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Qualité des services de santé Ontario

# Frequency of Testing for Dyslipidemia: A Systematic Review and Budget Impact Analysis

THETA

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# Abstract

## Background

Current Canadian guidelines recommend annual screening for hyperlipidemia in people with a Framingham risk score (FRS) of greater than 5%. In those with a FRS of less than 5%, lipid screening is recommended every 3 to 5 years.

## Objectives

We aimed to determine the most cost-effective frequency of lipid profile testing in adults with different levels of cardiovascular risk based on published literature, to determine current frequency of lipid screening in Ontario, and to calculate the cost of aligning current with recommended frequencies.

## Methods

We systematically searched for studies (from 2000 to 2012) evaluating the cost-effectiveness of lipid profile testing frequency in adults. Using the Canadian Community Health Survey and linked health administrative databases, we calculated the FRS for each survey respondent on every day from 2005 to 2011. Average current frequency of lipid testing was calculated according to the total number of patient days spent in each FRS category and the number of lipid tests occurring on those days. Extrapolating these outcomes to the Ontario population, we estimated the expected budget impact of aligning current rates of lipid testing with rates recommended by the Canadian Cardiovascular Society (CCS) guidelines.

## Results

No studies evaluated the cost-effectiveness of lipid monitoring frequency. Our database analysis revealed that people in the very low risk group are tested an average of once every 4.4 years, those in the low risk group are tested once every 2 years, those in the intermediate risk group are tested every 1.4 years, and those in the highest risk group are tested annually. If we compare these rates to those recommended by the CCS guidelines, an additional 3.6 million tests would be needed to achieve recommended rates of lipid testing. At a cost of $14.48 per test, the expected cost to the province would be $52.2 million.

## Limitations

The results were analysed in aggregate, leading to the potential for ecological fallacy. In addition, because data pertaining to drug prescriptions in Ontario are only available for people over 65 years of age, the analysis did not account for the influence of statin treatment on the frequency of lipid testing.

## Conclusions

Our findings show that there is currently no evidence to inform the optimal frequency of lipid testing. People in Ontario at low-low, low, intermediate, and high risk are being tested once every 4.4, 1.9, 1.4, and 1.0 times per year, respectively. According to the CCS guidelines, this represents under-testing in the low and intermediate groups. Achieving the recommended rates of testing would cost approximately $52.2 million. Given the large cost of implementing such a change and the uncertainty on which CCS guidelines are based, it would be prudent to await the results of further research before making such a large investment.

# Plain Language Summary

We conducted a systematic search for studies that attempted to identify the most cost-effective frequency of lipid profile testing in adults. None were found. In the absence of alternative evidence, the Ontario Health Technology Assessment Committee recommended testing according to the Canadian Cardiovascular Society (CCS) guidelines. These guidelines recommend annual monitoring of lipid levels in those with an annual risk of cardiovascular events greater than 5%. In those with a risk of less than 5%, testing is recommended every 3 to 5 years. We then conducted an analysis using Ontario administrative databases and the Canadian Community Health Survey to estimate the current frequency of lipid testing in Ontario. The results show that people in Ontario at very low, low, intermediate, and high risk are being tested once every 4.4, 1.9, 1.4, and 1.0 times per year, respectively. We estimated that it would cost approximately $52.2 million to increase province-wide rates of lipid testing to levels recommended by CCS guidelines. Given the lack of evidence supporting the CCS guidelines and the large cost of implementation, we think it prudent to await the results of further research before implementing this strategy.

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# List of Abbreviations

| | |
|---|---|
| **CCHS** | Canadian Community Health Survey |
| **CHD** | Coronary heart disease |
| **CI** | Confidence interval(s) |
| **CVD** | Cardiovascular disease |
| **FRS** | Framingham Risk Score |
| **HDL** | High-density lipoprotein |
| **HQO** | Health Quality Ontario |
| **HTA** | Health Technology Assessment |
| **ICES** | Institute for Clinical and Evaluative Sciences |
| **IHD** | Ischemic heart disease |
| **LDL** | Low-density lipoprotein |
| **OHTAC** | Ontario Health Technology Advisory Committee |
| **THETA** | Toronto Health Economics and Technology Assessment |

# Background

The Toronto Health Economics and Technology Assessment (THETA) Collaborative was commissioned by Health Quality Ontario to evaluate the cost-effectiveness and predict the long-term costs and effects of techniques for disease treatment. Published economic evaluations are reviewed, and the structure and inputs of the economic model used to estimate cost-effectiveness are summarized. The results of the economic analyses are presented for technique versus comparator, and the budget impact of implementing each intervention is estimated.

Health Quality Ontario conducts full evidence-based analyses, including economic analyses, of health technologies being considered for use in Ontario. These analyses are then presented to the Ontario Health Technology Advisory Committee, whose mandate it is to examine proposed health technologies in the context of available evidence and existing clinical practice, and to provide advice and recommendations to Ontario health care practitioners, the broader health care system, and the Ontario Ministry of Health and Long-Term Care.

**DISCLAIMER:** Health Quality Ontario uses a standardized costing method for its economic analyses. The main cost categories and associated methods of retrieval from the province's perspective are described below.

**Hospital costs**: Ontario Case Costing Initiative cost data are used for in-hospital stay, emergency department visit, and day procedure costs for the designated International Classification of Diseases diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may be required to reflect accuracy in the estimated costs of the diagnoses and procedures under consideration. Due to difficulties in estimating indirect costs in hospitals associated with a particular diagnosis or procedure, Health Quality Ontario normally defaults to a consideration of direct treatment costs only.

**Non-hospital costs**: These include physician services costs obtained from the Ontario Schedule of Physician Benefits, laboratory fees from the Ontario Schedule of Laboratory Fees, drug costs from the Ontario Drug Benefit Formulary, and device costs from the perspective of local health care institutions whenever possible, or from the device manufacturer.

**Discounting**: For cost-effectiveness analyses, a discount rate of 5% is applied (to both costs and effects/QALYs), as recommended by economic guidelines.

**Downstream costs**: All reported downstream costs are based on assumptions of population trends (i.e., incidence, prevalence, and mortality rates), time horizon, resource utilization, patient compliance, health care patterns, market trends (i.e., rates of intervention uptake or trends in current programs in place in the province), and estimates of funding and prices. These may or may not be realized by the Ontario health care system or individual institutions and are often based on evidence from the medical literature, standard listing references, and educated hypotheses from expert panels. In cases where a deviation from this standard is used, an explanation is offered as to the reasons, the assumptions, and the revised approach.

The economic analysis represents ***an estimate only***, based on the assumptions and costing methods explicitly stated above. These estimates will change if different assumptions and costing methods are applied to the analysis.

**NOTE: Numbers may be rounded to the nearest decimal point, as they may be reported from an Excel spreadsheet.**

# Introduction

Cholesterol is an essential lipid for normal cell function. However, high levels of total cholesterol (TC) and of low-density lipoprotein (LDL), and low levels of high-density lipoprotein (HDL) are associated with an increased risk of coronary heart disease (CHD) and cardiovascular disease (CVD). Together, these diseases are the leading causes of death and disability worldwide.

There is a direct relationship between lipid levels and cardiovascular events. In addition, there is robust evidence that reduced lipid levels are associated with a reduction in cardiovascular events and mortality. Since their introduction in 1987, 'statins' (3-hydroxy-3-methylglutaryl coenzyme A, HMG-CoA, reductase inhibitors) have proven to be highly efficacious in reducing lipid levels. Contemporary

guidelines (1-3) describe thresholds for the initiation of pharmacologic therapy; these thresholds are based on underlying cardiovascular risk.

Lipid measurement is essential for calculating an individual's risk of CHD and thereby determining when to initiate therapy. Canadian treatment guidelines (1) suggest the use of the Framingham risk score (FRS) to ascertain underlying cardiovascular risk. The FRS predicts the 10-year risk of developing cardiovascular disease based on age, sex, presence of dyslipidemia, hypertension, diabetes, and smoking status. These guidelines recommend annual monitoring of lipid levels in those with a FRS of greater than 5%. In those under 5%, testing is recommended every 3 to 5 years.

The purpose of this analysis was to systematically review the literature surrounding optimal rates of lipid testing. We also aimed to determine whether current lipid testing in Ontario meets best practice and the expected investment or disinvestment needed to achieving best practice across the province.

## Expert Panel

In August, 2012, an Expert Advisory Panel on Appropriate Use of Lipid Measurements was convened. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representation from the community laboratories. The role of the panel was to contextualize the evidence produced by THETA and HQO and provide advice on the appropriate use of lipid measurements within the Ontario health care setting. However, the views expressed in this report represent that of HQO and not necessarily those of the Expert Advisory Panel members.

# Economic Literature Review

## Objective

To determine the most effective and cost-effective frequency of lipid profile testing in adults with different levels of cardiovascular risk.

## Methods

### Literature Search

#### *Search Strategy*

An economic literature search was performed using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EconLit for studies published from January 1, 2000 to November 29, 2012. See Appendix 1 for detailed search strategies. Abstracts were reviewed by a single reviewer. Potentially relevant full-text articles were retrieved and evaluated against the following inclusion/exclusion criteria. Reference lists were also examined for any additional relevant studies not identified through the search.

### Inclusion Criteria

- English-language full-text publications.
- Published between January 1, 2000, and November 29, 2012.
- Cost-utility analyses were prioritised for inclusion. If cost-utility studies were not available, cost-effectiveness, and cost-benefit and cost-consequence analyses were considered. Costing studies were considered in the absence of all other types of economic analyses.
- Studies comparing different intervals of lipid monitoring (TG, HDL, and LDL testing) in people with varying cardiovascular risk profiles and/or taking or not taking lipid lowering therapy.

### Exclusion Criteria

- Abstracts, posters, reviews, letters/editorials, and unpublished studies.

## Results

A total of 394 abstracts were reviewed and 12 full papers were retrieved. None included relevant populations, comparators, or outcomes.

# Economic Evaluation

Due to limitations in time and resources, an original economic model was not developed. However, a health technology assessment (HTA) is currently in progress at the University of Oxford, entitled "Optimal strategies for monitoring lipid levels in patients at risk or with cardiovascular disease: best marker for monitoring and cost-effectiveness of different monitoring frequencies."

This research will consist of a systematic review, individual patient data analysis, and a cost-effectiveness model. The objectives of this project are: to identify the relative ability of different lipid measures (single or combination) to detect important changes in lipid status, to estimate the incremental gains and costs of different strategies (lipid measurements and intervals) for risk assessment and monitoring of lipid levels in patients at risk of or with cardiovascular disease, to develop and populate an economic model of lipid monitoring, and to explore how the choice of lipid measure impacts on risk assessment of CVD compared with original risk scores. The interim results of this work were presented on September 18, 2013, with an estimated publication date of early 2015. Further details are available at: http://www.hta.ac.uk/project/2616.asp. It was agreed by the expert panel that attempting to produce a similar body of work would represent an inefficient use of HQO resources.

# Budget Impact Analysis

A budget impact analysis was conducted from the perspective of the Ontario Ministry of Health and Long-Term Care to determine current patterns of lipids testing in Ontario adults and the impact to the Ontario health budget that would be expected to result from the implementation of the Canadian Cardiovascular Society guidelines. All costs were reported in 2013 Canadian dollars.

## Objectives

The objectives of this analysis were:

- to determine the current frequency of lipid profile testing in Ontario
- to determine the expected budget impact of aligning current lipid screening practices in Ontario with rates recommended by the Canadian Cardiovascular Society guidelines

## Methods

### A: Determining current frequency of lipid screening

#### *Data Sources*

Data were acquired from the 2005 Canadian Community Health Survey (CCHS) and linked databases housed as the Institute for Clinical and Evaluative Sciences (ICES). ICES is an independent non-profit research organisation that acts as a large repository for annually updated, de-identified, individual-level health administrative data. Disease-based cohorts can be created using health administrative case definitions that link hospital inpatient and outpatient care, physician claims, and drug benefits data over time.

#### *Data Analysis Plan*

A data analysis plan was developed a priori in consultation with analysts at ICES. The proposal was reviewed by analytical experts at THETA and approved by the expert panel.

#### *Design Selection and Limitations*

A cohort study was selected as the most appropriate design to address the aims of the research question. In a cohort study, groups of patients are followed over time to measure rates of outcome(s) of interest.

#### *Cohort Definition*

All adult Ontario residents who completed the CCHS in 2005 were included in the initial cohort. Individuals were then excluded if they were aged 18 years or younger, if they had been diagnosed with ischemic heart disease (IHD) within the past 3 years, or if they were ineligible for OHIP coverage during this time period. See Appendix 2 for the list of administrative codes to determine diagnoses and comorbidities.

From this cohort, all males aged 40 or more years and all females aged 50 or more years were included. Of younger patients, those with any of the following conditions were included: diabetes, hypertension, obesity (defined as BMI > 27 kg/m$^2$), inflammatory disease, chronic renal disease, human immunodeficiency virus, hyperlipidemia, chronic obstructive pulmonary disease, or were current smokers. Ex ante, erectile dysfunction was excluded due to lack of a validated database code. See Appendix 2 for a detailed description of the databases and definitions used to identify each characteristic.

### *Cardiovascular Risk*

A modified FRS was calculated for each patient at baseline according to age, sex, the presence of dyslipidemia, hypertension, or diabetes, and smoking status. The scoring system used to calculate FRS was based on that reported by Patel et al. (4) This system differs from that reported by the Framingham Heart Study (5) in that rather than calculating a score based on cholesterol and blood pressure (which were not available in our databases), a score of 1 or 0 was assigned based on the presence or absence of dyslipidemia or hypertension. For patients under 30 or over 74 years of age (who are outside the bounds of the FRS), we used the scoring system for 30 year olds and 74 year olds, respectively.

Patients were grouped into four mutually exclusive FRS categories of low-low (< 1% to 5%), low (6% to 9%), intermediate (10% to 19%), and high (≥ 20%) cardiovascular risk according to baseline characteristics. Over the course of the observation period, the FRS was recalculated for each patient upon the happening of any of the following events: birthday; entry into diabetes or hypertension databases; change in lipid count or smoking status (if not present at baseline). Because smoking status and the presence of hyperlipidemia were not available at yearly intervals for all patients, it was assumed that patient status at baseline did not change over the course the observation period for these characteristics.

Therefore, patients were eligible to transition to a category of greater risk according to changes in age, diabetes status, hypertension, lipid count, or smoking status. It was assumed that patients did not decrease in risk over time. The time that each patient spent in each FRS group and the number of lipid profiles received during the time spent in each category was calculated.

### *Event of Interest*

The event of interest was the number of lipid profile tests received by each patient over the period of observation. A complete lipids profile was defined based on OHIP laboratory codes for total cholesterol (L055), high density lipoprotein (L117), and triglyceride (L243), all billed on the same day.

### *Outcome of Interest*

The outcome of interest was defined as the frequency of lipid profile testing per patient day for low-low (< 1% to 5% FRS), low (6% to 9% FRS), intermediate (10% to 19% FRS), and high (≥ 20% FRS) cardiovascular risk. The crude rate of lipid profile testing for each FRS risk category was determined by dividing the total number of lipid tests for each category by the total number of patient days in each group. To evaluate temporal trends, rates of lipid testing in each risk category were also calculated by fiscal year. We then compared the differences between actual rates for lipid testing in each risk strata and the rates recommended by the Canadian Cardiovascular Society Guidelines.

## B: Budget Impact

In this section, we first estimated the current number of people in Ontario who are eligible for primary prevention and the proportion within this population who are at low, intermediate, and high risk of cardiovascular disease according to the FRS. We extrapolated the difference in actual and recommended rates of lipid testing determined in Section A to the Ontario population level. To estimate potential budget impact, costs were determined as outlined below.

### *Costs*

The cost of a lipid profile was based on reimbursement prices listed in the Ontario Schedule of Benefits for Laboratory Services. Multiplying individual LMS units (L055, L117, and L243) by $0.517 resulted in a total cost of $14.48 per lipid profile.

### *Ethical Approval*

Confidentiality agreements and privacy impact assessment forms were completed and approved by ICES.

# Results

## A: Lipid frequency

A total of 33,402 people in Ontario completed the CCHS in 2005. After excluding people aged 18 or fewer years (3,665), those who were ineligible for OHIP at the CCHS completion date (78), individuals with IHD (2,984), and males under 40 years or age and females under 50 years of age with none of the qualifying conditions listed above (5,643), a total of 21,032 people who completed the CCHS in 2005 were eligible for primary prevention. The large majority of these people (79%) were low to low-low risk according to the FRS. Obesity was the most common cohort characteristic, followed by smoking and hypertension. Descriptive characteristics for each FRS group are presented in Table 1.

Table 2 shows that patients in the low-low and high FRS categories are currently being tested in accordance with the recommendations of the Canadian Cardiovascular Society guidelines. However, to achieve the target rate, patients in the low group would need to double the number of lipid tests they receive and those in the intermediate group would need to increase the number of lipid tests by 42%. The confidence intervals within each group are tight and rates were remarkably consistent over time.

## B: Budget Impact

In 2012, the Ontario population aged 18 or more years was 10,627,344 (6). Assuming that CCHS respondents are representative of the general population, the primary prevention population makes up approximately 63% of these people. Applying our observed distributions of cardiovascular risk, we calculated the expected number of people in each FRS category across the province (Table 3). We then multiply the number of people in each FRS category by the difference between observed and target testing rates to determine the number of additional tests that would result from implementation of OHTAC recommendations (Table 3). Multiplying the number of additional tests (3.6 million) by the average cost per test ($14.48) results in an expected budget impact of $52.2 million (95% CI, $50.7 million to $53.8 million).

**Table 1: Characteristics of Primary Prevention Cohort at Baseline by Framingham Risk Score**

| Variable | Value | Framingham Risk Score | | | | |
|---|---|---|---|---|---|---|
| | | < 1% to 5% | 6% to 9% | 10% to 19% | ≥ 20% | Total |
| | | n = 7,933 | n = 8,678 | n = 3,553 | n = 868 | N = 21,032 |
| Age | Mean ± SD | 34.85 ± 8.36 | 59.61 ± 11.24 | 67.33 ± 9.20 | 71.36 ± 7.50 | 52.06 ± 16.88 |
| | Median (IQR) | 35 (28-42) | 58 (52-66) | 67 (61-74) | 71 (66-76) | 52 (40-64) |
| Sex | F | 3,823 (48.2%) | 5,640 (65.0%) | 1,180 (33.2%) | 248 (28.6%) | 10,891 (51.8%) |
| | M | 4,110 (51.8%) | 3,038 (35.0%) | 2,373 (66.8%) | 620 (71.4%) | 10,141 (48.2%) |
| BMI > 27 kg/m$^2$ | | 4,251 (53.6%) | 3,392 (39.1%) | 1,544 (43.5%) | 442 (50.9%) | 9,629 (45.8%) |
| Current smoker | | 3,547 (44.7%) | 1,676 (19.3%) | 1,135 (31.9%) | 341 (39.3%) | 6,699 (31.9%) |
| Hypertension | | 722 (9.1%) | 3,073 (35.4%) | 2,010 (56.6%) | 652 (75.1%) | 6,457 (30.7%) |
| Inflammatory disease | | 288 (3.6%) | 384 (4.4%) | 154 (4.3%) | 32 (3.7%) | 858 (4.1%) |
| Diabetes | | 169 (2.1%) | 188 (2.2%) | 836 (23.5%) | 718 (82.7%) | 1,911 (9.1%) |
| Chronic renal disease | | 27 (0.3%) | 56 (0.6%) | 56 (1.6%) | 32 (3.7%) | 171 (0.8%) |
| COPD | | 22 (0.3%) | 250 (2.9%) | 265 (7.5%) | 108 (12.4%) | 645 (3.1%) |
| HIV | | 10 (0.1%) | ≤ 5 | ≤ 5 | ≤ 5 | // |
| Hyperlipidemia | | 9 (0.1%) | 63 (0.7%) | 217 (6.1%) | 387 (44.6%) | 676 (3.2%) |

**Table 2: Total Average Number of Years per Lipid Test**

| Framingham Risk Category | Average number of years per lipid test | | |
|---|---|---|---|
| | Mean | LCL | UCL |
| Low – low (< 1% to 5%) | 4.44 | 4.35 | 4.52 |
| Low (6% to 9%) | 1.99 | 1.97 | 2.02 |
| Intermediate (10% to 19%) | 1.42 | 1.40 | 1.44 |
| High (≥ 20%) | 0.98 | 0.96 | 1.01 |

Abbreviations: LCL, lower confidence level; UCL, upper confidence level.

**Table 3: Number of Tests and Cost Required to Achieve Recommended Rates of Lipid Testing**

| Framingham Risk Score | Number of people in Ontario* | Tests needed to achieve target rate Mean (95% CI) | Cost |
|---|---|---|---|
| Low – low (< 1% to 5%) | 2,835,078 | At target | $0 |
| Low (6% to 9%) | 3,101,325 | 3,076,613 (3,003,645 to 3,151,346) | $44,537,048 ($43,480,767 to $45,618,885) |
| Intermediate (10% to 19%) | 1,269,763 | 533,878 (508,617 to 562,507) | $7,728,415 ($7, 362,735 to $8,142,851) |
| High (≥ 20%) | 310,204 | -5,748 (-12,789 to 1,559) | -$83,729 (-$185,131 to $22,565) |
| Total | 7,516,370 | 3,604,707 (3,499,473 to 3,715,412) | $52,181,734 ($50,658,371 to $53,784,302) |

*Estimated based on 2012 Ontario adult population (6), assuming representativeness of CCHS respondents

# Conclusions

Canadian guidelines recommend testing lipid levels once every 3 to 5 years in people with a FRS of < 5%. Our results show that patients in this category are currently tested in accordance with the guideline, with an average rate of one test every 4.44 years (95% CI, 4.35-4.53). The guidelines recommend annual testing for those with a FRS of > 5%.

Based on our results, only patients in the highest FRS category (≥ 20%) meet these criteria with an average rate of one test every 0.98 years (95% CI, 0.96-1.01). Those in the low and intermediate categories receive an average of one test every 1.99 years (95% CI, 1.97-2.02) and every 1.42 years (95% CI, 1.40-1.44), respectively.

Across the province, an additional 3.6 million (95% CI, 3.5 million to 3.7 million) tests would be needed to meet recommended rates of lipid testing according to the CCS guidelines. At a cost of $14.48 per test, the expected budget impact to the province would be $52.2 million (95% CI, $50.7 million to $53.8 million).

The CCS guidelines are not based on evidence of effectiveness or cost-effectiveness of different rates of lipid testing. The recommended rates from which the budget impact is derived appear to be based primarily on expert opinion informed by a meta-analysis of the effectiveness of lowering LDL levels on cardiovascular outcomes (7). Given that an analysis designed to answer this question is currently underway at the University of Oxford, it may be prudent to await further information.

# Acknowledgements


**Editorial Staff**
Timothy Maguire

**Medical Information Services**
Corinne Holubowich, BEd, MLIS
Kellee Kaulback, BA(H), MISt

**ICES Analysts**
Lauren Webster, MPH
Andrew Calzavara, MSc

**Expert Advisory Panel Members**

| Name | Title | Organization | Location |
|---|---|---|---|
| **Panel Chair** | | | |
| Dr Eric A. Cohen | Deputy Head, Division of Cardiology<br>Associate Professor,<br>Department of Medicine | Sunnybrook Health Sciences Centre<br>University of Toronto | Toronto |
| **Panel Members** | | | |
| Dr Alykhan Abdulla | Medical Director<br>Vice President<br>Assistant Professor,<br>Faculty of Medicine | The Kingsway Health Centre<br>Academy of Medicine of Ottawa<br>University of Ottawa | Ottawa |
| Dr Milan Gupta | Division of Cardiology | McMaster University | Brampton |
| Dr Robert Hegele | Scientist<br>Distinguished University Professor | Robarts Research Institute<br>University of Western Ontario | London |
| Dr Ruth McPherson | Professor of Medicine,<br>Division of Cardiology | University of Ottawa Heart Institute | Ottawa |
| Dr Joel Goodman | Vice-President, Strategies and Innovation | Gamma-Dynacare Medical Laboratories | Brampton |
| Margaret Jin | Clinical Pharmacist,<br>Pharmacy Department | Hamilton Family Health Team | Hamilton |
| Debbie Kwan | Pharmacist, Toronto Western Family Health Team | University Health Network | Toronto |
| Eric Lui | Clinical Pharmacist | North York Family Health Team | North York |
| **Ministry of Health** | | | |
| Dr Garry Salisbury | Senior Medical Consultant | Ministry of Health and Long-Term Care | Kingston |
| Ms Laurie Sweeting | Senior Program Consultant, Diagnostic Services and Planning Branch | Ministry of Health and Long-Term Care | Toronto |

# Appendices

## Appendix 1: Literature Search Strategies

**Search date:** November 30, 2012
**Databases searched:** OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; CRD
**Limits:** 2000-current; English; Humans
**Filters**: Economic

Database: Ovid MEDLINE(R) 1946 to November Week 3 2012, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations November 29, 2012, Embase 1980 to 2012 Week 47
Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | exp Dyslipidemias/ use mesz | 60193 |
| 2 | exp Lipids/ use mesz | 875707 |
| 3 | *Dyslipidemia/ use emez | 6318 |
| 4 | exp *Hyperlipidemia/ use emez | 40897 |
| 5 | *Abnormally High Substrate Concentration in Blood/ use emez | 133 |
| 6 | exp *Hyperlipoproteinemia/ use emez | 4220 |
| 7 | (hyperlipemia? or hyper-lipemia? or hyperlipaemia? or hyper-lipaemia? or lipemia? or lipaemia? or hyperlipidemia? or hyper-lipidemia? or hyperlipidaemia? or hyper-lipidaemia? or lipidemia? or lipidaemia? or dyslipidemia? or dyslipidaemia? or dyslipoproteinemia? or dyslipoproteinaemia?).ti,ab. | 87727 |
| 8 | (hypercholesterolaemia? or hyper-cholesterolaemia? or hypercholesteremia? or hyper-cholesteremia? or hypercholesterolemia? or hyper-cholesterolemia? or hypercholesterolaemia? or hyper-cholesterolaemia? or hypercholesterinaemia? or hyper-cholesterinaemia? or hypercholesterinemia? or hyper-cholesterinemia? or cholesteremia? or cholesterinemia? or cholesterolemia?).ti,ab. | 50998 |
| 9 | (((high* or elevat* or raise*) adj5 cholesterol*) or high- cholesterol* or highcholesterol*).ti,ab. | 95653 |
| 10 | lipid disorder?.ti. | 734 |
| 11 | or/1-10 | 1060760 |
| 12 | exp Mass Screening/ use mesz | 94040 |
| 13 | mass screening/ use emez | 46521 |
| 14 | rescreening/ use emez | 95 |
| 15 | screen*.ti. | 232629 |
| 16 | (re-screen* or rescreen*).ti,ab. | 2220 |
| 17 | ((optimal or appropriate* or reasses* or re-assess* or frequen*) adj3 (interval* or screen*)).ti,ab. | 19438 |
| 18 | ((interval* or optimal) adj3 monitor*).ti,ab. | 3179 |
| 19 | *Time Factors/ use mesz | 1088 |

| | | |
|---|---|---|
| 20 | Unnecessary Procedures/ use mesz | 2898 |
| 21 | unnecessary procedure/ use emez | 1636 |
| 22 | or/12-21 | 332731 |
| 23 | 11 and 22 | 6751 |
| 24 | limit 23 to english language | 5902 |
| 25 | Animals/ use mesz | 5096326 |
| 26 | animal/ use emez | 1802180 |
| 27 | or/25-26 | 6898506 |
| 28 | 24 not 27 | 5435 |
| 29 | limit 28 to yr="2000 -Current" | 3060 |
| 30 | remove duplicates from 29 | 2374 |
| 31 | exp Economics/ or exp Models, Economic/ or exp Resource Allocation/ or exp "Value of Life"/ or exp "Quality of Life"/ use mesz | 1020848 |
| 32 | exp "Health Care Cost"/ or exp Health Economics/ or exp Resource Management/ or exp Economic Aspect/ or exp Economics/ or exp Quality Adjusted Life Year/ or exp Socioeconomics/ or exp Statistical Model/ or exp "Quality of Life"/ use emez | 1966688 |
| 33 | (econom* or cost* or budget* or pharmacoeconomic* or pharmaco-economic* or valu*).ti. | 489537 |
| 34 | ((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay").ti,ab. | 195723 |
| 35 | ec.fs. | 3422189 |
| 36 | 30 and 35 | 385 |

**Cochrane Library**

| ID | Search | Hits |
|---|---|---|
| #1 | MeSH descriptor: [Dyslipidemias] explode all trees | 4517 |
| #2 | MeSH descriptor: [Lipids] explode all trees | 30386 |
| #3 | (hyperlipemia? or hyper-lipemia? or hyperlipaemia? or hyper-lipaemia? or lipemia? or lipaemia? or hyperlipidemia? or hyper-lipidemia? or hyperlipidaemia? or hyper-lipidaemia? or lipidemia? or lipidaemia? or dyslipidemia? or dyslipidaemia? or dyslipoproteinemia? or dyslipoproteinaemia?):ti,ab,kw (Word variations have been searched) | 1616 |
| #4 | (hypercholesterolaemia? or hyper-cholesterolaemia? or hypercholesteremia? or hyper-cholesteremia? or hypercholesterolemia? or hyper-cholesterolemia? or hypercholesterolaemia? or hyper-cholesterolaemia? or hypercholesterinaemia? or hyper-cholesterinaemia? or hypercholesterinemia? | 5 |

| | | |
|---|---|---|
| | or hyper-cholesterinemia? or cholesteremia? or cholesterinemia? or cholesterolemia?):ti,ab,kw (Word variations have been searched) | |
| #5 | (((high* or elevat* or raise*) near/5 cholesterol*) or high- cholesterol* or highcholesterol*):ti,ab,kw (Word variations have been searched) | 8754 |
| #6 | lipid disorder?:ti,ab,kw (Word variations have been searched) | 399 |
| #7 | #1 or #2 or #3 or #4 or#5 or #6 | 31496 |
| #8 | MeSH descriptor: [Mass Screening] explode all trees | 4249 |
| #9 | screen*:ti | 5233 |
| #10 | (re-screen* or rescreen*):ti,ab,kw (Word variations have been searched) | 81 |
| #11 | ((optimal or appropriate* or reasses* or re-assess* or frequen*) near/3 (interval* or screen*)):ti,ab,kw (Word variations have been searched) | 569 |
| #12 | ((interval* or optimal) near/3 monitor*):ti,ab,kw (Word variations have been searched) | 140 |
| #13 | MeSH descriptor: [Unnecessary Procedures] explode all trees | 80 |
| #14 | #8 or #9 or #10 or #11 or #12 or #13 | 7355 |
| #15 | #7 and #14 from 2000 to 2012 | 107 |
| #16 | (econom* or cost* or budget* or pharmacoeconomic* or pharmaco-economic* or valu*) .ti. | 2954 |
| #17 | ((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay") .ti,ab. | 1370 |
| #18 | MeSH descriptor: [Economics] explode all trees | 19979 |
| #19 | MeSH descriptor: [Models, Economic] explode all trees | 1457 |
| #20 | MeSH descriptor: [Resource Allocation] explode all trees | 114 |
| #21 | MeSH descriptor: [Value of Life] explode all trees | 141 |
| #22 | MeSH descriptor: [Quality of Life] explode all trees | 12081 |
| #23 | #16 or #17 or #18 or #19 or #20 or #21 or #22 | 33236 |
| #24 | #15 and #23 | 25 |

**CRD**

| | | |
|---|---|---|
| 1 | MeSH DESCRIPTOR dyslipidemias EXPLODE ALL TREES | 272 |
| 2 | MeSH DESCRIPTOR lipids EXPLODE ALL TREES | 1021 |
| 3 | ((hyperlipemia? or hyper-lipemia? or hyperlipaemia? or hyper-lipaemia? or lipemia? or lipaemia? or hyperlipidemia? or hyper-lipidemia? or hyperlipidaemia? or hyper-lipidaemia? or | 40 |

| | | |
|---|---|---|
| | lipidemia? or lipidaemia? or dyslipidemia? or dyslipidaemia? or dyslipoproteinemia? or dyslipoproteinaemia?)):TI | |
| 4 | ((hypercholesterolaemia? or hyper-cholesterolaemia? or hypercholesteremia? or hyper-cholesteremia? or hypercholesterolemia? or hyper-cholesterolemia? or hypercholesterolaemia? or hyper-cholesterolaemia? or hypercholesterinaemia? or hyper-cholesterinaemia? or hypercholesterinemia? or hyper-cholesterinemia? or cholesteremia? or cholesterinemia? or cholesterolemia?)):TI | 65 |
| 5 | ((((high* or elevat* or raise*) adj5 cholesterol*) or high- cholesterol* or highcholesterol*)):TI | 5 |
| 6 | (lipid disorder?):TI | 0 |
| 7 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 | 1172 |
| 8 | MeSH DESCRIPTOR mass screening EXPLODE ALL TREES | 1820 |
| 9 | (screen*):TI | 2002 |
| 10 | ((re-screen* or rescreen*)):TI | 6 |
| 11 | (((optimal or appropriate* or reasses* or re-assess* or frequen*) adj3 (interval* or screen*))):TI | 5 |
| 12 | (((interval* or optimal) adj3 monitor*)):TI | 4 |
| 13 | MeSH DESCRIPTOR unnecessary procedures EXPLODE ALL TREES | 16 |
| 14 | #8 OR #9 OR #10 OR #11 OR #12 OR #13 | 2392 |
| 15 | #7 AND #14 | 49 |
| 16 | (#15):TI# FROM 2000 TO 2012 | 36 |
| 17 | ((econom* or cost* or budget* or pharmacoeconomic* or pharmaco-economic* or valu*)):TI | 11541 |
| 18 | (((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay") ) | 1593 |
| 19 | MeSH DESCRIPTOR economics EXPLODE ALL TREES | 13202 |
| 20 | MeSH DESCRIPTOR Models, Economic EXPLODE ALL TREES | 1328 |
| 21 | MeSH DESCRIPTOR Resource Allocation EXPLODE ALL TREES | 73 |
| 22 | MeSH DESCRIPTOR Value of Life EXPLODE ALL TREES | 116 |
| 23 | MeSH DESCRIPTOR quality of life EXPLODE ALL TREES | 1662 |
| 24 | #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 | 15205 |
| 25 | #16 AND #24 | 21 |

# Appendix 2: Patient Characteristic Databases & Definitions

| | |
|---|---|
| **Accrual Start/End Dates** | limited to the CCHS 2005 cycle, assumed to be in fiscal year 2005 |
| **Max Follow-up Date** | Start observation on the date the 2005 CCHS is completed (according to question ANC_Q01), end March 31st 2012 |
| **When does observation window terminate?** | March 31st 2012 |
| **Lookback Window(s)** | Three years |

- Sex – Determined according to the RPDB:
  - Male = 1
  - Female = 0

- Current smokers – Smoking status was determined from the CCHS ('at the present time, do you smoke cigarettes daily, occasionally or not at all?'). For each patient (in 2005), smoking status was reported a dichotomous outcome:
  - 'yes' = 1 if patients answered '1' or '2' to question SMKE_Q202
  - 'no' = 0 if patients answered '3' to question SMKE_Q202

- Diabetes – Diabetes status was determined by checking the Ontario Diabetes Database. For each patient (in 2005), the presence of diabetes was reported as a dichotomous outcome:
  - 'Yes' = 1 if the patient is found within the Ontario Diabetes Database (see Table 1).
  - 'No' = 0 if the patient is not found within the Ontario Diabetes Database

- Hypertension – Hypertension status was determined by checking the Ontario Hypertension Database. For each patient (in 2005), a diagnosis of hypertension was reported as a dichotomous outcome:
  - 'Yes' = 1 if the patient is found within the Ontario Hypertension Database (see Table 1)
  - 'No' = 0 if the patient is not found within the Ontario Hypertension Database

- BMI – BMI was determined from the height and weight reported in the 2005 CCHS.
  - For each patient, self-reported height in cm (MHW_N6B) and weight in Kg (MHW_N2A) was reported
  - BMI was calculated according to the following formula:

$$\text{BMI} = \frac{\text{mass in kg}}{(\text{height in meters})^2}$$

  - Individuals were dichotomized according to whether they have a BMI of over 27kg/m$^2$
    - 'Yes' = If the patient has a BMI of > 27kg/m$^2$
    - 'No' = If the patient has a BMI of ≤ 27kg/m$^2$

- Hyperlipidemia – The presence of hyperlipidemia was determined according to whether patients report taking prescription medications for blood cholesterol in the 2 to 5 CCHS. For each patient, the presence of hyperlipidemia was reported as a dichotomous outcome:

- 'Yes' = 1 if patients answered '1' to question DIA_Q11
- 'No' = 0 if the patients answered '2' to question DIA_Q11

- Inflammatory disease – Inflammatory diseases specifically mentioned by the CCS guideline for screening include systemic lupus erythematosis, rheumatoid arthritis, and psoriasis. We used a lookback window of three years. For each patient, the presence of any one of these diseases as was reported as a dichotomous outcome:
  - 'Yes' = 1 if the patient has a diagnosis of systemic lupus according to OHIP diagnostic code 695 or CIHI DAD M32.1, M32.8, M32.9; has rheumatoid arthritis according to OHIP diagnostic code 714 or CIHI DAD M06.9; has a diagnosis of psoriasis according to OHIP diagnostic code 696 or CICI DAD M07.0 to M07.3.
  - 'No' = 0 if the patient does not have any of these diagnoses.

- Chronic renal diseases – CRD was determined based on OHIP diagnostic codes and CIHI database. Use a lookback window of three years. For each patient, report the presence of chronic renal disease as a dichotomous outcome:
  - 'Yes' = 1 if the patient has an OHIP diagnostic code of 580, 581, 584, or 585
  - 'Yes' = 1 if the patient has an ICD-10 code of I12.0; I13.1; N03.2-N03.7; N05.2-N05.7; N18; N19; N25.0; Z49.0-Z49.2 Z94.0; or Z99.2.
  - 'No' = 0 if the patient does not have one of these OHIP or CIHI diagnostic codes.

- HIV positive – HIV status was determined by checking the Ontario HIV Database. For each patient, the presence of HIV was reported as a dichotomous outcome:
  - 'Yes' = 1 if the patient is found within the Ontario HIV Database (see Table 1).
  - 'No' = 0 if the patient is not found within the Ontario HIV Database

- Chronic obstructive pulmonary disease – The presence of COPD was determined by checking the Ontario COPD Database (according to the more specific but less sensitive definition). For each patient, the presence of COPD was recorded as a dichotomous outcome:
  - 'Yes' = 1 if the patient is found within the Ontario COPD database (see Table 1)
  - 'No' = 0 if the patient is not found within the Ontario COPD Database

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Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: EvidenceInfo@hqontario.ca
www.hqontario.ca

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