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Cognitive Health, a New Target for Healthy Aging

KNOWLEDGE SYNTHESIS

Québec

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Direction du développement des individus et des communautés

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Foreword

The Institut national de santé publique du Québec (INSPQ) is a public health expertise and reference centre in Québec. Its mission is to support Québec's Minister of Health and Social Services, regional public health authorities and health and social services institutions in fulfilling their public health responsibilities, by offering its expertise and specialized laboratory and screening services.

Over the course of the past few years, the INSPQ has carried out a variety of work related to healthy aging. Indeed, it has focused on several factors related to the health of seniors, including chronic health problems, the life habits of older adults, the improvement of their oral health, their maintenance in the labour market and the impacts of social isolation on this population.

In 2016, the INSPQ specifically identified aging as one of its priorities. It has, moreover, adopted a healthy aging perspective throughout its new scientific programming for 2017–2020. Cognitive health has been identified as an important element to consider. A consultation involving fifteen actors carried out in the fall of 2016 confirmed not only the relevance of this subject, but also the need to better understand the factors that promote or harm cognitive health. These actors belonged mainly to the health and social services network, and included several working in public health, but also included were actors from the Ministère de la Famille et des Aînés, the Carrefour action municipale et famille and from organizations representing retirees or seniors.

This knowledge synthesis, based on four recent literature reviews, addresses the above-mentioned need. It is intended to enlighten public health actors and equip them to position themselves with respect to the issue of cognitive health in Québec. This document will inform discussion during a planned deliberative forum on this subject.

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Key messages

Population aging is occurring particularly rapidly in Québec. Moreover, cognitive impairments increase with advancing age and become a more significant source of disability as seniors age. Cognitive impairments adversely affect the exercise of such mental functions as memory, judgment, attention, learning capacity and the ability to solve problems, and such impairment can have a significant impact on the ability to remain autonomous and on quality of life. The main types of cognitive impairment are: age-related cognitive decline, mild cognitive impairment and major neurocognitive Alzheimer's-type dementia for which there is still no cure.

- In Canada in 2015, Alzheimer's disease and related dementias were the second leading cause of mortality, responsible for 12% of deaths, the third leading cause of premature mortality and the fourth most significant health burden.
- Cognitive impairments have significant economic and health impacts for informal caregivers. They also have implications for the use of community, social and health services. In 2016, the annual cost to Canadians of caring for people with cognitive diseases was estimated to be at least $10.4 billion.
- Aging in itself does not explain the development of mild cognitive impairment or a major neurocognitive disorder. The cumulative effects of genetic inheritance and especially of the life course contribute to the strengthening or weakening of cognitive health.
- The brain has the potential to adapt to threats to its functional abilities. Given the presence of favourable conditions, it develops over the life course a cognitive reserve that allows it to function better and to develop adaptive abilities. It then becomes less vulnerable to the effects of age-related cognitive decline and can offset the pathological damage that occurs with the onset of major neurocognitive Alzheimer's-type dementia.
- There are levers for acting upstream both to foster cognitive health and to protect it by reducing known risk factors. Once an advanced age is reached, the combined effects of these levers have major impacts for seniors and their loved ones.
- The factors that contribute to the development of cognitive reserve are education, particularly education early in life, sustained cognitive stimulation throughout life and the adoption of a physically active lifestyle.
- Other factors are associated with the development of cognitive impairments, especially certain risk factors for cardiovascular and cerebrovascular diseases, including smoking, high blood pressure and diabetes.
- Countries like the United States (2007) and the United Kingdom (2014) have made cognitive health a priority public health issue. Thus, for example, the United States has established and gradually implemented a program of activities aimed at detailing the current state of scientific knowledge about the subject as well as current perceptions within the populace about how to protect and improve their cognitive health. The United Kingdom officially recognized cognitive health as a national public health priority in 2014. Since then, multiple partnerships have been established with the aim of addressing this issue. The implementation of a large-scale campaign to raise awareness about cognitive health among adults aged 40 to 60 years has also been placed on the agenda.

Summary

Given the global context of population aging, some countries have chosen to make cognitive health a priority public health issue. This subject is also of interest to Québec, but there is a need to better understand the factors that promote or harm cognitive health. Cognitive health is a field in full expansion and current research is attempting to resolve persistent questions. This is a subject of interest because the consequences of cognitive impairments are significant, particularly among older seniors. This knowledge synthesis is intended for actors within the health and social services network, including those working in public health, as well as for individuals and groups with an interest in the subject. It serves as an aid to reflection on the targets and levers within reach for maintaining, developing or protecting cognitive health. It is intended to inform public health actors and equip them to position themselves with respect to the issue of cognitive health in Québec.

The knowledge synthesis is based mainly on four sources:

- The World Alzheimer Report 2014 by Alzheimer's Disease International: *Dementia and Risk Reduction: An Analysis of Protective and Modifiable Factors* (executive summary and full report);
- The 2015 report of the Institute of Medicine in the United States: *Cognitive Aging: Progress in Understanding and Opportunities for Action*;
- The 2017 report of the National Academies of Sciences, Engineering, and Medicine in the United States: *Preventing Cognitive Decline and Dementia: A Way Forward*;
- And the 2017 report of the Lancet Commission in the United Kingdom: *Dementia Prevention, Intervention, and Care*.

The first two are comprehensive reviews of the literature and represent reliable benchmarks for current development of knowledge on the subject. The third, from 2017, contributes new elements concerning the effectiveness of interventions, while the fourth source of information sheds further light on two of the factors already being considered, namely social isolation and hearing loss. These four sources were chosen because, together, they enable definition of the main concepts related to cognitive health and documentation of the major types of cognitive impairment, along with their protective and risk factors.

Cognitive health and the main types of impairment

Cognitive health manifests itself through the exercise of the mental processes required to function autonomously and independently. The principal mental functions include memory, judgment, attention, language, executive functions, and the ability to learn and to solve problems. The increase in cognitive impairments that can be observed at advanced ages is partially explained by aging and partially by the cumulative effect of conditions experienced throughout the life course: a more or less favourable genetic background, varying levels of cognitive stimulation, more or less healthy life habits, greater or lesser exposure to various risk factors, and the medium- and long-term consequences of acute or chronic health conditions. Thus, there exist throughout the life course various potential levers for promoting or protecting cognitive health.

The main types of cognitive impairment are age-related cognitive decline, mild cognitive impairment and, in the context of this synthesis, major neurocognitive Alzheimer's-type dementia. Age-related cognitive decline reflects the deterioration of cognitive performance that results from normal aging. Mild cognitive impairment is manifested by a perceptible deterioration of mental functions, without

significant disruption of normal functioning, and this occurs in about 20 to 40% of seniors.[1] About 40% of people with mild cognitive impairment will eventually develop a major neurocognitive disorder, although it is not currently possible to identify who, among those with mild cognitive impairment, will follow this path. Major neurocognitive Alzheimer's-type dementia is caused by progressive and irreversible brain damage that increases gradually, resulting in more and more severe disabilities. There is still no cure for these conditions. According to the Institute for Health Metrics and Evaluation,[2] in 2015 in Canada, Alzheimer's disease and related dementias were the second leading cause of mortality, responsible for 12% of deaths, the third leading cause of premature mortality and the fourth most significant health burden. Between 2005 and 2015, their significance rose sharply.

The natural history of severe cognitive disorders is still poorly understood, but there is a growing suspicion that a silent period of around 15 to 20 years precedes the clinical diagnosis of Alzheimer's-type neurocognitive disorders. This reality underlines the importance of gaining an understanding of the various mechanisms of action of the factors studied and identifying the optimum time to intervene effectively. Thus, interventions targeting certain influencing factors are considered relevant throughout life, whereas other factors are considered more relevant for midlife adults or seniors. In addition, work is still needed to clarify the effectiveness of interventions aimed at fostering or protecting cognitive health. The complexity of the subject may explain why the positions of authors vary somewhat from one synthesis to another.

Cognitive reserve and cerebral reserve

It is possible to develop new neurons throughout life and the brain has the ability to cope with the presence of cognitive impairment. In fact, the brain is malleable and its potential is not predetermined, which enables it, given favourable conditions, to adapt when damage threatens its ability to function. Cognitive reserve is developed by means of cognitive stimulation. Moreover, education early in life is particularly significant for the medium and long term in this regard. Subsequently, the sustained presence of new cognitive stimulation throughout life keeps the brain active. Such stimulation helps build synaptic links and increase the brain's efficiency, which proves very useful when cognitive impairment occurs. In addition, cognitive reserve makes it possible to adapt to the presence of areas made dysfunctional by disease, by mobilizing and adapting healthy areas of the brain so they can carry out the cognitive functions that are threatened. This is why regular integration of new learning activities throughout life is of great interest.

Cerebral reserve refers to the structural characteristics of the brain. Brain volume and numbers of neurons may initially have some importance. Conditions during gestation and early childhood play a role in this regard. In addition, physical activity contributes to cerebral reserve by increasing cerebral vascularity and fostering the development of new neurons.

Influence factors

The factors likely to affect cognitive health have been classified according to whether they promote cognitive health or they represent risk factors for cognitive impairment. The first category includes education and intellectual stimulation, a physically active lifestyle, cognitive training and, subject to further study, social interaction, diet and sleep quality. There is broad consensus in the reviews studied concerning education, intellectual stimulation and a physically active lifestyle. However, it

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1 In this document, "persons aged 65 years and older" are referred to by the term "seniors."

2 It should be noted that the grouping of diseases here differs from that of Statistics Canada. Thus, cancers are grouped according to their sites, and hypertensive heart disease is isolated as a cause. These differences enhance the accuracy of their national and supranational comparisons.

remains difficult to identify interventions that have been proven effective, although some elements stand out in this regard.

The risk factors have been grouped according to whether they are associated with cardiovascular or cerebrovascular diseases, with lifestyle, with other medical conditions or, finally, with the environment. Smoking, hypertension and diabetes are the main vascular risk factors for which the evidence for intervention is most robust. Individual risk factors that have drawn attention include depression and the presence of visual or auditory impairments. Environmental factors that can be considered include air pollution, occupational exposure to neurotoxic substances and traumatic brain injuries. Suboptimal management of medication can be added to these factors of interest, because seniors are more medicated than younger adults and many drugs have documented negative effects on cognition. The potentially higher risk attached to the combined effects of these factors must be considered. Tables 2, 3 and 4 presented on pages 30 to 32 of this document detail the current state of knowledge about each of the factors being considered.

In addition, there is strong interest in deepening and improving understanding of the relationships between the factors studied, age-related cognitive decline and cognitive impairments. It will be necessary to remain vigilant in coming years to keep abreast of new knowledge being acquired in this area.

What is being done elsewhere

Countries like the United States (2007) and the United Kingdom (2014) have made cognitive health a priority public health issue. Thus, for example, the United States has established and gradually implemented a program of activities aimed at detailing the current state of scientific knowledge about the subject as well as current perceptions within the populace about how to protect and improve their cognitive health. The United Kingdom officially recognized cognitive health as a national public health priority in 2014. Since then, multiple partnerships have been formed with the aim of addressing this issue. The implementation of a large-scale campaign to raise awareness about cognitive health among adults aged 40 to 60 years has also been placed on the agenda.

Currently, awareness-raising tools are circulating among the general public to inform people about useful ways of maintaining or protecting cognitive health. A rapid analysis indicates that the factors supported by broad consensus correspond to those for which the evidence seems most robust.

1 Introduction

Population aging is a global reality that is occurring at varying speeds in different regions of the world. It refers to the increasingly marked rise in the number of persons of advanced age (75 to 84 years, and 85 years and over) and is occurring particularly rapidly in Québec. It reflects, among other things, improved hygiene conditions and better control over the majority of infectious diseases, and it calls for a revised analysis of the risks to health and well-being. Currently, health problems threatening the integrity and quality of life are mostly chronic diseases, and several of these are influenced by life habits, including physical inactivity, smoking and the presence of diet-related risks. As people age, these diseases become more common and are characterized by their duration, their often concomitant presence, and the appearance of medium- and long-term disabilities which can affect the autonomy and independence of seniors.[3] Major neurocognitive disorders are included among these diseases.[4]

In recent years, certain developed countries, the United States and the United Kingdom in particular, have demonstrated an interest in acting upstream of cognitive impairments and have clearly positioned cognitive health as a public health issue. Since 2012, many studies have focused on the influence, positive or negative, in the medium or long term, of a large number of factors on cognitive health. In Québec, cognitive health is a concept of relatively recent concern, and public health authorities have not yet added intervention in this area to their mandates.

In 2016, the Institut national de santé publique du Québec (INSPQ) made healthy aging one of its priorities and identified cognitive health as an important element to consider. A consultation involving fifteen actors carried out in the fall of 2016 confirmed not only the relevance of this subject, but also the need to better understand the factors that promote or impair cognitive health. These actors belonged mainly to the health and social services network, and included several working in public health, but also included were actors from the Ministère de la Famille et des Aînés, the Carrefour action municipale et famille and from organizations representing retirees or seniors.

The aim of this knowledge synthesis is to inform decision-makers and public health actors, as well as other concerned actors within civil society, and to equip them to position themselves with respect to the issue of cognitive health in Québec. It serves as an aid to reflection on the targets and levers within reach for maintaining, developing or protecting cognitive health, so as to help offset the manifestations of the more severe forms of cognitive impairment and lessen their impacts on the quality of life of the persons affected and of those close to them.

The knowledge synthesis includes four sections. The first section describes the methodological aspects of the report: it presents the main sources of information on which the synthesis is based and explains the difficulties encountered in evaluating, on the one hand, the scope of factors likely to influence cognitive health and, on the other hand, the effectiveness of interventions; it also introduces the main concepts it is important to master when considering cognitive health. The second section describes the types of cognitive impairment that are the focus of this text and documents the significance and consequences of the most severe forms of cognitive impairment. The third section first describes the main factors associated with the protection of cognitive health, followed by the main risk factors. These are then grouped together according to whether or not they contribute to the development of cognitive reserve, a concept discussed in the first section, or whether or not they can potentially have an adverse effect on cognitive abilities. The fourth section briefly summarizes the

[3] In this document, "persons aged 65 years and older" are designated as "seniors."

[4] In the International Classification of Diseases (ICD-10), dementias are included under major neurodegenerative disorders. In this text, the term "major neurocognitive disorders" will generally be used.

positions taken by the United States, the United Kingdom and Canada with respect to placing cognitive health on the agenda as a public health issue. It also describes the intervention targets usually selected for the development, maintenance or protection of cognitive health. The conclusion reviews the arguments in favour of positioning public health authorities to address this issue.

2 Methodology

2.1 Objectives pursued and main sources of information

The main objectives of this knowledge synthesis are:

1. to acquaint readers with the difficulties involved in developing knowledge about the various factors that can influence, in the medium or long term, the occurrence of cognitive impairments;
2. to describe the main concepts that must be mastered to gain an understanding of the levers for acting on cognitive health;
3. to describe the main types of cognitive impairment affecting seniors as well as the consequences and impacts of the most severe types of cognitive impairment;
4. to identify the main influence factors that could be modified by preventive action targeting adults and seniors;
5. to describe the strategies used by countries similar to our own which have positioned themselves to address cognitive health as a public health issue;
6. to identify the key messages circulating among the general public to help people take individual action to protect their cognitive health.

Various documents were consulted in order to support these objectives. Two documents produced by the World Health Organization (1, 2) situate the subject in a more global context. The first, entitled *Dementia: a public health priority* (2012), outlines the importance at the global level of addressing the burden of major neurocognitive disorders and of acting on all fronts; the second, entitled *World Report on Ageing and Health* (2015), stresses the importance of implementing systemic and longitudinal interventions to counter problems related to the functional limitations of seniors, regardless of the origin of their disabilities.

The knowledge synthesis itself is based on four documents, which provided much of the information on the challenges and limitations involved in developing knowledge on this subject, on the main concepts related to this field of knowledge that must be mastered and on the nature of the various types of cognitive impairment. Above all, they enabled the description of the factors most likely to influence cognitive health. These are recent, large-scale studies that reflect the growing interest in this subject. They were produced by recognized organizations; namely, Alzheimer's Disease International[5] (3, 4), the Institute of Medicine (5) and the National Academies of Sciences, Engineering, and Medicine (6) in the United States,[6] as well as the British journal *The Lancet,*[7] one of whose commissions produced the document entitled *Dementia prevention, intervention, and care*, which appeared in July of 2017 (7). Three of these documents are based on systematic reviews. The documents produced by Alzheimer's Disease International in 2014 and by the Institute of Medicine in 2015 are literature reviews that have served as benchmarks for most of the subsequent work focused on upstream interventions targeting cognitive impairments. The National Academies 2017 report provides a detailed description of the challenges related to effective intervention; it relies on a systematic review of studies of interventions produced at the request of the Academies by the

[5] Their 2014 report is a literature review that was produced in collaboration with King's College of London (*The Global Observatory for Ageing and Dementia Care*); this source will be referred to as "the Alzheimer 2014 report."

[6] These two sources will be referred to using the following labels: "the Institute of Medicine 2015 report" and "the National Academies 2017 report."

[7] A *Lancet* commission produced a report on prevention, intervention and care of major neurocognitive disorders in 2017. Reference to this source, herein, will be made using the following term: "the Lancet Commission 2017 report."

Agency for Healthcare Research and Quality[8] (8). It serves as a useful complement to the Institute of Medicine 2015 review. The Lancet Commission 2017 report, the most recent, incorporates the results of the first two reviews, but has the merit of further examining two factors that, although not new, had not received comparable attention. These documents do not all examine the factors likely to influence cognitive health with the same level of thoroughness. This is taken into account by the author of the present review and attention is focused on the common problems raised in more than one document; the fact that these reports examine upstream interventions is also taken into account.

Annex 1 describes the specific contribution of each of these four documents, listing the factors that were integral to the production of this synthesis. It also identifies the sources used to document mortality, premature mortality and the overall burden of major cognitive disorders in Canada, as well as the sources of information on the main consequences of major cognitive disorders. Finally, it details the analysis processes used in producing this report.

2.2 Limitations to consider

The literature consulted details the impediments to forming judgments about the mechanisms of action of factors likely to influence cognitive health, as well as about their scope; difficulties are also associated with carrying out studies on the effectiveness of interventions aimed at promoting factors that support cognitive health, or at reducing the effects of those that harm cognitive health. Five elements are of particular interest: 1) the natural history of the disease; 2) the exposure parameters; 3) the association between some of the factors studied and vascular diseases, which are also associated with the development of cognitive impairments; 4) the difficulty, given the current state of knowledge, of drawing extrapolations from some of the knowledge produced; and 5) the impediments to carrying out studies aimed at gathering evidence about the effectiveness of interventions. Regarding this fifth element, the National Academies 2017 report made use of supplementary strategies to form more nuanced judgments about the effectiveness of interventions, and these will be briefly presented. The numerous questions regarding this subject that remain unanswered are the impetus behind the current expansion of knowledge in this field.

Natural history of the disease

The subject here is major neurocognitive disorders whose clinical picture resembles that of Alzheimer's-type dementia. It is becoming increasingly apparent that these diseases have a latency period of 15 to 20 years. It has been observed that during this preclinical stage, factors that may negatively influence cognitive health can improve without intervention. These include, for example, improvement of blood pressure, improvement of total cholesterol level, and lowering of body mass index (4). The explanatory hypothesis is that these changes are among the first manifestations of the disease. Thus, for such factors, it is necessary to clarify at what point the improvement of a given factor positively influences the course of the disease and at what point changes linked to the development of the disease instead lead to an improvement of the factor. The term used to describe this phenomenon is "reverse causality."

To influence the course of the disease, it is necessary to intervene before this preclinical phase: this is the "window of opportunity." This is one of the reasons for identifying the periods of life during which interventions targeting specific factors are more likely to bear fruit. The groups regularly identified are midlife adults[9] and seniors (aged 65 and older). The National Academies 2017 report defines midlife adults as those between 35 and 65 years, whereas the Lancet Commission 2017

[8] This agency is overseen by the US Department of Health & Human Services.

[9] "Midlife adults" are distinguished from "seniors", which refers to those aged 65 and older.

report applies this label to those between 45 and 65 years. In the Alzheimer 2014 report, the authors use a life course model[10] to situate the various factors that promote or harm cognitive health, and in this model adulthood begins at age 20. This model introduces the importance of the intrauterine environment prior to birth and the marked influence of socioeconomic status, education and nutrition during childhood and adolescence.[11] Among adults, it is mainly lifestyle and life habits that influence cognitive health and, in particular, the presence of risk factors for cardiovascular and cerebrovascular diseases.

Exposure parameters

The effect of influence factors varies according to the time exposure occurs, its intensity and its duration. Moreover, for some factors, this effect is reversed with time. For example, the goal is to intervene as early as possible to reduce arterial hypertension (AHT) to prevent major neurocognitive disorders; but on the other hand, it seems that AHT may also be a factor that protects against cognitive impairment in some seniors, particularly in the presence of atherosclerosis.

The role of factors associated with vascular diseases

Several risk factors like hypertension or smoking are associated with the development of cardiovascular and cerebrovascular diseases, which are themselves associated, sometimes strongly, with the development of cognitive impairments. It is sometimes possible to distinguish the direct effects of primary risk factors when specific relationships can be drawn between the factor studied and certain physiological or anatomical alterations observed in cases of cognitive impairment, but this is not always the case.

The difficulty of extrapolating from intervention evidence

Current knowledge is characterized by the following limitations: the literature does not demonstrate whether interventions considered effective for one type of impairment, for example age-related cognitive decline, will also be effective for other types of cognitive impairment; the results concerning the effects of short-term interventions cannot be extrapolated to the long term; and when studies are few and results modest, findings may be considered inconclusive.

The impediments to obtaining evidence about the effectiveness of interventions

Randomized clinical trials[12] offer optimal conditions for establishing how effectively a given intervention acts on cognitive impairments, but their constraints are numerous. For ethical reasons, some risk factors do not lend themselves to this type of study. These would include, for example, exposure to tobacco or the modulation of treatment in the presence of diabetes or depression. In addition, the study of interventions targeting life habits (e.g., physical activity or diet) requires that the interventions be precisely defined; an intervention's nature, frequency and intensity must be specified, along with variations associated with age, gender, cultural parameters, etc. These requirements are not suited to the reality of everyday life. Furthermore, it is necessary to intervene at the right time (within the window of opportunity) and long-term monitoring is often required, which increases the likelihood of having to contend with the appearance of new health problems or drop out due to mortality, relocation or abandonment. Other factors also need to be evaluated: thus a

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[10] The model used was developed by Muller, M. et al. (2014) and is entitled: *Hypothesized model of the origins and life course of brain aging*.

[11] For factors occurring very early in life, it is more difficult to establish clear associations with major neurocognitive disorders in seniors.

[12] Randomized clinical trials are also called randomized controlled trials. These are studies in which people are divided randomly into at least two groups: those who receive the intervention and those who only seem to receive the intervention. The term used in this document, because of its widespread use, is "randomized clinical trial".

group intervention can act positively by creating a sense of belonging and can also produce benefits related to the simple presence of social interaction. Another issue concerns certain characteristics of the measures used, such as their robustness or their acceptability (e.g., biological markers). These measures have to be repeated over many years, because their results could change after two, five or even ten years. New studies will continue to meet these requirements more effectively, but their results will not be available for several years.

Supplemental strategies for forming more nuanced judgments about the effectiveness of interventions

In addition to the results produced by the Agency for Healthcare Research and Quality, the National Academies 2017 report used supplementary information to support their evaluation of the effectiveness of interventions, and the reasons for this are as follows. Randomized clinical trials are better suited to the study of unique interventions, whereas here it is necessary to contend with the complexity of the phenomena studied. Indeed, specific characteristics such as, for example, the long latency period, the presence of co-morbidity and the diverse realities of seniors explain the difficulty of obtaining high-quality results. Supplementary sources of information, specified in Annex 2, were therefore used to broaden reflection on the relevance of the interventions studied. This reflection was informed by the following: 1) consideration of the results provided by large-scale observational studies, 2) application of the Bradford Hill criteria to evaluate the plausibility of the relationship between a given factor and its effect on cognitive function, and 3) an analysis of the risks and costs associated with the interventions studied and a more comprehensive analysis of their overall benefits.

The current expansion of knowledge

This knowledge synthesis is based on recent documents. There is currently a marked interest in deepening and improving understanding of the links between the factors studied and the different types of cognitive decline. It will be necessary to remain vigilant in coming years to keep abreast of new knowledge being acquired in this area.

2.3 The main concepts to be mastered

Cognition

Cognition comprises several mental functions, all necessary for a person to function well and autonomously. These mental functions include, among others, memory, judgment, attention, language, executive functions, concentration and the ability to learn and solve problems. Their integrity preserves autonomy and independence, conditions associated with quality of life. Their impairment diminishes the ability to care for oneself as an individual and the ability to participate within a social collective. In this synthesis, the term “cognitive abilities” refers to the exercise of these mental functions. Cognitive health refers globally to the development and maintenance of cognitive abilities.

The concept of the cognitive health of seniors

The concept of the cognitive health of seniors is adapted from a definition that has received the endorsement of three American national health institutes; namely the National Institute on Aging, the National Institute of Mental Health and the National Institute of Neurological Disorders and Stroke (9). The concept refers to the preservation of the mental functions required to maintain social bonds, a sense of purpose and the use of skills enabling one to function independently. These skills are useful when illness or accidents occur: they promote functional recovery and adaptation to the residual functional impairments. In this text, the concept of the cognitive health of seniors is more specifically focused on the abilities of the individual. In 2015, the WHO proposed a holistic view of the health of

seniors (2). In this perspective, the health of seniors depends on the presence of functional skills allowing them to accomplish that which they feel is worthwhile. In doing so, the intrinsic abilities of individuals, meaning their mental and physical abilities, are mobilized; however, these abilities are influenced by the characteristics of the environment with which they interact regularly, even daily. The WHO introduced here the importance of a dynamic equilibrium between individual health, both physical and mental, and the environment. Some of the factors studied seek to foster this equilibrium.

Cognitive reserve

It is possible to develop new neurons throughout life, and this reality is underestimated. In fact, the brain is malleable and its potential is not predetermined, which enables it, given favourable conditions, to adapt when damage threatens its ability to function. Genetic inheritance influences cognitive potential, but its original significance can be gradually offset by the positive consequences of cognitive stimulation that is sustained throughout life (10). Education early in life is particularly significant for the medium and long term in this regard (3, 4, 5, 7, 9). And in general, education level is considered an indicator of cognitive stimulation (4), a fact worth noting since the education levels of Québec seniors are rising with each generation, a trend that will continue over the course of the next decades (11). Factors that stimulate cognitive abilities throughout life, such as physical activity or successive new learning experiences, are associated with a reduced risk of major neurocognitive disorder later in life (3, 4, 5, 7), and this also applies to those who are genetically predisposed to Alzheimer's disease (7).

But the value of sustained cognitive stimulation extends beyond this: it would appear to develop the brain's potential to adapt to pathological brain damage. This is explained by the concept of cognitive reserve, developed by Stern in 2003 (12) and regularly referred to thereafter. It can be broken down into two mechanisms. The first is tied to the development and maintenance of a wealth of synaptic connections through cognitive stimulation over the life course: the greater efficiency of these rich networks helps counteract or minimize, at least for a while, the consequences of anatomopathological brain damage. The second mechanism acts differently: when there is a loss of functionality related to the destruction of nerve cells in certain areas of the brain, the brain will react by adapting other healthy brain parts, enabling them to perform the threatened functions. This concept was developed after it was observed that similar types of brain damage did not necessarily result in the same types of cognitive impairment. Cognitive reserve would explain this ability of the brain to adapt and thus maintain its functionality as long as possible. The presence of a high cognitive reserve in seniors carries two advantages: the effects of cognitive aging will occur in a brain with optimized functioning; and in the event of anatomopathological damage, the adaptability of the brain will delay the more severe cognitive manifestations. All the documents consulted incorporate this concept. There also exists a cerebral reserve, which is tied to the structural characteristics of the brain: its greater or lesser initial volume is significant, as is the potential development of certain areas of the brain in response to certain stimuli including, in particular, physical activity.[13]

[13] This structural reserve may be very valuable, for example, in the case of traumatic damage that reduces the number of healthy neurons, but this does not imply that smaller brains operate less optimally than larger brains.

3 Cognitive decline

3.1 Cognitive decline and its principal manifestations in seniors

The causes of cognitive decline, as identified in the context of this synthesis, are age, mild cognitive impairment and major Alzheimer's-type neurocognitive disorders.[14] These three causes allow for discussion of most cases of cognitive impairment and it is plausible that all can be influenced proactively by the same factors. Other major neurocognitive disorders[15] that have been excluded represent a small proportion of all major neurocognitive disorders and some have known causes that are associated with specific preventive interventions.

Age-related cognitive decline

Age-related cognitive decline refers to the deterioration of cognitive performance that is considered a normal part of aging. As is the case for the human body's other organs, the brain changes with age, both structurally and in terms of its ability to carry out its diverse functions. This is generally a gradual and ongoing process that begins at adult age and affects all cognitive functions, albeit unevenly. This process varies greatly from one individual to another.

Several myths and prejudices are derived from an alarmist understanding of the effects of aging on cognition (13). In fact, seniors remain capable of learning; occasional memory loss is common, but not pronounced enough to indicate the presence of cognitive impairment; and studies do not reveal the presence of productivity issues among seniors in the workplace. The accomplishment of previously well-learned tasks is generally little affected and knowledge decline occurs later, after age 90 (5). Age-related cognitive decline affects cognitive abilities whose level of development will have previously been influenced by an individual's life course.

Mild cognitive impairment

Mild cognitive impairment is identified by affected persons themselves, by family members and by clinicians during testing. The level of deterioration of cognitive functions is noticeable and distinctive, but it does not significantly interfere with the ability to carry out daily living activities (6, 14). Mild cognitive impairment is relatively common in seniors and, according to some studies, affects about 22% of people; however, this frequency varies considerably (from 0.1% to 42%) depending on the indicators measured. What is of particular interest is the uncertainty regarding its evolution. One systematic review suggests that less than a quarter of people with mild cognitive impairment will develop a major neurocognitive disorder over the subsequent three to ten years, that mild cognitive impairment can regress in some people, and that it can also recur (14). The Lancet Commission 2017 report indicates that around 39% of people diagnosed with mild cognitive impairment after testing in a specialist setting will develop major neurocognitive disorders (7). Thus, people with mild cognitive impairment are at greater risk of developing major neurocognitive disorders, but it is not yet possible to identify those whose mild cognitive impairment will evolve into a major neurocognitive disorder. Because there are still too many unknowns surrounding cognitive impairment, the United Kingdom's "National Screening Committee" positioned itself against screening for this condition in 2014, following a close analysis based on the committee's standard criteria[16] (14). To be able to assert that

[14] The definitions used for the three causes of cognitive decline discussed in this document are those proposed in the 2017 National Academies report.

[15] Examples of other causes of cognitive decline not included in this synthesis: mental health problems, kidney failure and chronic vitamin insufficiency, effects of certain medications, craniocerebral trauma, etc.

[16] Fifteen criteria are used: four of them focus on the disease studied, four on the tests used, three on the treatment options and the last four on the impacts of the screening program on those affected and their families.

the clinically verified presence of mild cognitive impairment signifies the presence of the early stages of a major cognitive disorder, it would be necessary to identify clinical or biological markers establishing this connection.

Alzheimer's-type dementia

The two main causes of major neurocognitive disorders are Alzheimer's disease and vascular dementia. More and more studies are documenting the presence of vascular disease in cases of major neurocognitive disorders of different types, and particularly of Alzheimer's disease; these are therefore major neurocognitive disorders of mixed origin (3, 4, 5, 6, 7, 10). In this synthesis, the factors studied are mainly considered in relation to major neurocognitive disorders that are clinically similar to Alzheimer's disease.[17] These major neurocognitive disorders are manifested by cognitive impairments severe enough to interfere with the autonomy of the person affected. Major Alzheimer's-type neurocognitive disorders stem from irreversible damage to brain tissue, mainly characterized by the destruction of brain cells, called neurons. Such damage is also associated with an accumulation of beta-amyloid proteins and tau proteins considered to be toxic[18] (10). The progression of the disease results in an increasing number of cognitive impairments, which worsen over time and may be accompanied by mood and behaviour disorders. The symptoms result in progressive dependence on others to assist with daily living and domestic activities, and the need for assistance increases as the disease progresses (1). Here, the significance of the brain's vasculature must be recalled. Despite its low weight of about 1.4 kg, the brain is one of the human body's most energy-intense organs, consuming almost 20% of the body's total energy. Consequently, vascular damage has documented impacts on brain functioning (10). Moreover, chronic diseases affecting vascular integrity remain common and represent significant causes of mortality in Canada. According to data from the Institute for Health Metrics and Evaluation, this was the case, in 2015, for ischemic heart diseases,[19] the leading cause of mortality, for cerebrovascular diseases (in 4th place), and for diabetes (in 8th place) (15). These diseases have recognized risk factors, often the same ones, which can be acted on proactively.

In the general population, more than 95% of cases of major neurocognitive disorder will develop after the age of 65 (10) and about 80% occur after the age of 75 (7). Recently, minor improvements have been observed in rates of mortality and incidence for major neurocognitive disorders in some Western countries, including the United Kingdom, the United States (4, 7) and Canada (7). These could be explained by improved levels of education and improved life habits, but also possibly by better control of common chronic diseases, within a context where rates of obesity and diabetes appear to be increasing (4,7).

3.2 The consequences of cognitive impairments

In general, cognitive impairments increase with advancing age and become a significant source of disability among older seniors. The WHO estimates that after age 65, the prevalence of major neurocognitive disorders doubles every five years (1). Because of the interpersonal variability of manifestations of age-related cognitive decline and uncertainty about the frequency and evolution of

[17] They exclude, among others conditions, major Lewy body neurodegenerative disorders, major fronto-temporal neurodegenerative disorders, disorders resulting from infectious diseases or a traumatic brain injury and those resulting from a major, but isolated, stroke.

[18] Beta-amyloid proteins are associated with the formation of plaques, and tau proteins with the formation of tangles, two pathological phenomena typical of brains afflicted with Alzheimer's disease.

[19] Ischemic diseases are diseases characterized by a reduced blood supply.

mild cognitive impairment, the data describing the magnitude of the problem and its various consequences apply mainly to major neurocognitive disorders.

The duration of an Alzheimer's-type dementia is seven to ten years, with individual variations (1). As of 2017, no effective curative treatment exists, either to cure the disease or to significantly slow its progress. It is a disease that generates a lot of anxiety in adults and seniors at many levels: there is the fear of being afflicted oneself and of the resulting loss of one's autonomy, independence and quality of life; the fear of the repercussions on one's family, given the increasing need for multiple types of support arising from the disease; and fear of the possibility of being called upon oneself to support loved ones. Responding to the needs of affected people involves the participation of a large number of actors over long periods of time, whether these be family members, the extended social network, community resources, the health and social services system or the various living environments of the affected people. Thus, an article produced in 2016 by Statistics Canada (16) documented the nature of the needs of persons suffering from a major neurocognitive disorder living in a private home in Canada and the frequency with which such help was needed.[20] Below is an excerpt from the abstract:

> "The vast majority of people with dementia [Alzheimer's disease and other forms of dementia] in private households received assistance with medical care (81%), housework and home maintenance (83%), meal preparation (88%), emotional support (90%), transportation (92%), and managing care (92%). Among those receiving assistance, 85% relied, at least in part, on family, friends or neighbours. The primary caregiver tended to be a spouse (46%) or an adult child (44%), most of whom were daughters (71%). The majority of primary caregivers lived in the same household (83%) and provided daily care (86%)."

Mortality, premature mortality and overall burden

The Statistics Canada data for 2013 on the leading causes of death ranked Alzheimer's disease 8th in a table where cancers are grouped together as a single cause of death and where hypertension is included under heart diseases (17). The methodology used by the Institute for Health Metrics and Evaluation[21] does more to highlight the importance of Alzheimer's-type dementia; cancers are broken down according to site (e.g.: lung, breast) and hypertensive heart disease is isolated as a cause of death. Recent data, drawn from work published in *The Lancet* (18), reveal that in 2015 in Canada Alzheimer's-type dementia was the second leading cause of death, all ages and both sexes combined, and was responsible for 12% of deaths. It was preceded in importance by ischemic heart disease and followed by lung cancer and cardiovascular and cerebrovascular diseases (15). This percentage rose to 19.7% among women aged 70 and older. 0 shows the rank attributed to this cause for deaths, premature deaths and overall burden,[22] as well as the percentage change observed for these indicators between 2005 and 2015 (15).

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[20] The sources used in this article come from the 2010-2011 Canadian Community Health Survey, from the 2011-2012 Survey of Neurological Conditions in Institutions in Canada, and from the 2011 Survey on Living with Neurological Conditions in Canada.

[21] The link to the data on Canada is as follows: http://www.healthdata.org/canada.

[22] The global burden refers to the disability-adjusted life-years (DALY). It is based on the years of life lost due to premature death and the years lived with disability. This allows for calculation of the total number of years of full health that have been lost due to a given cause.

Table 1 In Canada, 2015 rankings for Alzheimer's-type dementia for cause of deaths overall, cause of premature deaths and overall burden, and percentage change observed between 2005 and 2015

Indicator	Rank	Percentage change 2005–2015
Cause of death	2	+19.0%
Cause of premature death	3	+12.5%
Cause of overall burden	4	+14.2%

Persons afflicted and prevalence data

In Canada, in 2016, the work carried out by a team of experts convened by the Alzheimer Society of Canada (19) estimated that 564,000 Canadians were living with major neurocognitive disorders. Of these, 65% were women and 35% were men. The report mentions that, according to analyses by the Mental Health Commission of Canada, this number would rise to 747,000 if it included those with mild cognitive impairment, which would increase prevalence estimates by about 50%. Without these additions, that number is projected to rise to 937,000 in 2031.[23] The 2014 data indicate that in Canada, among seniors, the prevalence of major neurocognitive disorders was 10.9% for women and 7.1% for men, for an overall prevalence of 9.2% for both sexes. In the 85 and over age group, the prevalence was much higher and was estimated, in 2014, to be 37.1% for women and 28.7% for men.

In Québec, in 2014–2015, the INSPQ set the prevalence for major neurocognitive disorders among seniors at 7.5%, which corresponded to 107,345 people.[24] In the 85 and over age group, the prevalence rose to 29.8% for women and 23.5% for men (20). The methodologies used differ slightly, but the prevalence was similar.

Economic and health impacts and impact on informal caregivers

According to the Alzheimer Society of Canada, every person with a major neurocognitive disorder directly or indirectly solicits the help of at least two caregivers. This means that 1.1 million Canadian men and women will have acted as caregivers in 2016, and this number will rise to nearly 2 million in 2031; caregivers are mainly women (21).

Given that the needs of the persons afflicted are diverse and numerous, and that they increase throughout the illness, they have an impact on informal caregivers. The financial impacts identified include reduced participation in the labour market and a reduction in income, lifetime earnings and savings. Many negative health impacts have also been documented, including increased depression, anxiety and stress, an increase in health risk behaviours, a higher incidence of chronic diseases, and increases in heart disease and premature mortality[25] (19).

Given the major disabilities associated with the disease and the significant impacts on caregivers, delaying the onset of clinical manifestations of the disease has huge impacts. Of relevance here are the results of a recent study published in 2014 (22) and cited in the Lancet Commission 2017 report

[23] If you take into account people with mild cognitive impairment, this number would rise to 1,435,923 in 2031.

[24] This number does not account for people under 65 years who are affected or for those who have not been diagnosed. Clinicians believe that these additions would raise the number to about 120,000 people.

[25] Drawn from Figure 11, on p. 58. The source for the Figure was the *National Population Health Study of Neurological Conditions*. Personal communication with Christina Bancej, January 2015.

confirming the potential effects of a higher cognitive reserve.[26] Alzheimer's disease was observed to progress differently among more educated seniors as compared to less educated seniors. In the first group, later onset of the clinical stage of major neurocognitive disorders was observed, followed by a more rapid decline thereafter. This resulted, however, among more educated seniors, in a long preclinical period during which the cognitive impairments were less significant and, consequently, there was less need for support. These results underline the benefits of taking preventive action to delay arrival of the clinical stage of the disease and to decrease its duration.

In 2016, the annual cost to Canadians of caring for people with major neurocognitive disorders was estimated at $10.4 billion (21), an amount that is most likely conservative given that the calculation was based on an estimated 564,000 sufferers.

[26] In this study, seniors were monitored over a period of 20 years.

4 Protective factors and risk factors for cognitive health

Socioeconomic status is a significant marker for cognitive health, and this association persists throughout life. But it is also correlated with several health conditions and their consequences, as well as with levels of development observed during the first years of life. It is identified both as a determinant and as a confounding factor, and it is difficult to determine how to interpret its significance in a study where several factors are examined. Thus, it is not separated out as a specific factor, but remains omnipresent and is significantly tied to the presence of inequalities in health affecting cognitive health (5).

4.1 Factors that promote cognitive health

Six factors are identified in the literature examined as potentially beneficial to cognitive health: education and intellectual stimulation, physical activity, cognitive training and, subject to additional studies, diet, social interaction and sleep quality.

Education and intellectual stimulation[27]

Globally, having only a primary level education or lower is the single factor most strongly associated with the occurrence of major neurocognitive disorders later in life (1, 4, 5, 7). The influence of this factor is much less significant in developed countries. The Alzheimer 2014 report also points to the potential significance of a stimulating environment during the first years of life. Furthermore, education level is an indicator whose scope and consistency are among the strongest linked to cognitive ability levels throughout life (4, 5).

Cognitive training

Efficacy data associated with cognitive training among seniors are based largely on a single study.[28] Three cognitive functions were targeted: problem solving, memory and speed of information processing. The intervention consisted of specific individual training and training in small groups, for a period of five to six weeks, two sessions of booster training and feedback on performance results; the strategies used were applied to activities of everyday living (e.g., remembering a grocery list, understanding a medication dosage). Results showed moderate improvement after two years and modest improvement after five and ten years for each of the targeted functions. The ability to independently perform instrumental activities of daily living was reported to be higher after five years in groups trained in problem solving and after ten years in those trained for memory and speed of information processing (6).

This study produced the following findings: there are timeframes for observing improvement in targeted functions and it is possible to achieve long-term effects that apply to daily living; the training program used to achieve these comprised diverse interventions. However, the authors concluded that it was not possible to extrapolate these results to the use of commercial computer applications that offer to improve cognition, because they target very specific cognitive functions repetitively, with specific potential effects limited to the short term. However, these results strengthen interest in the benefits of engaging in stimulating cognitive activities over the long term, even if it is not possible to

[27] In this review, the complexity of work tasks was not identified as a separate factor promoting the development of cognitive reserve because it is strongly correlated with level of education.

[28] The ACTIVE study on *Advanced Cognitive Training for Independent and Vital Elderly*, of 10-year duration, with n = 2,082, and 25% of participants from ethnic minorities.

draw conclusions about their relative effectiveness. The activities mentioned included, for example, learning a new language, games (e.g., bridge or crosswords), crafts and social activities.

Physical activity

Physical activity is consistently associated with benefits for cognitive health, and this is consistent with neurobiological expectations. This can involve specific individual activities that help maintain and support cognitive health, at all ages, and does not necessarily require adherence to a structured program of physical activity. The Lancet Commission 2017 report states that data from observational studies point to an inverse relationship between exercise and the risk of developing a major neurocognitive disorder. The presence of contradictory results among intervention studies calls for a more nuanced judgment (6). The results of intervention studies are considered to be encouraging but inconclusive at this time, and focus specifically on age-related cognitive decline. Aerobic activities associated with muscle building appear to represent a winning combination (5). According to all the documents consulted, it would be necessary to conduct randomized clinical trials to identify which physical activities effectively benefit cognitive function.

Analysis of the benefits, risks and costs involved leads to the following observations: physical activity is an important factor for healthy aging with well-documented benefits that include improvements in quality of life related, on the one hand, to maintaining mobility and independence and, on the other hand, to lower risks for many chronic conditions (depression, AHT, osteoarthritis, metabolic syndrome, diabetes, stroke, coronary heart disease and injuries resulting from falls). Musculoskeletal injuries and hospitalizations related to physical activity do not seem more significant for seniors than for other age groups, and the balance weighs strongly in favour of the benefits of such activity. Costs vary according to type of activity and are typically minimal (e.g., walking) (6). Physical activity is also associated with the development of cognitive reserve and cerebral reserve (12). This analysis led the National Academies 2017 report to include physical activity among their recommendations for delaying or decreasing age-related cognitive decline. In 2010 the WHO also produced recommendations for standards to meet in this regard during the various stages of life (23).

Diet

Epidemiological results link certain diets,[29] particularly Mediterranean-style diets, to the prevention of Alzheimer's disease; and the presence of underlying biological mechanisms strengthens their credibility (4, 5). Yet the vast majority of intervention studies do not currently consider complete diets, and their results concerning cognition have been negative (6). However, new intervention studies target dietary habits, which has the benefit of more closely reflecting the daily eating habits of people, and thus better meeting the need for information about the medium- and long-term cognitive effects of diet. The literature reviews examined concluded that there is currently insufficient data to justify interventions targeting cognitive health.

Several vitamin or dietary supplements are regularly purported to have positive effects on cognition. Current data suggests an absence of benefits and the reviews examined tend toward the same conclusions regarding the use of nutraceuticals[30] and most vitamin supplements. Although their use does not usually produce any negative effects, their cost can be an issue considering the absence of results. However, encouraging studies have suggested the effectiveness of vitamin B12 in

[29] The dietary ingredients regularly considered to be beneficial include the following: less meat, more nuts, vegetables and whole grains, as well as the use of monounsaturated fats such as olive oil.

[30] Definition: product derived from food sources, but made available in the form of a tablet, powder, liquid or other medicinal form usually not associated with food, and that is purported to have a beneficial or protective physiological effect linked to chronic diseases [translation]. Retrieved on August 30, 2017 from the following website: https://www.oqlf.gouv.qc.ca/ressources/bibliotheque/GDT_fiches/nutraceutique.html.

conjunction with a folic acid supplement for certain subgroups at greater risk due to high blood levels of homocysteine. This is associated with an increased risk of cardiovascular and cerebrovascular diseases and with cognitive impairment, which, in these cases, is largely determined by food intake of vitamin B12 (6, 8).

Social interaction

A growing body of evidence suggests that social interaction could help prevent cognitive decline and major neurocognitive disorders and that it could have positive effects on cognition. These assumptions are derived from observational studies on the negative cognitive impacts of social isolation and loneliness, and several plausible mechanisms could explain these relationships: the direct neurobiological effects linked to social isolation, as well as its indirect effects, such as decreased sleep quality and physical activity and an increased risk of depression. However, social isolation can either result from cognitive impairment or contribute to it; it may be the result of a depression or instead contribute to the development of one.

Evaluation of the effectiveness of interventions aimed at increasing social interaction is hindered by several difficulties (5). Many parameters must be considered when evaluating results: higher levels of cognitive ability would encourage participation in social activities; different social activities mobilize different cognitive functions; women seem to respond better to social engagement; and some social activities may generate stress. In addition, social activities often include more than one component (e.g., participation and physical activity), which complicates the analysis of results. Although there are several benefits to encouraging seniors to get involved in various social activities, controlled trials would be needed to identify the specific social interactions that are beneficial and their conditions for success (6). The National Academies 2017 report and the Alzheimer 2014 report view this as an encouraging avenue for action; the Lancet Commission 2017 report, based on recent meta-analyses, identifies social isolation as one of the modifiable factors worth acting on to support cognitive health among seniors.

Sleep quality

Sleep plays a role in memory consolidation and elimination of toxins such as beta-amyloid and tau proteins in the brain (10). A substantial body of evidence supports the existence of a link between sleep quality, cognitive decline and Alzheimer's disease: poor sleep quality produces metabolic and inflammatory changes that are likely to promote cardiovascular disease and diabetes as well as an increase in beta-amyloid proteins. In cases of sleep apnea, inflammatory and hypoxic phenomena have been observed, which can have neurodegenerative consequences. The effects of good or bad sleep quality are plausible, but lack empirical evidence. It is also possible that, in some cases, the presence of cognitive impairment promotes poor sleep quality (5, 6). However, studies are few in number and current data, while encouraging, still do not suffice to confirm these links (4, 6, 8).

4.2 The main risk factors for cognitive health[31]

The main risk factors for cognitive health were grouped according to whether they are associated with the main risk factors for cardiovascular or cerebrovascular diseases, with lifestyle, with certain medical conditions or with the physical environment.[32]

[31] Among the literature reviews examined, only the IOM 2015 report studied the following risk factors: air pollution, occupational exposures, substance abuse, visual impairment and suboptimal management of medications.

[32] This classification system is informed by reading on the subject; however, this particular grouping of risk factors was selected by the author of this knowledge synthesis.

4.2.1 RISK FACTORS FOR CARDIOVASCULAR AND CEREBROVASCULAR DISEASES

This section focuses on the primary factors that are directly linked to the development of cognitive impairment. Thus, there will be no discussion of metabolic syndrome.[33] Smoking, which could also be included in the lifestyle section, is discussed in this section because of its association with vascular diseases.

Arterial hypertension (AHT)

Epidemiological data associate AHT with vascular diseases and major neurocognitive disorders. In addition to strokes that are clinically very evident, there exist more discrete forms of cerebrovascular disease that manifest as a result of silent cerebral infarction and microvascular damage (5, 8). These are significant risk factors for major neurocognitive disorders. In addition, decreased cerebral blood flow may increase production or reduce evacuation of toxic proteins in the brain. Antihypertensives are powerful tools for acting at both levels and contribute to risk reduction. They have protective effects if treatment occurs early enough in adult life to take effect before the onset of neurocognitive disease. The presence of AHT at advanced ages can, inversely, play a protective role with respect to cognitive impairment by maintaining blood perfusion when vascular permeability is decreased due to hardening of the arteries, in particular, in the presence of atherosclerosis. This said, control of AHT among seniors remains an issue because it is a documented source of cardiovascular morbidity and mortality in this age group and, despite this reality, its control declines regularly with advancing age (4). Despite the current limitations of efficacy studies, the National Academies 2017 report considers it justifiable to treat AHT in midlife adults to prevent or delay Alzheimer's-type dementias on the basis of the following factors: the methodological limits of intervention studies,[34] the favourable indications of several prospective cohort studies and the strong plausibility of a causal relationship. Moreover, the risks associated with AHT treatments are relatively small, and the treatments are inexpensive. The Alzheimer 2014 report also points out that during the 2011 "WHO and World Economic Forum," the WHO pointed to interventions aimed at preventing cardiovascular diseases, including antihypertensive treatment, as one of the "best buys" for reducing non-communicable diseases. To prevent or delay cognitive impairment, it is important to intervene as early as possible in adulthood. The Lancet Commission 2017 report also identifies AHT as a modifiable factor that merits intervention targeting midlife adults (4, 5, 6, 7).

Diabetes

The focus here is type 2 diabetes. Transversal and longitudinal observational studies have consistently demonstrated the presence of associations between diabetes and increased long-term risk for mild cognitive impairment and major neurocognitive disorders. High insulin levels promote amyloid accumulation, a fact that establishes the biological plausibility of the association. A meta-analysis conducted in 2012 estimated that the incidence risk of Alzheimer's disease increases by almost 50% for those diagnosed as diabetic. Thus, early diagnosis and careful treatment would have the potential to improve cognitive health, in particular by acting to reduce cardiovascular and cerebrovascular diseases. Here again, intervention studies are confronted with significant methodological limitations and the link between diabetes interventions and cognitive impairment has not been established. The Institute of Medicine 2015 study underlines the need to remain vigilant to avoid the negative effects of diabetes treatment on cognitive functioning, which are related to the risks of hypoglycemia. Type 2 diabetes remains a factor that evokes marked interest, although

[33] Metabolic syndrome is characterized by the presence of three of the following five elements: abdominal obesity, hypertriglyceridemia, high blood pressure, high fasting blood glucose and low levels of high-density lipoproteins (5).

[34] The committee observed that given the widespread use of antihypertensive treatments for purposes of primary, secondary and tertiary prevention of several chronic diseases, there could be an increase in the difficulty of studying the relationship between antihypertensive treatments and cognitive impairment using prospective randomized controlled trials.

questions remain regarding the optimal treatment and its modifying effects in the presence of other factors. The presence of type 2 diabetes increases with age, and this increase has become more pronounced among seniors in recent years. The Alzheimer 2014 report attributes this trend to the increased presence of obesity resulting from a more sedentary lifestyle; it identifies type 2 diabetes as a modifiable factor to be considered throughout life, with data on seniors found to be particularly robust; the Lancet Commission 2017 report identifies diabetes as a modifiable factor that merits intervention specifically among seniors, for cognitive purposes.

Hypercholesterolemia

Cholesterol is related to the generation and deposit of beta-amyloid plaques. Studies associate hypercholesterolemia treatment with improved vascular health and a reduced risk of stroke and, consequently, with the prevention of cognitive decline and major neurocognitive disorders. Studies were most focused on the effects of statins.[35] The Alzheimer 2014 report could not recommend hypercholesterolemia treatment for cognitive purposes, but called for further study to improve understanding of its role. According to the National Academies 2017 report, this is an encouraging avenue to pursue and merits intervention among midlife adults. This said, intervention studies have yet to provide conclusive evidence of the cognitive benefits of hypercholesterolemia treatment.

Obesity

Certain complications arise from obesity itself. For example, the secretion of inflammatory proteins generated by excess adipose tissue is associated with cognitive decline and cognitive dysfunction; an increased resistance to insulin, an excess of insulin and negative effects on cerebral health have also been observed. But obesity is not analyzed separately in this synthesis, because several primary factors of interest associated with obesity have already been addressed (e.g., diabetes, hypercholesterolemia). The Alzheimer 2014 report, the Institute of Medicine 2015 report and the Lancet Commission 2017 report all identify obesity as a modifiable factor that merits intervention among midlife adults.

Smoking

The direct links between smoking and cognitive impairment have often been studied, and the associations between smoking and a higher incidence of major neurocognitive disorders are well established. But these relationships are complex and difficult to interpret: among smokers, there is a relationship between the risk of cognitive impairment and the level of smoking engaged in, except among the heaviest smokers; and the risks for ex-smokers are the same as for people who have never smoked (4). Thus, recommendations in favour of smoking cessation are based mainly on the well-established relationships between smoking and cardiovascular and cerebrovascular diseases, and on the links between these diseases and cognitive impairment, and in particular Alzheimer's-type dementias. The WHO points out that, at the global level, smoking cessation could lead to a 13.9% reduction in Alzheimer's-type dementias. Thus, the WHO positions smoking as one of the main modifiable risk factors for major neurocognitive disorders (1). The Institute of Medicine 2015 report and the Alzheimer 2014 report identify smoking as a modifiable factor that can be acted on throughout life and the Lancet Commission 2017 report identifies it as a modifiable factor that merits intervention among seniors.[36]

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[35] This is a class of drugs routinely used to treat hypercholesterolemia.

[36] The full version of the Alzheimer Report raises the possibility of a potential and plausible association between smoking among seniors and the risk of major neurocognitive disorders, although there remain inconsistencies and uncertainties tied to this assertion (p. 49).

4.2.2 RISK FACTORS RELATED TO LIFESTYLE

Traumatic brain injury

Traumatic brain injuries occur at all ages and their consequences vary depending on their severity; they can be isolated or repetitive. They occur in the following circumstances, in particular: during team sports activities, during military service, due to accidents resulting from chronic alcohol abuse or abuse of other substances and, among seniors, due to falls. Severe injuries causing brain damage usually result in persistent cognitive sequelae and major functional disabilities. It is more difficult to identify the consequences of moderate cerebral injuries in the medium and long term: although many studies associate these with an increase in cognitive problems later in life, doubts persist regarding this assertion. Among military veterans (U.S. data), traumatic brain injuries are associated with a higher risk of major neurocognitive disorder. Among seniors, when a traumatic brain injury occurs, for example during a fall, the length of the interval between the time of the injury and its evaluation is independently associated with the severity of the cognitive consequences (5).

Stress

Stress is often studied by focusing on the presence of major stress events. Thus, the loss of a child is associated with more rapid cognitive decline later in life. Younger and less educated parents are more vulnerable in this regard. The Alzheimer 2014 report examined early life stressful events and reported an increase in the risk of major Alzheimer's-type neurocognitive disorders among people who had experienced the death of a parent during childhood. Feeling stressed on a daily basis and experiencing high levels of stress both have long-term cognitive consequences: an increase in memory disorders in the former case, and a faster rate of cognitive decline in the latter case. Perceived social stress contributes to the appearance of health problems attributed to increased cortisol levels; these problems include the development of cardiovascular diseases and the presence of indirect links to cognitive decline and major neurocognitive disorders. But this factor is difficult to study. Among the interventions explored, meditation and mindfulness[37] present encouraging results; however, these must be consolidated (4, 5).

Alcohol

The conclusions regarding alcohol are mixed. Although light to moderate consumption is not a factor associated with loss of cognitive function, and may even play a protective role among adults, it is impossible given the current state of knowledge to establish what amount of alcohol may be beneficial throughout life. However, it is well documented that excessive alcohol consumption produces cognitive impairment (4, 5).

Substance abuse

The substances studied were cannabis, methamphetamine, chronic use of opiates and methadone. There is insufficient information to establish links between abusive use of these substances earlier in life and cognitive performance later in life, during old age (5).

4.2.3 RISK FACTORS RELATED TO OTHER MEDICAL CONDITIONS INCLUDING MEDICATION MANAGEMENT

The three factors selected are: depression, both for its importance and its particular characteristics, auditory impairment and visual impairment. The optimal management of medications has also been selected for inclusion, although this was only addressed by the Institute of Medicine 2015 report,

[37] Mindfulness refers to vigilant awareness of one's own thoughts, actions and motivations. It is used in the West as a therapy for reducing stress and preventing relapses of depression. Retrieved on August 21, 2017 from: https://fr.wikipedia.org/wiki/Pleine_conscience.

because medication use is an important factor among seniors and several medications have well-documented cognitive consequences.

Depression

One person in five will experience at least one episode of depression during his or her lifetime. Depression occurring in midlife adults is associated with a two-fold increase in the risk for cognitive decline or a major neurocognitive disorder later in life. Moreover, there are several elements that suggest the presence of biological plausibility. However, many issues need to be resolved to clarify understanding of the links between depression and cognitive impairments; for example, the links between depression and cognitive symptoms, which are not always part of the clinical picture; the variability of responses to treatment depending on the person; and the absence of clear markers indicating response to treatment. There is also the possibility of reverse causality because depression could also be part of the natural history of major neurocognitive disorders, during a preclinical phase. Finally, negative cognitive effects have also been associated with the treatment of depression, especially among older populations (5, 6). The Lancet Commission 2017 report identifies depression as a modifiable factor that merits intervention among seniors. The Alzheimer 2014 report considers the data on adults insufficient and the data on seniors more robust, while at the same time questioning the direction of the relationship between depression and cognitive disease, given the risk of reverse causality.

Visual impairment

The loss or diminishment of visual acuity is relatively common among seniors and the data are sufficiently robust to establish links to cognitive health, after controlling for mental state and the presence of co-morbidity. The mechanisms explaining these links are poorly understood; they could include a reduction in social activities and an increased risk of falls (5).

Auditory impairment

Peripheral hearing loss received strong attention in the Lancet Commission 2017 report. Their meta-analysis highlights strong associations between the presence of peripheral hearing loss and the subsequent incidence of major neurocognitive disorders. This association is all the more important given that this is a common problem, with hearing loss occurring in nearly a third of people aged 55 and over. The appearance of major neurocognitive disorders has been documented beginning at age 55, which prompts the authors to include hearing loss as a modifiable factor for midlife adults (45 to 65 years), with intervention targeting the prevention or correction of hearing loss. Hypotheses for explaining the cognitive risk include the following: more social disengagement, the increased cognitive effort required to compensate for the impairment, particularly in the presence of cerebral vulnerability (e.g., vascular disease), and the acceleration of cerebral atrophy. However, questions remain regarding the effects of peripheral hearing loss when combined with aging or with vascular impairment, and regarding the nature and effectiveness of interventions aimed at preventing or delaying these diseases. Hearing impairment is also examined in the Institute of Medicine 2015 report and its significance for the cognitive functioning of seniors is recognized (5, 7).

Visual and auditory impairments are sensory losses that are among the most common disabilities faced by seniors and their presence increases with advancing age (2, 5).

Optimal management of medications

Advanced age is accompanied, in more vulnerable people,[38] by the more frequent occurrence of chronic diseases. There is often co-morbidity and the evolution of these problems sometimes requires an increase in or diversification of pharmacological treatments. At the same time, aging is accompanied by physiological changes that make seniors more sensitive to the desired and undesired effects of medication, regardless of whether or not it is prescribed. Risk control becomes increasingly complex as the number of medications and the number of prescribers increases. Studies estimate at between 25 and 30% the proportion of undesired drug effects that might be prevented (5).

Moreover, a large number of drug classes have well-documented negative effects on cognition. The Institute of Medicine 2015 report recalls that, according to the practice guidelines developed in 2012 by the American Geriatrics Society, medication classes with a high risk of cognitive disorders, cognitive decline, delirium and major neurocognitive disorders include: anticholinergics,[39] benzodiazepines, H2-receptor blockers, tricyclic antidepressants, sedative hypnotics and corticosteroids. Antihistamines, which are anticholinergics, as well as benzodiazepines, are in widespread use. Antihistamines, some of which are available over the counter, pose well-documented cognitive risks. As for benzodiazepines, their use is associated with an increased risk of delirium, cognitive dysfunction, falls and motor vehicle accidents, for which reasons they should rarely be indicated.[40] Strategies have been suggested for reducing the inappropriate use of these drugs, in particular when they are being prescribed, since this provides a key opportunity to act preventively. The proposed strategies include the use of computer software to support the decision-making process—sometimes with links to the patient's electronic file, as well as the use of consultant pharmacists and educational approaches directly targeting the user.

4.2.4 Risk factors related to the physical environment

Air pollution

There is an increasing amount of evidence indicating that ambient air pollution is associated with a decrease in cognitive performance among midlife adults and seniors. Here the main issue is pollution linked to ambient levels of fine particulate matter. Air pollutants also indirectly affect cognitive function through their contribution to the development of certain conditions including ischemic heart disease, stroke, various lung conditions and other chronic diseases. Thus, there seems to be a valid argument for the environmental control of air pollution in general and for prevention of harmful exposure among seniors in particular (5).

Workplace exposures

The exposure factors identified include neurotoxic substances and noise exposure. It is difficult to demonstrate the effects of medium- and long-term exposure to neurotoxic substances on cognitive health, given the number of variables that must be documented over a long period of time. However, studies have shown that lead exposure results in a medium- and long-term decrease in cognitive performance. This calls for vigilance and preventive intervention in the environment in general, as well as in the workplace. For other substances that carry a risk of neurotoxicity (e.g., organic solvents, organophosphates), the recommendation is to be proactive in workplaces where these are used and

[38] This would include people with, for example, an unfavourable genetic background, suboptimal living habits or the presence of risk factors.

[39] Anticholinergics include antihistamines, antidepressants, antimuscarinics (urinary incontinence), antiparkinson agents, antipsychotics, antispasmodics and musculoskeletal relaxants.

[40] Recognized uses: in the presence of epilepsies or specific neurological conditions, during alcohol withdrawal, in the presence of a severe generalized anxiety disorder, for anesthetic purposes and/or for palliative care.

to implement effective prevention programs to avoid neurotoxic exposure among all workers. Vigilance is also required when neurotoxic products are used in recreational or leisure contexts and levels of exposure should be verified (5).

Workplaces can be significant sources of noise. Whatever its origin, the presence of hearing loss is associated with decreased cognitive performance. This was discussed in the section on medical conditions affecting cognitive health (5).

4.3 Key points

The number of protective or risk factors studied and their assessment varies from one review to another and their description presents certain difficulties. For some factors, there are few studies specifying their links to cognitive impairment and, for others, it remains difficult to unequivocally identify the mechanisms establishing the plausibility of these links. In addition, because carrying out intervention studies is complex, the data about the effectiveness of interventions is insufficiently robust for the majority of these factors. This is why the National Academies 2017 report identifies only three intervention targets that appear to justify action. These are cognitive training and physical activity to delay age-related cognitive decline and arterial hypertension treatment to prevent or delay mild cognitive impairment or Alzheimer's-type dementias. The National Academies 2017 report considers that the experimental evidence is insufficiently robust to justify the launching of broad public information campaigns by public health actors. This said, they consider it appropriate to indicate in places where information is made accessible to the public (e.g., websites) the potential impact of these three interventions on cognitive health. They also consider it appropriate for actors in the health care and public health networks to describe the cognitive benefits of these factors when promoting them as a means of preventing or controlling other diseases or conditions. Annex 3 reproduces the wording of these recommendations.

The following three tables are intended to set forth the significant details of the various factors under study. Table 2 includes the factors likely to influence the development of cognitive reserve. The subsequent two tables list the factors likely to help prevent or delay cognitive impairments, which may be attributable to vascular conditions, neurotoxic exposure, inflammation or traumatic injury: Table 3 focuses on vascular factors and Table 4 focuses on the other factors that have been described in this report, which relate to lifestyle and to certain health and environmental conditions. It seems clear that planning to intervene to maintain, develop or protect cognitive health implies considering a large number of potential targets.

Table 2 Factors affecting cognitive reserve

Factor*	Characteristics	Details
Education and intellectual stimulation *Alzheimer Report, IOM, NA, Lancet Commission*	Attaining at least a primary level education is the most important protection factor overall for reducing the incidence of major neurocognitive disorders (WHO 2012). Level of education is associated with the development of cognitive reserve. Learning new things throughout life promotes the maintenance and development of cognitive abilities.	Completing primary level education is not an issue in Canada; it can be deduced, however, that there is an incentive to focus on the quality of learning during early childhood. Learning is a source of cognitive stimulation throughout life, including among seniors.
Cognitive training *NA*	Certain programs of long duration using diverse strategies helped improve some cognitive functions among seniors in the medium and long term.	Identified as an effective intervention target for addressing age-related cognitive decline. Computer-based cognitive training programs do not meet current efficacy criteria.
Physical activity (counterweight: sedentarity) *Alzheimer Report, IOM, NA, Lancet Commission*	This affects both cognitive reserve and cerebral reserve (structural changes).	NA: identifies physical activity as an intervention target for all ages, for reducing age-related cognitive decline; Lancet Commission: identifies sedentarity as a modifiable factor for seniors, for reducing the risk of major neurocognitive disorders.
Diet *IOM, NA and Alzheimer Report*	Inconclusive data despite the presence of associations with Alzheimer's-type dementias. Among the various vitamin or dietary supplements, only one encouraging option (NA): the use of vitamin B12 supplemented by folic acid for the most at-risk populations (high levels of homocysteine), but evidence must be consolidated.	New studies are currently targeting various dietary habits.
Social interactions (counterweight: social isolation) *IOM, NA and Lancet Commission*	Studies suggest that social interaction may have effects on cognition. Social isolation and loneliness are risk factors associated with cognitive decline and major neurocognitive disorders.	To be fostered throughout life as a source of cognitive stimulation. IOM and NA: support interventions for improving social interactions that target seniors; encouraging avenue worth pursuing; Lancet Commission: identifies social isolation as a modifiable factor to target among seniors.
Sleep quality *Alzheimer Report, IOM, NA, Lancet Commission*	Biological plausibility. Associated with cognitive decline and Alzheimer's disease.	Insufficient empirical evidence.

* Information sources: Alzheimer Report for the Alzheimer 2014 report, IOM for the Institute of Medicine 2015 report, NA for the National Academies 2017 report and Lancet Commission for the Lancet Commission 2017 report.

Table 3 Cardiovascular and cerebrovascular risk factors, harmful to cognitive health

Factor*	Characteristics	Details
AHT *Alzheimer Report, IOM, NA, Lancet Commission*	Strong associations that can be explained mainly by its association with cardiovascular and cerebrovascular diseases. Among seniors, AHT may play a protective role given the presence of atherosclerosis.	Alzheimer Report, NA and Lancet Commission: identify AHT as an intervention target for midlife adults for preventing, delaying or reducing - mild cognitive impairment and Alzheimer's type dementias.
Diabetes *Alzheimer Report, IOM, NA, Lancet Commission*	Strongly associated with risk of mild cognitive impairment and Alzheimer's-type dementias. Carefully control blood sugar levels to avoid episodes of hypoglycemia.	To prevent, delay or reduce mild cognitive impairment and Alzheimer's-type dementias: ▪ Alzheimer Report: evidence particularly robust for intervention targeting seniors; ▪ Lancet Commission: identifies this as a modifiable factor for seniors; ▪ NA: difficult to verify positive effects of treatment on cognitive impairment; studies should be pursued given the strong documented association.
Hypercholesterolemia *Alzheimer Report, IOM and NA*	Biological plausibility, but evidence is insufficient. Treatment is not associated with cognitive improvement among seniors.	Alzheimer Report: not identified as a risk factor; IOM and NA: encouraging avenue to pursue for intervention among midlife adults.
Obesity *Alzheimer Report, IOM, NA, Lancet Commission*	Obesity often includes several other risk factors for cardiovascular and cerebrovascular diseases; thus it is difficult to isolate its effect. Specific inflammatory effect associated with excess adipose tissue.	Alzheimer Report: insufficient data for midlife adults; robust data against making it an intervention target for seniors; Lancet Commission: identifies obesity as a modifiable factor for midlife adults.
Smoking *Alzheimer Report, IOM, NA, Lancet Commission*	Direct links difficult to prove; its associations with cardiovascular and cerebrovascular diseases explain its importance. Ex-smokers have the same risk level as those who never smoked.	Alzheimer Report and IOM: intervention target for all ages; Lancet Commission: modifiable factor for seniors.

* Information sources: Alzheimer Report for the Alzheimer 2014 report, IOM for the Institute of Medicine 2015 report, NA for the National Academies 2017 report and Lancet Commission for the Lancet Commission 2017 report.

Table 4 Other factors harmful to cognitive health

Factor*	Characteristics	Details
Traumatic brain injuries *IOM*	Diverse sources of injuries and diverse levels of severity: ▪ Robust evidence for severe injuries; ▪ Uncertainty for mild to moderate injuries.	Possible exposure throughout life: ▪ Greater vulnerability among seniors (encourage rapid assessment); ▪ Higher rate of major neurocognitive disorders among American veterans.
Stress *Alzheimer Report and IOM*	Biological plausibility. Studies focus on specific events, as well as on sustained stress at work, social stress, and stress due to war or discrimination.	Insufficient data. Particular vulnerabilities: ▪ Loss of a parent for a child; ▪ Loss of a child for a parent, with a higher risk for younger or less educated parents.
Alcohol *Alzheimer Report and IOM*	Current data do not identify light and moderate alcohol consumption as a risk factor for cognitive impairment.	Association not demonstrated except in presence of alcohol abuse (risk of major neurocognitive disorder).
Substance abuse IOM		Association not demonstrated.
Depression *Alzheimer Report, IOM, NA, Lancet Commission*	Presence of an association with cognitive decline and major neurocognitive disorders. Presence of biological plausibility, but a lot of grey areas relating to the mechanisms that would explain the links with cognitive impairment. Reverse causality: depression may also be associated with the preclinical phase of major neurocognitive disorders.	Alzheimer Report, IOM: intervention target for midlife adults, taking into consideration reverse causality factor;Lancet Commission: identifies depression as a modifiable factor for seniors; Warning: possibility of negative cognitive effects of treatment, particularly for seniors (AHRQ).
Visual impairment *IOM*	Documented risk for seniors, possibly connected to a reduction in social activities and an increased risk of falls.	IOM: suggests intervention among seniors.
Auditory impairment *IOM and Lancet Commission*	Risk for seniors, possibly connected to a reduction in social activities. The Lancet Commission documents an increased risk of cognitive decline and major neurocognitive disorders in the presence of peripheral hearing loss.	IOM: intervention target for seniors; Lancet Commission: considers peripheral hearing loss a significant modifiable factor for midlife adults.

* Information sources: Alzheimer Report for the Alzheimer 2014 report, IOM for the Institute of Medicine 2015 report, NA for the National Academies 2017 report and Lancet Commission for the Lancet Commission 2017 report; and AHRQ for Agency for Health Research Quality.

Tableau 4 Other factors harmful to cognitive health (continued)

Factor*	Characteristics	Details
Optimal management of medications *IOM*	Several classes of medication have well-documented cognitive effects. The risk of cognitive effects depends on the medications (nature, dose, dosage, duration) and their combined effects.	Optimal management of medication among seniors is a real issue: ▪ More drugs are used in the presence of concomitant chronic diseases; ▪ Over-the-counter drugs also included.
Air pollution *IOM*	Associations have been observed between air pollution and cognitive impairment. Complex subject.	Greater vulnerability of seniors.
Exposure to neurotoxins *IOM*	Possibility of exposure to neurotoxic substances at work (lead, volatile substances, organophosphates). Caution concerning the possibility of such exposure when engaging in certain hobbies (lead paint, glue).	Possible exposures throughout life. ▪ Act upstream; ▪ For lead, the medium- and long-term negative effects are documented.

* Information sources: Alzheimer Report for the Alzheimer 2014 report, IOM for the Institute of Medicine 2015 report, NA for the National Academies 2017 report and Lancet Commission for the Lancet Commission 2017 report.

For seven of these factors, in 2014, a team of researchers carried out work intended to calculate the relative contribution of each factor to the risk of developing a major neurocognitive disorder, because they are considered modifiable (24). The risk factors that were selected are: type 2 diabetes, AHT and obesity in midlife adults, depression, physical inactivity, smoking and low educational attainment level. This was calculated at the global level, for Europe, the United Kingdom and the United States. An overall score was also calculated, taking into account the interdependence of several of these factors, to estimate the possibility of reducing the risk of major neurocognitive disorders by acting on these factors. The results of this work are presented in Annex 4. The calculated percentages of risk reduction are 28% worldwide, 31% percent for Europe, 30% for the United Kingdom and 31% for the United States, assuming that effective interventions exist through which to act on these factors.

This annex also includes the results of additional work carried out by the 2017 Lancet Commission for the United Kingdom, which, in addition to the above factors, considered two other risk factors, namely hearing loss and social isolation. The data in the table takes into account the interdependence of the factors. The Lancet Commission 2017 report also indicates the time of life when it is useful to act on each of these factors. The total calculated percentage of risk reduction is 35% for these nine factors, assuming that effective interventions exist through which to act on the factors.

These calculations indicate that there is significant potential to act prospectively.

5 Placing cognitive health on the public health agenda in the United States, the United Kingdom and Canada, and common intervention targets

The first part of this section broadly summarizes the strategies used to place cognitive health on the public health agenda in the United States, the United Kingdom and Canada. The United States and the United Kingdom are distinguished by their explicit intention to act upstream of cognitive impairments. In recent years, they have produced various documents not only testifying to their willingness to take action in this area, but also describing the nature of their engagement and the means each of them is using to move forward. Research was carried out to identify similar commitments made by other developed countries, but this proved less productive. The author therefore decided, in this report, to limit study to the examples provided by the United States and the United Kingdom, especially since the reality of these countries closely resembles that of Canada and their experiences could therefore prove useful to us. It would be possible, in the future, to extend this quest for information to include the experiences of other countries to broaden reflection on the subject. The Australian experience, in particular, could be added to the examples provided. This section also describes the current positioning of Canada with regard to this issue. The second part of this section identifies the common intervention targets for promoting cognitive health, based on relevant sources.

5.1 Placing cognitive health on the public health agenda in the United States, the United Kingdom and Canada

The United States

Since 2005, the American Congress has provided funds to the Centers for Disease Control (CDC) specifically to support the establishment of medium- and long-term plans for concerted action aimed at developing cognitive health. In 2007, the CDC and the Alzheimer's Association of America together developed a systematic approach described in a document entitled *The Healthy Brain Initiative*: *A National Public Health Road Map to Maintaining Cognitive Health* (25, 26). The principles underlying this approach include: a firm grounding in science, an emphasis on primary prevention, a community and population approach and a commitment to eliminating cognitive health disparities. The document establishes ten priorities to be worked on specifically in the following years. These include, among others, determining what the public understands about cognitive health[41] (27, 28), conducting systematic reviews to identify influence factors and effective interventions (5, 6, 8), carrying out research and developing a surveillance system. The document also reflects the desire to include cognitive health, in 2020, among the national health objectives that will serve as the foundation for regional and local public health action plans. As a result, many partnerships were formed, including one with the National Institute on Aging, and updates on the progress of these initiatives are produced and made available online.[42] At a conference on healthy aging conducted by the White House in 2015, one of the key themes identified was the optimization of cognitive health.

The United Kingdom

In 2014, in the context of an initiative spearheaded by public health authorities, representatives of 26 national organizations and 32 specialists agreed on the relevance and the importance of promoting cognitive health and reducing the risk of major neurocognitive disorders in the British

[41] In 2009, a special issue of *Gerontologist* was devoted to this and a summary of the results was also produced thereafter.

[42] https://www.cdc.gov/aging/healthybrain/resources.htm.

population (29). These actors stressed the particular importance of strengthening existing strategies for addressing the modifiable risk factors for the main non-communicable chronic diseases, because these also have the potential to improve brain health and reduce the number of major neurocognitive disorders. They highlighted the concept of cognitive reserve and recalled the relevance and importance of acting early in life and throughout life and of acting upstream, both at the individual level and within communities. They were also concerned by health inequalities. At the end of 2014, reducing the risk of major neurocognitive disorders became one of the seven public health priorities of the United Kingdom (30). The strategies for achieving this include raising awareness within the population about how to protect cognitive health and, to this end, conducting a large-scale campaign among adults aged 40 to 60 years. Partnerships are being formed at many levels, in particular within the education, research and health communities.

Canada

At present, Canada's attention is more focused on the issues related to major neurocognitive disorders. The *National dementia research and prevention plan*, produced in 2014 by the Government of Canada (31), underlines the importance of major neurocognitive disorders and is particularly focused on investments in research on major neurocognitive disorders and the main neurodegenerative disorders. The government has invested in integrating major neurocognitive disorders into the Chronic Disease Surveillance System. References to preventive action are minimal in the plan. In 2016, the Standing Senate Committee on Social Affairs, Science and Technology examined the subject of major neurocognitive disorders in Canada (32) and offered 29 recommendations covering various aspects connected to the issue: research, public awareness, training and education, early detection and more accurate diagnosis, support for caregivers, contribution of health and community care services, and accommodation options. In June of 2017, Bill C-233, *An Act respecting a national strategy for Alzheimer's disease and other dementias*, was adopted. The federal strategy focuses on improving the clinical diagnosis of major neurocognitive disorders and their treatment, on improving the quality of life of people with major neurocognitive disorders and that of their caregivers, on the development and dissemination of information, both to health professionals and to the general public, to promote the importance of prevention of and early intervention in Alzheimer's disease and other major neurocognitive disorders (33).

To summarize, their positioning may differ, but the United States and the United Kingdom have both clearly indicated their desire to promote early intervention upstream of cognitive impairments and have made this a specific area of intervention. As regards Canada, the position set forth in the *Act respecting a national strategy for Alzheimer's disease and other dementias* affirms the importance of educating health professionals and the general public about the importance of taking preventive action. This could be an interesting aspect to leverage, in the follow-up to this report, to justify the identification of cognitive health as a public health issue and thus improve our effectiveness at acting upstream of cognitive impairments.

5.2 Common intervention targets for cognitive health

Four sources of diverse origin were selected to illustrate the strong convergence of results concerning the intervention targets recommended for maintaining and protecting cognitive health. The Institute of Medicine 2015 review (5) included explicit recommendations in this regard and these have been included. Alzheimer's societies are actively focused on prevention and this is why the advice provided by Alzheimer's Disease International (35) and the Alzheimer Society of Canada (36) was also selected. Finally, in the context of our work, we observed that the National Institute on Aging (34) in the United States used the same type of recommendations. Four separate sources

seemed sufficient to form an initial compilation and analysis of proposed choices, illustrating the commonalities in their messages and the results of the knowledge synthesis. Table 5 identifies these intervention targets and their sources.

Table 5 Common intervention targets for cognitive health

Intervention target	Sources References below table			
	1-IOM	2-NIA	3-AA	4-ASC
Be physically active	√	√	√	√
Act on the main risk factors for cardiovascular diseases:				
▪ Hypertension,	√	√	√	√
▪ Diabetes,	√	√	√	√
▪ Smoking,	√	√	√	√
▪ Hypercholesterolemia,		√	√	√
▪ Obesity.			√	√
Prevent and treat depression.		√	√	√
Optimally manage medications that have effects on memory, sleep and cerebral functions.	√	√		
Promote social interaction.	√	√	√	√
Promote intellectual stimulation and diverse learning experiences.	√	√	√	√
Get sufficient sleep and treat sleep disorders if necessary.	√	√	√	
Prevent falls and injuries.		√	√	√
Avoid excessive consumption of alcohol.				√
Favour a healthy diet.		√	√	√

1. IOM for the Institute of Medicine of the National Academies. 2015. *Cognitive Aging: Progress in Understanding and Opportunities for Action*, Washington, DC: The National Academies, p. 7.
2. NIA for National Institute of Aging: https://www.nia.nih.gov/health/cognitive-health-and-older-adults.
3. AA for Alzheimer's Association: http://www.alz.org/news_and_events_lifestyle_changes_help_reduce_risk.asp[43].
4. ASC for Alzheimer Society of Canada: http://alzheimer.ca/en/Home/About-dementia/Alzheimer-s-disease/Risk-factors.

This table reveals that the majority of the selected intervention targets focus on healthy lifestyles and on the main factors for preventing chronic diseases.

[43] The formulations used in this document are particularly dynamic: *Break a Sweat, Hit the Books, Butt Out, Heads Up!, Fuel Up Right, Catch Some Zzz's, Take Care of Your Mental Health, Buddy Up, Stump Yourself*.

6 Conclusion

Cognitive health has become a subject of interest because cognitive impairments occur most frequently in old age and the current context is characterized by rapid demographic aging, particularly among the oldest population segments. Moreover, major cognitive impairments are now a significant cause of mortality and morbidity in Canada and in Québec, especially among seniors aged 70 years and older. They last for many years and deprive people of their independence and autonomy; they also have important consequences for their loved ones, the health care and services system, community organizations and the wider communities in which sufferers and their loved ones live. Furthermore, the estimated costs are very high and will continue to increase.

Although there is no cure for major neurocognitive disorders at present, there exist levers for acting upstream. Preventing cognitive impairment or even delaying the onset of its most severe forms carries significant benefits. As this report illustrates, many recent literature reviews have synthesized the available knowledge on various factors of interest. Some factors strengthen cognitive reserve, which, on the one hand, contributes to the ability to better cope with age-related cognitive decline by enhancing cognitive abilities and, on the other hand, increases the brain's resilience in the event of severe impairment, making it possible to delay the clinical manifestations of major neurocognitive disorders. Other factors harm brain health by producing traumatic, vascular, neurodegenerative or inflammatory brain damage.

The main factors that strengthen cognitive reserve are education, intellectual stimulation throughout life and, according to the recommendations of the National Academies in 2017, cognitive training and physical activity. The main factors that harm brain health are AHT, smoking and hyperglycemia, and these factors are also associated with the development of cardiovascular and cerebrovascular diseases. Other factors of interest are physical inactivity and social isolation. Interventions targeting these various factors are appropriate at different times of life.

In recent years, studies have documented a slight decline in the incidence of major neurocognitive disorders in several developed countries. The hypotheses put forward to explain this change point to the most robust factors: an improvement in education levels, the adoption of healthy living habits associated with the prevention of cardiovascular and cerebrovascular diseases, and better control over the risk factors associated with these diseases. These observations imply that more intensive efforts to support this trend could make a difference.

This synthesis confirms that acting preventively on relevant factors would have a significant impact on the incidence and prevalence of cognitive diseases and that this would have beneficial effects on both the people affected and their families. The socioeconomic impacts of such change would also be major. This is a field of knowledge in full expansion, and it will be necessary to keep abreast of new knowledge as it becomes available.

This knowledge synthesis focuses on the main factors likely to influence cognitive health. It also identifies the approaches that have been adopted by countries concerned by this issue. It constitutes a useful information base for actors interested in reflecting on how the Québec public health sector might position itself with respect to cognitive health.

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29. UK Health Forum. May 2014. Blackfriars Consensus on promoting brain health: Reducing risks for dementia in the population, *Public Health England*, 7 p.

30. Public Health England. 2014. From evidence into action: Opportunities to protect and improve the nation's health, PHE publications gateway number: 2014404, 28 p.

Documents used for Canada

31. Government of Canada. 2014. National dementia research and prevention plan, 14 p.

32. Standing Senate Committee on Social Affairs, Science and Technology. 2016. *Dementia in Canada: A National Strategy for Dementia-friendly Communities*, Senate of Canada, 56 p.

33. Bill C-233: *An Act respecting a national strategy for Alzheimer's disease and other dementias*. Available at: http://www.parl.ca/DocumentViewer/en/42-1/bill/C-233/royal-assent

Websites with messages aimed at promoting cognitive health or brain health

34. https://www.nia.nih.gov/health/cognitive-health-and-older-adults

35. http://www.alz.org/news

36. http://www.alzheimer.ca/en/Home/About-dementia/Alzheimer-s-disease/Risk-factors

Annex 1

Complementary information about methodology

Description of the documents on which the knowledge synthesis is based

The Institute of Medicine report: Published in 2015 and entitled *Cognitive Aging: Progress in Understanding and Opportunities for Action,* this document focuses on factors that can be targeted by promotion and prevention interventions. It describes the current state of knowledge on a wide range of factors associated with both medium- and long-term cognitive health. The authoring committee carried out a preliminary selection process to identify evidence-based factors that could be targeted broadly through public health interventions (Table 1). The report is distinguished by the significant range of expertise represented within the members of the authoring committee, both in terms of their fields of expertise and their diverse work settings (universities and American research institutes). This depth of expertise also characterizes the document's review committee.

Table 1 The institute of Medicine 2015 report: factors selected

Factors associated with lifestyle and physical environment	Health and medical factors	Factors associated with general approaches

▪ Physical activity and exercise
▪ Education and intellectual engagement
▪ Social isolation, loneliness and social engagement
▪ Diet, use of vitamins
▪ Alcohol
▪ Smoking
▪ Substance abuse
▪ Physical environment:
  ▪ Air pollution
  ▪ Occupational exposure
▪ Stress
	▪ Medications
	▪ Cerebrovascular and cardiovascular disease risk factors:
	  ▪ Hypertension
	  ▪ Hyperlipidemia
	  ▪ Type 2 diabetes
	  ▪ Obesity
	▪ Depression
	▪ Traumatic brain injury
	▪ Hearing and visual loss
	▪ Sleep
		▪ Cognitive stimulation and training
		▪ Use of dietary supplements and nootropics*

* *Nootropics* are drugs, medications, plants and other substances that improve or are thought to improve cognitive function [translation]. http://www.psychomedia.qc.ca/lexique/definition/nootrope-medicament, retrieved on 14-09-2017.

The National Academies report: Published in 2017 and entitled *Preventing Cognitive Decline and Dementia: A Way Forward*, this report complements the previous one by documenting the effectiveness of interventions intended to influence cognitive health. Its analysis integrates the results of a review carried out by the Agency for Healthcare Research and Quality, which specializes in the production of evidence-based work. Table 2 lists those factors identified in the National Academies report whose results are considered to be convincing or sufficiently promising to warrant further research.

Table 2 The National Academies 2017 report: factors selected for effectiveness studies

Factors recommended as a focus for intervention and identified as a research priority	Promising factors identified as a research priority
▪ Cognitive training	▪ Diabetes treatment
▪ Blood pressure management for people with HT	▪ Depression treatment
▪ Increased physical activity	▪ Dietary interventions
	▪ Lipid-lowering treatment/statins
	▪ Sleep quality interventions
	▪ Social engagement interventions
	▪ Vitamin B12 plus folic acid supplementation

The Institute of Medicine 2015 and the National Academies 2017 include as an intervention target age-related cognitive decline, whereas the other two documents focus mainly on major neurocognitive disorders, which generally fall into the category of Alzheimer's-type dementia.

The Alzheimer Report: Published in 2014 and entitled *Dementia and Risk Reduction: An Analysis of Protective and Modifiable Factors*, this report uses a life-course approach to identify the factors likely to influence lifelong cognitive health (Table 3). Responsibility for each chapter was assigned to experts in the area discussed. They examine the most recent evidence concerning the influence factors within the scope of their expertise and analyze the results of studies that focus on these factors. They also cast a critical eye on the validity of the data studied and their limitations. The conclusions reached by the authors have the benefit of providing public health actors with great clarity. Many collaborators from Brazil and the United States also participated in the production of the document.

Table 3 The Alzheimer 2014 report: factors selected

Developmental factors	Psychological factors	Lifestyle	Cerebrovascular and cardiovascular disease risk factors
▪ Early life stress	▪ Depression	▪ Smoking	▪ Hypertension
▪ Education	▪ Stress	▪ Alcohol	▪ Obesity
	▪ Sleep disorders	▪ Physical activity	▪ Hypercholesterolemia
		▪ Cognitive stimulation	▪ Diabetes
		▪ Diet, vitamins and dietary supplements	

The Lancet Commission report: Published in 2017 and entitled *Dementia Prevention, Intervention, and Care*, this document focuses analysis on nine factors (Table 4). While they draw on previously accomplished work for seven of them, the authors carried out additional work to deepen knowledge concerning two of the factors: social isolation and hearing loss.

Table 4 The Lancet Commission 2017 report: risk factors selected according to the time of life to intervene

Time to intervene	Factors selected
Early life	▪ Level of education
Midlife adults (defined as between 45 and 64 years)	▪ Hearing loss ▪ Hypertension ▪ Obesity
Older adults	▪ Smoking ▪ Depression ▪ Physical inactivity ▪ Social isolation ▪ Diabetes

Data sources for mortality, premature mortality and overall burden

The data used to document the rates of mortality and premature mortality and the overall burden of major neurocognitive disorders in Canada were drawn from two sources: the first uses data from Statistics Canada to describe the relative importance of causes of mortality; the second uses data processed by the Institute for Health Metrics and Evaluation[44] responsible for the production of national, supranational and global data for the measurement of the global burden of diseases, whose 2015 summary analysis was used for this report. The disease groupings used to establish the relative importance of causes of mortality and premature mortality are different in these two sources. In compiling its data, Statistics Canada groups all cancers together and does not isolate hypertensive heart disease as a cause. The Institute for Health Metrics and Evaluation proceeds differently. To ensure more accurate comparisons between countries and regions throughout the world, it is necessary to distinguish the causes of cancer and to use more detailed groupings for vascular diseases. Data can thus be extracted from their data bank by country for indicators related to the global burden. This allows for comparisons between countries, on the supranational or global level.

Data sources documenting the consequences of cognitive impairment

The data on the consequences of cognitive impairment were drawn mainly from Canadian sources and secondarily from Québec sources. The source of several data elements was the Alzheimer Society of Canada and in particular a report produced in 2016 by a group of 20 experts on population health working within, among other organizations, several Canadian universities, research institutes, the Public Health Agency of Canada and the Canadian Institute for Health Information. This documentation includes a critical analysis of various sources that have, over the years, collected data on the incidence and prevalence of Alzheimer's disease in Canada. The data on the type of assistance needed come from Statistics Canada. Finally, the supplementary Québec data come from

[44] This American Institute, created in 2007, possesses leading expertise in the analysis of national, supranational and global health trends. Many of its studies have been published in *The Lancet*. In May 2015, this Institute signed a major agreement with the WHO to improve data used to establish health trends. Reference: http://www.healthdata.org/about/history.

work carried out in 2017 by the chronic diseases surveillance team at the INSPQ for the purpose of assessing, for 2014–2015, the results of monitoring indicators for the prevalence and incidence of major neurocognitive disorders drawn from various sources of administrative data available in Québec.

Quality analysis process used

The following quality analysis processes were used in the production of this report:[45]

- At several points during the drafting of the report, the four collaborators identified at the beginning of the document were able to iteratively respond to and comment on the progress of the report from the perspective of their fields of expertise: healthy aging, the public health vision of the INSPQ, concerns about healthy public policies and concerns related to the subsequent steps in knowledge transfer.
- At the end of the process, a manager in the Bureau d'information et d'études en santé des populations (Office of population health information and studies) at the INSPQ also commented on the document.
- Five readers external to the INSPQ read and commented on the document:
  - Two regional public health directors likely to be confronted with this new issue;
  - The coordinator of the project team for the writing of the 2018 report of the National Public Health Director that will focus on aging, at the Ministère de la Santé et des Services sociaux;
  - And two readers external to the INSPQ and to the public health network: an experienced neurologist in charge of the memory clinic for seniors suffering from cognitive impairment at the Centre hospitalier universitaire de Québec; and a researcher and professor in the department of medicine at the Université de Montréal who, among other things, directs the Cognitive Health and Ageing Research Laboratory (LESCA) at the Centre de recherche de

[45] The persons who participated in the review of this document are identified under the section heading *TRANSLATION*
Nina Alexakis Gilbert, Angloversion

LINGUISTIC REVISION

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Annex 2

Description of supplemental information strategies used by the National Academies in 2017

Description of supplemental information strategies used by the National Academies 2017 report[46]

Supplemental **observational studies** used included longitudinal population-based cohort studies, studies of risk factors and neurobiological studies. The latter allowed for better understanding of the neurobiological effects of the factors being studied or of proposed interventions and the mechanisms they involve.

Application of the Bradford Hill criteria[47] was used to assess whether or not credible causal inferences could be made based on the evidence suggesting the presence of an association between a given factor and cognitive effects. The following criteria were used:

- The chronological relationship confirming that exposure to the factor predates the occurrence of the consequences;
- The strength of the association;
- The presence of a dose-response relationship;
- The specificity of the effects observed or the absence of other explanations;
- The consistency of findings among different populations; and
- A plausible explanation of the mechanisms underlying the observations.

Analysis of the risks and costs of interventions and their potential benefits for noncognitive results helped to bolster some favourable judgments, and to strengthen some negative judgments regarding certain interventions.

[46] National Academies of Sciences, Engineering, and Medicine. 2017. *Preventing Cognitive Decline and Dementia: A Way Forward.* Washington, DC: The National Academies. 132 p.

[47] The description of the Bradford-Hill criteria is derived from p. 123 of the following document: The Association of Faculties of Medicine of Canada. 2017. AFMC Primer on Population Health, Public Health Educators' Network, 498 p.

Annex 3

Recommendations made in the National Academies 2017 report

Recommendations made in the National Academies 2017 report[48,49]

Conclusions concerning cognitive training (pp. 36–37 of the report):

- Some data from randomized clinical trials suggest that cognitive training may delay or slow age-related cognitive decline, based on measurements of performance on cognitive tests and of instrumental activities of daily living. This conclusion is largely based on the "ACTIVE" clinical randomized trial.
- There is no data from randomized clinical trials to support the assertion that cognitive training can prevent, delay or slow mild cognitive impairment or Alzheimer's-type dementia.
- Currently, there is no data to support the idea that the beneficial long-term cognitive effects suggested by the "ACTIVE" trial apply to computer-based "brain training" applications. The intervention program used in the "ACTIVE" trial includes sustained cognitive training and social engagement in a group setting. This differs substantially from commercial computer-based applications whose effects seem to be more short-term and to apply only to specific and repeated cognitive tasks.
- The encouraging data obtained from randomized clinical trials on cognitive training interventions, bolstered by additional data from prospective observational cohorts on the benefits of cognitively stimulating activities, supports the communication to the public of the fact that cognitive training may be a tool that can delay or slow age-related cognitive decline. However, current data do not allow the committee to draw conclusions about the relative effectiveness of different approaches or techniques used in cognitive training.

Conclusions concerning blood pressure management (p. 44 of the report):

- Blood pressure management for people with hypertension, particularly for midlife adults, is supported by encouraging, but inconclusive evidence, as a way to prevent, delay or slow Alzheimer's-type dementia. Data from randomized clinical trials do not offer strong support for the use of blood pressure management in hypertensive patients to delay or slow age-related cognitive decline or prevent, delay or slow mild cognitive impairment or Alzheimer's-type dementia, although one trial provides some positive evidence of an impact on Alzheimer's-type dementia. However, when considering prospective cohort studies and knowledge of the natural history and biology of the disease, the effects of blood pressure management on the incidence of Alzheimer's-type dementia in hypertensive patients are consistent with a causal relationship. Moreover, there are recognized cardiovascular benefits that result from blood pressure management.

[48] Reference: National Academies of Sciences, Engineering, and Medicine. 2017. *Preventing Cognitive Decline and Dementia: A Way Forward.* Washington, DC: The National Academies. 132 p. DOI: https://doi.org/10l17226/24782.

[49] These conclusions and recommendations are drawn from the original report; although not directly quoted, the wording of the original text is closely followed.

Conclusions concerning increased physical activity (p. 51 of the report):

- Increased physical activity as a means of slowing age-related cognitive decline is supported by encouraging but inconclusive evidence. What emerges from the results of all the randomized clinical trials examining different types of physical activity interventions provides an indication of the effectiveness of increased physical activity for delaying or slowing age-related cognitive decline. These effects are consistent with the presence of a causal relationship when prospective cohort studies and knowledge of the underlying neurobiological processes are considered. Moreover, increased physical activity has documented effects on cardiovascular health and other aspects of health.
- There is currently insufficient evidence to conclude that increased physical activity can prevent, delay or slow mild cognitive impairment or Alzheimer's-type dementia.
- Evidence is insufficient to determine what specific types of physical activity would be particularly effective in preventing cognitive decline and major neurocognitive disorders.

Recommendation for communicating with the public (p. 52 of the report):

When communicating with the general public about the current state of knowledge, the National Institutes of Health, the Centers for Disease Control and Prevention and other interested organizations should clearly indicate that the positive effects of the following interventions are based on encouraging, but inconclusive evidence:

- Cognitive training—a broad set of interventions, such as those targeting reasoning, memory and speed of information processing—to delay or slow age-related cognitive decline;
- Blood pressure management for people with hypertension to prevent, delay or slow Alzheimer's-type dementia;
- Increased physical activity to delay or slow age-related cognitive decline.

Currently, there is insufficient experimental evidence to justify a public information campaign that would encourage the adoption of these specific interventions to prevent these conditions. Nevertheless, it is appropriate for the National Institutes of Health and other concerned bodies to provide relevant information about the potential impacts of these three interventions on cognitive outcomes in locations accessible to the general public (e.g., websites). It is also appropriate for public health actors and health care professionals to mention the potential cognitive benefits of these interventions when promoting their adoption for the control of other diseases and health conditions.

Annex 4

Prevalence and attributable fractions

Table 1 Prevalence and attributable fractions for seven risk factors considered to be modifiable, worldwide and for Europe*

RISK FACTORS	DATA FOR WORLD		DATA FOR EUROPE	
	Prevalence	Attributable fraction and confidence interval	Prevalence	Attributable fraction and confidence interval
Type 2 diabetes	6.4%	2.9% (1.3%-4.7%)	6.9%	3.1% (1.4%-5.0%)
AHT in midlife adults	8.9%	5.1% (1.4%-9.9%)	12.0%	6.8% (1.9%-13.0%)
Obesity in midlife adults	3.4%	2.0% (1.1%-3.0%)	7.2%	4.1% (2.4%-6.2%)
Depression	13.2%	7.9% (5.3%-10.8%)	18.5%	10.7% (7.2%-14.5%)
Physical inactivity	17.7%	12.7% (3.3%-24.0%)	31.0%	20.3% (5.6%-35.6%)
Smoking	27.4%	13.9% (3.9%-24.7%)	26.6%	13.6% (3.8%-24.2%)
Low educational attainment	40.0%	19.1% (12.3%-25.6%)	26.6%	13.6% (8.5%-18.6%)
Adjusted combined effect**		28.2% (14.2%-41.5%		31.4% (15.3%-46.0%)

* Norton S., Matthews F. E., Barnes D., Yaffe K. & Brayne C., 2014. *Potential for primary prevention of Alzheimer's disease: An analysis of population-based data. Lancet Neurology,* 13(8), 788–794. DOI:10.1016/S1474-4422(14)70136-X.

** Adjusted for the non-independence of risk factors.

Table 2 Prevalence and attributable fractions for seven risk factors considered to be modifiable, United Kingdom and United States*

RISK FACTORS	DATA FOR THE UNITED KINGDOM		DATA FOR THE UNITED STATES	
	Prevalence	Attributable fraction and confidence interval	Prevalence	Attributable fraction and confidence interval
Type 2 diabetes	4.1%	1.9% (0.8%-3.1%)	10.3%	4.5% (2.0%-7.3%)
AHT in midlife adults	12.4%	7.0% (1.9%-13.3%)	14.3%	8.0% (2.2%-15.1%)
Obesity in midlife adults	11.8%	6.6% (3.9%-9.8%)	13.1%	7.3% (4.3%-10.8%)
Depression	13.9%	8.3% (5.5%-11.3%)	19.2%	11.1% (7.5%-15.0%)
Physical inactivity	34.0%	21.8% (6.1%-37.7%)	32.5%	21.0% (5.8%-36.6%)
Smoking	20.0%	10.6% (2.9%-19.4%)	20.6%	10.8% (3.0%-19.8%)
Low educational attainment	23.6%	12.2% (7.6%-16.9%)	13.3%	7.3% (4.4%-10.3%)
Adjusted combined effect**		30.0% (14.3%-44.4%)		30.6% (14.5%-45.3%)

* Norton S., Matthews F. E., Barnes D., Yaffe K. & Brayne C., 2014. *Potential for primary prevention of Alzheimer's disease: An analysis of population-based data. Lancet Neurology,* 13(8), 788–794. DOI: 10.1016/S1474-4422(14)70136-X.

** Adjusted for the non-independence of risk factors.

Table 3 Weighted attributable fractions for nine risk factors considered to be modifiable by the Lancet Commission 2017 and classification of the factors according to the time of life to intervene (United Kingdom)**

Time to intervene	Factors selected	Attributable fraction**
Early life	▪ Level of education	7.5%
Midlife adults (defined as between 45 and 64 years)	▪ Hearing loss ▪ Hypertension ▪ Obesity	9.1% 2.0% 0.8%
Older adults	▪ Smoking ▪ Depression ▪ Physical inactivity ▪ Social isolation ▪ Diabetes	5.5% 4.0% 2.6% 2.3% 1.2%
Combined effect of factors		35%

* The Lancet Commission. 2017. *Dementia Prevention, Intervention, and Care*, 62 p., Published online July 20: htpp://dx.doi.org/10.1016/S0140-6736(17)31363-6; data drawn from Table 1 presented on p. 5.

** The attributable fractions have been weighted to establish the relative contribution of each risk factor to the risk of developing a major neurocognitive disorder.

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