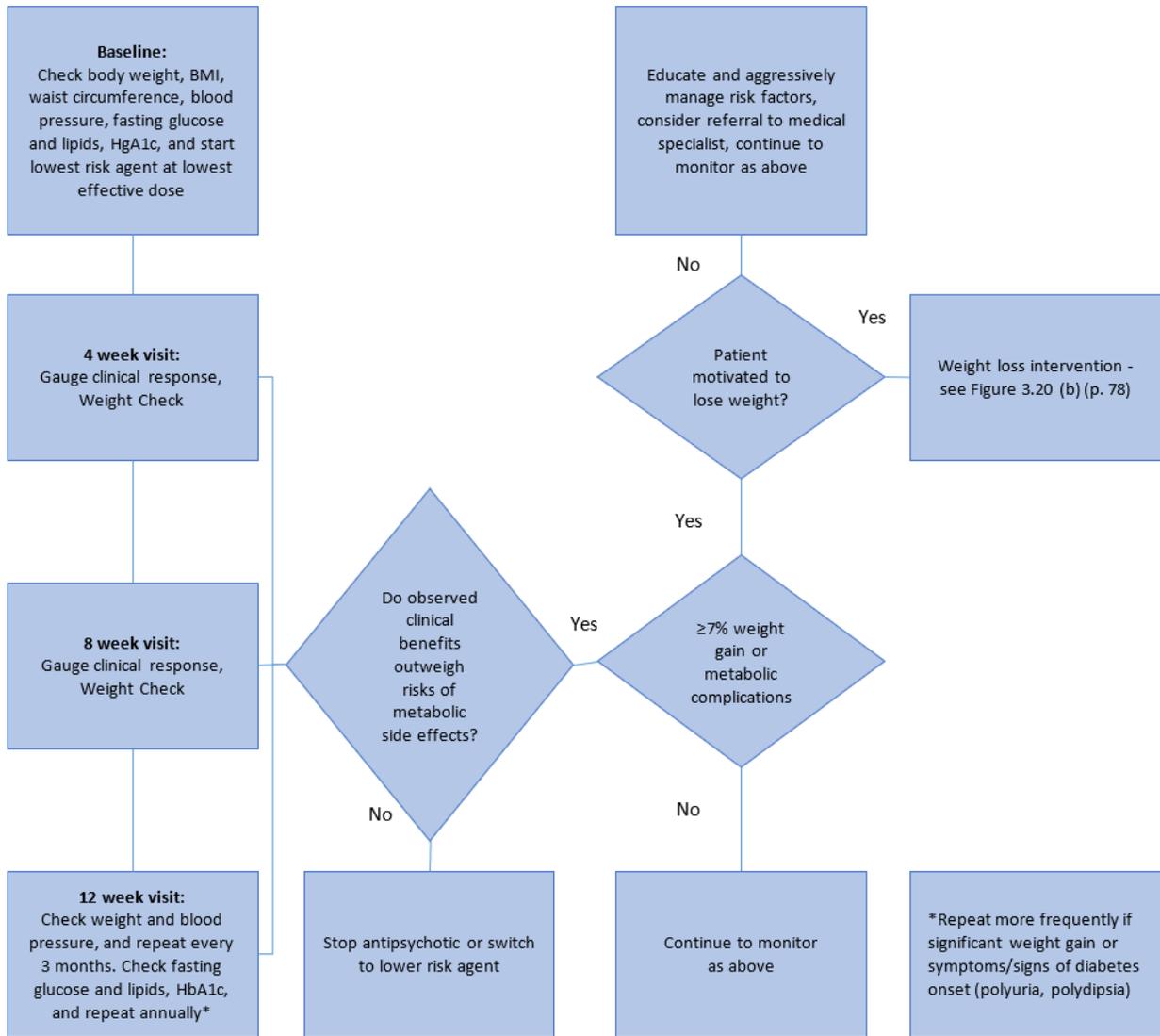
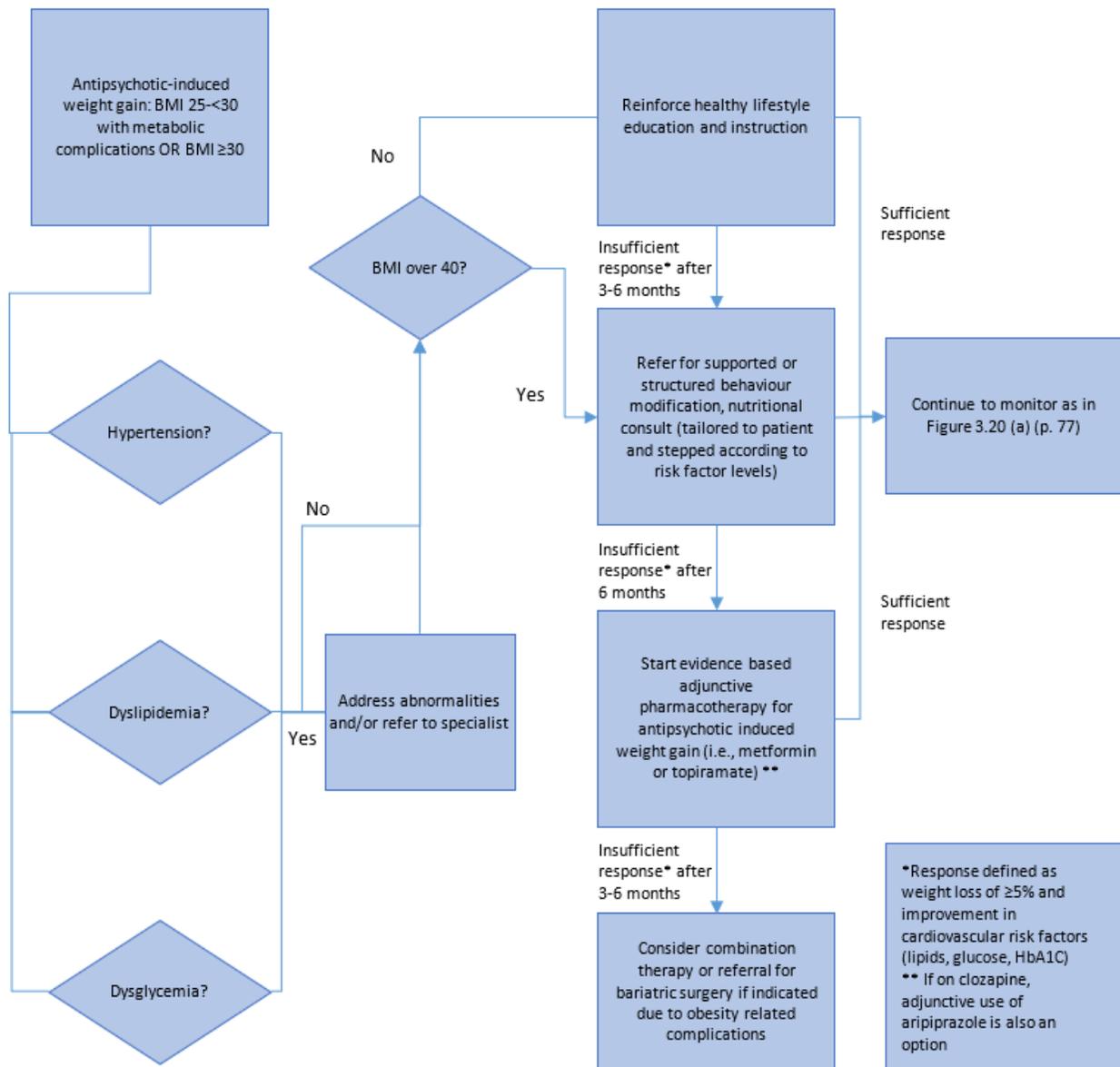


Figure 3.20: Cardiometabolic monitoring of individuals receiving anti-psychotics as mental health treatment

b) Suggested algorithm for managing antipsychotic-related weight gain.



D. PHARMACOLOGICAL AND SURGICAL INTERVENTIONS

- When pharmacological and surgical interventions are combined with psychological supplements via behavioural health interventions, treatment adherence and long-term sustainability are enhanced⁴¹⁹
- Antipsychotics are currently the only medication that effectively treat psychosis⁴³² and reduce risk of mortality.⁴³³ Other psychotropic medications, including mood stabilizers and antidepressants, can also lead to weight gain, and adversely affect lipid and glucose metabolism.⁴³⁴ Healthcare providers need to consider these factors when making treatment choices⁴³⁵ and implement integrated education,

assessment, and care for those with mental health concerns and at risk for weight gain

E. INTERVENTIONS FOR SUBPOPULATIONS

- Based on limited research about the experiences of lesbian women, overweight and obesity were associated with more public identification as a lesbian, more depressive symptoms, increased heavy drinking, and longer relationship length. These findings suggest health promotion and weight loss intervention programs for lesbians should incorporate psychological, relationship, and alcohol use components to reduce overweight and obesity⁴³⁶

3.1.13 Parkinson's Disease (PD)

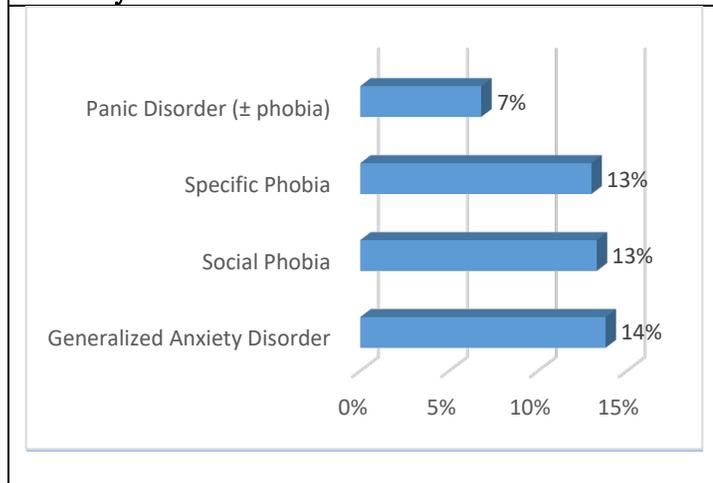
PD is a neurodegenerative disorder that affects mainly dopamine-producing (“dopaminergic”) neurons in a specific area of the brain called substantia nigra. The symptoms may include tremor, slowed movement, rigidity of the limbs, as well as gait and balance problems. The symptoms generally develop slowly over years.⁴³⁷

Prevalence and Incidence of PD with Mental Health Problems or Illnesses

A. ANXIETY

- A meta-analysis of 45 studies reported an average point prevalence of anxiety disorders in PD of 31%, with non-episodic anxiety being more prevalent than episodic anxiety⁴³⁸
- Estimates among subtypes of anxiety-related conditions range from 6.8 to 14%. Of the samples, 31% fulfilled the criteria for current multiple anxiety disorders. Based on anxiety rating scale cut-off scores, clinically significant anxiety symptoms were present in a weighted average of 25.7%. (Figure 3.21)⁴³⁸

Figure 3.21: Average Point Prevalence of Anxiety-Related Conditions in PD



B. DEPRESSION

- Depression affects 44%-51.7% of all people with PD⁴³⁸
- Depression and PD share overlapping symptoms such as reduced facial expression, problems with sleeping, fatigue, psychomotor retardation, and reduced appetite.

These similar symptoms may contribute to the underdiagnosis of depression in patients with PD⁴³⁹

- Risk factors for the development of depression in PD are being female, having family problems, early manifestations of disease, “atypical” parkinsonism, concomitant affective disorders such as anxiety, apathy, sleeplessness, and psychoses,⁴⁴⁰ history of depression, concomitant moderate cognitive disorder, and a higher daily dose of levodopa⁴⁴¹

C. IMPULSE CONTROL DISORDERS

- Prevalence estimates of impulse control disorders in PD have been reported to be 6%. Among this group, most were men (81%), had a mean age-at onset of PD of 48 years and disease duration of 8 years. Punding was the most frequent behavioural problem (57%), 42% exhibited aggressive hypersexuality, 27% compulsive eating, 24% pathologic shopping, and 21% compulsive medication⁴⁴²

D. PTSD

- A longitudinal study conducted in Taiwan reported an increased risk of developing PD in people with PTSD (HR=3.46, 95% CI 1.72–6.96) compared with individuals without PTSD⁴⁴³

Mental Health Screening

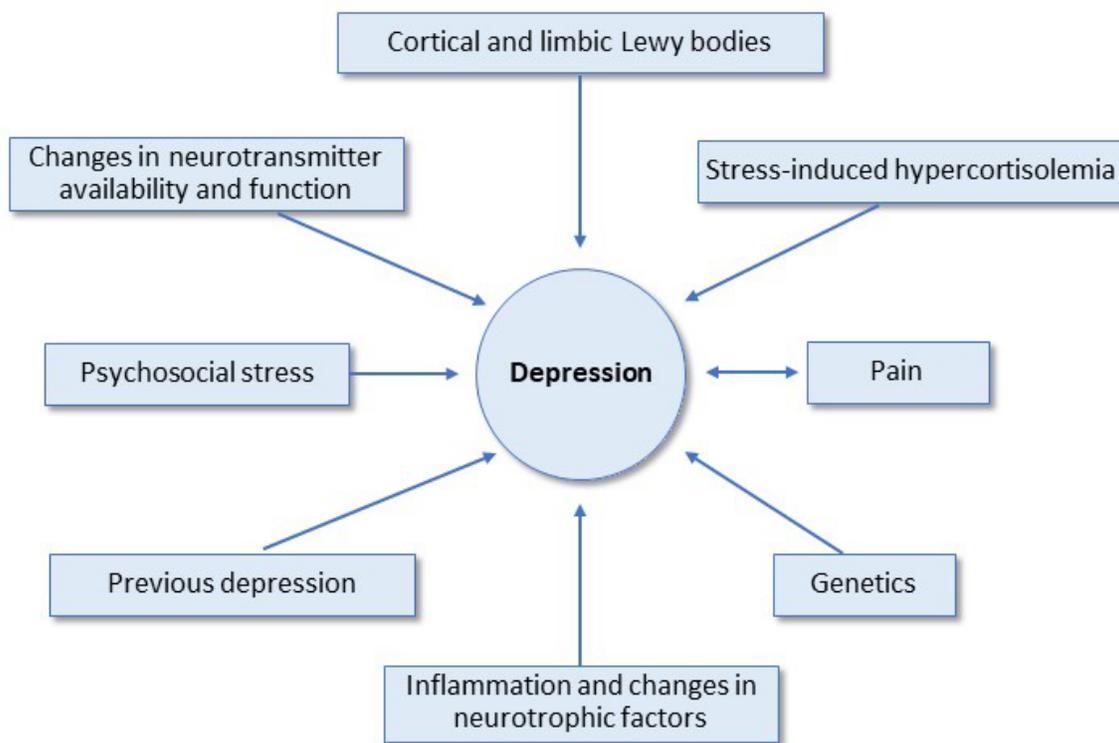
- The Movement Disorder Society recommends that the selection of screening tools needs to be guided by testing aims. The most suitable scales for screening for depression disorders are the Ham-D and BDI scales, the geriatric depression scale, the HADS, and the Montgomery Asberg Depression Rating Scale (MADRS)^{441,444}
- Use of the Ham-D and BDI, the Montgomery rating scale, and the Zung self-rating scale are considered more useful for assessment of the severity of the symptoms of depression⁴⁴¹
- Up to 68% of individuals with Parkinson’s are reported to have depression;⁴⁴⁵ there appears to be higher prevalence among men (65%) compared to women (35%)²²⁶
- Some research suggests there are gender effects of depression in PD. For example, partitioning items of the BDI has shown to be useful in identifying that melancholy features prominently in women, while classical factors associated with depression in PD (apathy and loss of libido) features more prominently in men⁴⁴⁶

Common Pathways

- The literature suggests various factors related to PD that can contribute to depression (Figure 3.22)⁴⁴⁷
- A systematic review of imaging studies reported increased neural activity in the prefrontal regions and decreased functional connectivity between the prefrontal- limbic networks in individuals with depression. Both nigrostriatal and extra-nigrostriatal pathways (especially the frontal region and its connecting areas) are dysregulated in mood disorders in PD⁴⁴⁸

- The neurochemical changes in PD involving dopamine, norepinephrine, and 5-hydroxytryptamine are also related to the pathophysiology of depression and anxiety⁴⁴⁸
- Familial susceptibility factors might have a role in shared pathophysiology, as first degree relatives of people with PD show an increased risk of experiencing anxiety and depressive disorders⁴⁴⁸
- Certain genetic markers, DNA sequences with a known physical location on a chromosome, have linked PD with mental health outcomes such as depression. These include glucocerebrosidase (GBA) variants rs76763715, rs421016, rs387906315 and rs80356773⁴⁴⁹
- The link between anxiety and PD is thought to be due to impairments of noradrenaline, serotonin, dopamine, and GABA synthesis⁴¹⁵

Figure 3.22: Factors Contributing To Depression In Individuals With PD⁴⁴⁷



Management of PD and Mental Health

A. DEEP BRAIN STIMULATION

- An investigation of deep brain stimulation on non-motor symptoms for individuals with moderate to severe PD reported improved depression 6 months post-operatively. Improvements in depression are maintained over time and correlate with improvements in sleep quality and quality of life⁴⁵⁰

B. EXERCISE

- Physical activity can improve clinical status in areas such as function, fatigue, depressive symptoms, sleep disorders, and quality of life.⁴⁵¹ The American College of Sport Medicine activity guidelines can be applied to patients with PD: aerobic exercise, strengthening, and balance training flexion is recommended three times a week for at least 30 minutes⁴⁵²
- Mind-body exercises may improve motor function, depressive symptoms, and quality of life, however, more needs to be known about specific factors such as gender, severity of disease, specific drug use, and intervention cycle⁴⁵³

C. PHARMACOLOGICAL INTERVENTIONS

- Antiparkinsonian medications might improve mood disorders by alleviating motor manifestations and disability, fostering feelings of disease mastery, or restoring dopaminergic signalling⁴⁵⁴

D. PSYCHOLOGICAL INTERVENTIONS

- Results for CBT and other modes of therapy are promising for acute management of depression and anxiety; longer term effects after treatment have been variable⁴⁵⁵
- Treatment of PD patients with signs of anxiety must be directed primarily to optimizing anti-parkinsonism therapy, with decreases in “off” periods

3.1.14 Respiratory Diseases (Chronic)

Chronic respiratory diseases are chronic diseases of the airways and other parts of the lung. Some of the most common are asthma and chronic obstructive pulmonary disease (COPD). Most of these diseases have a major impact not only on the individual with the disease but also on the family.⁴⁵⁶

Prevalence and Incidence of Chronic Respiratory Diseases with Mental Health Problems or Illnesses

A. ANXIETY

- Anxiety is more frequent (21-28%) among people with COPD compared with the general population or people with other chronic health conditions^{457,458}
- Individuals with anxiety tend to have their first hospitalization earlier in the natural course of COPD.⁴⁵⁹ It is reported that they tend to more intensely irritated by their shortness of breath, and have higher rates of mortality and readmission after an exacerbation⁴⁶⁰
- Respiratory failure, the number of acute exacerbations in the previous year, and the COPD evaluation test (CAT) score representing symptoms and quality of life of COPD are reported to be strongly related to anxiety in COPD^{461,460,462}
- A systematic review and a meta-analysis reported that anxiety increases the risk of hospitalization⁴⁶³

- The highest risk of death related to COPD and anxiety tends to occur among females⁴⁶⁴

B. DEPRESSION

- Depression is common with COPD, with a prevalence reported to be between 9-27%^{465,466,467,457, 468}
- A systematic review reported a pooled odds ratio of 3.74 (95% CI 2.4-5.9) for depression in those with COPD compared to those who did not have the condition⁴⁶⁸
- Respiratory failure, the number of acute exacerbations in the previous year, and the COPD evaluation test (CAT) score representing symptoms and quality of life of COPD are reported to be strongly related to depression in COPD^{461,460,462}
- A systematic review and a meta-analysis reported that depression increases the risk of hospitalization⁴⁶³

C. PTSD

- In a longitudinal study of people with PTSD, an increased risk of asthma (hazard ratio (HR)=2.30, 95% CI 1.60-3.30) was reported among those 20-64 years of age⁴⁶⁹

D. PSYCHOSIS

- A regression analysis of 28,002 adults in 16 countries from the WHO World Mental Health (WMH) Surveys that assessed psychotic experiences reported, after adjustment for several comorbid mental health conditions, significant association between asthma and subsequent psychotic experiences (OR=1.6, 95% CI 1.2-2.1)⁴⁷⁰

E. SUICIDE IDEATION AND BEHAVIOUR

- A systematic review examining suicide ideation and physical illness in older adults found suicidal behaviour was associated with COPD¹³³

F. ESTIMATES OF MENTAL HEALTH COMORBIDITIES BY SUBPOPULATIONS

- Women are more susceptible to the development of depression and/or anxiety in acute exacerbation of COPD⁴⁷¹
- Age, body mass index, and duration of illness have been reported to be related to COPD combined with depression and/or anxiety in some studies, but not in others. This may be due to variability across countries and different cultural backgrounds within countries⁴⁷²

Mental Health Screening

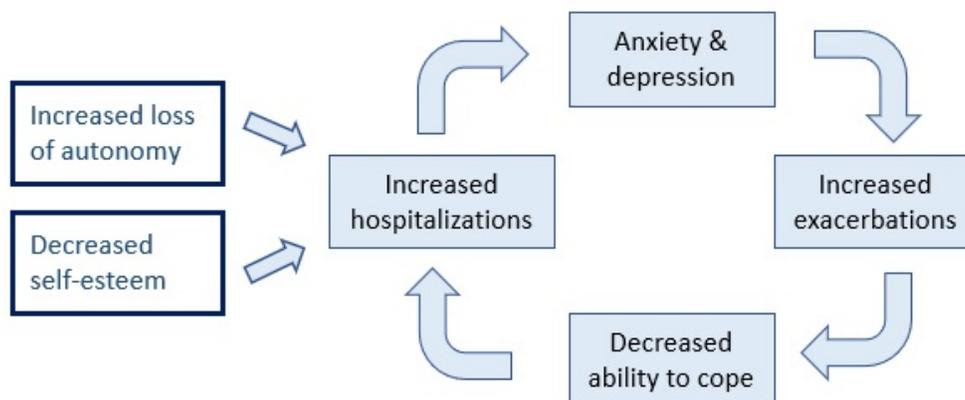
- The literature reports the use of the Ham-A and Ham-D, however, there is no consensus on the evaluation tools and diagnostic criteria of COPD with depression and anxiety

- Increases in maximum respiratory volume per second (VEMS) are correlated with higher anxiety (Ham-A Rating) and depression (Ham-D Rating Scale) scores⁴⁷³

Common Pathways

- The pathophysiology of depression and anxiety in chronic respiratory diseases may be explained by multiple risk factors, systemic inflammation, and response to COPD symptoms (Figure 3.23)
- Smoking, COPD, and depression are mutually reinforcing. Depression has a role in the initiation and maintenance of smoking, smoking leads to the development of COPD, and COPD contributes to the development of depression⁴⁷⁴
- COPD is associated with chronic hypoxemia; a known after effect of recurrent nocturnal hypoxemia is depressed mood⁴⁷⁵
- Both depression and COPD have been associated with processes that affect the brain microvasculature. There is evidence for systemic inflammation and elevated biomarkers of oxidative damage⁴⁷⁶ (e.g., soluble tumor necrosis factor receptor-1 (sTNFR-1) has strong association with depression in people with COPD)⁴⁷⁷
- A systematic review of stigma-related experiences in non-communicable respiratory disease reported that these experiences were significantly correlated with psychosocial, behavioral, physical, treatment, and work-related domains⁴⁷⁸
- In women, links to depression may involve female sex hormone secretion and reaction to social stress; severe breathing difficulties and subjective feelings about low social function are stronger in women when compared to men⁴⁷⁹
- Common diseases coexisting with COPD, such as heart disease, gastroesophageal reflux disease, and lung cancer, can worsen mental health. The greater the number of comorbidities, the greater the risks of depression and/or anxiety (OR=2.14, 95% CI 1.28–3.60)⁴⁷²
- Glucocorticoid inhalation is unlikely to accumulate in the body and lead to poor mental health. However, it is unknown if this is also true for oral or intravenous glucocorticoids. Glucocorticoid receptors in the hippocampus of the brain are activated by excess glucocorticoids in the body, causing degeneration and necrosis of hippocampal neurons, which can induce depression⁴⁷²
- The pathogenesis of panic and anxiety in COPD may be related to anxiogenic effects of hyperventilation, misinterpretation of respiratory symptoms, neurobiologic sensitivity to CO₂, lactate, or other signals of suffocation, and the stress of coping with chronic disease^{480,474}

Figure 3.23: Simplified shared etiology of COPD and mental health (anxiety)⁴⁶⁵



Management of Chronic Respiratory Diseases and Mental Health

Pharmacological Interventions

- A Cochrane review of pharmacological interventions for depression in COPD reported insufficient evidence about the efficacy or safety of antidepressant use³²¹
- The choice of antidepressant depends on the pattern of depression. Late-onset depression or geriatric vascular depression develops after COPD diagnosis and is more refractory to antidepressant treatment. Early-onset depression develops prior to the diagnosis of COPD and is often reflective of a genetic vulnerability to depression⁴⁷⁴
- Medications with the lowest potential to interfere with cytochrome P450 system should be considered; up-regulation of this system can make the lungs more susceptible to oxidant damage⁴⁸¹
- A Cochrane review of pharmacological interventions for the treatment of anxiety in COPD found insufficient evidence of benefit for any of the medications included⁴⁸²

Psychological/Behavioural Interventions

- Behavioural interventions that include Personalized Intervention for Depressed Patients with COPD (PID-C), a treatment mobilizing people to participate in their care, are more effective than usual care. Problem Solving-Adherence intervention integrating problem solving into adherence enhancement procedures found comparable results for depression to PID-C⁴⁸³
- An RCT of older adults (67-85 years) hospitalized for COPD with controlled breathing techniques as the intervention reported significantly improved dyspnea, anxiety, and mobility in the intervention group⁴⁸⁴
- A Cochrane review of psychological treatments in COPD reported limited evidence that psychological therapies (CBT-based approach) may be effective for treating COPD-related depression. Depressive symptoms improved more in the intervention groups compared to: 1) no intervention (attention placebo or standard care), 2) educational interventions, and 3) a co-intervention (pulmonary rehabilitation)⁴⁸⁵

Models of Care

- The inter-connectedness of stigma-related experiences to these conditions (e.g., stigma related to smoking, a common cause of respiratory disease, and having a mental health condition) highlights the need for integrated approaches⁴⁷⁸
- Although the measurement and management of symptoms tends to be the primary focus for clinicians, individuals with asthma or COPD are typically more concerned with the overall impact of their condition on their quality of life⁴⁸⁶
- Management of chronic respiratory diseases should aim for individualized care. For example, individuals with COPD tend to prefer treatments that provide symptom relief (e.g., dyspnea), positive physician relations, and improve quality-of-life. Individuals with asthma prefer treatments that increase symptom-free days and may be willing to trade days without symptoms for a reduction in adverse events and greater convenience⁴⁸⁷
- Pulmonary rehabilitation is beneficial for those with comorbidities and has been shown to reduce the severity of depression and cardiovascular risk factors, including blood pressure^{488,473}
- Mindfulness-based cognitive therapy may impact affective and sensory perceptions related to difficulty in breathing (dyspnoea), however, more research is needed⁴⁸⁹

The National Institute for Health and Care Excellence (NICE) has guidelines for the use of stepped approaches to psychological and/or pharmacological treatment of depression in people with long-term conditions, including respiratory conditions⁵⁷²

3.2 Implications for Health Education, Services, and Policy

In this section various physical health and mental health comorbidities were discussed based on screening, prevalence/incidence estimates, what is currently known about shared etiology, and their management. While there are attributes that are unique to the different physical and mental health comorbidities that were discussed, many commonalities were present as well. These are discussed as means to provide suggestions for practice and policies related to physical and mental health comorbidities.

3.2.1 Health Education

Stigma which can occur with both physical (e.g., obesity, lung cancer, arthritis) and mental health important public health concerns,⁴⁹⁰ with negative effects including anxiety,⁴⁹¹ stress,⁴⁹² depression,⁴⁹³ reduced self-esteem/self-efficacy,⁴⁹⁴ reduced or delayed care-seeking,⁴⁹⁵ and lowered adherence to treatment.⁴⁹⁶ Studies also suggest that, as physical health worsens, the risk of experienced discrimination increases.⁴⁹⁷ Public health campaigns focused on reducing health condition-related stigma can help educate the public and subsequently minimize burden for those diagnosed with a physical or mental health condition. Coordinated, interdisciplinary, and well-conceptualized efforts across the

health care continuum have the potential to reduce the barrier of stigma and facilitate improvements in care and quality of life.¹³⁸

Successfully addressing stigma, through targeted efforts aimed at intrapersonal, interpersonal (e.g., clinician, family), and society (e.g., social attitudes, policy) levels, is important in reducing the burdens associated with both physical and mental health conditions.

3.2.2 Health Services

The collaborative care model, is recognized as a best practices mechanism to provide for optimal management of physical and mental health comorbidities^{2,3,4}

Across all of the physical and mental health comorbidities that have been discussed, the need for more integrated health services were consistently identified. Better integrated health and social services contribute to:⁴⁹⁸

- better screening and management of physical and mental health comorbidities which reduces reliance on higher cost acute care services;
- mitigate morbidity, and prevent premature death;
- ease of transitions across the health care continuum;
- improved health care access, sustainability, and stability; and
- improved community health, including social services and/or education.

Currently, the collaborative care model, broadly defined as multi-professional approaches that employ structured management, scheduled follow-up, and inter-professional communication, is recognized as a best practices mechanism to provide for optimal management of physical and mental health comorbidities.^{2,3,4} These approaches, which are particularly relevant for services addressing mental health, addiction, and physical comorbidity, have been challenging to address. Specific evidence-based models and approaches for collaboration across mental health, addiction, and physical health include the Canadian Collaborative Working Group on Shared Mental Health Care, the Chronic Care Model, and the Tiered Model. Common features across these approaches include a focus on a broad continuum of severity, multi-sectoral involvement, multiple levels of collaboration that align with different types of needs and levels of severity; and a distinction between service- and system-level initiatives.⁴⁹⁹

The collaborative model of care may also include stepped care approaches which have been adopted in several international evidence-based clinical guidelines such as those of the National Institute for Health and Clinical Excellence. Stepped-care approaches, which offers end-users interventions of low intensity first (e.g., problem solving, psycho-education) and, where needed, progresses them to more intensive treatment options, has been shown to foster well-being and reduce healthcare costs.^{500,501} As noted by system stakeholders and researchers, enhanced efforts for the integration of stepped depression care in primary care are needed. This includes reducing barriers related to effective education programs for practitioners and care managers, reimbursement, as well as

communication and monitoring systems.^{502,503} To build appropriate capacity for collaborative health services will require both increases in human resources and enhancements in technology that facilitate sharing information across functional boundaries securely.⁴⁹⁹ In particular, the potential for integrated mobile apps that monitor both physical and mental health symptoms may improve efficiencies in care provision.

3.2.3 Health Practice

Models of Care

Collaborative primary care models that include allied health professionals such as dietitians, occupational therapists, social workers, and substance use disorder specialists integrated with well-established models of mental health services delivery such as peer support, include specialized services for physical health (e.g., diabetes), and encompass alternative mechanisms of delivery such as telehealth will help to address the complex needs of those with physical and mental health comorbidities.

The care of individuals with physical and mental health co-morbidities includes primary health care settings, hospitals, mental health, allied health services, and social services. Primary care is the foundation and is in need of integrating services such as mental health promotion, screening, and treatment,⁵⁰⁴ which will promote both physical and mental well-being.⁵³ Services, such as those aimed at mental health promotion and screening, must align with policy-level directives to create equitable, accessible, and appropriately resourced primary health care.⁵⁰⁵ For example, issues such as access to social workers, psychiatrists, psychologists, and substance use disorder experts need to be addressed, particularly for those who face additional barriers to receiving specialty health services due to factors such as cost, living in rural or remote areas, or being newcomers to Canada.⁵⁰⁶ The Mental Health Commission of Canada endorses that primary health care must increase the availability and coordination of both community-based mental health services as well as appropriate access to intensive, acute, and highly specialized services, treatments, and supports.⁵⁰⁷ In alignment with these priorities, collaborative primary care models that include allied health professionals such as dietitians, occupational therapists, social workers, and substance use disorder specialist integrated with well-established models of mental health services delivery such as peer support, include specialized services for physical health (e.g., diabetes, cardiovascular, respiratory care), and encompass alternative mechanisms of delivery such as telehealth will help to address the complex needs of those with physical and mental health comorbidities. Furthermore, long-term issues of fair compensation for primary care physicians who provide mental health care⁵⁰⁸ must be resolved to foster equity of service access for individuals struggling with mental health problems and illnesses.⁵⁰⁹ Care that is collaborative, integrated, tailored, and flexible (e.g., home visits, extended hours, provide online service delivery, group virtual visits) will also better meet the needs of those with physical and mental health comorbidities. As the prevalence of comorbidities in the aging Canadian population rises, it is evident that collaborative care models will be increasingly critical. Strategies that have been identified to facilitate integrated care include:^{510,511,512}

- having registries of people with complex needs to track preventative care, disease/illness management, and referrals to secondary and tertiary care
- providing health care system navigation supports
- implementing shared decision-making approaches
- adequately resourcing secondary and tertiary mental health services
- supporting competency development among practitioners to deliver high-quality health care to people with mental health problems and illnesses
- training practitioners in the recovery model, including stigma and discrimination, illness perceptions, trauma-informed care, positive communications, and social support interventions
- evidence-based and clear screening guidelines, pathways to management, and integration with social services

It is also evident that receiving collaborative care as compared to usual care has been found to be beneficial among those with mental health issues and illnesses for improving adherence and functional status.⁵¹³ Demonstration projects for providing coordinated care for high-cost and high-need individuals have also proven to be cost-effective. Specifically, the Hamilton Family Health Team model for collaborative care (the HFHT-model) which involves placing various health professionals within existing general practitioners practices to form Family Health Teams that can then offer coordinated mental and somatic health care has shown positive intended effects.⁵¹⁴

Finally, at the organisation level, efforts to foster relationships between mental health and physical health representative organisations are needed. For example, advocacy work to include people living with physical and mental health problems within reviews of relevant clinical and intervention guidelines would lead to the development of more relevant interventions for mental and physical health care.

Pharmaceutical Interventions

For many of the physical and mental health comorbidities reviewed in this report, high-quality efficacy and safety data on the use of psychiatric medications, such as anti-depressants, in the context of specific physical health conditions were lacking and in need of well-designed RCTs to clarify the balance between benefits and harms. For example, it is questioned if anti-depressants would be beneficial for those with chronic kidney disease and depression, as good kidney function is needed to help eliminate end-products of drug metabolism. Studies with long follow-ups are needed to demonstrate a sustained benefit of pharmacologic treatment and evaluate whether end-points, such as hospitalization and mortality, are affected without too many side-effects. In addition to better data, decision-making tools are needed by practitioners to help determine appropriate pharmacologic treatment pathways for different physical and mental health comorbidities.

Screening and Assessment

Appropriate screening for mental health problems and illnesses in those with chronic physical conditions needs to be priority. Health care professionals will need to expand their use of standardized screening tools that capture various psychosocial factors in the populations they work with.

A recurring issue among the assessment of physical and mental health comorbidities was the heterogeneity of mental health measures used which contributes to variability in estimates of prevalence and incidence. Issues with mental health screening in those with physical health conditions include a lack of consistent guidelines and implementation, varying symptom profiles, and a lack of clear guidelines for follow-up should someone screen positive. Appropriate screening for mental health problems and illnesses in those with chronic physical conditions needs to be priority. Health care professionals will need to expand their use of standardized screening tools that capture various psychosocial factors in the populations they work with. Tools to assess physical and mental health comorbidity should screen for symptoms, stress, quality of life, risk factors, and protective factors. Brief screening tools such as the two-item PHQ can be easily offered in busy clinic settings as part of questionnaires that used to register clients. If more comprehensive assessment is needed, people can be scheduled for an assessment with standardized instruments validated for their particular circumstances (e.g., condition diagnosis, gender). Finally, more research is needed to identify comprehensive screening tools with sound psychometric properties.

Trauma-Informed Care

While a history of trauma is clearly linked to many health issues, a paucity of literature describing approaches to care of physical and mental health comorbidities lacked discussion about trauma-informed care. Furthermore, it is recognized that exposure to multiple adverse childhood experiences (ACEs) is a major risk factor for the development of many physical and mental health conditions. To sustain improvements in health services requires a shift in focus to include ACE-informed service provision. The Sustainable Development Goals provide a platform to help implement strategies to reduce the life-course effect of ACEs on physical and mental health.⁵¹⁵

Challenges of Multi-morbidities

While comorbidities were the focus of this report, there were numerous studies located in the searchers that discussed multi-morbidities. In contrast to comorbidity which is a disease-centric concept, multimorbidity implies a patient-centred model of care, which does not prioritize a particular index disease and entails more comprehensive evaluation of individual complexity. This may be an approach to consider in the care of those with comorbidities also. Higher prevalence of multi-morbidity can lead to higher medical care utilization and expenditures which has implications for healthcare delivery reforms that focus on care management. For example, the model known as DIAMOND (Depression Improvement Across Minnesota Offering a New Direction) included both an integrated care component and bundled payments to primary care providers for depression. This model has been found to be effective in reducing depression remissions, and is based on

the IMPACT (Improving Mood–Promoting Access to Collaborative Treatment) intervention that uses a collaborative approach for providing treatment.⁵¹⁶ In summary, the increasing prevalence and incidence of comorbidities and multi-morbidities points to the need for even better integration care models.

Psychological, Lifestyle, and Peer Approaches

Additional health service gaps include clear consensus about the need for evidence-based psychological interventions among the different physical and mental health comorbidities. While CBT is considered a cornerstone of mental health care, the literature does not demonstrate its efficacy across all comorbidity types, such as applications in CVD. This suggests further investigative work is needed to determine its efficacy across on physical health conditions. Similarly, the literature was limited in discussion about lifestyle interventions such as physical activity and diet as adjuncts to the care for comorbid physical and mental health conditions. Finally, while peer support approaches are a recommended model for health care, particularly for those facing mental health problems and illnesses, there was very limited discussion of its potential for the care of those with physical and mental health comorbidities. As noted in the obesity literature, most interventions do not include mental health professionals. Future studies should assess the effects of interventionist professions in addition to primary and secondary outcomes for adults with different lifestyle-related conditions, including obesity.⁴²⁰

Contextual Factors: Gender and Equity and Priority Seeking Populations

Multidisciplinary care for equity and priority-seeking populations with physical and mental comorbidities, should focus person-in-environment orientations and their service agencies. For example, helplessness experienced by those with CVD may intertwine with factors such as perceived injustice, discrimination, poor family relationships, and previous trauma. For people with a community or extended-family orientation, interventions that focus on connections with others may be more effective than interventions that focus on improving perceptions of individual control.¹⁷⁸ It is important to recognize contextual factors such as non-traditional families, same-sex partners, and chemical dependency. It is also critical to identify issues that might mask health symptoms, such as fears of prejudice or legal ramifications.

The literature about physical and mental health comorbidities yielded limited research about the effects of race and ethnicity. Race and ethnicity may influence individuals coping with stressors⁵¹⁷ and access to resources and quality health care. Services aimed at physical and mental health comorbidity care of those from diverse backgrounds need to include culturally sensitive practices. For example, minorities and immigrants with CVD may not be accustomed to intensive Western-style exercise programs. Alternatives such as integrative therapy (e.g., tai chi, yoga) and community-oriented approaches (e.g., Aboriginal ceremonies and rituals) may be better adopted by those from diverse backgrounds.

While there was limited research that examined physical and mental health comorbidities among LGBTQ populations, research that compared transgender and non-transgender older adults reported that transgender older adults have significantly worse physical health as measured by the Health-Related Quality of Life Scale and depressive symptomology.⁵¹⁸ It

is recommended that effective interventions for populations such as these will need to consider factors such lifetime victimization, stigma, and distinct social support networks.⁵¹⁹

Manifestations and outcomes of physical and mental health conditions differ between men and women due to both sex (molecular, cellular, epigenetic mechanisms) and gender (adopted or imposed social norms, behaviours, identities and expectations).⁵²⁰ In the literature about physical and mental health comorbidities, there was limited reference to sex and gender differences. As identified by others, this raises issues about the development and uptake of sex and gender influences into care guidelines and health practice.⁵²¹ For example, there are important knowledge gaps that exist about the different impacts of menopause and andropause in relation to physical and mental health comorbidities.

3.2.4 Health Policy

Policy targets aimed at shaping positive food environments, healthy eating, food security, physical activity, affordable childcare and housing, social assistance, as well as health and income equity⁵⁸⁰ have potential to help prevent and manage physical and mental health comorbidities.

Mental health policy has the potential to better shape the prevention and management of physical and mental health comorbidities. However, mental health services are poorly resourced and interventions for those with mental health problems are reported to be inadequate. Pharmacotherapy, particularly antipsychotic medication use, is also the mainstay of therapy programs, but has important cardio-metabolic risk factors. While the implementation of routine metabolic screening and monitoring practices have improved, reports in the literature suggest much more can be done to ensure these are consistently offered.

There is much to be gained from using positive mental health approaches to prevent and manage physical and mental health comorbidities. First is the recognition that 70% of mental health problems in Canadian adults have their onset in childhood and adolescence⁵²² and these are linked to earlier childhood experiences. Many non-communicable diseases also are linked to earlier life experiences and are shaped during key developmental periods such as emerging adulthood.

3.2.5 Health Research

There is a need to advance knowledge in the screening, prevention, characterization, and management of different physical and mental health comorbidities. Research that addresses knowledge gaps about appropriate tools for mental health screening in different physical health conditions and among equity-seeking and priority populations can help to identify the benefits in relation to anticipated improvements in one's overall health. Measures that can estimate trends in physical and mental comorbidities are also needed. In particular, assessments that can reduce the variability across tools used for assessment and diagnosis will help to accurately monitor trends and develop appropriate interventions.

There is much work that could be done to better understand the shared etiology of mental and physical health comorbidities. For example, a better understanding of genetic underpinnings and the role of the human gut microbiome could lead to targeted interventions and more personalized approaches to care. Better knowledge about integrated care implementation and outcomes are needed, and innovations such as those in nanomedicine, mobile health, and imaging need to be critically evaluated.

While there is evidence that the collaborative care model is effective in improving mental health outcomes, including substance use problems,⁵²³ it remains unclear what components of the model are necessary for success. Future research could aim to investigate what combination of components in the model might be most effective. In addition, investigations aimed at developing data systems that provide reliable and valid mental and physical health services data that can be analysed in an integrated and strategic manner may better inform provision, policy, and future research.

Finally, future research about physical and mental health comorbidities needs to be co-produced with those who have lived experiences, their families, and carers. Recently, the Canadian Institutes for Health Research introduced initiatives that fosters patient-oriented which aims to focus on patient-identified priorities which are believed to lead to better health outcomes.

4. Which Interventions Work? For Whom? How? In Which Contexts?

Realist synthesis begins with testable program theory of how a program should work in the real world. Evidence, from secondary data from documents, is used to refine and shape the program theory. For this report, an adapted a socio-ecological framework (Figure 4.1) with program theories to explain mental health promotion at different systems levels, beginning with the policy level is used as a frame of reference for the rapid realist synthesis. It is important to note that boundaries are permeable across systems levels. This section of the report is subdivided into categories that correspond with the systems levels of the framework.

4.1 Level 1: Healthy Public Policy for Mental Health: Mental Health Promotion/Mental Health in All Policies (MHiAP)

In the first, outer ecological layer of the model, we will discuss an overarching policy strategy for promoting mental health, both for people living with chronic conditions, and at risk for, or living with, mental health stress and illness, *and* for people living with serious mental illnesses and at risk for, or living with chronic physical diseases. However, in line with our health promotion emphasis, and our adoption of the dual continuum model of mental health, we include the latter two populations as part of a general population mental health promotion strategy, that focuses not just on people who are ill, or at risk of getting ill (mentally or physically), but also on promoting general mental health flourishing in the wider population. This approach recognizes that even people living with mental and physical illnesses have the potential to live a flourishing, joyful life, and that while we must try to prevent and manage illness, we must also try to promote and strengthen health assets, including structurally (social, economic and cultural) supportive environments, community resilience and life coping skills. Below is our program theory for how MHiAP is meant to work:

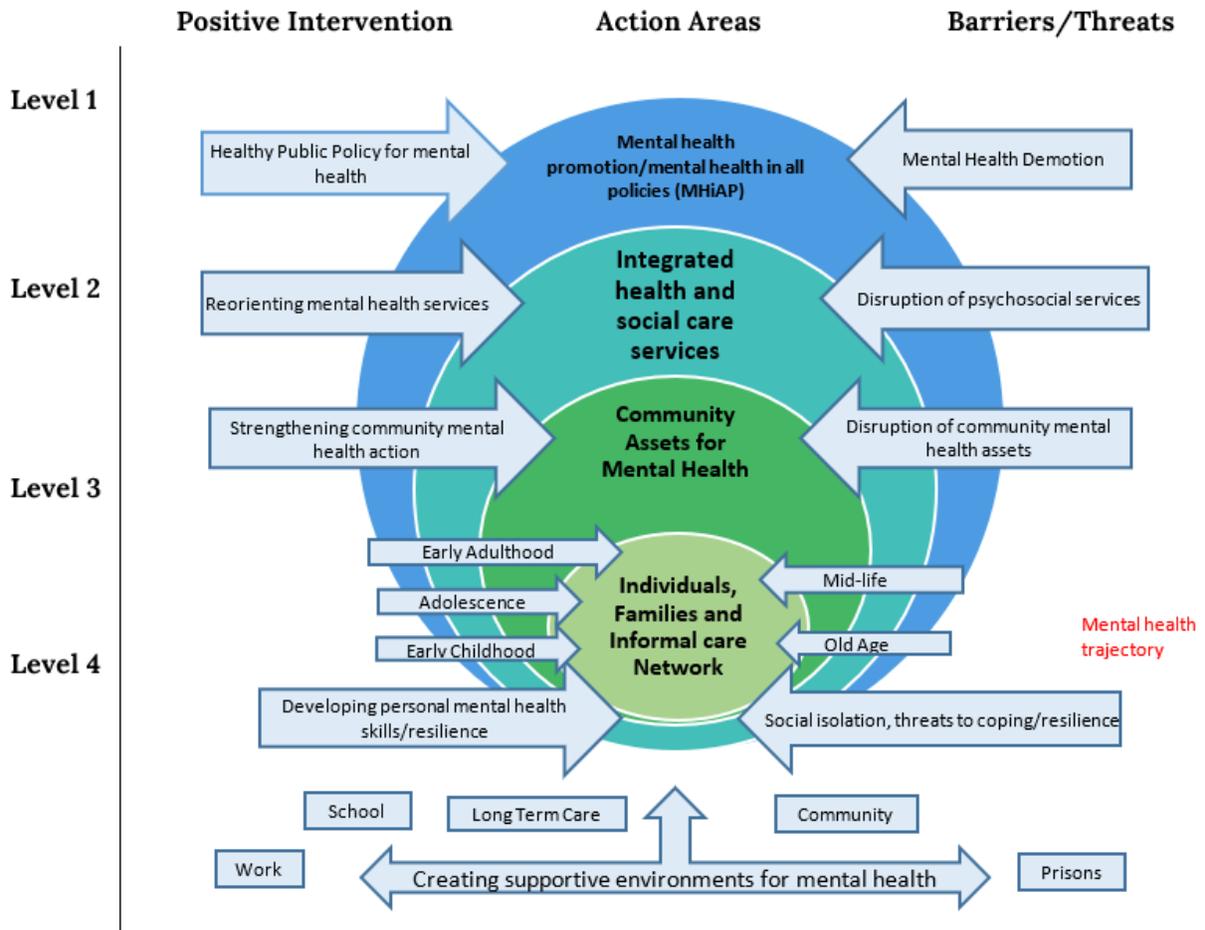
A Program Theory for Mental Health in All Policies (MHiAP)

A MHiAP strategy → Intersectoral governance for mental health → Changes in policies (usually signaled by some sort of strategic document/plan) → policy actions (legislative, regulatory, budgetary/investment tools) to promote mental health → Impact on social determinants of mental health → Improved mental health outcomes (e.g. increased well-being, happiness, improved coping and resilience, reduced mental stress, reduced incidence of mental illness, reduced harms from substance misuse, reduced incidence of suicide).

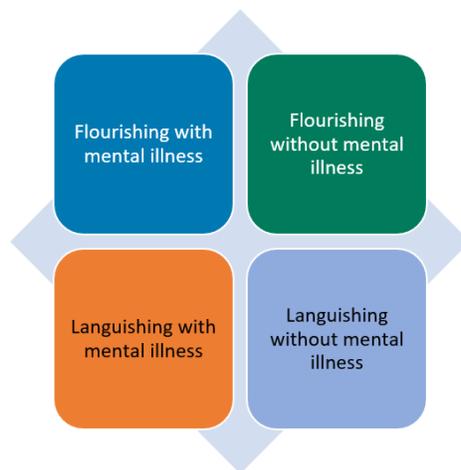
Below, is an outline of what we know about how HiAP is adopted as a policy agenda, is implemented as an intersectoral governance strategy, and sustained as an institutionalized

process that leads to better outcomes, in terms of what types of combinations of contexts-mechanisms-outcomes lead from one part of the theory to the other.

Figure 4.1: A Socio-ecological model of mental health promotion interventions + the Dual Continuum Model of Mental Health



The Dual Continuum of Mental Health



Agenda Setting for a MHiAP Strategy

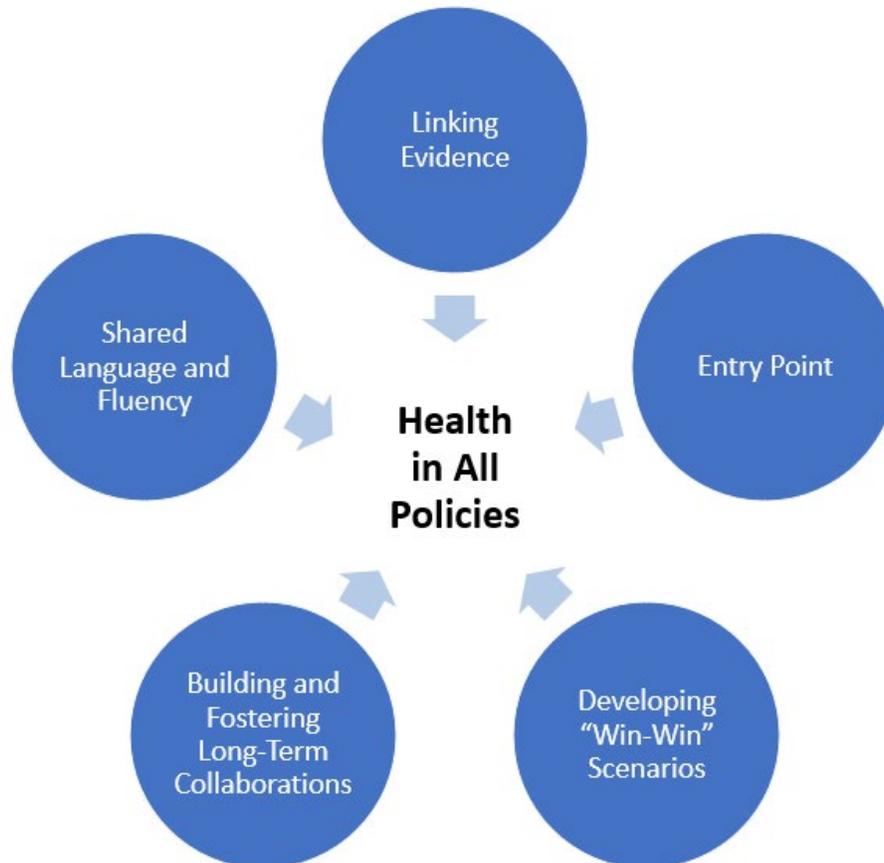
A 'Health in All Policies' approach to intersectoral collaboration has been gaining ground globally as a policy-level agenda aimed at addressing the wider social determinants of health. Advocates of HiAP highlight the importance of mental health promotion as central to successful HiAP approaches, and as a means to contribute to addressing health equity and inequality.^{9,10} Conversely, advocates of mental health promotion have identified HiAP as a key policy framework for advancing mental health and physical health.^{11,12} Evidence discussing the implementation of HiAP is currently limited, as much of the explicit policy initiatives have been initiated only recently; however, there is a growing field of work that tracks well with a realist approach^{524,525} and can contribute to identifying C-M-O-Cs that will inform conditions where HiAP approaches will make substantive positive contributions to societal well being.^{526,10} Of note are Shankardass et al. (2018),⁵²⁷ who adopt a realist/systems approach to HiAP and identify four key sub-systems relevant to successful HiAP initiation, implementation and sustainability (Executive (leadership); Intersectoral (across sectors); Intrasectoral (within sectors); and, Extra-governmental). Within these sub-systems there are several components that the authors argue are mechanistically related to successes/failures in HiAP adoption/uptake, implementation and sustainability. In the Canadian context, we can identify in the Executive sub-system, led by policy elites, the lack of an explicit policy agenda for implementing HiAP, either at the federal level or in most provinces (with the exception of Quebec and Newfoundland).^{528,529,10} This is an ongoing reality recognized almost a decade ago (Greaves & Bialystok, 2011). Some advocates of HiAP have recognized the deficit in the health promotion and population health fields of a theoretically reflective understanding of the policy development process in relation to work on the social determinants of health,⁵³⁰ and so have begun to integrate a more sophisticated understanding of the latter in their HiAP work.^{531,526} Following Exworthy (2008),⁵³⁰ many have adopted a policy 'streams' (problem, policy, political) process approach based on the work of Kingdon (2011),⁵³² which is premised on the idea that 'policy windows' are opened when these three streams are coordinated, which can come about partly by chance, and partly through the strategic action of policy networks and policy entrepreneurs.

Recent research shows there is emerging interest in Canadian policy networks in pushing forward an HiAP agenda, with strong leadership from the Quebec government and the National Collaborating Centre on Healthy Public Policy.⁵³³ While mental health has been on the HiAP agenda in most of the key background documents,¹¹ it suffers from a lack of parity in focus in relation to physical health conditions within the broader field of health promotion, as it does in relation to the health care system's prioritization of physical health. This may lead to some pessimism regarding the prospects of a Mental HiAP agenda, as it requires overcoming the burdens of reversing disproportionate awareness, attention and resources to both health care over health promotion, and physical health promotion over mental health promotion, as well as the other issues associated with HiAP implementation.^{526,10}

Based on a review of the emerging literature on HiAP adoption and implementation, we propose five simple rules for successful HiAP initiation: 1) Developing a shared language and fluency around a broader understanding of 'health' to include well-being and happiness, and general welfare; 2) Linking evidence for how HiAP initiatives are able to

contribute to sustainable economies and sustainable health systems (both theoretical and empirical); 3) Having an ‘entry point’ to initiate an HiAP agenda; 4) Developing ‘win-win’ scenarios, goals, and objectives across sectors;¹³ and 5) Building and fostering long-term collaborative partnerships and engagement with intersectoral stakeholders. See Figure 4.2.

Figure 4.2: Five Simple Rules at the Policy Level



The notion of simple rules comes from complexity science, and the study of complex systems, such as health care systems.^{534,534,535,536,17} Given the unpredictability, diversity and variability of complex systems, prescriptive rules do not provide the flexibility needed to adapt to changing conditions. Simple rules are guidelines for successful systems adaptability. Based on our realist review of evidence, we propose that these five simple rules can act as linkages across systems levels. They are particularly critical, at the policy level, to influence change in language and in partnerships and engagement at other systems levels--setting the stage.

While the simple rules approach is sometimes accused of avoiding ‘big bang’ solutions,⁵³⁷ and encouraging incrementalism, this would be an inaccurate characterization of the complex systems approach. In fact, the Canada Health Act itself can be read partly as both a ‘big bang’ solution *and* an example of using broad principles of action to guide or steer divergent policy implementation processes in the provinces. Despite the perennial concerns in Canada about threat to the principles of Medicare, what is more remarkable, is that despite the autonomous powers of the provinces in health system development, there

has been so much relative stability and coherence around the central principles, and this is reflected strongly in Canadians' deeply valuing those principles, making any major reversal in direction toward a less universal, less public system politically unviable.⁵³⁸ Evidence shows that rather than reversing direction, Canadians overwhelmingly support the expansion of the principles of Canada's universal public health system to cover things like prescription medication for all.⁵³⁹ This latter example shows how, given the right policy window, a long term policy issue network, with a well-framed communications strategy, can quickly galvanize public opinion to support a fairly major policy change. As the Final Report of the Advisory Council on the Implementation of National Pharmacare demonstrates, this combination of broad policy frameworks, with specific sets of universal principles and a more complex, time-staggered, jurisdiction-variant mode of implementation, is a model of policy change that works, even (or especially) in highly complex constitutional federations like Canada.⁵⁴⁰ It is important that, particularly at the federal level, policy-makers continue to build on the success of the Canada Health Act, and develop policy coalitions around expanding coverage that is universal, comprehensive, accessible, portable and public, to a wider set of services for the 21st Century.

In the Canadian context, not only is mental health well placed to be included in any HiAP policy agenda, it may in fact be the key entry point for raising the awareness and urgency of a HiAP approach at the federal and provincial levels. First, with the help of key policy elites, such as Senators Kirby and Wilson, and with the establishment of the MHCC, much of the foundational work in boosting awareness has already taken place. In this collective work, Canadian researchers, practitioners, policy-makers and people with lived experience have worked on developing a more inclusive, shared language around mental health, that by its nature tends to be less 'deficit-focused' and more positive and strengths-based (which relates to simple rule 5 above).

The dual or 'two'-continuum model, depicted at the base of Figure 4.1, is taken from transformative ideas in the MHCC document, *Changing Directions, Changing Lives: The Mental Health Strategy for Canada*.⁵⁰⁷ The model is based on conversations with mental health policy-makers who recognized that new, strategic directions for Canadian mental health policy will only happen with shifts in public perceptions of mental health-mental illness. These policy-makers also acknowledged how language is one critical determinant in how we think about and how we describe mental health-mental illness. The two-continuum model is a "road map" for mental health transformation in Canada.¹⁹ The model proposes that to some degree, every individual is somewhere on a continuum of mental health and illness. This holistic approach recognizes that at any point in an individual's life, mental health needs may shift, as is true of our physical needs. The purpose of this model is to decrease stigmatization and to promote awareness that "at the core we're all the same" (p. 465). Even the language of 'flourishing' points toward a rhetorical broadening of focus and is likely to overcome some of the tendency of advocates from the health sector to slide back into an exclusively epidemiological focus on patterns of disease, which disregards health as a resource for everyday life. Second, the MHCC and others have done very important work establishing the evidence base for investments in mental health promotion (which relates to simple rule 2 above). Finally, existing cross-government, intersectoral work in mental health in Canada (e.g. The 'Tripartite Agreement' on improving mental health and wellness services between the First Nations Health Council, the Government of

Canada and the Province of BC; the Public Health Agency of Canada's Mental Health Promotion Innovation Fund) can be used as a platform for demonstrating how win-win scenarios can be developed and implemented (which relates to simple rule 4 above). In this respect, mental health should be considered foundational to a HiAP approach, just as a HiAP approach should be considered foundational in furthering the promotion of mental health as a critical resource for everyday life.

In lieu of a full blown, explicit HiAP initiative, governments continue to pursue a variety of mainly issue-focused intersectoral collaboration strategies, which have an ongoing direct impact, and indirectly, provide a context for any future more comprehensive approach, coordinated across all health-relevant policy development, implementation and evaluation. However, it is clear from the literature that an explicit HiAP approach has several advantages over ad hoc intersectoral collaborations. First, it embeds formal governance mechanisms with clear terms of reference to develop and sustain intersectoral policy-making for health across governments. This encourages accountability through regular reporting processes, and can lead to establishing frameworks for implementation and evaluation of HiAP initiatives. Second, it provides an opportunity for government to coalesce and concentrate skills and capacities for intersectoral collaboration (e.g., Canada has many experienced professionals and policy practitioners with intersectoral collaboration experience, yet they tend to be dispersed in various parts of the policy system), and to encourage training in the implementation and evaluation of HiAP. Finally, formal HiAP governance mechanisms and skilled practitioners of intersectoral collaboration can act as much needed supports and facilitators of ongoing, issues-based initiatives. The latter can also serve as advocates and conduits to higher-level policy forums, such as Cabinet-level meetings, and Deputy ministerial committees, where executive leadership is enacted and major social investment strategies are decided upon.

4.2 Level 2: Reorienting Mental Health Services: Integrated Health and Social Services

Beyond the HiAP approach, which tends to focus on 'upstream' population health and the social determinants, a key role for public policy is to provide the regulatory, legislative and financial context for the transformation of health and social services more broadly in society. For Canadians, 'health reform'¹⁴ is an ongoing reality, that is complex and multi-faceted, with varying objectives across provinces, and widely differing governance strategies and outcomes. However, a common recurrent theme is the need to develop *integrated, collaborative systems of health and social care* to address the increasingly complex needs of an ageing population, with the concomitant multimorbidity of chronic diseases, both physical and mental being the driving force of this complexity. While these efforts require many transformational changes at the health and social service/organizational level, which will be addressed in the following section, there is a strong role for high-level policy in successfully moving towards the ideal system. It is generally acknowledged, based on decades of research evidence,¹⁵ that comprehensive primary health care, as originally outlined in the Alma Ata Declaration,¹⁶ is the overarching framework for efficiently, effectively, and equitably organizing health and social services in order to produce optimum health in populations.

The **program theory** at this level is: by providing *universal financial coverage, under government control and regulation, with equitable distribution of services, comprehensive coverage, and with low or no co-payments*, then you attain “*greater first contact access and use, more person-focused care over time, greater range of services available and provided when needed, and coordination of care.*” (Starfield, 2012, p. 20).

Canadian provincial governments, constitutionally designated to provide health, education and most other social services to Canadians, have operated since 1966 under the *Medical Care Act*, and since 1984 under the *Canada Health Act (CHA)*, which offers financial incentives to provinces to provide universally accessible, comprehensive and equitable health insurance coverage to their populations, although limited mainly to physician and hospital-based services. In relation to mental health services in particular, the protection provided by the CHA has serious gaps, leaving “a lack of universal coverage for psychological counseling, prescription drugs, home care and other community supports”.⁵⁴¹ Along with other initiatives to expand Canada’s commitment to providing universal coverage of health services, such as the ‘Pharmacare for All’ movement,⁵⁴⁰ the Federal Government should use its legislative, regulatory and fiscal muscle to provide leadership on expanding Canadians’ access to psychological services, improved home care through publicly funded, relational care-based assisted living and long term care arrangements, and community-based extended health and social supports, that go beyond the narrow, physician-determined concept of ‘medical necessity’. In Figure 4.1, we have depicted lifespan mental health needs (and the contexts where you find these needs) as the foundational level of the socio-ecological framework.

At the provincial level, a commitment to supporting collaborative, integrated health and social care systems, means dedicated financing, legislative and regulatory changes. There are multiple models of practice available to help implement such changes, such as: continuing community care, collaborative care models (CCMs), the primary care behavioral health (PCBH) model;⁵⁴² patient-centred medical homes, community health centres, community mental health teams, multispecialty community providers, Local Integrated Health Networks (LHINS), primary care networks, and many others. There are also multiple ways of remunerating physicians and other health and social service providers in order to procure their services, including improving existing fee-for-service agreements, capitation formulas, salaried contracts, and pay-for-performance. There seems to be no ‘silver bullet’ in terms of specific interventions that will ‘solve’ the integration problem. However, a combination of the CCM and the PCBH models might provide an optimal combination to address a wide range of mental health issues at the primary care level.⁵⁴³

Nevertheless, at the policy level, there does seem to be some generic lessons based on the underlying principles of health system reform, that have started to be synthesized over the past two decades of work in health system change and implementation science in integrated care systems.^{544,545,546,547,14} The first common finding is that while ‘integration’ sounds like a simple plea, it is not. Many authors have noted the ambiguity and complexity inherent in the call for ‘integrated care’.^{548,549,547} Kodner breaks down the complexity into five dimensions (foci, type, level, breadth and degree), each with several sub-dimensions.

Nevertheless, despite the ambiguous nature of this “imprecise hodgepodge” and the fact that “not only is it a difficult concept to understand, but also one that in the final analysis is enormously challenging to implement and manage” (p.12-13),⁵⁴⁶ we see consistent advocacy, from even the more skeptical researchers, for its pursuit by policy-makers in order to address the increasingly complex care needs of their citizens. Part of the reason for this seeming paradox (ambiguity and contradictory empirical support, yet consistent advocacy and commitment), is that most experts in this amorphous field recognize that ‘integrated care’ signifies an entry point at this systems level for transformation--from thinking about (predominantly) physical health needs to physical-mental health needs. The simple rules from Figure 2 may apply at this level as well. The right integrated care model has the capacity to provide a shared language and opportunities for greater collaboration and generation of win-win integrated care (mental-physical) scenarios (rather than a set of prescriptive interventions/directives).

One influential Canadian framework for integrated care, notable for its continuing/community care perspective was developed by Hollander and Prince after extensive consultations with experts and policy/decision-makers across Canada (2008).⁵⁴⁵ What makes this framework interesting is that it is one of the few integrated care frameworks that starts from the non-medical community level of care, and then asks what collaborations need to be made to primary care and hospital-based systems. Most other frameworks^{544,546,550} start from the opposite perspective, starting with existing systems of primary care, and expanding them out to include integration with broader community and social services. In this framework, ‘client-centred’ care contrasts with provider-driven objectives. This framework is based on commitment to a comprehensive range of services (psychosocial, physical care) with sufficient and sustainable funding, based on what clients need--first and foremost (pp. 48-49).⁵⁴⁵ We believe this integrated care framework can work if it is backed with real funding commitments and specific investments in administrative functions and information technology supports to facilitate transformational change processes.

Integrating care via simple rules allows relatively autonomous actors to use their contextual knowledge to come up with creative implementation solutions. At the integrated care level, there are some important contextual factors to consider. In order for clients to have a voice in decision-making (e.g., priority physical and social/mental needs), power differentials need to be ‘smoothed.’ Differential power dynamics impede effective collaborative practice among different service providers,¹⁷ but they also relegate clients to a marginalized role with respect to decisions around their care needs. Physicians are considered the top of the healthcare hierarchy, and this conceptual approach can break the success of any reform program or change initiative.

Canadian policy researchers have understood for a long time that physicians play a central role in the health system, and that the history of the Canadian health system’s evolution has certain path-dependent features that make negotiations with physician associations often difficult and protracted.^{551,552,537} As Best et al.¹⁷ noted ‘physician engagement’ in transformational change processes is still a foundational principle for any successful health system transformation, even though it is important to emphasize that this has less to do with their intrinsic relative value in an integrated system of care (a key indicator of a

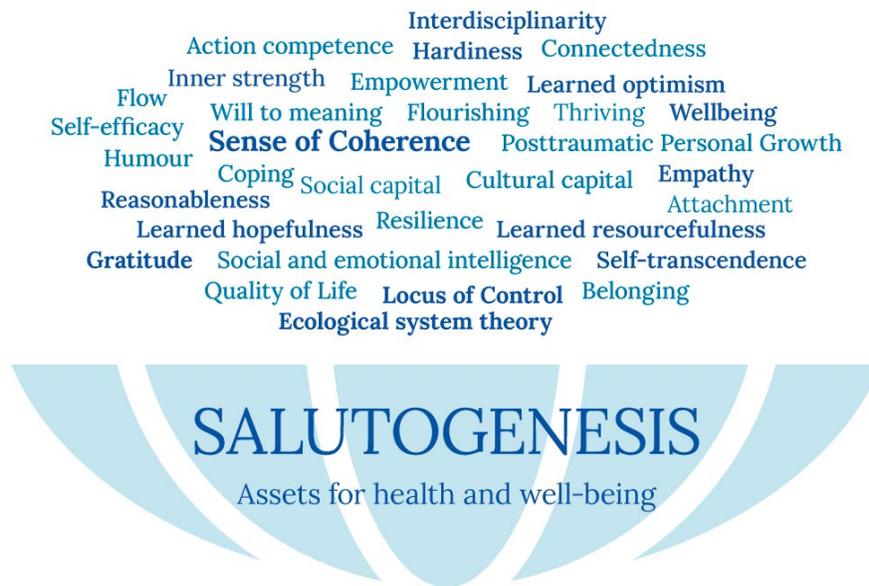
transformed system would be an equitable rebalancing of the value assigned to the many different professions and service workers that form part of an ideal multidisciplinary care team), and more to do with their strategic institutionalized positioning within the health care system. Sociologists of health have developed very influential theories of medical professional power,^{553,554,555} and have debated the relative dominance and autonomy of physicians in health systems across the world, under changing political and economic conditions. In Canada, physician autonomy still characterizes the relationship of physicians to the healthcare system as a whole, and furthermore, that this sustained autonomy is often a factor in the difficulty of major system transformation.¹⁴

Rather than a confrontational approach, tackling the instrumental self-interest of physicians in terms of their financial and work autonomy, governments have tended to try various efforts to enrol them as collaborators, based on the shared values of Quadruple Aim. Quadruple Aim is often used as a means to rally physicians and other healthcare providers around universal quality improvement healthcare goals of enhanced population health, enhanced patient experiences, enhanced cost effectiveness and enhanced service provider experiences (i.e., joy at work).⁵⁵⁶ Quality councils in Canadian provinces and territories promote physician engagement in Quadruple Aim initiatives, including leadership development, knowledge development and communications strategies. Education and financial incentives for integrated care development may be generating some power shifts.^{557,558}

4.3 Level 3: Strengthening Community Mental Health Action: Community Assets for Mental Health

At this systems level, community “assets” for mental health are the chosen foci, as they bring together three important theoretical approaches to mental health: mental health promotion;¹⁸ the two-continuum approach;¹⁹ and, the Canadian Mental Health Association’s framework for support approach.^{20,21} Morgan & Ziglio⁵⁵⁹ define health assets as: *‘as any factor (or resource) which enhances the ability of individuals, groups, communities, populations, social systems and/or institutions to maintain health and wellbeing and to help to reduce health inequalities’*. This approach, founded on the salutogenic⁵⁶⁰ understanding of health and well-being has been demonstrated as theoretically compatible with a mental health promotion approach, as well as with the two-continuum model and the framework for support. It has also underpinned a relationship with positive psychology,⁵⁶¹ where it is seen as the umbrella concept that encapsulates a variety of key aspects and dimensions of positive psychological development, including coping, sense of coherence, flourishing, well-being, and many others (Figure 4.3).⁵⁶²

Figure 4.3: Salutogenic Understanding of Health and Well-Being



Van Bortel et al.,⁵⁶³ in a recent review of the salutogenic approaches application globally, identify community health assets as including, among other things: “family and relationships or supportive networks, intergenerational solidarity, community cohesion, religious tolerance and harmony” (2019, p. 2). Building on these connections, we can derive a tentative program theory as below:

The **program theory** at the community level is: by helping to *co-create, strengthen and sustain community mental health assets*, people can be supported to live happy, joyful, flourishing lives, whether or not they are living with mental or physical illness *and* they can be empowered to help co-produce and shape the mental health services they receive in community through context-appropriate co-produced mental health service planning

As Trainor et al.²¹ argue, this means shifting from a ‘service paradigm’ to a ‘community process paradigm’, where not only is it recognized that community and personal resources are critical for mental health promotion and recovery, but that the whole system needs to shift to a person-centred approach that develops services from the perspective of the person-in-community, rather than from the perspective of the service professionals and administrators exclusively. This is a key way that this program theory connects to the *integrated health and social services level*. It is clear from the literature on integrated care, that a major failing of implementation is often related to the failure to make this paradigm shift that is recommended by Framework for Support model. As a recent review of integrated care makes very clear, there are real tensions between a political economy of health care/organizational perspective that is aimed mainly at integrating care to deal with cost pressures within the overall health and social care system, and that of a truly person-

centred care approach. The authors conclude: “Recognizing rather than resolving these tensions would mean accepting that relationship-based care offering time and space for patients to be seen and heard is likely to be a necessary (if not sufficient) condition that can contribute to the achievement of integrated patient care. Moreover, provision of this care needs to be understood as not necessarily aligning with organizational or system objectives of reduced cost.” (p. 480).⁵⁴⁷

Another tension that has been identified in relation to the assets-based approach, is that its reliance on concepts of community cohesion and social capital can lead, if not reflexively and critically implemented, to the marginalization of stigmatized members of the community and thereby increase health inequity (Wakefield & Poland, 2016),⁵⁶⁴ particularly if the social capital resources are mainly of the ‘bonding’ type which can reinforce exclusivity and homogeneity, as opposed to ‘bridging’ and ‘linking’ social capital that operates to strengthen ties between heterogeneous groups within the community and make linkages between marginalized groups and people in positions of power that can ally with them.⁵⁶⁵ Part of the reason for emphasizing multi-level approaches, is that leaving too much responsibility for producing mental health and well-being to the community and individuals, without paying attention to the wider socio-economic context (influenced profoundly by macro-level public policy), means that community assets can be overwhelmed and even deteriorated by too much stress on their resources and capacities for resistance to a policy context that far from being supportive of mental health promotion, can often actively undermine it.

In a Canadian community-based participatory action research realist evaluation,²² collaboration across a community depended on power-sharing and co-governance. It took time for partners to establish trust in each other’s commitment to power equity. In a recent realist synthesis on inter-organizational collaborations,⁵⁶⁶ inter-organizational collaboration is defined as a “negotiation between people from different organisations with a commitment to working together to secure improvements which could not have been achieved by acting alone (Dickinson and Glasby 2010). This realist synthesis proposes a series of context-mechanism-outcome configurations (CMOCs). Many of the CMOCs are similar to those derived through community-based participatory action research.²² Table 4.1 contains our adaptations of inter-organizational CMOCs. Based on our review of literature at the other systems levels, there is evidence that these “collaboration” CMOCs are relevant to each systems levels and our simple rules approach.

4.4 Level 4: Developing Personal Health Skills/Resilience: Individuals, Families and Informal Supports

This level looks mainly at the personal resources individuals utilize to help them develop resilience, hope, confidence and well-being. Below we see the model the Framework for Support developed for what they call the Personal Resource Base, which again is very compatible with a mental health promotion, a two-continuum model, and the assets-based approach. Although the authors of the Framework have developed their models for people living with mental illness, this approach clearly applies to the general population other than perhaps the ‘practical understanding of the illness’ dimension, and certainly to those living

with chronic physical conditions that might not yet have developed a mental illness. There are many resources and interventions that aim at strengthening individual coping skills and resilience to bolster mental health and prevent the worst impacts of mental illness (e.g., self-aid, mutual aid, via peer support networks).

Figure 4.4: The Personal Resource Base²¹

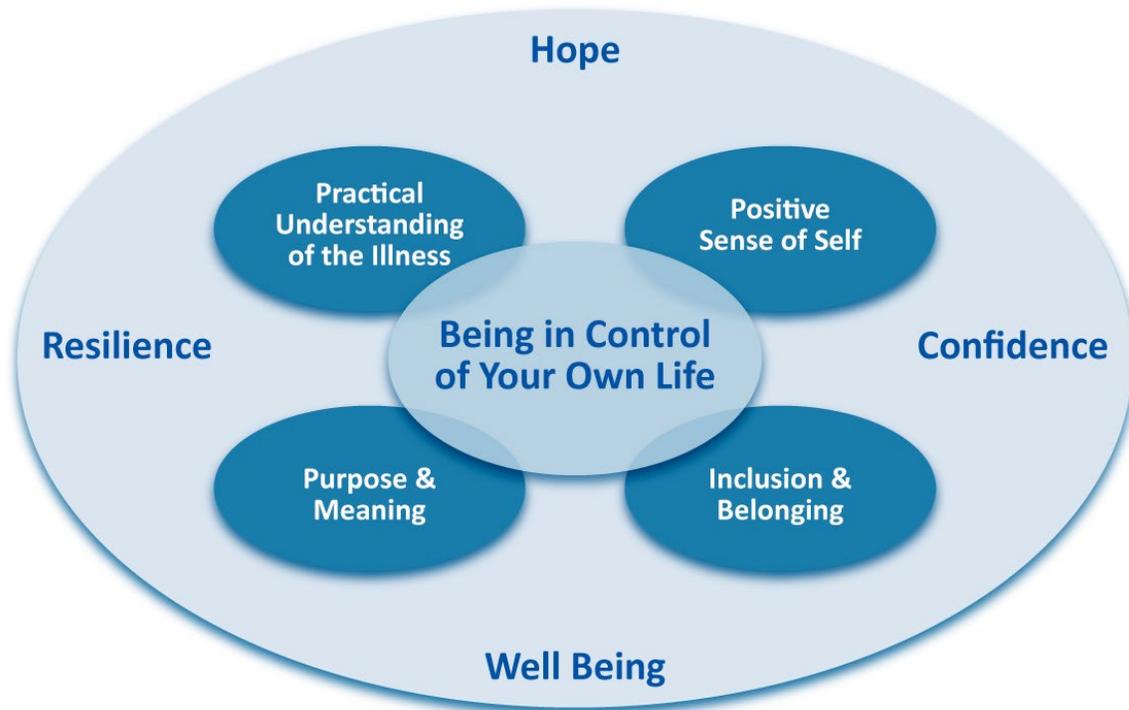


Table 4.1. Context-Mechanism-Outcome (CMO) Configurations to Complement Simple Rules	
Trust	Trust develops over time as partners at different systems levels earn trust through respectful, reliable interactions. CMO: High trust (context) creates partnership synergy (mechanism) leading to successful outcomes at all systems levels (e.g., mental health services delivery).
Formalization	Policy, especially at the highest level (national government) is an important context for successful outcomes at all systems levels. CMO: Formalization through policy (context) creates greater initial trust (mechanism) leading to greater uptake of mental health inclusion, mental health awareness at all systems levels.
Shared Vision	Shared vision, values and goals help bind diverse stakeholders at different systems levels. CMO: Having a shared vision (context) reduces the potential for conflict (mechanism) leading to improved trust/high trust (outcome) at all systems levels.
Commitment/ Accountability	Commitment and accountability are evidenced by partner investment. Is there evidence of preparation to act and to be accountable for actions taken? This is a litmus test for partners at each systems level. CMO: Evidence of preparedness and accountability (context) results in reduced conflict (mechanism) leading to greater trust (outcome) among partners at each systems level.
Power	Power differentials are a significant threat to collaboration at every systems level. CMO: Power imbalances among partners (context) creates partner domination (mechanism) leading to reduced trust, blocked mental health services delivery at each systems level.
Faith	Faith is belief and confidence in others-an important ingredient/context at every systems level. CMO: High faith (context) creates partnership synergy (mechanism) leading to enhanced mental health services delivery at each systems level.
Authenticity	Authenticity or genuineness is an important leadership component. It is also a necessary component of partner collaboration at any systems level. CMO: Authentic collaboration of partners (context) increases faith among partners (mechanism) leading to increased agreement over common goals, such as mental health services delivery (at each systems level).

Leadership	<p>There need to be effective leaders at each systems level. Effective leaders are authentic/genuine and they use positive psychology approaches to move others towards collaboration--at every systems level.</p> <p>CMO: Positive, authentic leaders (context) create more effective integration of different partners/cultures (mechanism) leading to greater trust among partners at each systems level (outcome).</p>
Culture	<p>Culture is an amalgamation of values, beliefs, attitudes--all influencing what we say and do at any systems level-national to individual.</p> <p>CMO: Cultural closeness or coherence (context) decreases conflict (mechanism) leading to greater trust among partners at each systems level.</p>
Flexibility	<p>In complex systems, there is a lot of unpredictability. At each systems level, there needs to be flexibility with respect to directives, guidelines, actions-so that partners can adapt within their own contexts.</p> <p>CMO: Greater flexibility in directives/guidelines (context) increases the likelihood of goal achievement (mechanism) leading to more efficient, effective mental health services delivery (outcome) at each systems level.</p>
Entry Point	<p>Within complex systems, there needs to be a designated entry point as a frame of reference for partners.</p> <p>CMO: Designated entry points (context) provide clarity (mechanism) leading to more confidence (e.g., consistent model for mental health services delivery) (outcome) at every systems level.</p>

5. Highlights and Recommendations

The intent of this report was to synthesize knowledge about common physical and mental health comorbidities related to their prevalence, incidence, and healthcare-related cost estimates across the lifespan and among priority and equity-seeking populations. In addition, the aim was to conduct a rapid realist review to help determine interventions that may work in different contexts and for different people.

A number of conclusions and recommendations arise from this review.

5.1 Health Education, Practice, Programming, and Policy

- All of the physical and mental health comorbidities highlighted in this report have shared biological, psychosocial, and environmental etiological pathways. Policies and preventive programming that are aimed at these pathways, particularly at psychosocial and environmental targets, are recommended. These should include addressing resource allocation to mental health promotion, screening and monitoring practices, and interventions
- Policies aimed at life course, population health, and mental health promotion have the potential to prevent or delay the development of physical and mental health conditions. Exemplars of policy targets include food environments, healthy eating, food security, physical activity, affordable childcare, affordable housing, social assistance, employment, as well as health and income equity
- Comprehensive, integrated, and tailored management programming that include shared decision-making will help to address the multiple underlying factors contributing to physical and mental health comorbidities. At a broader level, these practices can reduce health system costs
- As part of integrated health programs and practices, stepped-care models show potential to further optimize care for those with physical and mental health comorbidities. To facilitate the delivery of these approaches, supportive administrative and reimbursement structures will be needed that are inclusive of allied health professionals who can work collaboratively with other practitioners to support the end-user's physical and mental health needs
- Public health campaigns, which help to dispel myths and stigma associated with having chronic conditions, could minimize potential of mental health impacts that occur around the time of diagnosis. Exemplars of positive messaging could include showing individuals with health conditions leading healthy productive lives and working effectively with their health care team
- Better integration of primary care with social services is needed to address the multi-faceted complex needs of those with mental and physical health comorbidities. These services need to be accessible, particularly to groups that face barriers to access such as those residing in rural and remote communities. Established effective models of care applied to mental health such as peer support approaches may help to further support the needs of individuals with physical and mental health comorbidities

- Collaborative care models need to include all health disciplines including allied health professionals and substance use disorder specialists
- Health research should continue that informs practice, programming, and policy and include ongoing exploration of the determinants of health condition comorbidities, optimal delivery and integration of health and social services, and exploring policy alternatives to optimize population mental health should continue

5.2 Physical and Mental Health Comorbidities

Arthritis

a. Osteoarthritis (OA)

- Case finding for depression in people with OA has been recommended by the National Institute for Health and Care Excellence⁵⁰
- To optimize psychosocial well-being, models of care should incorporate strategies aimed at maintaining function, using positive language to describe the condition, increasing social participation, and maintaining employment
- Multi-modal interventions that include cognitive behaviour therapy, neuroscience education, centrally-acting drugs, and exercise could improve both OA-related pain and mental health^{70,66}

b. Rheumatoid Arthritis (RA)

- Psychological evaluation and care are recommended to be among the therapeutic objectives.⁸⁶ Clinicians recommend use of the Hospital Anxiety and Depression Scale (HADS) for screening,⁸⁶ however its validity and reliability in this population has not been assessed
- Better physical and mental health outcomes for those with RA are likely to result from integrated mental health care provided within routine clinical practice⁵⁶⁷
- The goals of care should aim to engage and motivate the person toward goal-setting, attend to psychological needs of caregivers, generate trust and empathy, negotiate treatment options, and promote self-efficacy⁸⁶

c. Psoriatic Arthritis (PsA)

- Screening tools used include the HADS, General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9); however, validation studies are needed⁹³
- Treatment escalation driven by non-inflammatory symptoms may increase adverse events and appears to provide modest improvements in mental health-related areas (e.g., quality of life)⁹⁸
- Joint guidelines of care recommend people with psoriasis should be informed about the association of psoriasis and anxiety and depression and asked about signs and symptoms¹⁰⁰
- Psoriasis-specific therapy is recommended as a measure to improve psoriasis-associated anxiety and depression in individuals with psoriasis¹⁰⁰

Cancer

- Screening is recommended at different stages of cancer (e.g., pre-treatment, periodic follow-ups post-treatment, and survivorship periods)
- Important considerations in cancer care are risk of potential re-traumatization of PTSD when individuals undergo pelvic, breast, or rectal examinations. Relapses of a depressive disorder may occur after mastectomy, and relapses of manic or depressive episodes in bipolar affective disorder may occur due to essential treatment with corticosteroids
- Addressing underlying secondary or disease-related causes can promote mental health. Examples included treating symptoms such as hypothyroidism that arise from radiotherapy with head and neck cancer and vitamin B₁₂ deficiency after pelvic irradiation
- Use of antidepressants should be determined on an individual basis; SSRI are suggested to have a positive safety profile¹⁴⁰
- Collaborative care appears to be more effective than pharmacological and psychological interventions for depression reduction¹⁴⁴
- While some complementary therapies such as lavender, passionflower, and saffron may produce benefits comparable to standard anxiety and antidepressant medications. These results need to be confirmed with larger RCTs.¹⁴¹
- Life review programs may help reduce depression and anxiety¹⁴⁵
- Stepped care approaches for mental health interventions in cancer are recommended and should include the following considerations:¹⁴⁶
 - i. Psychotropic medications should be guided by clinical parameters, particularly interactions with chemotherapies, to identify specific contraindications;
 - ii. Psychological therapies such as CBT can help in understanding the thoughts, feelings, and behaviours that can cause or maintain symptoms of depression or anxiety (e.g., treatment refusal, avoidance behaviour, or excess reassurance seeking);
 - iii. Providing availability of specialist psychological therapy with appropriate expertise. Therapeutic expertise needs include complex illness beliefs, challenging side effects (e.g., psychosexual), physical disfigurement, and end-of-life issues.
- Integrated mental and physical cancer care approaches are also recommended. One reported model of the UK NHS Cancer Strategy includes:¹⁴⁷
 - i. Collaborative screening and treatment;
 - ii. Cancer clinical nurse specialist delivery of supervised CBT interventions for depression, and
 - iii. Guidance to GPs by liaison psychiatrists to optimise the prescribing of antidepressant medication.
- In Canada, examples of integrated mental and physical cancer care approaches exist.
- Better integration between primary and tertiary cancer care is understood to lead to improved coordination, continuity and quality of care.

- There is some preliminary evidence that comprehensive education and care (CEC) programs are more effective than basic health education and rehabilitation to improve anxiety and depression in those with hepatocellular carcinoma who underwent surgical resection¹⁵⁰
- Psychotherapy combined with psychoeducation and exercise appears to be more effective in improving depressive symptoms when compared to psychoeducation alone¹⁵¹

Cardiovascular Disease (CVD)

- Various studies recommend that all people diagnosed with CVD be screened for depression, particularly at key periods such as post myocardial infarction or major surgical interventions
- For people that have had an acute coronary syndrome, depression screening is recommended while in hospital and rescreening should occur two months after the acute event.¹⁸² Individuals with chronic heart failure also have a high frequency of depression and should be screened at least annually
- Longer-term face-to-face CBT has shown benefit for improving depression.²¹⁰ Internet-based CBT has limited evidence and has been indicated to be unsuitable for moderate-to-severe depression or anxiety.²¹⁰ Furthermore, treatment adherence may be low.²⁰⁹
- Cardiac rehabilitation programs for CAD and congestive heart failure for older adults (64 years+) offered in their home is effective for reducing depression. Tailored interventions combined with psychosocial interventions are likely to be more effective in decreasing depression in older adults with heart disease compared to usual care²²³
- For those with CHD, aerobic exercise in a group setting improves depression and cardiovascular function²⁰⁶
- CBT in combination with exercise may help improve depression symptoms²¹¹ and reduce subsequent cardiovascular events²¹²
- Anti-depressant medications are reported to improve depression in individuals with CVD, however, efficacy needs to be balance with potential risks.²¹⁵ For example, tricyclic anti-depressants have been shown to lengthen cardiac myocyte action potentials²¹⁵
- Combination therapies appear to reduce depression after ACS. Combined therapeutic approaches of stepped care have been reported to be effective in improving depression symptoms²¹⁶
- Anxiety and depression may be more effectively improved in programs offering CBT plus an HF education program²¹⁷
- Compared with usual care or center-based cardiac rehabilitation, home-based interventions may have heightened benefit in reducing anxiety²¹⁹
- Home-based robot-assisted rehabilitation coupled with a home exercise program helps to improve depression, quality of life, and condition impact in people who have had a stroke²²⁰

- Individuals living in rural settings admitted to hospital for ACS may be prone to heightened anxiety. The development and testing of protocols for anxiety reduction in rural settings may be needed¹⁷⁵
- Problem-solving therapy may help prevent mood disorder diagnosis in individuals who have had a stroke²¹³

Dementia

- Primary prevention strategies that target shared metabolic pathways, such as those contributing to CVD, may prevent depression in AD
- NICE guidelines suggest psychological treatments for people with mild-to-moderate dementia who have mild-to-moderate depression. Antidepressants are indicated for those with a pre-existing severe mental health problem⁵⁶⁸
- Several brief psychotherapeutic interventions have been shown to be effective in this population.²⁵³ Behavioural therapies are more commonly applied in the later stages of dementia, while modified cognitive-behavioural strategies appear to be more successful with those in the earlier stages of cognitive decline²⁵⁴
- CBT programs for persons with dementia should involve their caregivers, both as CBT coaches for the care recipient and as treatment partners²⁵⁵
- Based on social support research findings, depression management at the time of dementia diagnosis should include interventions to increase social engagement²⁵⁶
- Physical activity interventions can improve physical function in older people with dementia, however, evidence for an effect on depression is limited²⁴⁹
- Bright light therapy may help to reduce depression and agitation in persons with dementia residing in long-term care facilities²⁵⁷

Diabetes Mellitus (DM)

- Mental health screening is recommended at least annually
- The initiation of new anti-diabetic medication may be a time of heightened vulnerability to depression. Clinicians should be aware that women, patients starting an AD at a young age, those with a low SES, and a history of anxiety or dementia may need to have their physical and mental health tracked closely²⁶⁷
- Targeting the three well established inter-related major pathophysiologic pathways between DM and mental health may optimize both physical and mental health. The pathways include hyperglycaemia, microvascular dysfunction, and inflammation
- Holistic, preventive services focusing on healthy diet, physical activity, healthy weight management, to promote both physical and mental health is recommended
- Antidepressants may both moderate depression severity and improved glycemic control
- Collaborative care with stepped care approaches that include choice of psychotherapy and pharmacotherapy presents good results for treatment of depression and anxiety in diabetes⁵⁶⁹
- Examining indicators of low-grade inflammation as a prognostic tool for choosing the treatment modalities in individuals with both depression and T2DM may have beneficial effects for cardiovascular risk mitigation and management

- Interventions such as diabetes self-management education and pharmacist-led group shared medical appointment visits may improve glycemic control^{291,293}
- Depression in T2DM varies among ethnic groups, which suggest the need to address stressors unique to racial/ethnic minorities to improve diabetes-related outcomes²⁹²
- Integrated interventions co-developed with end-users, their family members, and provider stakeholders may positively impact on both diabetes and depression-related outcomes, particularly among specific ethnic groups²⁹⁴
- Integrated interventions that use patient prioritized planning (incorporated financial, social and emotional needs for primary care patients with T2DM and depression) may improve HbA1c and depression symptoms²⁹⁵
- Usual care plus psychotherapy for depression via home telehealth (home monitor that captures clinical measures) may improve glycemic control and generate significant healthcare cost savings²⁸⁹

Epilepsy

- The BDI-I and BDI-II have been well-validated as a depression screening tool in epilepsy³⁰⁵
- Clinicians need to consider that there are various subtypes of depression in people with epilepsy in order to best screen and manage symptoms³⁰⁶
- Individuals with PTSD may be at elevated risk of developing epilepsy
- Among intervention options oxcarbazepine, venlafaxine, and lamotrigine may improve mood and CBT may improve both depression and epilepsy outcomes.³¹³ Specialist epilepsy nursing and self-management education, have some evidence of benefit. At present it is not possible to advocate any single model of service provision for self-management in epilepsy³¹⁴

Frailty

- Screening of mental health in frailty is recommended but complicated as mental health may be considered part of the condition's definition
- The task force of the International Conference of Frailty and Sarcopenia Research (ICFSR) recommend the following guidelines for managing frailty:³²⁷
 - Address polypharmacy, the management of sarcopenia, the treatable causes of weight loss, and the causes of exhaustion (depression, anaemia, hypotension, hypothyroidism, and vitamin B₁₂ deficiency)
 - All persons with frailty should receive social support as needed to address unmet needs and encourage adherence to a comprehensive care plan
 - Include a multi-component physical activity programme with resistance-based training
 - Provide protein/caloric supplementation when weight loss or undernutrition are present
- At this time, there is insufficient evidence to support therapies such as cognitive therapy, problem-solving therapy, vitamin D supplementation, and hormone-based treatment³²⁷

Huntington's Disease (HD)

- Mental health-related comorbidities reported in HD have included depression, irritability, anxiety, apathy, hallucinations, psychosis, suicide ideation and attempts, obsessive/compulsive disorders, and perseveration³³⁶
- The Irritability Scale of the Beck Depression Inventory-II, and the Hospital Anxiety and Depression Scale for depression are recommended screening tools³³⁶
- Mental health management should be based on the identification of underlying environmental or somatic (e.g., pain, side effects of medications) triggers causing changes in mood or behaviour
- International Guidelines for the Treatment of Huntington Disease suggest mindfulness-based cognitive therapy and Acceptance and Commitment Therapy, personalized cognitive stimulation, establishing routines, a structured programme of activities, and psycho-education for the family regarding diversion strategies to mitigate confrontations³³⁴
- For depression that is resistant to medications, electroconvulsive therapy (ECT) may be suggested under the guidance of a psychiatrist³³⁴
- Suicide risk should be assessed regularly, including at diagnosis and when the disease starts to impact on daily activities. Individuals with active suicidal ideation and a plan require immediate psychiatric evaluation³³⁴

Inflammatory Bowel Diseases (IBDs)

- Reducing stress with support from psychological interventions improves health-related quality of life³⁵³
- There is insufficient evidence to recommend online psychological interventions. The research literature about benefits of CBT is mixed^{357,358,359}
- The British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults suggest psychological intervention (psychotherapy, patient education and relaxation techniques) for anxiety, pain, and stress levels to improve mood⁵⁷⁰
- Mindfulness as an adjunct to pharmacological therapy may improve psychological symptoms in IBD and facilitate coping with symptoms during a disease flare-up^{360,361,362}
- Gut directed hypnotherapy has an established evidence base for the control of IBS symptoms, however more research is needed to determine if there are mental health benefits^{363,364}

Kidney Disease (Chronic) or CKD

- Some studies support mental health screening programs and suggest screening for depression should take place at key transition points such as at the initial evaluation, dialysis initiation, and regular intervals thereafter³⁶⁶
- The benefits vs harms of anti-depressant medications need to be considered. The medications are broken down by the liver and end products may not be removed

sufficiently by the kidneys or through dialysis. Further concerns are increased risk of drug interactions and accumulation of toxic metabolites³⁶⁶

- Chronic disease self-management programming that includes activities such as exercise therapy may foster mental health.³⁶⁶ CBT may be beneficial during changes in dialysis regimen³⁶⁶
- Nurse-led, in-center breathing training programs for individuals on maintenance hemodialysis may improve depression³⁷²

Metabolic Syndrome (MetS)

- Screening and monitoring of MetS in individuals with mental health conditions, particularly those taking anti-psychotic medications, is part of standard care
- The HADS is a reliable screening tool for current major depressive episode and generalized anxiety disorder in middle aged and elderly populations with and without MetS.
- A systematic review reported there was some indication of a possible protective effect of drug combinations including aripiprazole for diabetes and hyperlipidaemias. Long-term prospective studies are required for accurate appraisal of diabetes risk, hypertension, and hyperlipidaemia in those exposed to antipsychotic medication polypharmacy⁴⁰⁶
- SSRIs have been shown to reduce cytokine levels⁴⁰⁸ and may be protective against MetS
- Mental health based primary care of individuals accessing services of a community mental health center may improve diabetes HbA1c monitoring and metabolic monitoring of anti-psychotic medication treatment⁴⁰⁷

Obesity

- A typical tool used for mental health screening is the Patient Health Questionnaire-9 or PHQ-9
- Screening is particularly recommended in sarcopenic obesity, defined as being the presence of loss of muscle and obesity typically related to aging
- Current guidelines related to management of overweight and obesity in adults align with risk profiles for CVD⁴³¹ and integrates guidelines for cardiometabolic monitoring for those with weight gain related to anti-psychotic medication use
- Mobile health (mHealth), health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices may have potential in managing obesity and mental health but further research is needed
- Interventions for obesity should involve mental health professionals.⁴²⁰ Behavioural interventions, that involve treatments that are taken to modify behaviour, emotions, and cognition to improve psychological and physical well-being are integral⁴¹⁹
- Research has indicated that when pharmacological and surgical interventions are combined with psychological supplements via behavioural health interventions, treatment adherence and long-term sustainability are enhanced⁴¹⁹

- Psychotropic medications that treat psychosis and mood stabilization may contribute to weight gain and adversely affect lipid and glucose metabolism.⁴³⁴ Healthcare providers need to consider these factors when making treatment choices⁴³⁵ and implement integrated education, assessment, and care for those with mental health concerns and at risk for weight gain
- Health promotion and weight loss intervention programs for lesbians should incorporate psychological, relationship, and alcohol use components to reduce overweight and obesity⁴³⁶

Parkinson's Disease (PD)

- The most suitable scales for screening for depression disorders are the Ham-D and BDI scales, the geriatric depression scale, the HADS, and the Montgomery Asberg Depression Rating Scale (MADRS)^{441,444}
- Physical activity can improve the clinical status in areas such as function, fatigue, depressive symptoms, sleep disorders, and quality of life.⁴⁵¹ The American College of Sport Medicine activity guidelines can be applied to patients with PD: aerobic exercise, strengthening, and balance training flexion is recommended three times a week for at least 30 minutes⁴⁵²
- Mind-body exercises may improve motor function, depressive symptoms, and quality of life, however, more needs to be known about specific factors such as gender, severity of disease, specific drug use, and intervention cycle⁴⁵³
- Early identification of mental health symptoms and appropriate multidisciplinary management of depression may improve the quality of life of people with PD⁵⁷¹
- Antiparkinsonian medications might improve mood disorders by alleviating motor manifestations and disability, fostering feelings of disease mastery, or restoring dopaminergic signalling.⁴⁵⁴
- CBT is promising for acute management of depression and anxiety⁴⁵⁵
- Unilateral subthalamic nucleus deep brain stimulation on non-motor symptoms for individuals with moderate to severe PD may also improve depression, sleep quality, and quality of life⁴⁵⁰

Respiratory Diseases (Chronic)

- The literature reports the use of the Ham-A and Ham-D, however, there is no consensus on the evaluation tools and diagnostic criteria of COPD with depression and anxiety
- The inter-connectedness of stigma-related experiences to these conditions highlight the need for integrated approaches⁴⁷⁸
- Management of chronic respiratory diseases should aim for individualized care. For example, individuals with COPD tend to prefer treatments that provide symptom relief (e.g., dyspnea), positive physician relations, and improve quality-of-life. Individuals with asthma prefer treatments that increase symptom-free days and may be willing to trade days without symptoms for a reduction in adverse events and greater convenience⁴⁸⁷

- Pulmonary rehabilitation is beneficial for those with comorbidities and has been shown to reduce the severity of depression and cardiovascular risk factors, including blood pressure^{488,473}
- The National Institute for Health and Care Excellence (NICE) has guidelines for the use of stepped approaches to psychological and/or pharmacological treatment of depression in people with long-term conditions, including respiratory conditions⁵⁷²
- Personalized behaviour and problem solving-adherence interventions provide similar improvements in depression⁴⁸³
- Older adults (67-85 years) hospitalized for COPD who are offered controlled breathing technique interventions reported significantly improved dyspnea, reduced anxiety, and better mobility⁴⁸⁴
- For individuals with COPD, depression symptoms were shown to be more improved among those receiving psychological therapies (CBT-based approach) compared to standard care, educational interventions, or a co-intervention (pulmonary rehabilitation)⁴⁸⁵

5.3 Mental Health Promotion

Based on an adapted a socio-ecological framework (Figure 4.1) that draws upon program theories to explain mental health promotion at different systems levels, four broad guidelines for mental health promotion to help prevent and manage physical and mental health comorbidities are recommended.

Level 1: Healthy Public Policy for Mental Health: Mental Health Promotion/Mental Health in All Policies (MHiAP)

People living with mental and physical illnesses have the potential to live a flourishing, joyful life. We must also try to promote and strengthen health assets, including structurally (social, economic and cultural) supportive environments, community resilience and life coping skills.

A Program Theory for Mental Health in All Policies

A MHiAP strategy → Intersectoral governance for mental health → Changes in policies (usually signaled by some sort of strategic document/plan) → policy actions (legislative, regulatory, budgetary/investment tools) to promote mental health → Impact on social determinants of mental health → Improved mental health outcomes (e.g. increased well-being, happiness, improved coping and resilience, reduced mental stress, reduced incidence of mental illness, reduced harms from substance misuse, reduced incidence of suicide).

Agenda Setting for a MHiAP Strategy

A 'Health in All Policies' approach to intersectoral collaboration has been gaining ground globally as a policy-level agenda aimed at addressing the wider social determinants of health. Advocates of HiAP highlight the importance of mental health promotion as central

to successful HiAP approaches, and as a means to contribute to addressing health equity and inequality;^{9,10} conversely, advocates of mental health promotion have identified HiAP as a key policy framework for advancing mental health and physical health.^{11,12}

Based on a review of the literature on HiAP adoption and implementation, we propose five simple rules for successful HiAP initiation: 1) Developing a shared language and fluency around a broader understanding of ‘health’ to include well-being and happiness, and general welfare; 2) Linking evidence for how HiAP initiatives are able to contribute to sustainable economies and sustainable health systems (both theoretical and empirical); 3) Having an ‘entry point’ to initiate an HiAP agenda; 4) Developing ‘win-win’ scenarios, goals and objectives across sectors;¹³ 5) Building and fostering long-term collaborative partnerships and engagement with intersectoral stakeholders.

In the Canadian context, not only is mental health well placed to be included in any HiAP policy agenda, it may in fact be the key entry point for raising the awareness and urgency of a HiAP approach at the federal and provincial levels. First, with the help of key policy elites, such as Senators Kirby and Wilson, and with the establishment of the MHCC, much of the foundational work in boosting awareness has already taken place. In this collective work, Canadian researchers, practitioners, policy-makers and people with lived experience have worked on developing a more inclusive, shared language around mental health, that by its nature tends to be less ‘deficit-focused’ and more positive and strengths-based.

Level 2: Reorienting Mental Health Services: Integrated Health and Social Services

Beyond the HiAP approach, a key role for public policy is to provide the regulatory, legislative and financial context for the transformation of health and social services more broadly in society. For Canadians, ‘health reform’¹⁴ is an ongoing reality, that is complex and multi-faceted, with varying objectives across provinces, and widely differing governance strategies and outcomes. However, a common recurrent theme is the need to develop *integrated, collaborative systems of health and social care* to address the increasingly complex needs of an ageing population, with the concomitant multimorbidity of chronic diseases, both physical and mental being the driving force of this complexity. While these efforts require many transformational changes at the health and social service/organizational level, there is a strong role for high-level policy in successfully moving towards the ideal system. It is generally acknowledged, based on decades of research evidence,¹⁵ that comprehensive primary health care, as originally outlined in the Alma Ata Declaration,¹⁶ is the overarching framework for efficiently, effectively, and equitably organizing health and social services in order to produce optimum health in populations.

The **program theory** at this level is: by providing *universal financial coverage, under government control and regulation, with equitable distribution of services, comprehensive coverage, and with low or no co-payments*, then you attain “*greater first contact access and use, more person-focused care over time, greater range of services available and provided when needed, and coordination of care.*” (Starfield, 2012, p. 20).

Integrating care via simple rules allows relatively autonomous actors to use their contextual knowledge to come up with creative implementation solutions. At the integrated care level, there are some important contextual factors to consider. In order for clients to have a voice in decision-making (e.g., priority physical and social/mental needs), power differentials need to be ‘smoothed.’ Differential power dynamics impede effective collaborative practice among different service providers,¹⁷ but they also relegate clients to a marginalized role with respect to decisions around their care needs. Physicians are considered the top of the healthcare hierarchy, and this conceptual approach can break the success of any reform program or change initiative.

Level 3: Strengthening Community Mental Health Action: Community Assets for Mental Health

At this systems level, community “assets” for mental health are the chosen foci, as they bring together three important theoretical approaches to mental health: mental health promotion,¹⁸ the two-continuum approach;¹⁹ and, the Canadian Mental Health Association’s framework for support approach.^{20,21}

The **program theory** at the community level is: by helping to *co-create, strengthen and sustain community mental health assets*, people can be supported to live happy, joyful, flourishing lives, whether or not they are living with mental or physical illness *and* they can be empowered to help co-produce and shape the mental health services they receive in community through context-appropriate co-produced mental health service planning.

We propose a series of context-mechanism-outcome configurations (CMOCs). Many of the CMOCs are similar to those derived through community-based participatory action research.²² Based on our review of literature at the other systems levels, there is evidence that these “collaboration” CMOCs are relevant to each systems levels and our simple rules approach and are outlined as follows.

Context-Mechanism-Outcome (CMO) Configurations to Complement Simple Rules	
Factor	CMO
Trust	High trust (context) creates partnership synergy (mechanism) leading to successful outcomes at all systems levels (e.g., mental health services delivery).
Formalization	Formalization through policy (context) creates greater initial trust (mechanism) leading to greater uptake of mental health inclusion, mental health awareness at all systems levels.
Shared Vision	Having a shared vision (context) reduces the potential for conflict (mechanism) leading to improved trust/high trust (outcome) at all systems levels.

Commitment/ Accountability	Evidence of preparedness and accountability (context) results in reduced conflict (mechanism) leading to greater trust (outcome) among partners at each systems level.
Power	Power imbalances among partners (context) creates partner domination (mechanism) leading to reduced trust, blocked mental health services delivery at each systems level.
Faith	High faith (context) creates partnership synergy (mechanism) leading to enhanced mental health services delivery at each systems level.
Authenticity	Authentic collaboration (context) increases faith (mechanism) leading to increased agreement over common goals, such as mental health services delivery (at each systems level).
Leadership	Positive, authentic leaders (context) create more effective integration of different partners/cultures (mechanism) leading to greater trust among partners at each systems level (outcome).
Culture	Cultural closeness or coherence (context) decreases conflict (mechanism) leading to greater trust among partners at each systems level.
Flexibility	Greater flexibility in directives/guidelines (context) increases the likelihood of goal achievement (mechanism) leading to more efficient, effective mental health services delivery (outcome) at each systems level.
Entry Point	Designated entry points (context) provide clarity (mechanism) leading to more confidence (e.g., consistent model for mental health services delivery) (outcome) at every systems level.

Level 4: Developing Personal Health Skills/Resilience: Individuals, Families and Informal Supports

This level looks mainly at the personal resources individuals utilize to help them develop resilience, hope, confidence and well-being. There are many resources and interventions that aim at strengthening individual coping skills and resilience to bolster mental health and prevent the worst impacts of mental illness (e.g., self-aid, mutual aid, peer support networks).

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Appendix A: Search Strategy

The purpose of the search strategy is to: 1) obtain literature about common physical and mental health co-morbidities that outlines their prevalence and incidence across the lifespan and among priority populations and equity-seeking groups (scoping review); and 2) obtain literature about common physical and mental health co-morbidities and effective strategies in which to prevent and mitigate them across the lifespan and among priority populations and equity-seeking groups (rapid realist review).

Working Definitions

Comorbidity: the co-occurrence of at least one mental and at least one physical disease or disorder in the same person, regardless of the chronological order in which they occurred or the causal pathway linking them⁹. For the purposes of this project, multimorbidity would be considered as inclusion criteria for comorbidity.

Non-communicable conditions: Physical health conditions as indicated by the WHO's top 20 leading causes of disease burden and other global burden of disease estimate studies that include diabetes, cardiovascular and chronic respiratory diseases, rheumatoid arthritis, osteoarthritis, inflammatory bowel disorders, kidney disease, neurological conditions (Alzheimer's disease, dementia, Parkinson's disease).

Mental health conditions: Depressive and anxiety disorders, bipolar and related disorders, schizophrenia spectrum and other psychotic disorders, obsessive-compulsive and related disorders, trauma- and stressor-related disorders, substance use and addictive disorders, and feeding and eating disorders.

Where applicable, the most recent edition of the International Classification of Diseases will be used to screen for the NCDs and mental health conditions. For the mental health conditions, however, it is anticipated that older versions will need to be used. In addition, the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders Revision IV and 5 will be used.

Populations: Women/men, immigrant, refugee, ethnocultural and racialized (IRER) communities, First Nations, Inuit and Métis, 2SLGBTQ+, linguistic minorities, rural, low income, aging (>65 years).

Databases: MEDLINE, EMBASE, CINAHL, PsycInfo, Sociological Abstracts, and EBM Reviews Multifile

Search Limiters: English language, full texts, human, January 2010–

⁹ Benjamin G. Druss & Rosalynn Carter. Mental disorders and medical comorbidity. 2011. Robert Wood Foundation

1. Searches of Academic Databases

Search 1: Broad Mental and Physical Health Terms

Code A	Concept (Broad Terms)	Code B	Concept (Complementary Terms)
BT1	Multimorbid* or Comorbid*	CT1	Psychiatr* or psychol* or mental*
		CT2	Prevalence or incidence

Search 2: Search of Non-communicable Diseases

Code A	Concept (Mental Health)	Code B	Concept (Physical Health)
MH1	Depress* or affective disorder	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke*
			or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheim* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or nephr* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
PH12	Frail*		
MH2	Anxiety*	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
			or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheim* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or nephr* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
PH12	Frail*		

Code A	Concept (Mental Health)	Code B	Concept (Physical Health)
MH3	Bipolar* or Manic*	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheim* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or neph* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
		PH12	Frail*
		MH4	Schizophr* or Schizoaff*
PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*		
PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis		
PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*		
PH5	Diabetes or diabetes mellitus		
PH6	Bowel* or colitis* or ulcerative colitis or crohn's		
PH7	Neoplas* or tumor or cancer or malignan*		
PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheim* or Parkin* or epilepsy		
PH9	Kidney dis* or urol* or neph* or renal dis*		
PH10	Obes*		
PH11	Metabolic Syndrome		
PH12	Frail*		

Code A	Concept (Mental Health)	Code B	Concept (Physical Health)
MH5	Psychos* Psychot*	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or Amnestic or Alzheimer* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or neph* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
		PH12	Frail*
MH6	Obsessive-compulsive or neurosis	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheimer* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or neph* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
		PH12	Frail*

Code A	Concept (Mental Health)	Code B	Concept (Physical Health)
MH7	Trauma* or PTSD or post-traum* or stressor	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or Amnestic or Alzheim* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or neph* or renal dis*
		PH0	Obes*
		PH11	Metabolic Syndrome
		PH12	Frail*
MH8	Substance* or addict* or compuls* drug abuse or drug dependence	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheim* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or neph* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
PH12	Frail*		

Code A	Concept (Mental Health)	Code B	Concept (Physical Health)
MH9	Feeding dis* or eating dis* or anor* or Bulimia or Binge Eating Disorder	PH1	Hyperten* or high blood pressure
		PH2	Cardiovasc* or heart* or coronary* or myocar* or stroke* or cerebrovas* or ischem*
		PH3	Respir* or asthma or lung dis* Or pulmon* or COPD or dyspnea or emphys* or bronchitis
		PH4	Arthr* or osteoarthr* or rheumatoid arthr* or spondylarthr* or musculoskeletal*
		PH5	Diabetes or diabetes mellitus
		PH6	Bowel* or colitis* or ulcerative colitis or crohn's
		PH7	Neoplas* or tumor or cancer or malignan*
		PH8	Neurocogn* or neurol* or dementia or amnestic or Alzheimer* or Parkin* or epilepsy
		PH9	Kidney dis* or urol* or neph* or renal dis*
		PH10	Obes*
		PH11	Metabolic Syndrome
		PH12	Frail*

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Search 3: Broad Mental and Physical Health Terms with Priority and Equity-Seeking Populations

Code A	Concept (Comorbid)	Code B	Combine With Priority Groups
CM1	Multimorbid* or comorbid*	PG1	Disadvan* or hard-to-reach or marginalise* or marginalize* or vulnerable or socioeconomic or inequalit* or inequit* or unequal*
		PG2	Emigrant* or foreign* or foreign born or immigrant* or migrant* or im/migrant* or refugee*
		PG3	Ethni* or ethnic minorit* or minority population* or race* or racial* or racial minorit* or visible minorit*
		PG4	Aged or aging or elder* or old age* or older or senior* or frail*
		PG5	Countryside or remote or rural
		PG6	Education* or litera* or illitera*
		PG7	Income* or poor or poverty
		PG8	Sex* or women
		PG9	Aborig* or Indig* or First Nations or Inuit or Métis
		PG10	2SLGBTQ+ or GLBT or Person* or Non-Heterosexual* or sexual or minorities or gay or gender minor* or Lesbian or bisexual or homosexual or queer or pansexual
		PG11	Canada and French Quebec and English

2. Grey Literature Searches

1) Theses/dissertations:

- Proquest Dissertations and Theses
- Theses Canada Portal
- Networked Digital Library of Theses and Dissertations (NDLTD)

2) Conference proceedings/papers:

- PapersFirst
- ProceedingsFirst

3) International, national & provincial non-profit organizations (addressing the identified disease groups and priority populations)

a. International

- World Health Organization
- Mental Health International
- Mental Health Foundation: UK - <https://www.mentalhealth.org.uk/>
- MIND UK <https://www.mind.org.uk/>
- International Research Community on Multimorbidity
- Equally Well – Australia - <https://www.equallywell.org.au/>

- Equally Well – New Zealand
- <https://www.tepou.co.nz/initiatives/equally-well-physical-health/37>
- Equally Well - UK - <https://equallywell.co.uk/>
- b. National
 - Alzheimer’s Society of Canada
 - Anxiety Disorders Association of Canada
 - The Arthritis Society of Canada
 - The Asthma Society of Canada
 - Autism Canada
 - Canadian Centre on Substance Use and Addiction
 - Canadian Diabetes Association
 - Canadian Frailty Network
 - Canadian Hypertension Society
 - Canadian Lung Association
 - Canadian Mental Health Association
 - The Centre for ADHD Awareness, Canada
 - Crohn’s and Colitis Canada
 - Heart and Stroke Foundation of Canada
 - Metabolic Syndrome Canada
 - Mood Disorders Society of Canada
 - Obesity Canada
 - OCD Canada
 - Parkinson Canada
 - Schizophrenia Society of Canada
 - Diabetes Canada
 - Cardiac Health Foundation of Canada
 - Huntington Society of Canada
 - Kidney Foundation of Canada
 - The Centre of Excellence for Women’s Health (for relevant studies using sex and gender-based analysis)
- c. Provincial non-profit organizations
 - Provincial chapters of national non-profit organizations listed above
 - Provincial non-profits (e.g., National Organization of Immigrant and Visible Minority Women of Canada)
 - Medical Psychiatry Alliance (<https://www.medpsychalliance.ca/>)
- 4) Government departments or agencies (international and national)
 - Ministries of Health (federal and provincial), including departments of chronic disease and primary care
 - Provincial and regional health authorities (Vancouver Coastal Health and others in BC and Canada)
 - Public Health Agency of Canada

- Centre for Health Services and Policy Research (CHSPR), University of British Columbia
- Health Quality Council, Saskatchewan
- Institute for Clinical Evaluative Sciences (ICES), Ontario
- Institute of Health Economics (IHE), Alberta
- Agency for Healthcare Research and Quality (AHRQ), USA
- Public Health Ontario

5) National & provincial healthcare provider associations (international and national)

- Canadian Medical Association
- Canadian Psychiatric Association
- Canadian Psychological Association
- Canadian Nurses Association
- Canadian Physiotherapy Association
- Canadian Association of Occupational Therapists
- Dietitians of Canada
- Provincial chapters of associations listed above

The grey literature checklist Grey Matters, developed by the Canadian Agency for Drugs and Technologies in Health (CADTH), and the New York Academy of Medicine's Grey Literature Report will also be mined for organizations relevant to the review. Although some grey literature sources may use standardized subject headings to index their publications, the vast majority rely on information being extracted by keyword. In general, keywords from the detailed strategy in the table below will be used to query the identified sources, providing for context dependent modification.

6) Cited reference checking (reference mining and snowballing)

Useful supplementary strategies for unearthing relevant studies are referencing mining and snowballing, techniques that are two sides of one coin. Reference mining involves combing through bibliographies and reference lists of key articles to find similarly relevant literature. Snowballing involves the use of a cited reference database such as Web of Science, or a parallel feature in Google Scholar and other databases to determine who has cited the article in question.

7) Personal contacts

For discovering the most current literature, works that have yet to be indexed or even works in progress, working through personal contacts are an effective method. As the search evolves, we will compile a list of relevant key authors to follow up with.

Background:

Purpose of the search strategy: 1) obtain literature about common physical and mental health co-morbidities that outlines their prevalence and incidence across the lifespan and among priority populations and equity-seeking groups; and 2) obtain literature about common physical and mental health co-morbidities and effective strategies in which to prevent and mitigate them across the lifespan and among priority populations and equity-seeking groups. The following will be applied to the abstract screening:

1. Does the abstract refer to at least one of the following mental health conditions:

- Depressive disorders (includes major depression, depression)
- Bipolar and related disorders (includes Manic depressive)
- Anxiety
- Schizophrenia spectrum (Schizoaffective)
- Psychotic disorders (includes psychosis)
- Obsessive-compulsive disorders (includes neurosis)
- Trauma- and stressor-related disorders; example post-traumatic stress disorder
- Substance use and addictive disorders (includes compulsive disorders, drug abuse, drug dependence, gambling)
- Feeding and eating disorders (includes anorexia, bulimia, binge eating disorder)

AND

2. Does the abstract refer to at least one of the following physical health conditions:

- Diabetes (includes diabetes mellitus)
- Cardiovascular (includes hypertension or high blood pressure, myocardial infarction, coronary heart disease, stroke, cerebrovascular accident, ischemic heart disease)
- Chronic respiratory diseases (includes asthma, lung disease, pulmonary, chronic obstructive pulmonary disease, COPD, dyspnea, emphysema, bronchitis)
- Arthritis (rheumatoid arthritis, osteoarthritis, spondyloarthritis, musculoskeletal arthritis)
- Inflammatory bowel disorders (includes colitis, ulcerative colitis or crohn's)
- Cancer (neoplasm, tumor; all types)
- Kidney disease (includes nephritis, renal disease)
- Obesity
- Metabolic syndrome
- Frail or frailty
- Neurocognitive conditions: dementia, amnestic, amnesia, Alzheimer's disease, dementia, Parkinson's disease, epilepsy

Note: abstract may refer to multimorbidities or comorbidities and be specific about the health conditions; in this case select it and it will be screened at the full text review

3. Does the study focus on adults (18 years+)

4. Is the abstract written in English?

Exclude: Traumatic brain injury, studies of children and adolescents (include adults 18 years+), exclude animal studies

Search includes all study types: intervention, epidemiology, qualitative

Added Inclusion and Exclusion Criteria for Full Text Screening

The following mental and physical health condition combinations had a high level of search hits.

1. Depression and diabetes
2. Depression and cardiovascular disease or hypertension
3. Depression and Alzheimer's dementia or dementia
4. Depression and cancer
5. Depression and respiratory conditions
6. Depression and arthritis
7. Anxiety and cardiovascular disease
8. Anxiety and cancer

The following criteria were applied:

1. Select intervention, systematic reviews/meta-analyses, cohort studies, qualitative studies (exclude retrospective, case-control, cross-sectional, case series, case studies, letters to editor, narrative reviews)
2. Select studies that include at least one of the following priority or equity seeking populations.

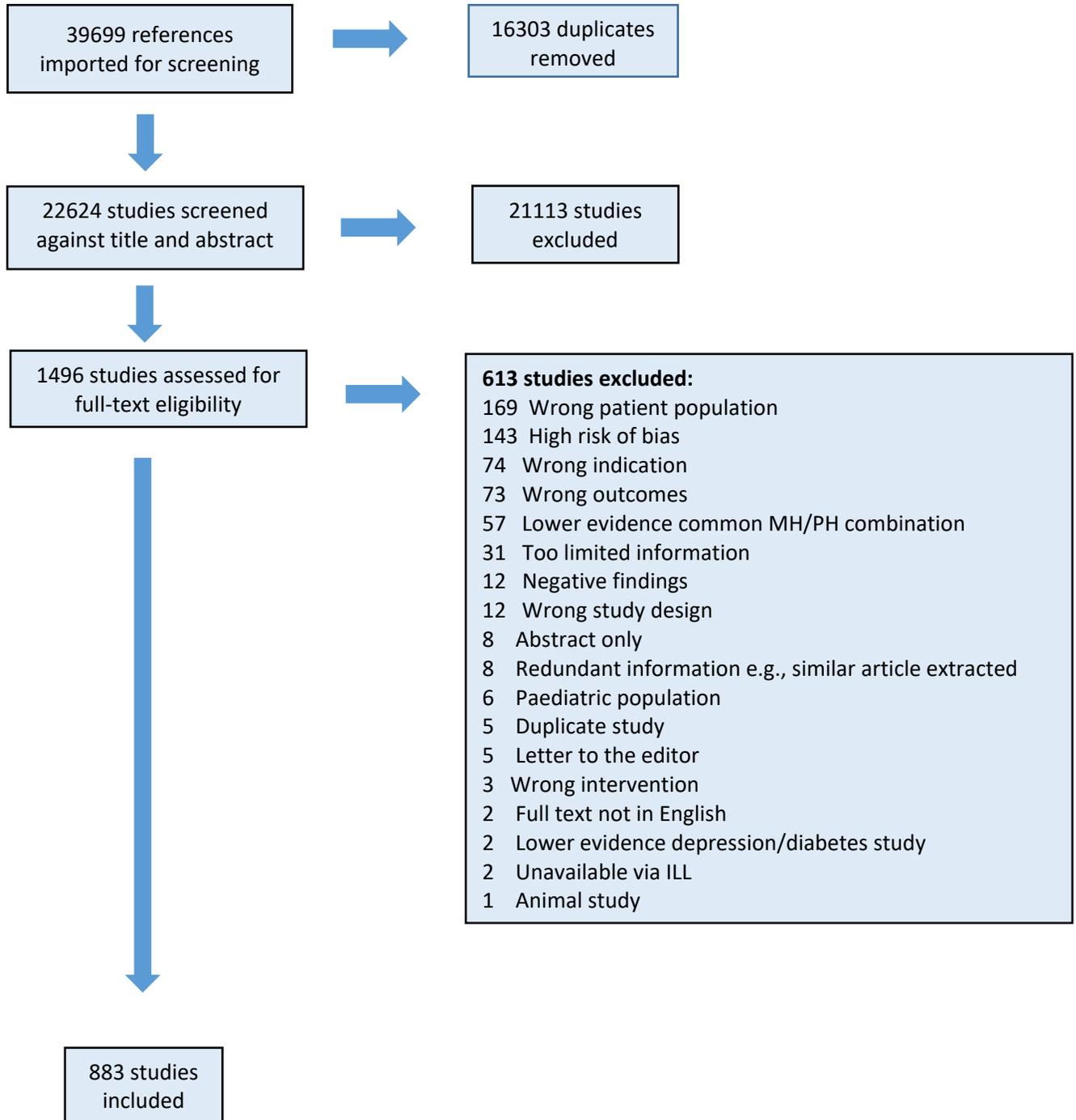
Additional criteria for all studies:

Exclude studies:

- Where factors such as depression and/or anxiety symptoms are a secondary outcome variable, or part of another construct (e.g., quality of life, patient outcome measures) or not discussed in any depth
- Where primary mental and physical health comorbidities are not the main construct
- Validation studies of measurement tools where depression and anxiety are a subscale

Appendix B: Search Strategy Results

PRISMA Results





Mental Health
Commission
of Canada

Commission de
la santé mentale
du Canada



Mental Health Commission of Canada

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[in/Mental Health Commission of Canada](https://www.linkedin.com/company/mental-health-commission-of-canada)