Issue: Type II Diabetes Prevention & Screening
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Evidence *in* Context

Health research — synthesized and contextualized for use in Newfoundland & Labrador

Prevention and Screening for Type 2 Diabetes *in* Newfoundland and Labrador

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APPLIED HEALTH RESEARCH
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About This Report

About NLCAHR

The Newfoundland and Labrador Centre for Applied Health Research, established in 1999, contributes to the effectiveness of the health and community services system of the province and the physical, social, and psychological well-being of the population. NLCAHR accomplishes this mandate by building capacity in applied health research, supporting high quality research, and fostering more effective use of research evidence by decision makers and policy makers in the province's health system.

About the Contextualized Health Research Synthesis Program

In 2007, NLCAHR launched the Contextualized Health Research Synthesis Program (CHRSP) to provide research evidence that would help guide decision makers in the provincial health system on issues of pressing interest to Newfoundland and Labrador. Instead of conducting original research, CHRSP analyzes findings from high level research already conducted in the subject area, such as systematic reviews, meta-analyses and health technology assessments. Findings are then synthesized and subjected to a systematic process of contextualization: they are analyzed in terms of their applicability to the conditions and capacities of the unique context of Newfoundland and Labrador. Our contextual analysis includes assessing the specific forms an issue may take in this province as well as the applicability of any proposed solutions and methods to locally available resources, infrastructure, human resources, cultural conditions and financial capacities. CHRSP uses a combination of external experts and local networks to carry out and contextualize the research synthesis and to facilitate the uptake of the results by research users. CHRSP focuses on three types of projects: health services/ health policy projects, health technology assessment (HTA) projects, and projects that combine the two to examine processes for the organization or delivery of care involving a health technology.

Who Should Read This Report?

This report provides a synthesis of the relevant research-based evidence on synthesis of the relevant research-based evidence on reducing the incidence of Type 2 Diabetes and its medical complications in the adult population of Newfoundland and Labrador. This report is intended to inform and assist decision makers in Newfoundland and Labrador's four Regional Health Authorities and the Departments of Health and Community Services and Seniors, Wellness, and Social Development. The findings of our synthesis are based on an international search of the literature and may also be applicable to other countries, but are specifically interpreted for the context of Newfoundland and Labrador.

Decision makers from other jurisdictions, especially those with similar potential clients, geography and resources, may also find the content helpful. The report includes explanations of research terms and technical language; as such, there is no need to have a specialized medical or health background in order to understand its content.

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Type 2 Diabetes Prevention and Screening *in* Newfoundland and Labrador

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Acronyms

ACEIs	Angiotensin Converting Enzyme Inhibitors
ADDITION	Anglo Danish-Dutch Study of Intensive Treatment in People with Screen Detected Diabetes in Primary Care
AMSTAR	Assessment of Multiple Systematic Reviews
ARB	Angiotensin Receptor Blockers
BMI	Body Mass Index
CAD	Coronary Artery Disease
CDA	Canadian Diabetes Association
CEA	Cost Effectiveness Analysis
CHRSP	Contextualized Health Research Synthesis Program
CPCSSN	Canadian Primary Care Sentinel Surveillance Network
CTFPHC	Canadian Task Force on Preventive Health Care
CUA	Cost-Utility Analysis
CVD	Cardiovascular Disease
DASH	Dietary Approaches to Stop Hypertension
DHCS	Department of Health and Community Services (Government of Newfoundland and Labrador)
DPP	Diabetes Prevention Program
HbA1C	Glycated Hemoglobin
ICER	Incremental Cost-Effectiveness Ratio
iEHR/LABS	Interoperable Electronic Health Record and Laboratory System
NLMA	Newfoundland and Labrador Medical Association
NICE	The National Institute for Health and Care Excellence
OR	Odds Ratio
QALY	Quality-Adjusted Life Year
RCT	Randomized Controlled Trial
RR	Relative Risk
T2D	Type 2 Diabetes Mellitus
USD	American Dollars
USPSTF	U.S. Preventive Services Task Force

Glossary

Alpha-Glucosidase Inhibitors	A class of oral medications for type 2 diabetes that decrease the absorption of carbohydrates from the intestine, resulting in a slower and lower rise in blood glucose throughout the day, especially right after meals.
AMSTAR	**Assessment of Multiple Systematic Reviews:** An 11-item instrument used to assess the methodological rigor of systematic reviews
Angiotensin Converting Enzyme Inhibitors	A class of medication that is used to treat a variety of conditions such as high blood pressure.
Angiotensin Receptor Blockers	A class of medication that is used to treat conditions such as high blood pressure and heart failure.
Archimedes Model	Type of simulation model used in economic analyses.
Bariatric Surgery	Weight-loss surgery that makes changes to your digestive system to help you lose weight by limiting how much you can eat or by reducing the absorption of nutrients, or both.
Cardiovascular Disease	A group of disorders of the heart and blood vessels.
Cost	The cost per individual of the intervention (prevention or screening).
Cost-Utility Analysis	A form of evaluation that focuses particular attention on the quality of the health outcome produced or forgone by health programs or treatments.
Downs and Black Assessment Tool	A checklist that was developed to assess the methodological quality of both randomised controlled trials and non-randomised studies.
Fasting Plasma Glucose	This is a type of blood test that measures glucose in the blood. It is completed after a period of fasting. Results of this test are used to help diagnose diabetes or prediabetes
Glycated Hemoglobin	This is a type of blood test used to diagnose diabetes. This test measures a person's average blood sugar level for the past few months (often abbreviated as HbA1C).
Heterogeneity	Used to describe the consistency or variation between trials in meta-analysis. The degree of heterogeneity can be quantified on indices, such as I^2 and can be tested with chi-square based statistical tests.
Health Technology Assessment	Research that that studies the medical, social, ethical and economic implications of the development, diffusion, and use of health technology.
Hyperglycemia	The medical name for high blood glucose.
Impaired Fasting Glucose (IFG)	A condition in which the fasting blood glucose level is consistently elevated above what is considered normal levels; however, it is not high enough to be diagnosed as type 2 diabetes. Considered a pre-diabetic condition.
Impaired Glucose Tolerance (IGT)	A condition in which blood glucose is elevated above the normal range after a meal/glucose load, but not quite high enough for diagnosis of type 2 diabetes. Considered a pre-diabetic condition.
Incidence	A measure that describes the occurrence of new disease in a population over a specific period of time.
Incremental Cost-Effectiveness Ratio (ICER)	A measure used to compare interventions that are not cost-saving (net cost greater than 0). It is the ratio of net cost to net gains in outcome (that is, the ratio of the difference in costs and difference in outcomes between two interventions) A lower ICER means the intervention is more cost-effective (it costs less per unit of outcome). ICERs are needed to compare interventions for different diseases.

Markov Chain	A type of model that is based on random probability distribution that describes a sequence of possible events in which the probability of each event depends only on the present state and not on any past states.
Meta-Analysis	A type of synthesis that uses statistical techniques to quantitatively combine the findings from primary research studies. A meta-analysis may or may not be applied to a systematic review of the literature.
Metabolic Syndrome	A combination of the medical disorders that, when occurring together, increase the risk of developing cardiovascular disease and diabetes.
Metformin	An oral antidiabetic drug in the biguanide class. It is commonly the drug of first choice used for type 2 diabetes to lower blood glucose (sugar) by influencing the body's sensitivity to insulin.
Normoglycemia	The medical term for normal levels of glucose content of the blood.
Oral Anti-Diabetic Drugs	Include a number of drug classes used to treat T2D e.g., biguanides, sulfonylureas, meglitinides, thiazolidinediones and alpha-glucosidase inhibitors.
Oral Glucose Tolerance Test	A test given to measure blood glucose levels over a period of time to determine the body's ability to handle glucose.
Prediabetes	A condition in which blood glucose levels are higher than normal but not high enough to be diagnosed as type 2 diabetes. Can be any combination of IFG and IGT).
Primary Prevention	Strategies used to protect healthy people from developing a disease or experiencing an injury in the first place.
Cohort Study	A study that follows a group of individuals over time. These individuals are similar in many ways but differ by a certain characteristic. This characteristic is compared to see whether it is associated with a particular outcome.
Quality-Adjusted Life Year(QALY)	A measure of health as a combination of the length of life and the health-related quality of life (HRQoL).
Ramipril	A drug in the angiotensin-converting enzyme inhibitor class used in the treatment of high blood pressure and certain heart conditions.
Secondary Prevention	Strategies used to reduce the impact of a disease or injury that has already occurred. This approach includes early detection or treatment of disease with the focus on slowing the progression or progress of disease/ injury.
Screening	A type of secondary prevention that aims to detect disease before symptoms are present in order to treat it early and avoid unnecessary complications.
Social Determinants of Health	The social and economic factors experienced through life that influence the health of populations.
Systematic Review	A literature review that tries to identify, select, appraise, and synthesize published and unpublished research evidence relevant to a specific research question.
Tertiary Prevention	Strategies used to help manage the impact of complicated, long-term health problems or injuries to prevent any further physical deterioration and to maximize quality of life.
Type 2 Diabetes	A chronic disease that affects the way the body processes glucose, a kind of sugar found in the blood.

The Research Question

"What interventions are likely to be effective in reducing the incidence of Type 2 Diabetes and its medical complications in the adult population of Newfoundland and Labrador?"

Developing the Research Question

At its initial meeting, the project team decided that this report should synthesize scientific evidence relative to two areas of Type 2 Diabetes (T2D) prevention:

- the effectiveness and cost-effectiveness of interventions to prevent diabetes in at- risk, asymptomatic adults; and
- the effectiveness and cost-effectiveness of screening on the early detection of T2D in adults and prevention of further medical complications.

With guidance from our subject expert, Dr. Laura Rosella, the project team created a broad research question that would encompass these two areas of study. In an effort to ensure that the amount of research evidence to be included in this report would be manageable, the team then narrowed its focus by using specific selection criteria (i.e., we placed limits on population, interventions and outcomes to be studied). Please see the Online Companion Document for the detailed list of the specific selection criteria we used to determine what evidence would be included in this report LINK

Key Messages from this Report

1. At present, there is an insufficient amount of high-quality evidence on the long-term clinical benefits and potential harms of screening for T2D. The limited evidence that is available showed no evidence of improved mortality through screening for T2D, either in the general population or in high-risk populations after 10 years of follow-up.

2. Overall, more robust evidence is needed to confidently evaluate the cost-effectiveness of screening interventions for T2D. In the limited studies available, there was some evidence to suggest that targeted opportunistic screening to detect and manage diabetes among high-risk

patients (i.e., patients with obesity and/or with high blood pressure) may be either cost-saving or cost less than $6,000 USD per quality-adjusted life year (QALY) gained. However, it should be noted that there was disagreement between studies on the range of cost.

3. Universal population screening of all adults aged at or over 45 years compared with no screening was not shown to be cost-effective at all, with a predicted incremental cost-effectiveness ratio (ICER) of close to CAD$200,000.

4. Evidence shows that some oral anti-diabetic drug classes and some other drug classes can effectively prevent the onset of T2D in specific at-risk populations. The authors describe these populations differently: as hypertensive, as high risk, as pre-diabetic, as having at least one cardiovascular disease or as having one cardiovascular disease risk). Other drug classes had no significant preventive effect. Additionally, some drug classes are more effective for promoting regression to normoglycemia than for reducing T2D incidence, depending on the individual's risk profile.

5. Good quality evidence shows that many effective lifestyle interventions (that promote modest weight loss through improved diet and/or increase physical activity) can decrease the incidence of T2D in both the short and long-term. Improvements in blood pressure, triglycerides, weight, BMI and waist circumference were also commonly reported. A key factor in the success of combination lifestyle interventions is adherence to lifestyle changes.

6. Most preventive interventions are considered cost-effective, with ICER of less than $20,000 USD per QALY.

7. There are a number of heterogeneous strategies that prevent T2D. The effectiveness of these interventions appears to be dependent on age, weight loss, and an individual's risk profile, among other factors. There is insufficient evidence to comment on the effectiveness of mixed interventions on cardiovascular outcomes or on all-cause morbidity and mortality.

Background

Statistics from the Diabetes Charter for Canada published by the Canadian Diabetes Association (CDA) reveal the prominence of Type 2 Diabetes in Newfoundland and Labrador (NL). CDA estimated a diabetes prevalence of 12% in the province (1) which is higher than the estimated national prevalence of 9% (2). Projections suggest a 40% increase in diabetes prevalence in NL between 2015 and 2025. The most recent CDA Charter also estimated that 25% of the province's population aged 20 years and older has pre-diabetes (1). The CDA report suggests that a constant incidence represents 9% of new cases that will drive up prevalence of T2D between 2010 and 2020 contributing to the burden of T2D in NL (3).

T2D is a progressive disease with serious potential medical complications. Once diagnosed, patients require multifactorial management to avoid diabetes-related complications including blindness, heart disease, and lower-limb amputation. Many of these complications can occur early in the progression of the disease. For some, these complications can occur even before a clinical diagnosis of diabetes has been made (4). Preventing T2D by lowering risk for the disease in adults is a way to avoid the progressive chronic health problems associated with this disease.

Decision makers in NL recognize the burden that T2D places on the individual as well as the strain it places on the province's healthcare system. The Department of Health and Community Services (DHCS) and the four Regional Health Authorities (RHAs) asked the Contextualized Health Research Synthesis Program (CHRSP) to identify and review the best available research-based evidence on the clinical and cost-effectiveness of approaches to reducing the incidence of T2D in NL to help inform diabetes resource allocation.

CHRSP personnel assembled a project team that included officials from the four RHAs and the DHCS, the Programs & Partnerships Coordinator of the CDA in NL and representatives of NL physician researchers. Dr. Laura Rosella, Assistant Professor at the Dalla Lana School of Public Health, Scientist at Public Health Ontario, and Adjunct Scientist at the Institute for Clinical Evaluative Sciences, agreed to serve as Subject Expert for the project. Dr. Michel Grignon, Director of the Centre for Health Economics and Policy Analysis of McMaster University agreed to serve as the project's Health Economist.

Synthesis of the Evidence

What evidence did we look for?

Our synthesis is based primarily on evidence from 22 systematic reviews published in the 2009-2014 time period. To supplement this review evidence, we also searched for randomized controlled trials and prospective cohort studies published too recently to have been included in our selected systematic reviews. The results of this search yielded 1 subgroup analysis of a randomized controlled trial, 1 population-based prospective study (pooled data) and 3 randomized controlled trials published between November 2013 and June 2014. For detailed descriptions of our inclusion criteria, search strategy, article selection, and critical appraisal of selected articles, see the Online Companion Document: LINK

How was the evidence appraised?

Appraising the Systematic Review Literature Our critical appraisal methodology for systematic reviews employed the Assessment of Multiple Systematic Reviews (AMSTAR), a validated measurement tool for evaluating the methodological quality of systematic reviews (5). A higher AMSTAR score can be taken as an indicator that the various stages of the review were conducted appropriately. A low AMSTAR score does not necessarily mean that the review should be discarded but that less confidence can be placed in its findings and that the review must be examined closely to identify its limitations. In Table 1 below, we provide the AMSTAR scores for the reviews included in the synthesis, ranked from the highest score to the lowest.

Table 1: AMSTAR Scores for Systematic Reviews in this Report

Quality Ranking	Review/Year	AMSTAR Score
High	Grant, 2009	100%
	Schellenberg, 2013	91%
	Gillett, 2012	82%
Moderate	Sherifali, 2013	73%
	Dunkley,2014	64%
	Dunkley, 2012	64%
	Merlotti, 2014	64%
	Phung, 2012	64%
	Phung, 2011	64%
	Yoon, 2013	64%
	Aguiar, 2014	55%
	Greaves, 2011	55%
	Johnson, 2013	55%
	Waugh, 2013	55%
	Yuen, 2010	55%
	Everson-Hock, 2013	45%
	Geng, 2013	45%
	Hopper, 2011	45%
Low	Geng, 2012	36%
	Shirani, 2013	36%
	Song, 2012	36%
	Malkawi, 2012	27%

As this table indicates, not all reviews were deemed equal in terms of methodological quality. We took this variability into account when formulating our conclusions. We also took into account the number of primary studies each review covered. In general, we assigned greater weight to higher quality and more inclusive systematic reviews.

Appraising the Primary Literature Recent primary articles included in our synthesis were appraised using the Downs and Black Assessment Tool, a checklist that was developed to assess the methodological quality of both randomized controlled trials and non-randomized studies (6). The table below provides Downs and Black scores for each primary study included in the synthesis, ranked from highest to lowest.

Table 2: Downs and Black Scores for Primary Literature in this Report

Quality Ranking	Primary Study/ Year	Downs and Black Score
High	Lian, 2014	89%
	Tokunago-Nakawatase, 2014	86%
	Long, 2014	82%
Moderate	Salas-Salvado, 2014	79%
	Hellgren, 2013	71%

Interventions & Outcomes in this Report

The high-level research evidence (systematic reviews and health technology assessments) we found on the effectiveness of interventions for reducing the incidence of T2D and its medical complications focuses on interventions that target individuals. In Table 3 below, we group this research by the categories of interventions examined. We also include the methodological strength of each study. High quality is assigned to studies that received an AMSTAR score between 80 and 100%; moderate quality is assigned to studies that received an AMSTAR score between 45 and 79%; and low quality is assigned to studies that received an AMSTAR score below 45%.

Because of the complex nature of the research on diabetes, the intervention categories we provide are not necessarily mutually exclusive. Where studies might be placed in more than one category, we have placed them in what we determined to be the most appropriate category rather than placing the same study within multiple categories.

Table 3: Intervention Categories Assessed

Intervention Category	Description of Studies	Systematic Reviews	Primary Research
T2D Screening and Follow-up Interventions	Studies that examined the clinical effects of using a systematic detection process to identify individuals with undiagnosed/ asymptomatic T2D.	**Moderate Quality** Sherifali, 2013 Waugh, 2013	**High Quality** Long, 2014
Drug Interventions	Studies that assessed the effectiveness of different drug classes on the primary prevention of T2D.	**Moderate Quality** Phung, 2011 Geng, 2013 Phung, 2012 **Low Quality** Geng 2012 Song, 2012	none
Lifestyle Interventions	Studies that assessed or compared programs and strategies aiming to produce changes in: • Diet • Exercise • Diet & exercise • Some educational component of individual or group advice Generally speaking, research evidence assessed lifestyle interventions that were comprised of various combinations of the components listed above.	**High Quality** Gillett, 2012 Schellenberg, 2013 **Moderate Quality** Aguiar, 2014 Dunkley, 2014 Everson-Hock, 2013 Greaves, 2011 Johnson, 2013 Yoon, 2013 **Low Quality** Malkawi, 2012 Shirani, 2013	**Moderate Quality** Hellgren, 2013 Salas-Salvado, 2014

Mixed Interventions	Studies that assessed the effects of a variety of interventions including lifestyle interventions, drug interventions, herbal medicines and other types of prevention for T2D on their own or in combination. • Diet, exercise, drugs, lifestyle advice in some combination • Diet, exercise and drugs in combination • Herbal medicines versus placebo • Herbal medicines in combination with lifestyle modification • Herbal medicines in comparison to lifestyle modification • Bariatric Surgery • Diet modification + Drugs • Vitamins • Micronutrients • Estrogens • Alcohol • Coffee • Indirect Lifestyle Intervention, computer assisted.	**High Quality** Grant, 2009 **Moderate Quality** Dunkley, 2012 Hopper, 2011 Merlotti, 2014 Yuen, 2010	**High Quality** Lian, 2014 Tokunaga-Nakawatase, 2014

We sought findings for the effectiveness of these interventions on two primary health outcomes:

- incidence of T2D, and
- changes in glucose levels.

We also considered other outcomes when they were mentioned in the literature, including:

- cardiovascular risk factors,
- body composition changes and
- all-cause morbidity and mortality.

We also sought economic research evidence that addressed the cost-effectiveness of interventions for T2D prevention and screening. We will discuss these economic findings in a separate section of this report.

Synthesis and Interpretation

Before proceeding to a detailed examination of the review evidence on each of the interventions we studied, we would like to make three general observations.

Population

In our search for high-quality evidence, we sought systematic reviews and recent primary research that focused on adults ≥ 18 years old who are at risk of developing T2D (it is worth noting that the vast majority of studies included individuals in mid-to-late adulthood). Studies varied considerably in terms of how the authors defined 'at risk' and in the terminology they used to describe risk. Various factors such as age, family history, race, blood glucose abnormalities, and vascular problems are known to increase a person's risk of developing T2D (7). The presence of these risk factors, in various combinations, can be conceived as a continuum of risk ranging from low risk to high risk. For the purposes of this project, 'at risk' will be used as a general term that encompasses the different ways the authors of the systematic and primary research defined the populations included in their studies. Also worth noting is that all populations under study were similarly 'at risk' of developing T2D, in that they were free of a T2D diagnosis at baseline even if there were different reasons for their inclusion in the literature.

Criteria Used to Define New Onset Type 2 Diabetes

Not all studies that looked at laboratory-confirmed T2D incidence as an outcome specified the criteria used to define or diagnose new onset diabetes. Those authors that did specify these criteria often commented that T2D was defined differently across trials or was defined according to the criteria of different national and international organizations. These differences reflect changes over the years in the prevailing cut-off values in the various laboratory tests used for the diagnosis of T2D, impaired glucose tolerance, impaired fasting glucose, and HbA1c.

Differences between populations and diagnostic criteria introduce an unmeasurable amount of heterogeneity among, and even within, the systematic and primary studies reviewed. Please refer to the Online Companion Document to see how individual studies defined 'at risk' or diagnosed Type 2 Diabetes. LINK

Complexity of Interventions

Another important point to consider is the complexity of the interventions we assessed. Differences in study design and intervention components permeate the literature, particularly with respect to lifestyle interventions. Authors commonly cited differences in setting, population and intervention components (including intervention follow-up period) as challenges for analyzing and/or interpreting the effectiveness of interventions (8–18). At times, this variability prevented meta-analyses or caused statistical heterogeneity that prevented direct comparisons of certain outcomes or interventions (14).

Diabetes Screening and Follow-up

For our first intervention category—diabetes screening and follow-up— we found two moderate-quality systematic review articles and one high-quality population-based prospective cohort study that investigated the clinical effects of screening for T2D in adults (19,20). Of the systematic review literature, the review by Sherifali et al. had slightly higher methodological quality than the Health Technology Assessment by Waugh et al. Both were limited by a lack of appropriate studies conducted in this area. The cohort study by Long et al. (22) was found to have a high methodological quality according to the Downs and Black checklist. We have also included a review by Selph et al. that was made available very recently (21). Although this study was published outside our original dates for inclusion, its relevance warranted its inclusion in this report.

… all of these reviews had a common specific objective: they all searched for new, direct evidence on whether screening for T2D improves health outcomes. Taken together, these updates found very little new evidence.

All included systematic reviews on screening were conducted with the express objective of updating national recommendations on T2D screening. The systematic review by Sherifali et al. was conducted to update the Canadian Task Force on Preventive Health Care guidelines on screening for T2D released in 2005 (19). The HTA by Waugh et al. was conducted in order to update the 2007 UK National Screening Committee guidelines on screening for T2DM (20). The review by Selph et al. (21) was conducted to update the 2008 U.S. Preventive Services Task Force review on diabetes screening in adults (22).

Despite some differences in the specific questions about T2D screening that the authors sought to update, all of these reviews had a common specific objective: they all searched for new, direct evidence on whether screening for T2D improves health outcomes. Taken together, these updates found very little new evidence. In particular, they found a paucity of high-quality RCT evidence (19,20).

Sherifali et al. were particularly focused on the clinical benefits of screening of T2D in asymptomatic adults ≥18 years deemed to be at high risk (risk was not defined in detail by the authors). They concluded that

> *…more research is needed to determine the effect of screening for T2D, the best approach to screening (detection that minimizes harm and is cost effective), and the best treatment once prediabetes or T2D is diagnosed* (19*, p.11*).

Waugh et al. assessed proposed population screening programs for T2D. They advised that the case for screening has become less conclusive since the previous HTA was conducted in 2007. Ultimately, these authors indicated that the case for universal screening of those aged ≥40 years remains unproven. They also passed along a useful message about screening for diabetes in their discussion of existing research, asserting that:

> *Much of the benefit from diagnosing and treating undiagnosed diabetes comes from treating hypertension and blood lipids, rather than blood glucose. If BP and cholesterol levels in the general population are now better controlled, the benefits of screening for diabetes will be less* (20, *p.xiii*).

All three updates agreed that available evidence suggested that mortality rates were not improved after 10 years of follow-up by screening for T2D (19–21).

The primary evidence presented by Long et al. does not directly measure the clinical effectiveness of screening for T2D. However, given that the study was of high methodological quality according to the Downs and Black assessment and that screening is an integral part of the design, we have included relevant findings from this study below.

Long et.al. conducted a population-based prospective cohort study using stepwise screening to identify participants with undiagnosed T2D. Stepwise screening is defined by the study protocol as the "*combination of a diabetes risk score with various biochemical tests as a screening strategy*" (24, p.12). Those with screen-detected T2D were then subject to "intensive multifactorial treatment" which consisted of "*theory-based health promotion materials concerning diet, physical activity, tobacco use and medication adherence*" (p.1713) and compared to screen-detected participants receiving usual care (24). Long et al. contend that the year after diabetes diagnosis is an important time for the encouragement of change and maintenance of healthy behavior and habit formation. The study focused clinically on cardiovascular disease (CVD) outcomes in the five years following diabetes diagnosis and the effective of intensive intervention in reducing CVD events. The authors claim that theirs is:

> *The first study to show that healthy behavior changes in the year after diagnosis of diabetes are associated with significant reductions in the risk of incident CVD over 5 years, independent of cardio protective medication use* (24).

It is important, however, to have clinically-supported evidence for T2D screening from randomized controlled trials (25). Until these studies are completed and are included in new systematic reviews, we must rely on the evidence of the more robust and comprehensive systematic reviews discussed above and particularly those studies with long-term follow-up.

Table 4 summarizes the systematic and primary research examined for this report. Please refer to the Online Companion Document for a more detailed analysis of the individual outcomes included in the screening evidence as well as for a list of the current recommended guidelines for screening of T2D in Canada. LINK

Table 4: Summary of the effectiveness of diabetes screening on health outcomes

Outcome	Evidence	Study/Methodological Strength
T2D Incidence	The authors found no new controlled studies on the clinical benefit of screening asymptomatic adults, aged ≥18, at average or high risk for T2D to support recommendations on screening practices. Former recommendations were based on three non-randomized studies and "*found no benefit from screening for microvascular complications or any good data for the effectiveness of screening for T2DM in any targeted population*" (p.3).	Sherifali, 2013/ Moderate
Change in Glucose Levels, Metabolic Syndrome	No evidence reported on the effectiveness of screening for this outcome.	No included studies measured this outcome
Cardiovascular Risk Factors and related clinical measures	The evidence did not show that population screening programs are effective in reducing CVD based on the Ely and ADDITION trials. It should be noted that the ADDITION trial was not formally a screening trial but it "*showed no benefit in cardiovascular outcomes from intensive management in people with screen-detected T2DM*" (p.1).	Waugh, 2013/ Moderate
	"*Patients with newly diagnosed Type 2 diabetes who increased their physical activity levels and abstained or reduced their alcohol intake in the year after diagnosis of diabetes had a lower risk of CVD events over 5 years compared with individuals who did not change their behavior. The association between modifying these health behaviors early in the disease trajectory and reduced CVD risk were independent of age, sex, study group, social class, occupation, and the prescription of cardio protective medication. The greater the number of healthy behavior changes made in the year after diabetes diagnosis, the lower the CVD risk*" (p.1717). Those who "*improved 3 or 4 health behaviors had lowest rate of CVD*" (p.1715). Those "*participants who didn't change health behaviors had 3.71 times higher CVD event rate*" (p.1715).	Long, 2014/ High
Body Composition Changes	"*Association between health behavior change and reduced CVD risk is likely, in part, mediated through changes in body composition*" (p.1717).	Long, 2014/ High
All-Cause Morbidity and Mortality	Evidence from one population-based cohort study addressed this outcome. It reported a non-significant reduction in mortality.	Sherifali, 2013/ Moderate
	No evidence that population screening programs are effective in reducing mortality and morbidity. The 10-year data from the ADDITION trial "*showed no reduction in cardiovascular, diabetes-related or total mortality events*" (p.xiii).	Waugh, 2013/ Moderate

KEY MESSAGE ABOUT SCREENING AND FOLLLOW-UP:

At present, there is an insufficient amount of high-quality evidence on the long-term clinical benefits and potential harms of screening. The limited evidence that is available showed no evidence of improved mortality through screening for T2D, either in the general population or in a high-risk population after 10 years of follow-up.

Drug Interventions

for People at Risk of Developing Type 2 Diabetes

When reading the evidence below concerning drug interventions for those at risk of developing T2D please consider the following: since T2D is a diagnosis based on blood glucose levels in theory, almost any drug that lowers blood glucose levels below the current diagnostic cut-points can be said to 'prevent' diabetes.

In total, we identified five meta-analyses that investigated the effect of various drug classes on the development of T2D:

- one on **angiotensin converting enzyme inhibitors** (11)**,**
- two on **angiotensin receptor blockers** (12,26) and
- two on **oral antidiabetic drug classes** (27,28).

Examples of these types of drugs are outlined in Table 5 below.

Table 5: Drug Classes Used in Interventions for T2D & Examples

Type	Drug Class	Example
Oral Antidiabetic drugs: prescribed uniquely for diabetes	**Alpha-glucosidase inhibitors**	Acarbose
	Biguanides	Metformin
	Sulfonylureas	Glyburide Gliclazide
	Glinides (or Meglitinides)	Nateglinide
	Thiazolidinediones (or known as Glitazones)	Pioglitazone Rosiglitazone
Other Drugs: not uniquely prescribed for diabetes alone	**Angiotensin converting enzyme inhibitors (ACEIs)**	Ramipril
	Angiotensin receptor blockers (ARBs)	Valsartan
	Calcium channel blockers	Diltiazem Verapamil
	Estrogens	
	Lipid-lowering drugs	
	Vitamins and micronutrients	Vitamins C and E

The articles reviewed for drug interventions studied individuals whose risk for T2D was described broadly in the following ways:

- non-diabetic adults with hypertension (11),
- non-diabetic adults with at least one cardiovascular disease or cardiovascular risk (12),
- adults with hypertension (26),
- high-risk adults (27), or
- pre-diabetic adults (28).

The criteria for enrolment in individual drug trials were not mentioned; however, given that drug trials are typically strict about selection and eligibility criteria, we caution the reader that the findings from these studies would likely apply to a very small portion of the population. Taken together, the evidence from all included systematic reviews most likely represents a small number of at-risk individuals.

We identified some overlap in the primary literature included in these meta-analyses and this overlap will be taken into account in the discussion below. The overlap was mainly between Geng 2012 and Song 2012 who looked at angiotensin receptor blockers**,** and Phung 2011 and Phung 2012 who examined oral anti-diabetic drugs. The methodological quality of evidence for this group ranged from low (12,26) to moderate (11,27,28).

Geng et al. determined that ACEIs have beneficial effects in preventing new-onset diabetes. These authors found that patients with hyper-tension, coronary artery disease or other cardiovascular disease or heart failure benefit from taking ACEIs as a means of lowering the risk of new-onset diabetes.

Geng 2013 was the only meta-analysis that examined the effect of angiotensin converting enzyme inhibitors (ACEIs). Nine randomized controlled trials (RCTs) were analyzed for the development of T2D in adults who, at baseline, were non-diabetic with hypertension. Geng et al. determined that ACEIs have beneficial effects in preventing new-onset diabetes. These authors found that patients with hypertension, coronary artery disease or other cardiovascular disease or heart failure benefit from taking ACEIs as a means of lowering the risk of new-onset diabetes. An analysis of the ACEI ramipril showed that it increased regression to normoglycemia significantly in adults with impaired glucose tolerance or impaired fasting glucose even though it did not significantly reduce the incidence of diabetes in this population (11). This might be a unique effect of ramipril, or (more likely) a class effect; however, Geng et al. only singled out this particular drug when reporting on a regression to normoglycemia.

Geng et al. (2012) and Song et al. assessed the effects of angiotensin receptor blockers (ARB)[1]. These two meta-analyses had many similarities. Both reviews were of low methodological quality. Differences

[1] In the primary studies assessed by Geng et al. (2012): 6/11 primary studies compared ARBs to a placebo, 2/11 used a non-ARB comparator, 2/11 used Ca channel blocker as comparator and 1/11 used a beta blocker. Out of the primary studies assessed in the Song et al.: 5/11 primary studies compared ARBs to a placebo, 2/11 used a diuretic and/or beta blocker as a comparator, 2/11 used a Ca channel blocker comparator and 1/11 used a non-ARB alternative.

in how diabetes was defined in different trials and the heterogeneity of trial populations are common weaknesses cited by the authors. Additionally, Geng et al. (2012) noted that the studies they included had different durations and Song et al. revealed that the trials they assessed had different study designs and different treatment strategies. Both gathered 11 RCTs each (six of which overlapped) and both chose similar populations to examine. Geng el al. (2012) included non-diabetic adults having at least one cardiovascular disease or some cardiovascular risk while Song el al. included subjects with either hypertension or other risk factors. Taken together, these studies found that ARBs have a beneficial effect on the prevention of T2D for the specific high- risk populations they described. In their concluding remarks, Song et al. explicitly included patients with essential hypertension, cardio-cerebrovascular disease, impaired glucose tolerance and heart failure as beneficiaries of ARB treatment. Song et al. also reported that there was no significant difference in all-cause mortality over the follow-up time of ARB trials evaluating new onset T2D in patients with essential hypertension, impaired glucose tolerance and/ or high cardiovascular risk (Song, 2012).

Phung et al. (2011) and Phung et al. (2012) examined the effect of oral anti-diabetic drugs on the development of T2D. Between the two, seven primary studies overlapped and they were both of moderate methodological quality. The main difference between these two analyses was the populations they studied and their main prevention objective. Phung et al. (2011) is a meta-analysis of 20 RCTs involving at individuals at high risk for T2D with a mean age range of 34-57. It focused on preventing the development of T2D. For this review, high risk included women who experienced "*gestational diabetes; patients with impaired glucose tolerance, impaired fasting glucose or* HbA_{1c} *39-46mmol/mol (5.7-6.4%); or people who are obese*" (p.948). In terms of prevention of T2D in these high-risk participants, thiazolidinediones showed the greatest risk reduction compared with controls followed by alpha-glucosidase inhibitors and biguanides. In the same meta-analysis, sulphonylureas and glinides did not show significant benefit for the high-risk population assessed. But the authors also advised that

> *although thiazolidinediones were found to be most effective, they are not without adverse effects. Of the trials which reported it, patients taking thiazolidinediones gained up to 3.1 kg more in body weight than those taking placebo* (29, p.962)*.*

Phung et al. (2012) assessed 13 RCTs in adults with prediabetes ranging in age from 45 to 64 and focused on how to promote regression from prediabetes to normoglycemia. Prediabetes was defined by the authors as individuals having IGT, IFG or AIC between 5.7% and 6.7%. These reviewers found that some oral antidiabetic drugs doubled the odds of a return to normoglycemia for pre-diabetic participants. This trend was shown specifically for thiazolidinediones and alpha-glucosidase inhibitors but not for bigunides and sulfonylureas (28).

Table 6 below provides a summary of the systematic and primary research. Please refer to the Online Companion Document for a more detailed look at the individual outcomes included in the drug intervention evidence. LINK

Table 6: Summary of the effectiveness of drug interventions on health outcomes

Outcome	Evidence	Study/ Methodological Strength
T2D Incidence	"*ACEI therapy was associated with a significant reduction in the risk of new-onset diabetes compared with beta-blocker/diuretics*[2]" (p. 2606). ACEIs therapy was associated with a significant reduction in the incidence of new-onset diabetes in non-diabetic participants with hypertension at baseline compared with control group "irrespective of BP at the follow-up" (p.2605). ACEI therapy was significantly associated with reduced risk of new-onset diabetes in patients with hypertension, CAD, CVD, heart failure. "*Ramipril did not significantly reduce incidence of diabetes*" (p. 2606) for participants with IGT/IFG.	Geng, 2013/ Moderate
	(Non-diabetic population with at least 1 CVD or CVD risk) ARBs were associated with a significant reduction in incidence of new-onset diabetes. ARBs were associated with "*significantly reduced risk of new-onset diabetes compared with placebo, beta-blocker, calcium channel blocker and non-ARBs"* (p. 239). "*ARBs were associated with significant reduction in the risk of new-onset diabetes in patients with hypertension, heart failure, IGT, cardio cerebrovascular diseases*" (p. 239). "*ARB therapy was associated with a significant lower incidence of new-onset diabetes in Western population and Japanese population*" (p.239).	Geng, 2012/ Low
	The oral anti-diabetic drug class, thiazolidinediones showed the greatest relative risk reduction for T2D in high-risk participants followed by alpha-glucosidase inhibitors and biguanides (all significant effects). "*Although thiazolidinediones were found to be most effective, they are not without adverse effects. Of the trials which reported it, patients taking thiazolidinediones gained up to 3.1 kg more in body weight than those taking placebo* [3,6]" (p. 962). Sulphonylureas and glinides showed no significant effect on the relative risk for T2D.	Phung, 2011/ Moderate
	ARBs significantly reduced the incidence of new-onset type 2 diabetes among patients with essential hypertension, cardio cerebrovascular disease, impaired glucose tolerance and heart failure.	Song, 2012/ Low

[2] Out of the 9 primary studies assessed by Geng et al. 2013, 5 compared ACEIs versus placebo and 4 compared ACEIs versus diuretic or ACEIs versus diuretic or beta blocker (in some combination). It should be noted that the comparator groups that were not placebo were heterogeneous.

Change in Glucose Levels, Metabolic Syndrome	The ACEI Ramipril "*significantly increased regression to normoglycemia*" (p. 2606) in patients with IGT or IFG.	Geng, 2013/ Moderate
	Oral antidiabetic drugs doubled the odds of a return to normoglycemia for pre-diabetic participants. Specific classes of drugs (thiazolidinediones and alph-glucosidase inhibitors) increased odds of regression to normoglycemia in patients with prediabetes. Specific drug classes biguanides, sulfonylureas were not associated with regression to normoglycemia = i.e., no statistically significant effect.	Phung, 2012/Moderate
Cardiovascular Risk Factors and related clinical measures	"*Since type 2 diabetes increases the risk of cardiovascular events, it could be assumed that reducing the incidence of new-onset type 2 diabetes would result in fewer events. However, our findings demonstrated that among ARBs trials evaluating new-onset type 2 diabetes, there were no significant differences in all-cause mortality, cardiovascular end points versus control therapy*"(p.1808).	Song, 2012/ Low
Body Composition Changes: Weight Change, BMI, Waist Circumference	No evidence reported on the effectiveness of drug interventions for this outcome.	No evidence reported on this outcome
All Cause Morbidity and Mortality	Significant differences in all-cause mortality were not shown in trials assessing ARB treatment.	Song, 2012/ Low

KEY MESSAGE ABOUT DRUG INTERVENTIONS:

Evidence shows that some oral anti-diabetic drug classes and some other drug classes can effectively prevent the onset of T2D in specific at-risk populations. The authors describe these populations differently: as hypertensive, as high risk, as pre-diabetic, as having at least one cardiovascular disease or as having one cardiovascular disease risk). Other drug classes had no significant preventive effect. Additionally, some drug classes are more effective for promoting regression to normoglycemia than for reducing T2D incidence, depending on the individual's risk profile.

Lifestyle Interventions

In the literature reviewed for this report, lifestyle Interventions for T2D were non-pharmacological in nature and were based on an adjustment of diet and/or exercise, and the receipt of advice from health professionals concerning one, the other, or both. Within systematic reviews, lifestyle interventions tended to be described in terms of their basic components without offering specific detail about the nature of individual programs or lifestyle advice and guidance offered. There were many variations in the way changes in diet and physical activity were implemented, resulting in an irreducible level of heterogeneity in the research evidence. The majority of the systematic reviews involved studies that considered diet and physical activity in combination, but some included a minority of studies that focused on making changes in *either* diet *or* physical activity, rather than both. In addition, one systematic review (18) and one primary study (29) focused exclusively on dietary changes. Another primary study focused primarily on physical activity (30). This research evidence also varied in terms of the duration of both the interventions tested and the follow-up provided. It should also be noted that, while many interventions were individualized, some were group-based and one systematic review examined community-based interventions (31).

Within systematic reviews, lifestyle interventions tended to be described in terms of their basic components without offering specific detail about the nature of individual programs or lifestyle advice and guidance offered. There were many variations in the way changes in diet and physical activity were implemented, resulting in an irreducible level of heterogeneity in the research evidence.

Studies examining lifestyle interventions assessed adults at risk of developing T2D, who were described using various terms:

- people at risk for T2D,
- people with pre-diabetes,
- people at high risk for T2D,
- people with hyperglycemia,
- people with elevated blood glucose,
- people from low socio-economic status (SES) populations.

Taken together, these terms were used to characterize populations of adults at moderate-to-high risk of developing T2D, but it is important to note that there was considerable variation in the way both population and risk were defined within these studies.

In total, we identified ten systematic review articles (8,9,13,15,17,18,31–34) that reported on lifestyle interventions. Six of the ten articles were of moderate quality (8,9,15,31,32,34), two were of high quality (13,17), and two were of low methodological quality (18,33). Individual systematic reviews included a minimum of seven articles and a maximum of 30. We detected some overlap in the primary research covered by this body of systematic research; however, we did not identify any major concerns. We have also included two primary studies that received a moderate rating on the Downs and Black checklist (29,30).

Overall, findings for lifestyle interventions converged on several outcomes including T2D incidence, change in glucose levels, and change in body composition. Findings for other endpoints, like cardiovascular outcomes and all-cause morbidity and mortality were mixed or unclear. These results will be discussed in detail below.

Seven out of ten systematic reviews addressed the incidence of T2D,[3] making it the most commonly reported outcome in this body of evidence. Incidence was reduced through the various lifestyle interventions examined (8,9,13,17,33,34). The only discrepancy in the findings on incidence was in regard to the effect of lifestyle intervention after several years of follow-up. Schellenberg et al. reviewed studies on high-risk individuals.[4] According to seven studies assessed in their review, "*lifestyle interventions decreased the risk for diabetes from the end of intervention up to 10 years after it*" (p. 543). Other reviewers, however, cautioned about the diminished effect of lifestyle interventions after several years. These authors suggest that this diminishing effect is caused by the inherent challenge of adhering to a healthy lifestyle. They claim that adherence to lifestyle advice has been seen to fluctuate between 20% and 90% (34). Adherence was also mentioned in the primary study by Salas-Salvadó et al. included in this category. In this case, a behavioral intervention promoting the Mediterranean Diet without calorie restriction was assessed as a way to prevent T2D in individuals at high cardiovascular risk. Participants received advice from dietitians and weekly support in their dietary choices. After a follow-up period of 4.1 years, these authors concluded that incidence of T2D was reduced for older persons at high cardiovascular risk following "*a long-term intervention with a high-quality dietary pattern akin to the traditional Mediterranean Diet and rich in EVOO [extra-virgin olive oil]*" (29, p.7). Adherence to the prescribed Mediterranean Diets was measured by a 14-item Mediterranean Diet screener. Through this process, adherence was shown to be better in Mediterranean Diet groups than in the control groups.

[Type 2 Diabetes] incidence was reduced through the various lifestyle interventions examined…[however] reviewers cautioned about the diminished effect of lifestyle interventions after several years. These authors suggest that this diminishing effect is caused by the inherent challenge of adhering to a healthy lifestyle.

Weight loss was the second most commonly reported outcome in this group of reviews. Five systematic reviews reported weight loss related to lifestyle interventions; however, the extent of the weight loss reported varied from study to study (8,9,13,15,32). Johnson et al. proposed that there was a "*strong trend*" towards weight loss in the intervention group versus the control group (15) but that effect sizes varied widely for this outcome across the studies they analyzed. Gillett et al. claimed that the greatest benefit of lifestyle interventions for individuals with impaired glucose tolerance (IGT) was seen "*in those with the highest compliance and [in those] who achieved*

[3] Reduced risk of T2D is also included within the number of articles assessing incidence.

[4] Schellenberg et al. examined two populations, those at high-risk for T2D and those with T2D. The review analyzed the two populations separately; given this report's focus on prevention, we only included those conclusions pertaining to high-risk individuals and excluded findings for people who already have T2D.

more of the intervention goals such as weight loss and dietary change" (p.138). These authors suggest that sustained weight loss through changes in diet and/or exercise can reduce the progression to T2D in this population. Another systematic review concluded that lifestyle interventions were "*modestly effective in reducing weight loss*" (8, p.9). Finally, Dunkley et al. and Greaves et al. both claimed that the weight loss achieved through the lifestyle interventions they assessed was clinically meaningful for T2D incidence reduction in the high-risk populations evaluated (9,32).

Three systematic reviews investigated specific changes in glucose levels, which is a precursor to developing T2D. The evidence indicated a significant reduction in fasting plasma glucose (8), a reduced progression to diabetes in people with impaired glucose tolerance (13) and an improvement in glucose measures (33). Shirani et al. also investigated changes in glucose levels; however, this review was distinct in that it evaluated the Dietary Approaches to Stop Hypertension (DASH) Diet as an intervention to improve glycemic control without the physical activity component. The DASH Diet was found to significantly reduce serum fasting insulin levels overall and in particular when prescribed over 16 weeks but not when the diet was prescribed for less than 8 weeks. Those with metabolic syndrome or hyperlipidemia showed significant reduction in fasting insulin on the diet but this effect was not shown in healthy participants without glucose impairments. Finally, the DASH Diet showed no beneficial effect on fasting blood glucose or Homeostatic Model Assessment insulin resistance (HOMA-IR) compared with the control diet (18).

Findings for cardiovascular outcomes and all-cause morbidity and morbidity were not delineated as clearly. Pragmatic lifestyle interventions investigated by one review found reductions in blood pressure and triglycerides in high-risk populations (9). Another systematic review found no benefit in cardiovascular outcomes for high-risk participants based on two trials involving comprehensive lifestyle interventions (17). A primary study by Hellgren et al. examined the results of a lifestyle intervention that focused on increasing physical activity in individuals with IGT in ordinary primary care. The strongest conclusion made by study authors was that an intervention focused on physical activity was feasible in a clinical setting and it improved cardiovascular risk factors. These authors also observed that more than just a basic intervention[5] was necessary to increase physical activity in participants over time. The intensive group[6] increased physical activity by 69% as compared to a 17% increase in the basic group and a 44% increase in the control group. The authors claimed that a change in physical activity led to changes in diet as well as weight loss and an improvement in cardiovascular risk factors (30). Success of the intervention group was likely augmented by the additional support of the health professionals who chaired the group activity sessions.

[5] The basic Intervention group included *"care as usual, a card giving participants the option to take blood glucose freely, a personal nurse contact to contact when needed, a prescription for physical activity, a step counter (if using the prescription)"*p.465 (30).

[6] The intensive intervention group included usual care with added opportunities for lifestyle changes. Usual care provided information about IGT orally and in writing as well as information brochures about diet and physical activity. Additional lifestyle change opportunities included: "*an invitation to participate in eight group sessions focusing on physical activity (six sessions the first six months and another two sessions the following six months). A lifestyle coach (nurse), a nutritionist and a physiotherapist chaired these sessions. The sessions were solely focused on physical activity and were held daytime"* p.465 (30).

One systematic review focused on all-cause morbidity and mortality in adults with impaired glucose tolerance but concluded that these outcomes were not analyzed well by the studies they examined. The only clear finding reported by these authors showed no difference between the intervention and control group but this was based on one study only (34).

Given the various ways in which diet and physical activity were combined to achieve lifestyle interventions, it is useful to consider which specific components the study authors identified as either enhancing or inhibiting effectiveness. The most commonly highlighted keys to success were:

- adherence to intervention targets,
- clearly-defined goals and objectives, and
- sufficient resources and support.

Authors of a high-quality Health Technology Assessment suggested that:

> *The key to success is sustained lifestyle change, especially weight loss. In conclusion, lifestyle measures can be highly effective in reducing progression to diabetes but adherence to lifestyle change is the most important factor* (13, p.69).

Table 7 outlines the specific components that, according to study authors, can enhance or inhibit the effectiveness of lifestyle interventions.

Table 7: Components that Enhance or Inhibit Lifestyle Intervention Effectiveness

Components that ENHANCE effectiveness	Components that INHIBIT effectiveness
Interventions for reducing weight and fasting plasma glucose (FPG) levels: Program delivery factors • delivering interventions face-to-face (individual and/or group) • An average of eight contacts per month (including face-to-face sessions, email, and phone calls) • A minimum of six (and preferably 12) months of follow up Beneficial lifestyle interventions: • 150–210 minutes of aerobic exercise per week (over 3–5 sessions) • 60–120 minutes of resistance training per week (1–3 sessions) • Recommending a specified macronutrient diet profile, energy restriction for weight loss, and setting a goal of losing 5-10% of total body weight. -Aguiar, 2014	**Interventions for reducing weight and fasting plasma glucose (FPG) levels:** Program delivery factors • Lack of evaluation of muscular performance • Cost of providing qualified personnel to supervise exercise programs -Aguiar, 2014
Adherence factors: • Close adherence to intervention guidelines maximizes their effectiveness -Dunkley, 2014	Adherence factors: • Poor compliance with guidelines (both for intervention content and delivery) accounts for variance in effectiveness. -Dunkley, 2014

Components that ENHANCE effectiveness	Components that INHIBIT effectiveness
Community-based lifestyle interventions • Having sufficient resources and facilitator knowledge • Having facilitators who know and understanding participants • Communicating clear and consistent information about healthy diet and exercise, whether from government sources, in media, or when delivering the interventions • Harnessing pre-existing motivators for participants to buy-in to the program • Enhancing participants' belief in, sense of control over, and self- confidence in their ability to cook, eat well, and be physically active • Addressing the role of the whole family in lifestyle choices • Community-based interventions were more widely accepted when they involved enjoyable, creative, and innovative activities and harnessed social inclusion or used enhanced social inclusion methods. -Everson-Hock, 2013	**Community-based lifestyle interventions** • Negative or misunderstood beliefs/ connotations about healthy diet and exercise • Actual or perceived affordability of healthy lifestyle choices • Health advice that contains unclear or inconsistent messages -Everson-Hock, 2013
• Adherence to lifestyle change • High compliance with the specific targets of lifestyle change -Gillett, 2011	• Cultural influences can make lifestyle changes more difficult • Decline in adherence to lifestyle changes over time decreases their effectiveness -Gillett, 2011
• Targeting both diet and physical activity • Using established behavior change techniques • Mobilizing social supports • Having a clear plan to support and maintain behavior change • Providing a higher frequency/higher number of contacts -Greaves, 2011	
• Having clearly defined physical activity objectives • Providing personal counseling sessions • Providing both diet and exercise interventions • Conducting intervention programs at the national level -Malkawi, 2012	• The cost of intervention delivery, health educator training, exercise equipment, and participant time can inhibit community-based interventions. -Malkawi, 2012

Specific details about the health outcomes assessed by these studies are outlined in the Online Companion Document. LINK

In Table 8 below, we provide a summary of the impact of lifestyle interventions on specific health outcomes, based on systematic and primary research for lifestyle interventions studied in this report.

Table 8: Summary of the impact of lifestyle interventions on health outcomes

Outcome	Evidence	Study/ Methodological Quality
T2D Incidence	Strong body of evidence of reduced progression to diabetes in people with IGT through lifestyle interventions.	Gillett, 2011/ High
	Comprehensive lifestyle interventions decreased risk for diabetes from the end of the intervention up to 10 years after it (based on results from 7 studies)	Schellenberg, 2013/ High
	Lifestyle interventions reduced incidence (based on 2 studies).	Aguiar, 2014/ Moderate
	Potentially reduce risk of developing diabetes, based on demonstrated weight loss.	Dunkley, 2014/ Moderate
	Risk Reduction of T2D among older persons with high- cardiovascular risk through long-term adherence to Mediterranean Diet supplemented with EVOO without energy restrictions. Note: *"Beneficial effect was mainly due to the overall composition of the dietary pattern, and not to calorie restriction, increased physical activity or weight loss because such lifestyle changes were not part of the intervention and between-group changes were negligible"* (p.8).	Salas-Salvado, 2014/ Moderate
	Set out to measure cumulative diabetes incidence at follow-up but *"this outcome was not typically measured in translational studies that included a comparator, probably because there was not sufficient statistical power to do so. Therefore, it is difficult to make direct inferences about the effectiveness of the intervention in reducing diabetes" (*p. 8).	Johnson, 2013/ Moderate
	Significant reduction in diabetes incidence found through lifestyle intervention. Found a drop off in effectiveness of lifestyle interventions after several years.	Yoon, 2013/ Moderate
	Significant reduction in cumulative diabetes incidence.	Malkawi, 2012/ Low
Change in Glucose Levels, Metabolic Syndrome	Lifestyle interventions significantly reduced fasting plasma glucose (FPG) in intervention group compared to control group.	Aguiar, 2014/ Moderate
	Good evidence that well-structured lifestyle interventions can improve glucose measures.	Malkawi, 2012/ Low
	DASH Diet significantly reduced fasting insulin overall, when prescribed over 16wks. The effect was not significant for fasting insulin when the diet was prescribed for less than 8 weeks. DASH Diet showed significant reduction in fasting insulin for individuals with metabolic syndrome or hyperlipidemia but this effect was not shown in healthy participants without glucose impairments. DASH Diet showed no beneficial effect on fasting blood glucose or HOMA-IR compared with the control diet.	Shirani, 2013/ Low

Cardiovascular Risk Factors and related clinical measures	Found insufficient evidence to report on the effectiveness of lifestyle interventions on CVD events and microvascular outcomes.	Schellenberg, 2013/ High
	Pragmatic Lifestyle interventions showed significant reductions in BP and triglyceride levels.	Dunkley, 2014/ Moderate
	Lifestyle intervention was found to be possible in primary care with limited resources and was found to influence severe risk factors for CVD. Significant decrease found in systolic and diastolic blood pressure, weight, BMI, waist circumference and sagittal diameter for the intensive intervention group. Significant decrease found in systolic blood pressure in the basic intervention group.	Hellgren, 2013/ Moderate
Body Composition Changes: Weight Change, BMI, Waist Circumference	Lifestyle measures consistently showed a reduction in the development of diabetes in those with IGT. The best results are seen in those who achieve more of their goals and those who adhere to the lifestyle change.	Gillett, 2011/ High
	Lifestyle interventions significantly reduced weight loss for the intervention group in 4/5 RCTs.	Aguiar, 2014/ Moderate
	Weight loss seen to be clinically meaningful for the incidence of diabetes despite a drop-off in intervention effectiveness with time.	Dunkley, 2014/ Moderate
	Group-based translational lifestyle interventions reduced weight by at least 4%. Translational lifestyle interventions reduced waist circumference in 7 studies.	Johnson, 2013/ Moderate
	Lifestyle interventions produced clinically meaningful weight loss.	Greaves, 2011/ Moderate
	Intensive intervention showed a significant difference in body weight, BMI, waist circumference and sagittal diameter in comparison with basic intervention and control groups but when adjusted for energy intake this difference was no longer seen.	Hellgren, 2013/ Moderate

KEY MESSAGE ABOUT LIFESYLE INTERVENTIONS:

Good quality evidence shows that many lifestyle interventions (designed to promote modest weight loss through improved diet and/or increase physical activity) can decrease the incidence of T2D. Improvements in blood pressure, triglycerides, weight, BMI and waist circumference were also commonly reported.

A key factor in the success of combination lifestyle interventions is adherence to lifestyle changes.

Mixed Interventions

For this category, articles either combined diet, exercise, and drug therapies in their analyses, or compared them, or studied a mixed intervention that was unique. Three systematic reviews and one primary study analyzed various combinations of non-drug and drug-based approaches to reducing T2D incidence or treating glucose impairment (14,16,35,36). We identified five systematic reviews and two primary randomized controlled trials (RCTs) that assessed mixed interventions for T2D. AMSTAR scores were mostly moderate for this group of studies except for one that had a perfect score (14). The two primary studies also displayed high methodological quality on the Downs and Black assessment (36,37).

Generally speaking, most of the available evidence for mixed interventions involved particular at-risk populations. For example, one article focused on reversing metabolic syndrome or preventing the development of T2D and CVD in adults with metabolic syndrome (10). Three other reviews included adults with impaired glucose tolerance or impaired fasting glucose (14,35,38), as did one primary study (36). Another primary study examined adults that had diabetic first-degree relatives (37). Only one article of this group looked more broadly at adults at high risk for T2D (16). These variations add to the challenges of synthesizing the findings on this category of interventions.

For this category, articles either combined diet, exercise, and drug therapies in their analyses, or compared them, or studied a mixed intervention that was unique.

Generally speaking, most of the available evidence for mixed interventions involved particular at-risk populations.

These variations add to the challenges of synthesizing the findings on this category of interventions.

It is also important to note that three of the systematic review articles overlapped. Merlotti 2014 is a very comprehensive systematic review and meta-analysis with a broad scope that included 71 studies of different design types to evaluate the effectiveness of different strategies for the prevention of T2D in high-risk adults. Six out of the ten studies covered by Hopper et al. 2011 are also included in Merlotti et al. 2014. Yuen 2010 is a smaller review that included 4 RCTs. These are all accounted for within Merlotti 2014 or Hopper 2011. We have considered these overlaps when drawing conclusions from these studies.

The highest quality systematic review in this synthesis (Grant, 2009) and one high-quality primary study (Lian, 2014) assessed Chinese herbal medicines (14,36). Grant's review found evidence to suggest that some Chinese herbal medicines can reduce the incidence of diabetes in adults with impaired glucose tolerance or impaired fasting glucose. The Lian study was a recent multi-center randomized trial that assessed the Tianqi capsule (a capsule containing 10 different Chinese herbal medicines) plus lifestyle education in adults with impaired glucose tolerance supported this finding (36). It found that this herbal

combination reduced the risk of diabetes by 32.1% compared with the placebo group. While the authors of both studies agreed that Chinese herbal medicines have potential, they agreed that more research is necessary to verify these findings as well as to examine possible side effects. Specifically, future research must address the lack of other trials that tested the same herbal medicine, lack of details on co-interventions, unclear methods of randomization, poor reporting, other risks of bias, and issues of sample size, length of treatment and follow-up (14,36). These cautions are in line with Canadian Diabetes Association's Clinical Practice Guidelines from 2013. Natural health products like herbal medicines are not currently recommended for glycemic control in individuals with diabetes because of insufficient evidence on the efficacy and safety of these products (39). We assume that this applies to all findings below regarding herbal medicines for those with glucose impairment as well.

Two overlapping reviews provided evidence that both non-drug and drug-based[7] approaches delayed or prevented T2D. Hopper et al. reported that both approaches were successful in reducing the progression to diabetes for populations defined as *"participants with established cardiovascular disease, one or more cardiac risk factors, risk factors for diabetes, or elevated body mass index as entry criteria"* (35). The reviewers noted that between the two, the non-drug approaches which involved either diet or exercise or both in combination were superior to drug-based approaches. Merlotti et al. included trials with populations that had prediabetes, impaired fasting glucose and impaired glucose tolerance. The authors found a variety of interventions to be effective. T2D incidence was reduced by: bariatric surgery,[8] glitazones, diet + physical activity, diets, physical activity or education, alpha-glucosidase inhibitors, metformin, lipid- affecting drugs, alcohol and cardiovascular drugs (16). These authors maintain that subject age and weight loss are important in determining effectiveness of an intervention. For example, although there was evidence that bariatric surgery was effective in reducing T2D, this was true only for morbidly obese patients. Intensive lifestyle modification and/or drugs were suggested as more appropriate prevention strategies for overweight and lean subjects.

On the other hand, the non-overlapping content from the Merlotti 2014 and Hopper 2011 reviews found evidence of interventions that *did not work* for diabetes prevention. Hopper et al. identified three primary studies that found that pioglitazone, ramipril and nateglinide were *not* beneficial for adults with impaired glucose tolerance and impaired fasting glucose. Similarly, Merlotti et al. found that incidence was not reduced in high-risk populations through the use of beta-cell stimulating drugs, vitamins or estrogens.

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[7] As mentioned in an earlier section, when reading the evidence concerning drug interventions for those at risk of developing T2D please consider the following: since T2D is a diagnosis based on blood glucose levels in theory, almost any drug that lowers blood glucose levels below the current diagnostic cut-points can be said to 'prevent' diabetes.

[8] "*Subjects undergoing bariatric surgery are completely different from other subjects. This raises two concepts, that are not mutually exclusive: one is that for morbidly obese subjects, weight loss is an adequate measure to prevent T2DM; the other is that T2DM is a different disease in overweight and in morbidly obese subjects; intuitively, the fact that T2DM appears in subjects with an excessive BMI, and often disappears after weight loss [102,103], suggests that the derangement of beta cells is of a lower degree, or that the mechanisms involved are different*" p. 722 (14).

Two systematic reviews assessed changes in glucose levels. In a population with impaired glucose tolerance, Grant et al. reported that a combination of herbal medicine and lifestyle modification normalized blood glucose levels significantly better than lifestyle alone (14). On the other hand, Dunkley et al. stated, *"results indicate that lifestyle interventions are more effective at reversing metabolic syndrome than pharmacological therapies"* (10, p.620). These differences may reflect the heterogeneity that exists amongst the Chinese herbal medicine trials discussed by Grant et al. in a previous paragraph.

Two out of the four reviews that set out to measure cardiovascular outcomes concluded that there was insufficient evidence to report on cardiovascular disease events (10) or on CVD mortality and morbidity (38). Grant el al. observed that, in Chinese studies of comparatively weak methodological quality, several herbal medicines successfully reduced total cholesterol and triglycerides compared to controls (14). Another review reported that there was no significant difference found for the relative risk of myocardial infarction and stroke outcomes according to four primary studies that analyzed drug therapies (35).

Similarly, evidence for all-cause morbidity and mortality was minimal. Just one review had enough data to report on this outcome. Hopper et al. reported that neither the drug approaches nor the non-drug approaches showed any difference in all-cause mortality (35).

A primary study by Tonkunaga-Nakawata et al. evaluated a unique intervention- an indirect, computer-based lifestyle intervention for first-degree relatives of those with diabetes called *Lifestyle Intervention Support Software* (LISS-DP). This software was developed to "*easily provide education regarding the incorporation of healthy dietary and physical activity behavior into participants' daily life*" (p.208). Recommendations were individualized to participants based on a self-administered questionnaire with LISS-DP support provided three times over a six-month period. The intervention helped participants to reduce their dietary intake for the intervention period but overall authors found:

> *This intervention was not associated with successful long-term modification of lifestyle, and no changes were found in the fat-energy ratio, physical activity expenditure level, and biomedical data such as BMI. There is a possible necessity for the offspring of patients with type 2 diabetes to continuously receive lifestyle interventions, such as with computer-based, non-face-to-face lifestyle intervention* (37).

Details of the health outcomes assessed by these studies are outlined in the Online Companion Document. LINK Table 9 summarizes the systematic and primary research for this set of interventions.

Table 9: Summary of the effectiveness of mixed interventions on health outcomes

Outcome	Evidence	Study/ Methodological Quality
T2D Incidence	Incidence of T2D was not reported in enough trials to enable a meta-analysis.	Dunkley, 2012/ Moderate
	"Both non-drug and drug-based approaches reduced progression to overt diabetes. Non-drug approaches (n=3495, 0.52 95%CI 0.46–0.58) were superior (p<0.05) to drug-based approaches (n=20,872, 0.70, 0.58–0.85)" (p.817). "*Diabetes was not prevented in three trials, which included the pioglitazone arm of IDPP-2, the Ramipril arm of DREAM and the nateglinide arm of NAVIGATOR (Figure 2)*" (p.817).	Hopper, 2011 / Moderate
	Those receiving Chinese herbs were more likely to have reduced incidence of diabetes than comparison group. Authors call this a potential treatment for those with IGF (serum insulin-like growth factor) or IFG (impaired fasting glucose) but findings are not conclusive given the lack of trials that tested the same herbal medicine, lack of details on co-interventions, unclear methods of randomization, poor reporting, and other risks of bias.	Grant, 2009/ High
	The risk of T2D was reduced through a variety of interventions with the following order of effectiveness: "*bariatric surgery (OR 0.16), followed by glitazones (OR 0.37), diet+physical activity (OR 0.43), diets (OR 0.44), physical activity or education (OR 0.53), alfa-glucosidase inhibitors (OR 0.54), metformin (OR 0.65), lipid-affecting drugs (OR 0.66), [moderate intake of alcohol (OR 0.65) and cardiovascular drugs (OR 0.74–0.76)*"(p.721).Incidence was not reduced through the use of beta-cell stimulating drugs, vitamins and estrogens.	Merlotti, 2014/ High
Change in Glucose Levels, Metabolic Syndrome	Both lifestyle and pharmacological interventions were statistically superior compared with control for reversing metabolic syndrome. The probability that lifestyle interventions were the most clinically effective was assessed to be 87% using mixed treatment comparison methods. "*Results indicate that lifestyle interventions are more effective at reversing metabolic syndrome than pharmacological therapies*" (p.620).	Dunkley, 2012/ Moderate
	A combination of herbal medicine and lifestyle modification normalized blood glucose levels significantly better than lifestyle alone. Statistically significant reduction of HbA1c when lifestyle and herbal medicines combined when compared to control or lifestyle modification alone. However note that, findings are not conclusive given the lack of trials that tested the same herbal medicine, lack of details on co-interventions, unclear methods of randomization, poor reporting, and other risks of bias.	Grant, 2009/ High
	Mixed interventions showed insufficient evidence of the effect on CVD morbidity and mortality.	Yuen, 2010/ Moderate

Cardiovascular Risk Factors and related clinical measures	Mixed interventions in this review insufficiently reported on CVD event outcomes.	Dunkley, 2012/ Moderate
	Chinese medicines "*Jian pi zhi shen huo xue, Jiangtang bushen tang, Tang kang yin, Liu wei di huang tang, and Xiaoke huayu pian* all showed a significant improvement compared to the control in reducing total cholesterol and triglycerides"(p. 24). However note that, findings are not conclusive given the lack of trials that tested the same herbal medicine, lack of details on co-interventions, unclear methods of randomization, poor reporting, and other risks of bias.	Grant, 2009/ High
	There was no difference in the risk of cardiovascular death between pharmacological and non-pharmacological interventions. However, "*there was a non-significant trend towards increased cardiovascular death when the drug sub-group alone was considered (1.27, 0.96– 1.68, p=NS), and a non-significant trend towards reduction in cardiovascular death when the non-drug sub-group (0.70, 0.46–1.07 p=NS) was assessed*" (p.821). No significant difference for relative risk of MI (myocardial infarction) and stroke outcomes through four drug trials.	Hopper, 2011/ Moderate
	Mixed interventions showed insufficient evidence of the effect on CVD morbidity and mortality.	Yuen, 2010/ Moderate
Body Composition Changes: Weight Change, BMI, Waist Circumference	Lifestyle interventions achieved greater weight loss than those in drug trials.	Hopper, 2011/ Moderate
	"*no statistical differences in body weight and BMI changes between the two groups [Tianqi group and the placebo group] at any of these time points*." p.653 i.e. for measurements made at 0,6 and 12 months.	Lian, 2014/ High
	Participants BMI normal at study outset, no need to reduce BMI.	Tonkunaga-Nakawata, 2014/ High
All Cause Morbidity and Mortality	Reported that none of the included studies reported on mortality or morbidity.	Grant, 2009/ High
	Drugs and Lifestyle interventions for prediabetes showed no difference in all-cause mortality outcomes in comparison to control groups.	Hopper, 2011/ Moderate

KEY MESSAGE ABOUT MIXED INTERVENTIONS:

There are a number of heterogeneous strategies that prevent T2D. The effectiveness of these interventions appears to be dependent on age, weight loss, and an individual's risk profile, among other factors. There is insufficient evidence to comment on the effectiveness of mixed interventions on cardiovascular outcomes or all- cause morbidity and mortality.

Economic Evidence

Recognizing the distinct differences between the methodologies used for studies of clinical effectiveness as compared against economic analyses, the current section of the report will deal with the economic evidence separately. Evidence obtained from systematic reviews of clinical effectiveness enables us to comment on a body of literature based on rigorous methods that have been developed to assess various primary studies together, often through pooling data in meta-analyses. In comparison, economic studies are much more difficult to combine because they vary along a number of dimensions such as the assumptions on which the analysis is based and the perspective employed in the study – economic analyses may examine the cost to the individual, the cost to the healthcare system or societal cost.

For this report, we will focus on the cost-effectiveness of various interventions from the perspective of the healthcare system. This will involve assessing direct medical costs (e.g., clinical services, hospitalization, and medications) of preventive efforts rather than assessing indirect costs (e.g., cost in time and travel incurred by patients to receive the treatment, lost time/productivity due to illness or premature mortality). We concentrated on economic literature that evaluated the screening and prevention of T2D through a structured form of economic evaluation called a cost-utility analysis (CUA).

A CUA is a type of economic analysis that allows us to assess the health benefit of an intervention (i.e., the additional quantity and quality of life an intervention provides) versus the cost of the resources required to implement the intervention. The key outcome variable considered is the additional cost of the new intervention per incremental unit of health gain and the key question is whether an intervention is cost-saving, cost-effective, or neither.

Calculating Cost Saving

An intervention would be considered cost-saving if it delayed or prevented a large enough number of cases so as to generate more savings to the healthcare system in the future than the up-front implementation cost. Determining whether or not an intervention is cost-saving involves calculating differences in the net cost (NC) of an intervention.

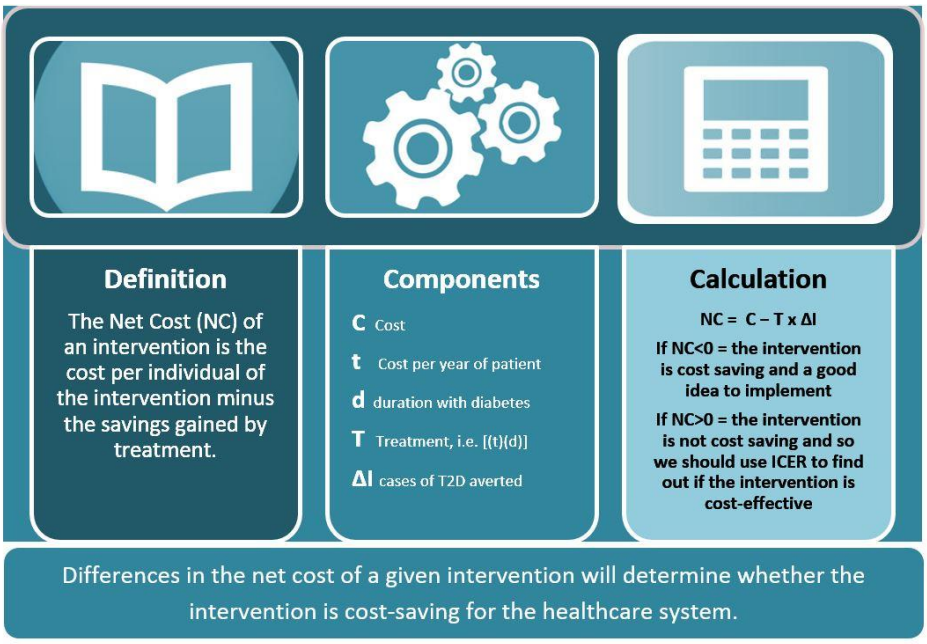

Figure 1: Calculating the Net Cost (NC) of an Intervention

Calculating Cost Effectiveness

If an intervention does not turn out to be cost-saving, it may still be cost-effective. An intervention can be deemed cost-effective if it is more costly up front than the expenditures it saves but generates enough gains in quality and quantity of life per extra dollar spent that taxpayers are willing to pay for it.

The incremental cost-effectiveness ratio is the main measure used to determine the cost-effectiveness of an intervention. See Figure 2.

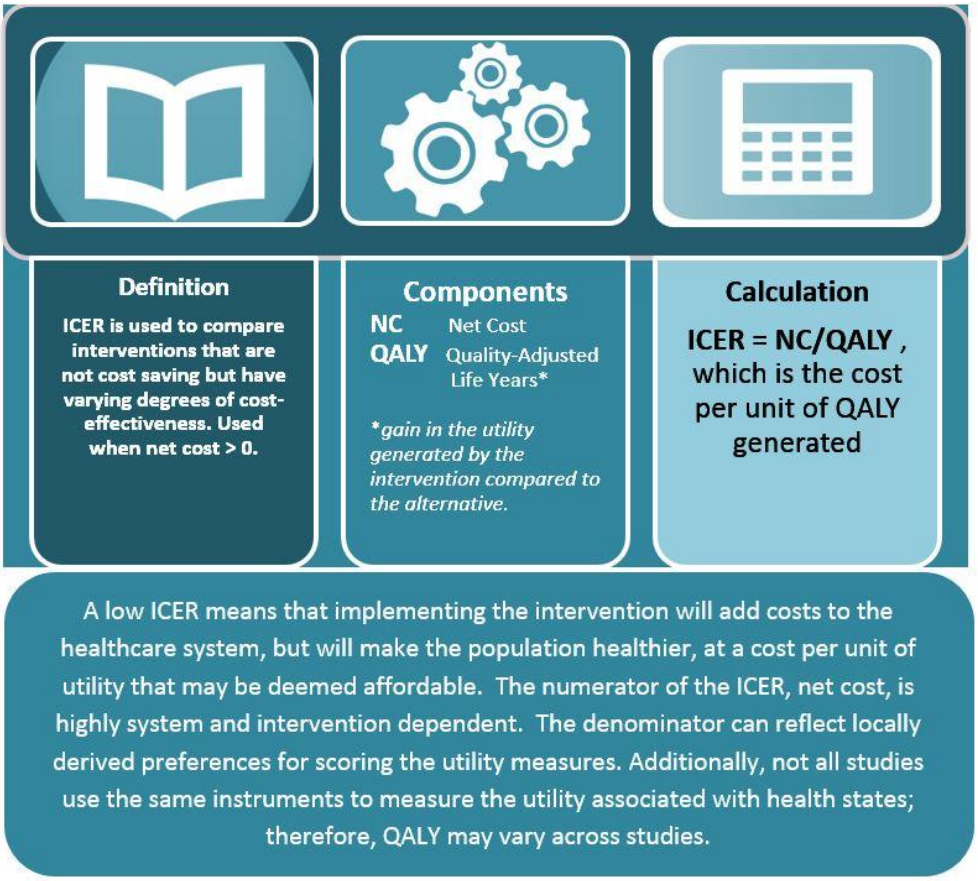

Figure 2: Calculating the Incremental Cost-Effectiveness Ratio (ICER) of an Intervention

It should be noted that the threshold of cost effectiveness is debated in the economic literature.

Cost is calculated in each economic analysis based on different assumptions, inferences, and contexts. Rather than conceiving of a fixed threshold for cost-effectiveness, it has been suggested that *"in principle, the threshold should depend on the budget available to a decision maker and the costs and benefits of alternative uses of that budget*" (40).

For this reason, any categorization of interventions as being cost-effective or not; has an associated ICER provided so that it is ultimately left to decision makers to decide whether or not an intervention is cost-effective relative to available resources. A more detailed description of economic parameters is described in the Online Companion Document. LINK

Types of Economic Evidence

In this review of the economic literature, we evaluated two types of evidence:

- **Evidence from empirical studies**
  This evidence considered similar, non-identical interventions aimed at changing lifestyles or detecting diabetes. For each intervention, it estimated values for the parameters: cost (C), cases of T2D averted (ΔI), treatment (T), and gain in QALY utility generated by the intervention and it calculated the resulting incremental cost-effectiveness ratio (ICER) (or the difference between C and (ΔI)(T) if negative).

- **Evidence from simulations**
  This type of evidence uses values for the parameters estimated in empirical studies to project the likely cost-effectiveness of these interventions in the long term beyond the period of observation.

Empirical evidence is more robust and internally valid but typically, it is restricted to a relatively short time period (a maximum of 10 years); however, we usually have reason to believe that the benefits of such interventions will be felt more strongly over longer periods. This is especially the case for primary prevention (a one-time intervention that is followed by several years of benefits). Therefore, to fully assess the economic impact of an intervention, we need to look at a combination of empirical (within-trial) studies and simulated (outside-of-trial) studies that use costs projected over longer periods.

Interpreting the Economic Evidence

Rather than synthesizing the economic findings, this report provides a narrative description of the economic literature on T2D screening and prevention. Because an ICER is heavily dependent on intervention, study design, and health-system context, we were unable to calculate any average ICERs (by using an approach similar to a meta-analysis).

An additional challenge to synthesis was the wide variation in economic evidence among key components analyzed in the literature, including:

- type of intervention studied
- comparator (placebo, standard, drug alone),
- target group (targeted by age and risk factors),
- setting (national /local)
- time discount rates (some studies use different total dependency ratios (TDR) for costs and benefits)
- time horizons, and
- methods used to measure quality of life (e.g., decision trees, Markov models, life-tables, or Archimedes models.)

In the narrative description that follows, we present the findings in a way that respects the approach used by the different study authors. We will consider which assumptions were made to derive values for C, T, and ΔI, and what instruments were used to assign utility values to various health states. Most

included studies identified used the self-administered questionnaire on quality of well-being (QWB-SA) but two used a different instrument, the EQ-5D.

Inclusion Criteria for Economic Evidence in this Report

Because such a limited number of economic studies met our inclusion criteria, we have maximized the quantity of economic information in this report by including *all* relevant studies, even those with methodological flaws. Since most of the methodological flaws uncovered in the literature could be easily corrected, we present these findings having made all necessary corrections. We recognize that this practice is not orthodox for clinical studies but in the case of economic evidence, we hope to convince the reader of the validity of our corrections.

We should further note that for studies based on self-reported healthcare services utilization (rather than direct observation of costs or imputation of average costs), we include the findings without giving much credence to the conclusions.

We also make clear in the narrative description our preferred economic model for evidence from the United States and what conclusions we can draw from that evidence in terms of achieving an ICER.

All individual studies that yielded either an ICER or a value for net costs were included in this report, either directly (if published after 2009) or indirectly (for individual studies that were included within one systematic review published in 2010). As stated previously, we focused on studies using an ICER statistic to compare intervention costs and studies and that calculated the ICER from a health system perspective. We did not include economic evidence that involved broader societal costs. As such, **direct** medical costs such as clinical services, hospitalization, and medications are considered in the interpretation of results while **indirect** costs of both the intervention and treatment are excluded. For purposes of clarity, indirect costs for an intervention include costs in time and travel incurred by patients; indirect costs for treatments averted include the cost in time and travel incurred by patients to receive a treatment. The largest component of indirect cost is typically the cost of lost productivity resulting from morbidity and premature mortality.

Narrative Description of the Economic Evidence

Dollar figures below are provided in United States Dollars (USD) unless otherwise specified. The conversion rate from Canadian dollars (CAD) to American dollars (USD) is 0.85 purchasing power parity (US$1,000 = CAD1, 176).

What We Found: Economic Evidence in this Report

We found only two economic reviews for either preventive interventions or for screening for T2D. These reviews are included in the narrative description that follows. Both describe variable findings within the studies they included (41,42):

- Both reviewers note a lack of consensus: some studies found an intervention to be cost-saving while other studies found a similar intervention to have an ICER well above $150,000 per QALY.
- One review identified intensive lifestyle interventions:

  - six to increase physical activity
  - five to change diet,
  - fourteen interventions combining diet and physical activity, and
  - nine interventions including drugs plus any of the preceding combinations (42).
- The other review examined all types of preventive interventions as well as screening and was organized around interventions rather than studies (41).

For the narrative description of the evidence that follows, we include the findings from these two reviews, revisiting some of the most important individual studies cited, and adding a description of twelve primary studies published since 2010.

Economic Evidence for Interventions to Prevent T2D

Overall, we found that reviews of **empirical studies** converged in their conclusions. Preventive interventions[9] were never cost saving in the short-to-mid run (10 years and less) but most were in the low range of ICER, between $4,000 and $30,000 per QALY (in 2015 USD). No short-run (within trial) studies were identified in Saha et al. or Li et al.

Ambitious follow-up studies conducted in the United States revealed that T2D prevention [for those with pre-diabetes] costs between $10,000 and $20,000 per QALY. The cost per QALY will likely be even greater in a Canadian context where the treatment cost is lower.

Five economic studies published since 2010 were also identified. One concluded that the intervention it examined was cost saving (43) but its data were derived from self-reported adverse events (hospitalizations) and as a result should be considered less reliable. The other four (two from the US, one from Britain and one from Spain) used actual treatment cost in both intervention and control arms (44–47). The ICER values of these economic studies ranged between $4,000 and $30,000 per QALY. The variation in the ICERs reflects differences among studies such as intervention components included, intervention costs used, length of follow-up period and participant characteristics. Ambitious follow-up studies conducted in the United States revealed that T2D prevention costs between $10,000 and $20,000 per QALY (44,45). The cost per QALY will likely be even greater in a Canadian context where the treatment cost is lower. Specific details for these individual study results can be seen in the economic section of the Online Companion Document. LINK

In reviewing **the simulation literature**, we uncovered an issue related to the models used to simulate cost. We would expect that, in the longer run (20 years to lifetime), interventions are at least as cost-effective as in the short run and could even become cost-saving. The review by Saha et al. disagrees with

[9] The majority of populations included in the economic literature that examined preventive interventions for T2D were described as high-risk, IGT, IFG, overweight/obese, or women with a history of gestational diabetes, or pre-diabetic patients. One review (Saha,2010) analyzed studies with both healthy populations and high-risk populations at baseline but a majority of the studies included were looking at at-risk/high-risk individuals.

this premise (42). It highlights a controversy among epidemiologists as to which model should be used to simulate cases of T2D averted. A Markov chain model can be used to simulate ΔI outside of the follow- up range. Alternatively, a more complex model, called Archimedes, can be used (48). The three studies identified in Saha et al. used a Markov model and found a lifetime ICER between $1,000 and $10,000. The one study using the Archimedes model found a much higher ICER of > $100,000 (48).

Our assessment sheds some light on this confusing technical debate. Markov chains and the Archimedes model are the main types of simulation models used in the literature we reviewed. The Archimedes model is sometimes preferred from an epidemiological perspective because it produces much more conservative estimates of ΔI than the Markov chain model. The only study reviewed that used the Markov approach for estimating cost effectiveness used a very high value for the cost of the intervention (48). We recalculated its analysis using a more conservative value for cost (approximately $4,000 per patient as in the Diabetes Prevention Program) and showed between $5,000 and $27,000 per QALY gained.

We can conclude that interventions to prevent T2D among those with pre-diabetes are not cost saving but their ICERs are in the low to medium range (USD 10,000 to 20,000).

Since Saha et al. and Li et al. were published, eight other English-language primary economic studies were conducted. These studies contain simulations of lifetime costs and benefits of the prevention of diabetes, yielding ten ICERs (13,49–55). These studies showed a range of cost-effectiveness from cost saving to an ICER of $30,000 per QALY (depending on the age of the individual when the intervention was applied). However, one of these studies used a societal perspective rather than a healthcare system perspective (53) and another was based on self-reported survey data, making its results less reliable (51). Neumann et al. found that the intervention studied was cost saving if applied to 30-to-50 year olds in Germany and would cost $30,000 per QALY if applied to patients aged 75 or older. However, these authors (53) used a societal perspective which is not fully comparable to CUA done from the narrower perspective of the health care system.[10] It is important to note that ICERs are generally, but not always, lower for cost estimates from the societal perspective than those from a healthcare system perspective. Castro-Rios et al. also found a preventive intervention to be cost saving in the long-term in Mexico but it is based on self-reported survey data which makes its results less reliable (51).

Most other studies were too heterogeneous to compare directly as a result of differences among individual studies or discrepancies in the values used to calculate cost. Despite these differences, studies followed the same pattern and converged toward a low cost per QALY, between $0 and $10,000 (13,49,50,52,54,55). Specific details for these individual studies can be seen in the Online Companion Document. LINK

[10] This includes somewhat difficult to justify estimates for indirect costs of the intervention and the disease.

We can conclude that interventions to prevent T2D among those with pre-diabetes are not cost saving but their ICERs are in the low to medium range (USD 10,000 to 20,000). ICER values are sensitive to national values of C and T as well as the population targeted. These values are also affected by adherence to the lifestyle intervention and whether or not non-adherers are allowed to switch to therapeutic treatments (metformin). For people who adhere to lifestyle changes, therapeutic treatments are less effective than these lifestyle changes. Conversely, therapeutic treatments are more effective for people who do not adhere to lifestyle changes. Non-adherers to lifestyle changes are those who cannot lose weight or cannot lose enough weight. On average, non-adherers lose only 1% weight versus 7% for adherers.

Economic Evidence for Screening Interventions to Detect T2D/ Subsequent Interventions to Prevent T2D Progression:

There is a weak economic case for untargeted screening of undiagnosed diabetics in the general population (starting at a given age) and then treating to prevent T2D complications. For this intervention, there are very few studies to draw on; furthermore, those available tend to contradict one another for reasons related to basic assumptions on ΔI and QALY.

Li et al. was the only economic review that evaluated the economics of screening. It set different screening strategies and populations against each other and against cases where no screening was undertaken. Its findings were based on only two primary studies (56,57). In this review, three relevant findings were uncovered:

- First, the authors reported that, one-time, opportunistic, targeted screening of hypertensive patients ≥45 years who were not diagnosed with T2D and who were followed by state-of-the-art treatment to prevent onset of diabetes and complications was not cost saving but was in the low range of ICERs (below $25,000 per QALY) compared with no screening.
- Second, Li et al. reported strong evidence that non-targeted "one-time universal opportunistic screening for undiagnosed type 2 diabetes among those aged 45 years and older compared with no screening"(p.1885) was not cost-effective (defined as > $100 000 per QALY or life year gained). This finding is attributed to small gains in quality and quantity of life relative to cost. There were no gains at all for the screening of all nondiabetics and relatively small gains even for newly-diagnosed diabetics.
- And finally, the review found strong evidence that universal population[11] screening for those aged 45 years and older compared with targeted screening in persons with hypertension would not be cost-effective at all (defined as >$100 000 per QALY or life years gained).

Since the review by Li et al. was published, two simulation studies calculating ICERs for screening interventions have been conducted and published, all in the US context (58,59). Other published studies, such as Khunti et al., report cost per case detected, attempting to answer the question: "how much does

[11] The age of population screening for adults in this case was not well defined. One of the studies cited age as > 25 and another cited US population. Li et al. 2010 conclude that they are unable to determine how the age of screening affects cost-effectiveness based on discrepancies in the studies their analyses were based on.

it cost to find one un-diagnosed diabetic?" These studies do not estimate the costs of treating those newly diagnosed diabetics or the gains produced by preventing/delaying complications of diabetes. Chatterjee et al., conducted a simulation over three years based on the costs of complications of T2D from data obtained from Kaiser Permanente, a large managed-care organization in the US.
This study involved three simulations:

- of opportunistic screening compared with no screening;
- of universal screening for diabetes or high-risk prediabetes, and
- of screening those with risk factors based on age, BMI, blood pressure, waist circumference, lipids, or family history of diabetes.

However, it should be noted that 58% of the study population was African American; the results of this study cannot necessarily be generalized to all populations. Chatterjee et al. found that, for the third type of screening, the savings on complications offset the initial cost of the opportunistic screening intervention for those at higher risk (this included those with BMI >35kg/m^2, systolic blood pressure $\geq$ 130mmHg, or age >55 years). All net costs are negative and, in some sub-groups, significantly different from 0 at the usual 5% threshold, but they are always very close to 0. Overall, costs savings are in the order of USD 100 per person and per year, and net costs savings are close to USD 10 per person/ per year. The highest absolute net cost saving was obtained among patients with a BMI greater than 35, with USD 15 per person per year. A safer way to describe such a study would be to state that opportunistic screening targeted at adults with higher risk for diabetes may be cost-neutral to the healthcare system over three years, and may yield benefits in quality of life to patients, but these benefits were not presented in the study (59).

…opportunistic screening targeted at adults with higher risk for diabetes may be cost-neutral to the healthcare system over three years, and may yield benefits in quality of life to patients, but these benefits were not presented.

Kahn et al. conducted a simulation using the course of a lifetime as its follow-up timeframe. An important assumption is that those diagnosed with T2D through screening would then receive state-of-the-art treatment to control their T2D and delay complications. These clinical parameters might differ from those observed in actual trials of screening because, in a trial, the compliance of individuals with treatment, once diagnosed, might vary—whereas the simulation assumes that all subjects comply fully. Readers should bear these assumptions in mind when considering any evidence based on simulations. Kahn et al. 2010 found that most screening strategies would yield ICERs in the low range, below USD 30,000. These authors used the Archimedes model to project the course of the disease in the intervention and the control groups and found the following, in ascending order of ICER:

- **Targeting hypertension** (> 140=90mmHg) every year or every 5 years costs less than USD 10,000 per QALY gained.
- **Screening all persons** aged 45-75 every 3 or 5 years **or** all persons aged 35-75 every 3 years costs roughly USD 10,000 per QALY gained.

- **Screening all persons** aged 45-75 every year, all persons aged 60-75 every 3 years, or all persons aged 30-75 every 6 months, costs between USD 15,000 and USD 30,000 per QALY gained (58).

The same authors also recommended targeted screening for individuals with hypertension between the ages of 35 and 75. However, there are several caveats associated with these findings:

- Differences across strategies are not statistically significant in a cohort of 325,000, because differences in outcome (QALY) are small over the population as a whole.
- The model found a lower ICER than previous models because it employed a treatment strategy based on more recent guidelines.
- The model allowed for repeated sequential screening, as opposed to one-time screening.
- It is not clear why Kahn et al. assume a gain in QALY from the combination of screening and intervention that is ten times larger than the gain assumed by Hoerger et al.
- Findings are sensitive to assumptions on QALY gains (58).

These two recent simulation studies seem to agree that the benefits of early detection per detected case decreases with age. This is because detecting T2D at age 35 gives an individual more time to benefit from delaying T2D complications than would be the case if T2D were not detected until age 65. On the other hand, the rate of detection varies with age: detection rates peak at age 55 when the prevalence of T2D is high and many are not detected; after age 55, rates of detection decrease. As a result, for older individuals, prevalence is high but detection rates are lower because chances are their T2D has already been detected.

These two recent simulation studies seem to agree that the benefits of early detection per detected case decreases with age. This is because detecting T2D at age 35 gives an individual more time to benefit from delaying T2D complications than would be the case if T2D were not detected until age 65.

Overall, even the case for screening in the best-case scenario (i.e. screening patients with hypertension) is not entirely clear although the estimated ICER (+/- USD 10,000 per QALY gained) is lower in more recent studies. More robust evidence is needed on this particular topic.

Key Economic Messages

The following key economic messages are based on these assumptions:

- We assume the cumulative incidence of T2D decreases by 11% due to the preventive intervention;
- We assume the cost of the intervention is $4,000;
- We assume that, on average, each patient with T2D lives 10 years with the illness;
- We assume the intervention will be cost-saving as long as t is greater than t_{min}= [4000/(0.11)(9.9)] (1+ 0.03).[10]
- We assume that, if the annual relative cost of treatment for T2D (relative to pre-diabetic patients) is lower than $4,900 (which is very likely in Canada), the intervention is not cost-saving. This includes the cost of treating diabetes-related complications.

What is the cost of preventive interventions for T2D?

Most preventive interventions are within the cost-effective range of less than USD 20,000 per QALY.

The ICER that results from the following formula: **ICER = C/QALY – [(d)(ΔI)/(1+p)^{10} (t/QALY)** yields values from USD 5,000 to USD 15,000 when **t** decreases from USD 4,000 to USD 2,000. With a more optimistic estimate of QALY at 0.29, ICERs vary between USD 3,000 and USD 8,000 for the same values of **t**.

KEY MESSAGE ON THE COST OF PREVENTION

Most preventive interventions are within the cost-effective range of less than USD 20,000 per QALY.

What is the cost of screening interventions for T2D?

More robust evidence is needed to evaluate the cost of screening interventions for T2D. In the limited studies available, there was some evidence to suggest that targeted opportunistic screening of at-risk individuals to detect and manage diabetes among high-risk patients (obese and/or with high blood pressure) may be either cost saving or cost less than USD 6,000 per QALY gained. However, it should be noted that there was disagreement between studies on the range of the cost. Universal population screening of all adults ≥ 45 years compared with no screening was not cost-effective at all, with a predicted ICER of close to CAD$200,000 per QALY gained.

KEY MESSAGES ON THE COST OF SCREENING FOR T2D

Overall, more robust evidence is needed to confidently evaluate the cost-effectiveness of screening interventions for T2D. In the limited studies available, there was some evidence to suggest that targeted opportunistic screening to detect and manage diabetes among high-risk patients (i.e., patients with obesity and/or with high blood pressure) may be either cost-saving or cost less than $6,000 USD per quality-adjusted life year (QALY) gained. However, it should be noted that there was disagreement between studies on the range of cost.

Universal population screening of all adults aged at or over 45 years compared with no screening was not shown to be cost-effective at all, with a predicted incremental cost-effectiveness ratio (ICER) of close to CAD$200,000 per QALY gained.

The Newfoundland and Labrador Context

Throughout the course of this project, we have tried to identify contextual factors unique to Newfoundland and Labrador that may influence the relevance and applicability of the research-based evidence to our province and its population. This section of the report addresses those contextual factors and is based primarily on an analysis of relevant administrative data and consultations with local decision makers, administrators, clinicians and stakeholder group representatives in the province.

Contextualization Approach

By 'contextual factors' we mean the local conditions, capacities and qualities that can have an impact on the reported effects of our included research evidence—such factors have the potential to enhance or to reduce the likely effectiveness, feasibility or acceptability of an intervention in Newfoundland and Labrador. Our Research Team helped us recruit key contextual advisors from across the province; team members also participated in contextualization interviews, often providing relevant documents and sources of data about the specific Newfoundland and Labrador context.

Below we consider the characteristics and circumstances that will come to bear on lifestyle interventions geared towards reducing the incidence of T2D in the adult population of Newfoundland and Labrador.

Contextualization Factors

Patient-Level Factors

The prevalence of T2D is greater in NL compared to other places in Canada (60). In considering the characteristics that contribute to an increased risk for developing T2D in the NL context, we identify below the factors we cannot change, such as an aging population, genetic factors, and the challenges inherent in our geography and climate, and those factors we might be able to change as we consider the applicability of interventions and ways to build better capacity for the people of this province to make healthier food and lifestyle choices.

Demographics & Diabetes Risk: Factors We Cannot Change

When considering the NL population in terms of diabetes risk, our informants identified the following non-modifiable demographic factors as contributing to an overall population risk for diabetes in NL:

- **Aging:** The ability to produce and use insulin declines as we age; therefore, older adults are at increased risk of developing T2D. The sharpest increase in the prevalence of diabetes occurs after the age of 40 (61). Given that NL has the highest median age in Canada at 44.6 years (62), demand for services to prevent, manage and treat T2D is particularly high and can be expected to increase as the population ages.
- **Geography & Climate:** Our key informants noted that certain geographical factors such as poor soil, short growing season, adverse climate and island geography make access to, and

affordability of, vitamin-rich foods a challenge in NL and are likely to challenge the efforts of health promotion interventions focused on diet and physical activity.

- **Genetics:** T2D has a hereditary component. Historically, the island of Newfoundland has had less genetic variation than other parts of Canada, with the majority of Newfoundlanders coming from limited areas in England and Ireland. The interplay between genes and factors such as age, physical activity, diet and obesity can contribute to the risk factor profile for the province's population (63).

Population- Level Risk: Factors We Can Change

When considering the population of NL in terms of diabetes risk and prevalence, our key informants identified the following factors as contributing to overall population risk for diabetes in NL; however, unlike aging and geographical factors that cannot be changed, certain population risk factors below have the potential to be improved with help from healthcare and social support systems:

- **Poor Population Health Status:** In provincial/territorial rankings of health status, NL has consistently had the lowest ranking of all Canadian provinces. Of particular relevance, Newfoundland and Labrador received a grade of D- on mortality from diabetes (64). The Canadian Diabetes Association estimates the prevalence of pre-diabetes for adults aged >20 years in NL to be 25.3% (1). Canadian Primary Care Sentinel Surveillance Network (CPCSSN NL) data from a sample of the province's adults shows us that the proportion of adults with diabetes has increased from roughly 5% in 2009 to 10.5% in 2014; this increase has coincided with an increase in other comorbid conditions (see Table 10 below). These numbers are in line with the trend shown in data published by Statistics Canada, measured for the total NL population over the age of 12 (see Table 11)(65). NL's poor health status scores can be looked at in two ways: they can be seen as obstacles to the success of disease prevention programs or as evidence that we have an opportunity to improve population health status in the province by implementing effective programs aimed towards lifestyle change.

Table 10: Prevalence of select medical conditions within CPCSSN-NL sample of adult population, by year

	Mean Prevalence (%) by year					
Year→ Condition ↓	2009	2010	2011	2012	2013	2014
Diabetes	5.1	6.2	7.6	8.5	9.6	10.5
Hypertension	11.1	13.3	15.7	17.3	19.1	21.2
Hyperlipidemia	13.2	15.8	19.0	21.5	23.3	25.2
Ischemic Heart Disease	3.0	3.5	4.2	4.7	5.2	5.9
Cerebrovascular Disease	0.4	0.5	0.6	0.7	0.8	0.9

Please see the Online Companion Document for more details LINK

- **Increased T2D Risk Factors:** T2D risk in NL is exacerbated by rates that are higher than the national average for overweight/obesity and high blood pressure together with the province's higher incidence of unhealthy lifestyle behaviors such as heavy drinking, smoking, physical

inactivity, and low consumption of fruits and vegetables (64,65). These are modifiable risk factors that, if addressed, could lower risk for developing T2D but that, for the moment, serve as potential obstacles to the success of T2D prevention programs or initiatives. The table below provides a comparison between Canadian and NL health indicators as well as a further breakdown of health indicators within the four health regions in Newfoundland and Labrador.

Table 11: Comparison of Health Indicators Linked to T2D and T2D Risk: Canada, NL, and NL Health Regions

Health Indicators linked to T2D Diabetes and T2D risk	Canada Total%	NL Total %	Eastern Heath%	Central Heath%	Western Heath%	Labrador -Grenfell Heath%
Diabetes	6.6	8.8	7.4	11.2	11.9	7.4
Overweight or obese	53.8	68.3	67.0	71.5	66.4	76.1
High Blood Pressure	17.7	24.0	21.3	30.6	28.0	21.8
Current Smoker: daily or occasional	18.7	20.8	19.7	21.0	24.0	24.3
Heavy Drinking	18.4	25.0	25.4	25.0	23.9	23.1
Leisure time physical activity: moderately active or active	54.4	48.0	49.0	40.0	53.8	47.9
Fruit and vegetable consumption; 5 portions or more per day	40.2	25.6	26.3	20.9	29.1	24.7

All data in the table above were published by Statistics Canada (66) based on Canadian Community Health Survey 2013/14. Overweight or obese measures were for adults 18 and older while all other measures were recorded for ages 12 and older.

- **Health Literacy/Adherence to Healthy Lifestyle Choices:** When evidence in this report indicated that lifestyle changes are inhibited when people hold negative beliefs or misunderstand information about healthy diet and exercise choices, we asked our key informants to characterize provincial literacy among adults about healthy diet and physical activity (31). While adult knowledge of healthy nutrition was characterized as being good, our key informants pointed out that understanding broader messages about healthy eating does not always mean this knowledge is applied to individual choices. Our key informants noted the need for more in-depth education about nutrition: not only do people need to be better educated about how to navigate food labels, they also need support in knowing how to plan and prepare healthy meals.

  Our key informants characterized adults in the province as being quite knowledgeable about healthy levels of physical activity. However, once again, there are challenges in applying this understanding and in becoming motivated to maintain appropriate exercise and activity levels. Factors that were cited as contributing to lower levels of physical activity in NL included:
  - time for, and access to, physical activity programs;
  - the need for more facilities, equipment, trained instructors;
  - the need for public transit to take people to recreational facilities;
  - a lack of recreational infrastructure in rural communities;
  - long winters and the difficulty in getting outdoors in inclement weather; and
  - the costs associated with accessing some recreational and exercise programs.

- **Lifestyle Factors and the Need to Support Healthy Options:** Not unexpectedly, today's fast-paced lifestyle was cited as a contributor to unhealthy food and lifestyle choices. Busy people tend to rely more on convenient "on-the-run" options for meals and these are often not as healthy. Where possible, supportive environments that make healthy food choices more available and affordable will contribute more success in making healthy food choices.

The Social Determinants of Health

The social determinants of health have an important role to play when it comes to diabetes prevention and management. Lower levels of education, income, and socioeconomic status, as well as increasing levels of poverty and hunger are associated with increased incidence, prevalence, and burden of disease (67). The important social determinants of health highlighted during our contextualization discussions included:

- **Literacy:** Poor literacy can be a barrier for the uptake of healthy lifestyle choices and positive change. Literacy in NL is lower than the Canadian average (68) and this can have a negative impact on health in situations where prevention information is in written form; where writing is required to register for programs, or where adherence is affected by people's understanding of medication labels and treatment instructions.
- **Employment:** Prevalent types of employment in the province can make a healthy lifestyle challenging. Seasonal work and commuting out-of-town or out-of-province for work can lead to fluctuating lifestyles that challenge consistent adherence to healthy behaviors for those travelling and for those remaining at home. In smaller communities, community capacity can suffer—commuting results in shortages in local tradespeople, volunteers, and community leaders who might support healthy lifestyle programming at the local level (69). Shift work also contributes to risk of chronic conditions because it results in abnormal eating and sleeping patterns.
- **Income:** The median family income in NL is among the lowest in Canada (1). For those with lower and/or unstable incomes, spending on housing, childcare or transportation often takes precedence over spending on healthy food and/or exercise. When healthier choices are not affordable, people turn to lower-cost foods that are often high in fat, sodium and calories. Key informants mentioned this is a serious problem for seniors living on low fixed incomes in NL.

Tradition and Lifestyle in NL

Our key informants suggested that changes to traditional lifestyle habits could contribute to T2D risk in this province. Traditional ways of life in Newfoundland and Labrador such as fishing, hunting and trapping once spread the majority of the population along the coastline in small isolated communities. Many families who once carried out traditional types of physical work have had to adjust their lifestyles in the face of modern economic realities. Whereas physical work was once a large component of the traditional lifestyle in the province, in its absence there is a need for scheduled exercise.

Local adherence to traditional foods and cooking methods may also pose a challenge to interventions that are aimed at changing the foods you eat and how you cook them. As the result of malnutrition, food scarcity and a short growing season, residents of Newfoundland and Labrador traditionally relied

heavily on preservation methods such as salting, smoking, pickling, and root cellars to preserve food for consumption year-round (70). Although improvements in transportation networks and refrigeration have decreased the province's incidence of deficiency-induced disease in the province, the legacy of the traditional Newfoundland and Labrador diet remains, such that even with access to fruits and vegetables, consumption of these items remains low when compared to foods that tend to be higher in fat, sugar and salt. The tradition of salting, smoking, and pickling foods is still widely practiced in the province. Low consumption of fruits and vegetables and high consumption of salt and sugar contribute to weight gain, high blood pressure and increased T2D rates. Although the persistence of traditional cultural food consumption and preparation might interfere with the effectiveness of prevention programs focused on healthy eating, it also provides a highly visible target for such programs.

Food Security and Access

Access to healthy foods is essential for the feasibility of dietary change among the NL population. Households with higher food insecurity are more commonly afflicted with health problems like diabetes, high blood pressure, and food allergies (71). A mere 10% of the fresh vegetables available in the province are produced here. NL residents rely on imported food; the high cost and uneven distribution of imported fresh goods creates inequities in access. A disruption in the food supply chain would result in a mere 2-3 day supply of fresh vegetables (72). Issues of security and access are particularly acute in areas of the province that remain isolated and where transport of food remains difficult. For some communities, stocking up on non-perishable foods is a cheap and practical solution for the transportation delays that inevitably occur. A large portion of the province's fisheries production of fresh, local seafood is exported and therefore unavailable to the province's residents (72). Between 2007 and 2011, measures in the province's Poverty Reduction Strategy have helped to lower food insecurity in the province (especially for those receiving government income supports). However, an increase in overall household food insecurity was reported between 2011 and 2012. This issue highlights the complexity of maintaining a healthy and sustainable food system for all residents of the province (73).

The Patient-Related Context: Conclusions

Overall, we have identified a number of key patient-related factors present in the NL context that are likely to impact the effectiveness of the lifestyle changes recommended in the literature. Although there are some factors we cannot change, there is significant room for the improvement of modifiable risk factors such as poor lifestyle behaviors. Careful consideration of how future initiatives and programming are matched to the patient-related factors presented in this report will be important for decision makers as they work towards optimizing the effectiveness of lifestyle interventions in the province.

Service Landscape Factors

The service landscape in NL includes a range of prevention and health promotion programs/initiatives related to healthy lifestyle. In describing the service landscape, our informants provided information on programs made available by the Canadian Diabetes Association and on programs/initiatives provided by various branches of provincial government.

Canadian Diabetes Association (CDA) Programming

The Canadian Diabetes Association offers the most targeted programming for the prevention of T2D. CDA offers various supports and programs[12] for people in NL at various stages of the disease. The table below focuses on program offerings for those with pre-diabetes.

Table 12: Canadian Diabetes Association (CDA) Programming

Program Name	Description
Information Sessions	Experts on diabetes-related topics make presentations on a variety of topics. Open to anyone with an interest, including persons with pre-diabetes.
DSupport (Peer Support)	Peer-support program developed in Atlantic Canada that matches participants (pre-diabetic, diabetic, or caregiver) with peers elsewhere in Canada. The program has had small success as a telephone service; CDA hopes to improve uptake by offering the program online.
Virtual Health Coaching	A free telephone-based service for adults living with pre-diabetes, Type 1 Diabetes or T2D. Professional health coaches provide two 45-minute telephone sessions and one 20-minute follow-up to evaluate success. Coaches help prioritize participants' health goals and identify ways for them to manage their health.
CDA Learning Series	This learning series aims to increase awareness of T2D over a range of topics. The series covers everything from risk awareness and symptom identification to the prevention or management of diabetes with a healthy lifestyle.

Our informant from CDA suggested that a provincial database with up-to-date data would help our local CDA branch target programs towards specific populations, both to raise the awareness of T2D risk and to develop and promote prevention programs. The absence of reliable statistics about the number and distribution of at-risk cohorts impedes the effectiveness of CDA prevention efforts in NL.

The Provincial Chronic Disease Prevention and Management Policy Framework

At the provincial government level, disease prevention policy does not target specific chronic diseases such as T2D; rather, the aim is to address a variety of chronic conditions that affect a large portion of the population and that have significant impact on quality of life. In 2011, the Department of Health and Community Services published *Improving Health Together: A Policy Framework for Chronic Disease Prevention and Management in NL*. The framework focuses on prevention, awareness, and self-management of chronic diseases in NL including T2D (74).

- **Provincial Chronic Disease Self-Management Program | *Improving Health My Way*:** While we did not identify provincial programming that exclusively targets T2D prevention, our key informants highlighted a key program called *Improving Health: My Way*[13] (the Stanford Chronic Disease Self-Management Program) that was implemented in NL as part of the province's chronic disease prevention and management policy. While it focuses broadly on awareness and

[12] Our focus in this report is prevention programs for diabetes; however, CDA offers two additional programs focused on T2D management for those already diagnosed with T2D as well: Firstly, they offer live interactive free webinars to those living with T1D or T2D; secondly, CDA offers diabetes self-management workshops to provide diabetes education to communities throughout the province. The Improving Health: My Way provincial government program is promoted at each of these workshops. The workshops have been an effective recruitment tool for the provincial program in Eastern Health.

[13] The program was developed by Stanford University and is sold to organizations and jurisdictions who want to avail of it. The province obtained a license to deliver this program in 2011. Strict rules govern how this program is delivered.

self-management of chronic disease, many components of the program are applicable to T2D prevention. According to Accreditation Canada, adaptions for a range of specific populations are being developed to improve the program by making it more disease-specific (75). This innovation could provide an opportunity to adapt *Improving Health: My Way* program in NL to increase the focus on preventing prediabetes and diabetes-related health risks.

Improving Health: My Way is sponsored by the province and is becoming a well-established, well-known program that is available free of charge in each of the four regional health authorities. The program uses a peer-support model in which lay people and health professionals help small participant groups address issues commonly faced by people with chronic disease and teaches them how to better manage their conditions(s). It is aimed towards adults with chronic disease risk factors and/or their caregivers. Participants learn about healthy eating and exercise, how to use medication, and how to cope with their chronic disease (75).

Feedback from participants has been positive, with reported increases in quality of life and improvements in clinical indicators. Testimonials from participants and support from health professionals have created growing interest. The effectiveness of this program was formally evaluated for the period from 2012 to 2014. In a small sample of 228 participants, a number of statistically significant improvements in health status were found. Improvements were reported in energy level, quality of life, communication with healthcare providers and confidence/self-efficacy in managing chronic conditions. Evaluations indicated significantly lower levels of health distress, perceived pain, and decreased interference of the chronic condition in sufferers' daily lives. Easier access and greater awareness, common challenges for many jurisdictions including NL, were highlighted as important ingredients for the continued success of this self-management program (76). In cases where participants have not adhered to the program, drop-out was usually attributed to the same health issues that prompted them to join, e.g., pain and illness. In some cases, evaluations noted that the program failed to align with patient expectations and they chose not to complete the sessions. Informants who had experience with this program identified other barriers in NL that could contribute to drop-out rates, including insufficient human resources, lack of participant readiness, and lack of social supports.

- **Provincial Prevention and Wellness Organizations and Initiatives:** Given that healthy eating and physical activity are key components of successful lifestyle interventions, maintaining and bolstering wellness and prevention efforts will be critical for T2D prevention in NL. There are a number of organizations within government that promote healthy lifestyle, including:

    - The Healthy Living Division of the Department of Seniors, Wellness and Social Development
    - The Provincial Wellness Advocacy Council,
    - The Regional Health Authorities,
    - The Regional Wellness Coalitions,

- Community agencies and NGOs (e.g., Food First NL –formerly the Food Security Network- and Recreation NL)

While not specifically targeted to the prevention of T2D or chronic disease management, the following initiatives focus on healthy eating and physical activity as components of a healthy lifestyle:

- the Provincial Wellness Plan (2006),
- the Provincial Healthy Aging Policy Framework (2007),
- the Recreation and Sports Strategy (2007), and
- the Poverty Reduction Strategy (2006).

The 2014 Provincial Health and Wellness Review Report

The Newfoundland and Labrador Center for Health Information (NLCHI) outlines recent health promotion and prevention efforts undertaken in the province in *The Provincial Health and Wellness Review Report (2014).* A comprehensive list of health promotion projects/initiatives submitted by the regions for the fiscal year 2013/2014 can be found in the report's appendix. The report highlights a number of successful initiatives for healthy living:

- School Health Liaison Consultants,
- Regional Wellness Coalitions,
- Family Resource Centers and Healthy Baby Clubs,
- The development of nutrition tool kits,
- Provincial Wellness Grants,
- The Eat Great and Participate initiative (77).

Our informants and NLCHI also identify challenges with the current provincial approach to health promotion and wellness:

- Leadership for physical activity,
- Prioritization across government,
- Resource coordination, and
- Evaluation (77).

Program coordination and consistency in setting priorities were also highlighted as particular challenges for wellness promotion initiatives at the provincial level. While the province sets wellness policies, the actual wellness programs are implemented either by the Regional Health Authorities or by individual organizations. Programs may be implemented differently in each region and are not necessarily coordinated among the RHAs.

- **Promoting Physical Activity:** Physical activity has been said to have "received variable programmatic attention across the health authorities" (76). RecNLs *Find Your Fit!* is one strategy our informants pointed out that involves a physical activity campaign to encourage an

active lifestyle by having municipal leaders and community ambassadors help promote physical activity and recreation in the province's communities. In our contextualization interviews, we learned that RecNL is also working to address the programming gap for adults by working with professors at Memorial University's School of Human Kinetics and Recreation to develop programs and training for adult fitness.

- **Promoting Healthy Eating:** Numerous efforts are underway to improve healthy eating in the province and a wealth of information has been gathered on which aspects of these campaigns could be augmented. The following improvements will enhance existing strategies:
    - The *Provincial Wellness Advisory Council Activity Plan* (2014) suggested that *an integrated and collaborative approach, which preserves and promotes health and prevents and controls disease, is needed to: reduce the incidence of many of the illnesses that currently contribute to the burden of illness in Newfoundland and Labrador; and prepare the health system for illnesses and threats to health that are expected to emerge as society and the physical environment change* (78).
    - In 2014, the Healthy Living Division of the Department of Health and Community Services, in partnership with other health stakeholders, developed a Healthy Eating Promotion Plan to raise awareness of healthy eating resources and programs and to strengthen partnerships that will increase access to healthy food (79). An inventory of healthy eating programs/initiatives has been created to help facilitate discussion on best approaches. Our key informants noted the following as ways to improve provincial healthy eating strategies:

        - promoting physical and economic access to nutritious food;
        - increasing access to healthy choices, particularly in rural areas where transportation and price are inherently challenging;
        - increasing awareness of healthy eating by developing more partnerships;
        - promoting healthy eating and available resources by social marketing or other media sources.

        In terms of framing messages to promote a healthier diet, our key informants converged on the following ideas:

        - messages need to be simple and accessible (i.e., understandable by those with low literacy; conveying lifestyle changes that are easy to implement);
        - key messages should target specific groups in the population;
        - messages need to be supported by a culture of care that promotes healthy eating (education alone is not sufficient);

- increased public awareness and resources around sugar consumption are required;
- healthy diet campaigns should focus on the promotion of homemade meals and cooking rather than targeting specific nutrients/components of food such as fat, salt and sugar (79).

Supporting a Healthy Built Environment

There is growing recognition and support for paying attention to the health impacts of the built environment in NL, although it is a relatively new area of focus for the province. The Provincial Wellness Advisory Council (PWAC) first identified this issue in 2011. In 2012, PWAC hosted a conference called *Building Healthy Communities: Bringing Health and Wellness to the Community Planning Table* with participation from public and private sectors. An outcome of the conference was the establishment of the Building Healthy Communities Collaborative (77). Several key informants recognized the opportunities that a healthier built environment will provide to support physical activity and healthy eating at the population level. They recognized that it is important for the province to continue working with groups outside of health such as municipal planners, to ensure that various opportunities for physical activity and healthy eating are made available. Educating people regarding healthy lifestyles is not sufficient – "the built environment must promote, or at least allow for, engaging in healthy behaviors" (79).

Barriers and Program Gaps

Diabetes Data: Our key informants pointed out the importance of access to reliable data upon which to make informed decisions about diabetes prevention and management programs. The current data gap could be addressed by implementing a system that would identify a wide range of diabetes indicators. This would include data on more than just T2D diagnosis. Suggested data variables that would improve the ability to prevent and manage T2D would include:

- data about risk factors such as:
  - diet and physical activity information
  - measured data on body weight, height, and blood pressure
  - other anthropometric measures for NL, for example, waist circumference,
- data about pre-diabetic cases,
- data about the frequency of testing,
- data that identifies diagnosed cases of T2D,
- surveillance data to follow patient progress,
- data that identifies complications over time, and
- diabetes care results.

Mindful of the need for better data, Western Health is piloting a Diabetes Registry that uses clinical data from the Meditech lab module that stores results of all clinical laboratory tests conducted in hospitals or clinics. Building on the experiences of Western Health, the NL Centre for Health Information is

developing a provincial Diabetes Registry using data from the Canadian Chronic Disease Surveillance System, the interoperable Electronic Health Record and Laboratory System (iEHR/LABS) project, and the regional Meditech systems. The long-term goal is to have lab data from all regions of NL feeding into the registry.

The difficulty obtaining representative data on T2D indicators in Newfoundland and Labrador was reflected in our own analysis of local data for the economic portion of this project. One of our key informants suggested that we use the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) to obtain data because this database holds the diabetes-related indicators we hoped to analyze for a substantial cohort of NL patients. CPCSSN is a multi-disease surveillance system based on primary care electronic medical record (EMR) data of 10 practice-based research networks across Canada. These networks include family physicians and nurse practitioners who use EMRs in their practice. Participants agree to contribute to the CPCSSN database de-identified, point-of-care patient data from their practices on a quarterly basis (80). Since we were interested in local data, we submitted a request for data[14] to the Atlantic Practice Based Research Network (APBRN), in an attempt to address the likely economic effectiveness of various diabetes interventions in the NL context.

Our experience in analyzing existing CPCSSN-NL data highlighted the detrimental impact of incomplete data samples on the ability to inform T2D-related healthcare decisions. When we received the requested data, we found several fields within the CPCSSN-NL dataset that were recorded inconsistently or not recorded at all. Missing data included:

- key values for body weight,
- low-density lipoprotein (LDL),
- high-density lipoprotein (HDL),
- systolic blood pressure/ diastolic blood pressure (SBP/DBP),
- glycated haemoglobin (HbA1c) values,
- fasting blood sugar (FBS) values, and
- total cholesterol (TC) values.

The ability to make projections about diabetes incidence in an effort to create diabetes prevention and management programs or initiatives is contingent on representative, up-to-date, quality data. Our experience in preparing this report highlighted the following key issues about the data required to make confident, representative projections. At minimum, the following barriers must be addressed:

1. **Data quality**: No matter which type of database or system is used to store patient information, ensuring quality data is imperative. Healthcare providers collect and record the point-of-care

[14] To gain access to CPCSSN-NL data we were required to submit an ethics application to the Primary Healthcare Research Unit. This Unit approves use of the local APBRN data. We were required to revise the variables we originally requested because we were advised that NL has a low number of providers in the database and that the possibility of provider identification was quite high. This meant that we were not able to gain access to a number of variables we first requested (i.e. provider number, date of birth and sex). In turn, this precluded access to some other variables like billing information that would have been linked to providers. Ultimately this limited what our Health Economist could say about the total cost of T2D to the system in NL.

data that is needed to inform decisions on where best to direct resources and programming/policy efforts. If this information is not entered consistently, key indicators may be missing or inconsistently recorded. Physician buy-in for any data collection system is crucial to obtaining complete point-of-care patient data. Decision-makers should note that, even for a database like CPCSSN, which has physician buy-in, there are still challenges in maintaining complete, representative data. In recognition of this issue, the Newfoundland and Labrador Medical Association (NLMA) is funding a project to improve the quality of CPCSSN data. Data completeness is one of several dimensions that help to provide useful data. Other dimensions include uniqueness, timeliness, validity, accuracy, and consistency (81).

2. **Collection of key indicators**: Other challenges arise when collecting diabetes-related indicators in NL. For example, data for blood pressure is often entered as text in the progress note of a medical chart (which is not accessible) rather than being entered into the blood pressure field of the chart (where it would be accessible). BMI is another important indicator for T2D risk. The problem with recording information on BMI is that *height* is rarely measured. CPCSSN is also working on ways to provide these data through patient self-reporting in the waiting room.

3. **Electronic Medical Record**: Another barrier to a comprehensiveness of NL data is the development of the Electronic Medical Record (EMR) for the whole province. Although Eastern Health and Western Health have developed laboratory interfaces for EMRs, Central Health has not yet worked with EMR vendors to develop a lab interface. Without a lab interface between physicians with EMRs and the relevant labs in Central Health, it will be difficult to obtain provincially-representative laboratory data.

Our CHRSP informants suggested one potential solution for the current data gap, which would be to use the existing CPCSSN infrastructure as the foundation for a province-wide database of primary care activities. The CPCSSN database provides a valuable resource for the kind of point-of-care data needed to inform decisions related to T2D. CPCSSN has recognized a number of key issues involved with data collection and input and is taking steps to improve these issues. Building a new database from scratch would delay the process by years and would potentially lack family physician buy-in that CPCSSN has already secured. The CPCSSN database is shared with NLCHI guaranteeing its availability to government through standard NLCHI procedure. Rather than building a new dedicated database for diabetes, our informant suggested that the province could consider building on the decade of work that has already gone into the CPCSSN database and take it to the next level. However, in order for CPCSSN to be representative at the provincial level, the base of participating physician would have to be increased.

Alternatively, another of our CHRSP informants pointed out that a diabetes/chronic disease registry is currently being developed, which will draw on laboratory data from all regions of the province, and that this may be a more efficient means of filling the data gap. It was further suggested that the number of physicians using EMRs (required for CPCSSN) will not increase until the province advances its EMR solution; at which point, this new data will feed into the EHR and the new diabetes/chronic disease registry. However, in order for this registry to effect prevention efforts for T2D, it will require buy-in at

the family physician level to capture key point-of-care level patient data, not indicated by laboratory data (e.g. body weight and height for BMI calculations, waist circumference).

Targeted Prevention Programing for Adults at Risk of T2D: As noted previously, the provincial government has adopted a broad approach to health and wellness promotion at the population level through its chronic disease prevention and management framework. Lacking within this framework are specific programs that target T2D prevention in adults. Existing programs for adults tend to address the management of existing T2D rather than prevention. Our subject expert suggested that it may be more effective to target risk factors for T2D early on, *before people become overweight or pre-diabetic*. A targeted approach may have a greater impact than a high-risk prevention approach alone.

Issues of Access: For diet and exercise programs or healthy lifestyle initiatives to be successful in NL, our contextualization interviews revealed three crucial issues of access that require support:

- the need for physical and economic access to healthy foods;
- the need for greater access to opportunities for utilitarian physical activity, safe space, equipment, and physical activity or recreation programs; and
- the need for access to allied health professionals outside the hospital setting to support healthy lifestyle initiatives and programs.

In addition to results from our own consultations, the report from the 2014-2015 Premier's Summit on Healthcare recommended improved access to physical activity in the community through more community services and supports. A suggested solution was to have more subsidization of recreation and physical activity to make programs more affordable (82).

Awareness and Understanding: T2D prevention will require increased awareness and understanding of one's health status, combined with understanding how to adopt healthier behaviors. The Premier's Summit on Healthcare identified a lack of awareness of services and supports as an issue with direct impact on population health (82). A lack of awareness is also at issue for the programs and services aimed at the diabetes prevention. Greater promotion of programs like *Improving Health: My Way*, or other services relating to T2D prevention or healthy lifestyle offered in the community could help improve lifestyle behaviors in NL. At the Premier's Summit, the development of a community health directory was suggested as a way to address this problem. If the population is unaware of the risks for T2D and if people do not recognize the role of unhealthy lifestyle behaviors in increasing diabetes risk, it is unlikely that people will seek appropriate support or adopt lifestyle changes to prevent developing the disease. This disconnect between awareness and action was reflected in the feedback we received from our key informants; it is further borne out in the overall poor population health indicators in Newfoundland and Labrador.

Additionally, the provision of accurate diabetes information through public media in the province is an important way to guard against misinformation about diabetes and negative stereotyping of people with

the disease or about the behaviors associated with developing the disease. Misinformation can result in discrimination against those with diabetes and a poor understanding of the complications associated with the disease (83).

Economic Factors

Based on our sample NL CPCSSN data, our health economist was unable to estimate the cost of T2D for the province. Ethics considerations about linking certain variables to physician encounters prevented access to the data required to make such projections. Instead, we obtained some idea of the economic burden of T2D from a model that was developed by the Canadian Diabetes Association.

While the economic literature reviewed in this report focused mainly on direct costs, indirect costs for T2D are particularly high (according to the CDA projections). In 2009, the NL Diabetes cost model created by the Centre for Spatial Economics projected that the total cost of diabetes in NL will reach $322 million by 2020 (3). Of this total amount, $260 million in indirect costs made up the largest portion (e.g., mortality and disability costs) while $62 million was attributed to direct costs (e.g., hospitalization).

Making a healthier lifestyle economically accessible in NL is a great challenge. It is clear that prevention efforts for T2D, whether through programming or promotion of healthy lifestyle, will be constrained by the available infrastructure as well as recruitment and retention costs to employ necessary health professionals to oversee such initiatives.

In the most recent budget, the government set out to directly support healthy living in the province in a number of ways:

- $5.9 million for community-based organizations and agencies which deliver programs and services to encourage healthy living.
- $1.84 million for programs and projects focused on recreation, physical activity and wellness.
- Over $1 million to support initiatives dedicated to encouraging healthy living and increased physical activity in school-aged children.
- Approximately $500,000 for programs which focus on healthy eating, physical activity, and mental health promotion.
- $350,000 to support new and expanded programs and services to help people quit smoking.
- $300,000 for age-friendly transportation services.
- $100,000 to support continued development of age-friendly communities throughout Newfoundland and Labrador.
- Funding for recreation and sport development initiatives for persons with disabilities (84,85).

Considerations for Decision Makers

The considerations listed below are based on the synthesis findings as refracted through the professional perspectives gathered from the clinicians, administrators, and decision makers on the project team concerning the NL context. Given the nature of our methodology and the limitations of the evidence available for our synthesis, we cannot firmly endorse any particular programs, services, or interventions. Instead, readers should regard the following as considerations that decision makers may wish to bear in mind as they contemplate the local relevance and applicability of the research-based evidence synthesized in the first part of this report to the implementation of policies and programs.

1. At this time, there is insufficient high-quality evidence on the clinical benefits and potential harms of screening for T2D. The limited evidence that is available shows no evidence of improved mortality through screening for T2D in the general population or in high-risk populations after 10 years follow-up.

2. The clinical and cost-effectiveness evidence examined in our synthesis converged most strongly around the effectiveness of lifestyle interventions for the prevention T2D in adults. The biggest challenge is that adherence to lifestyle changes can fluctuate widely. Despite this challenge, success of lifestyle interventions for T2D prevention can be enhanced in a variety of ways, including: the use of clearly defined goals and objectives, sufficient resources, and adequate supports for participants.

3. Currently, no specific provincial programs in NL target the prevention of T2D. Despite provincial health and wellness promotion and the province's Chronic Disease Framework, T2D rates are still on the rise. This situation might be improved by a provincial T2D prevention strategy with a more comprehensive focus on risk factors for developing diabetes in adults. A strategy that includes the appropriate implementation of initiatives that result in improved diet, increased physical activity, and prevention/reduction of excess body weight could help lower T2D levels in NL, as well as supporting the prevention of other chronic diseases.

4. The level of T2D risk in the NL adult population is affected by a combination of non-modifiable and modifiable factors. An important component to the success of future initiatives to lower incidence of T2D in the province will be a careful consideration of how modifiable and non-modifiable characteristics are distributed in the population and which types of programs and initiatives appropriately match these characteristics. In particular, the province has an opportunity to develop prevention programs and initiatives that will target modifiable risk factors to help curb risk and progression to pre-diabetes or T2D.

5. T2D risk pervades the province; however, some risk factors are more significant in certain adult populations/age groups. A reliable and comprehensive collection of data on diabetes and diabetes

risk- factor indicators will be required to guide the development of appropriate programs/prevention efforts in different areas of the province and for different population groups. Through access to reliable data, decision makers and community groups can more effectively direct resources and evaluate prevention and management outcomes. The minimum data set required for this purpose would include: anthropometric measures (body weight and height for BMI calculations, waist circumference), low-density lipoprotein (LDL), high-density lipoprotein (HDL), systolic blood pressure/ diastolic blood pressure (SBP/DBP), glycated haemoglobin (HbA1c) values, fasting blood sugar (FBS) values and total cholesterol (TC) values.

6. Health literacy in particular, and literacy levels in general will affect the uptake of T2D prevention messages in the province. A concerted effort should be made to ensure that all T2D prevention information is available in formats that are accessible to all people in the province, regardless of their literacy levels.

7. Physical and economic access to infrastructure, programming, professional expertise, and healthy foods are major challenges in Newfoundland and Labrador, particularly for those who live in rural areas. Investment in these areas will be important in helping adults in the province make and maintain required lifestyle changes to lower T2D risk.

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