Canada's Drug and Health Technology Agency

Choosing Wisely Canada™

Advisory Panel Guidance on Minimum Retesting Intervals for Lab Tests

About the Panel Members

An independent time-limited advisory panel of 7 core and 7 specialist members developed recommendations on minimum retesting intervals for lab tests.

The 7 core panel members were recruited from across Canada and brought together expertise in laboratory medicine, family practice, and patient lived experience. The core panel helped draft and develop consensus-based recommendations.

The 7 specialist panel members brought expertise in endocrinology, cardiology, pediatric cardiology, rheumatology, hematology oncology, gastroenterology, and general internal medicine and participated in developing consensus-based recommendations for the tests that corresponded to their clinical area.

The names and biographies of the 14 panelists are on the CADTH website. Declarations of conflicts of interest can be found in Appendix 3.

Core Panel Members

Dr. Daniel Beriault, PhD, FCACB
Head of Biochemistry, Department of Laboratory Medicine, Unity Health Toronto; Associate Professor at University of Toronto
Ontario

Dr. Manal Elnenaei, MBChB, Ph.D, FRCPath, EuSpLM
Head of the Medical Biochemistry Division, Department of Pathology and Laboratory Medicine, Nova Scotia Health Authority; Professor at Dalhousie University
Nova Scotia

Dr. Rosilene Kraft, MBC, MSc, Ph.D., P.Eng.
Patient Partner
British Columbia

Dr. Janet Simons, FRCPC Internal Medicine, FRCPC Medical Biochemistry
Medical Biochemist and Internist, Providence Health Care; Assistant Clinical Professor, University of British Columbia
British Columbia

Dr. Alexander Singer, MB BAO BCh. CCFP, FCFP
Family Physician, Associate Professor, Clinician-Teacher and Director of Research and Quality Improvement, Department of Family Medicine, University of Manitoba
Manitoba

Dr. Li Wang, MD, MSc, FRCPC
Medical Biochemist, BC Children's and Women's Hospital and Health Centre; Clinical Associate Professor, University of British Columbia
British Columbia

Dr. Yan Yu, MD, MPP, MBA, CCFP
Family Physician
Alberta and Northwest Territories

Specialist Panel Members

Dr. Natalia Calo, MD
Therapeutic Endoscopist, St. Michael's Hospital Division of Gastroenterology; Assistant Professor of Medicine at the University of Toronto
Ontario

Dr. Matthew Cheung, SM, MD, FRCP(C)
Clinician-Investigator and Clinical Hematologist, Odette Cancer Centre/Sunnybrook Health Sciences Centre; Professor, University of Toronto
Ontario

Dr. Nowell Fine, MD, SM, FRCPC, FACC, FCCS, FASE, FHFSA
Heart Failure Cardiologist and Echocardiologist and Associate Clinical Professor, University of Calgary
Alberta

Dr. Michael Khoury, MD
Pediatric Cardiologist and Assistant Professor at the Stollery Children’s Hospital, University of Alberta
Alberta

Dr. Ferhan Siddiqi, MD FRCPC MScHQ
Endocrinologist, Queen Elizabeth II Health Sciences Centre; Associate Professor, Dalhousie University; Chair, Canadian Society of Endocrinology and Metabolism Quality Improvement Committee
Nova Scotia

Dr. William Silverstein, MD
General Internist, Sunnybrook Health Sciences Centre; Chair of the Canadian Society of Internal Medicine’s Choosing Wisely Committee; Assistant Professor, University of Toronto
Ontario

Dr. Carter Thorne, MD, FRCPC, FACP, MACR
Consultant Staff Rheumatologist, Southlake Regional Health; Assistant Professor, University of Toronto
Ontario

In Partnership

Choosing Wisely Canada is the national voice for reducing unnecessary tests and treatments in Canada. Using Labs Wisely is a national consortium of over 150 hospitals committed to making a measurable impact on reducing low-value lab testing in Canada.

CADTH is a not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH and Choosing Wisely Canada have partnered to host the Advisory Panel on Minimum Retesting Intervals for Lab Tests in support of Using Labs Wisely.

Acknowledgements

We wish to thank the following patient groups for their time and insights on the impact of the frequency of testing for patients: Arthritis Consumer Experts (ACE) Joint Health; Canadian Arthritis Patient Alliance; Cassie and Friends Society for the Children with Juvenile Arthritis; Diabetes Canada; Gastrointestinal (GI) Society; JDRF Canada; Lupus Canada; Myeloma Canada; Pulmonary Hypertension Association Canada; Thyroid Foundation of Canada; and Thyroid Patients Canada.

We are grateful to the panel members who shared their time and expertise to develop these recommendations to support reducing unnecessary lab testing thereby contributing to the quality of health care services.

We also wish to thank Dr. Doug Helmersen and Dr. Jason Weatherald for generously sharing their clinical expertise with the advisory panel on BNP and NT-proBNP retesting for pulmonary arterial hypertension.

Table of Contents

Key Messages

What Is the Issue?

- Lab test overuse can contribute to further unnecessary follow-up and testing, negative patient experiences, potentially inappropriate treatments, and the inefficient use of health care resources. One review of lab testing in Canada found that around 22% of blood tests were likely unnecessary.
- One strategy to address lab test overuse is to establish minimal retesting intervals that suggest the minimum time before a test should be repeated based on the biochemical properties of the test and the clinical situation in which it is used.
- The importance of lab resource stewardship is being addressed by Choosing Wisely Canada through Using Labs Wisely, a consortium of more than 150 hospitals committed to driving the appropriate use of lab testing in Canada. Hospitals participating in Using Labs Wisely identified a need for guidance on the minimum retesting intervals for commonly used lab tests.

What Did We Do?

- Choosing Wisely Canada and CADTH partnered to convene an independent time-limited advisory panel to develop consensus-based recommendations for minimum retesting intervals for 7 commonly used lab tests (ANA, BNP and NT-proBNP, HbA1c, lipase, lipid panel, SPEP and TSH) in prespecified patient populations.
- The advisory panel included core and specialist members who were recruited from across Canada. The 7 core advisory panel members brought together expertise in laboratory medicine, family practice, and patient lived experience. Seven specialist members brought expertise in endocrinology, cardiology, pediatric cardiology, rheumatology, hematology oncology, gastroenterology, and general internal medicine.
- The Advisory Panel on Minimum Retesting Intervals considered patient group input, evidence from focused literature reviews, equity considerations, and clinical expertise. Through facilitated discussion, they reached consensus on the recommendations for minimum retesting intervals for 7 lab tests.

What Is the Potential Impact?

- The recommendations on minimum retesting intervals can support hospitals participating in Choosing Wisely Canada's Using Labs Wisely campaign in their effort to reduce unnecessary lab tests and their impact on patients, providers, health systems, and the environment.

- The recommendations may also be relevant to community and hospital lab stewardship efforts and may address overuse of the 7 included lab tests by supporting changes in lab test ordering in both in and outpatient settings.

Setting the Context

Overuse of Laboratory Tests

Laboratory testing is a critical component of effective patient care, providing health care professionals and patients with important information to make decisions regarding the diagnosis, treatment, and management of many diseases.[1] Lab testing is a high-volume medical activity in Canada, and it is estimated that over $5 billion is spent annually on laboratory testing by the provincial and territorial governments.[1]

Inappropriate lab testing can occur when tests are underused, misused, or overused.[1,2] Lab test overuse – which is the focus of Choosing Wisely Canada's (CWC) Using Labs Wisely campaign – can occur in situations where they are not indicated, where there is a potential that patient harm exceeds the possible benefit, or where the test results are unlikely to inform the course of treatment or management of conditions (e.g., test results may not reflect a clinically meaningful change).[2] Other practices that can substantially contribute to the overuse of lab tests include repeat ordering of the same tests on the same patient prior to the indicated test interval or unnecessary duplicate testing (i.e., when a test is ordered even if there is valid result on file).[2] A 2022 systematic review on inappropriately used clinical practices in Canada reported that approximately 22% of blood tests met the criteria for overuse (i.e., the potential of harms exceeded the potential benefits).[2] Lab test overuse can contribute to further unnecessary follow-up and testing, negative patient experiences, inaccurate diagnoses, potentially inappropriate treatments, and the inefficient use of health care resources.[1-3]

What are Minimum Retesting Intervals?

One strategy to help reduce lab test overuse is to establish minimum retesting intervals for appropriate use of lab tests. Minimum retesting intervals are meant to support clinical decisions around ordering and processing lab tests by specifying the minimum time before a test should be repeated, based on the biochemical properties of the test and the clinical situation in which it is used.[4] They can help identify and manage lab test requests that are potentially inappropriate (i.e., if a test is ordered within a time frame that would not provide clinically meaningful information), reduce patient harm due to unnecessary testing and treatment, and enable the creation of automated rules in laboratory information systems.

Minimum retesting intervals:

- Suggest a minimum time before a test should be repeated for specific clinical scenarios,
- Specify that a test would be not performed or should not be ordered within a set number of days, weeks, or months of a previous test.

Minimum retesting intervals are not recommendations on **testing frequency**, which is a suggested time frame for patient monitoring to support overall health (e.g., to assess therapeutic response or safety). In many cases, testing frequency will be longer than minimum retesting intervals. Minimum retesting intervals are also not recommendations on the clinical scenarios or indications in which the tests should be used.

Rationale and Objectives for the Guidance

CWC, a national campaign focused on tests and treatments, is reducing unnecessary lab testing through Using Labs Wisely.[5] Using Labs Wisely is a consortium of more than 150 hospitals committed to making a measurable impact on reducing low-value lab testing in Canada so that lab resources can be used more appropriately, and reduce the impact of unnecessary lab testing on patients, providers, health system, and the environment.[6]

Hospitals participating in Using Labs Wisely identified a need for guidance on the minimum retesting intervals for 7 commonly repeated lab tests. CWC surveyed a small sample of hospitals participating in Using Labs Wisely and identified heterogeneity in the retesting intervals for these lab tests.

In partnership with CWC, CADTH convened a time-limited advisory panel to support hospitals by developing guidance on minimum retesting intervals for 7 lab tests used in prespecified patient populations or clinical scenarios. These tests are:

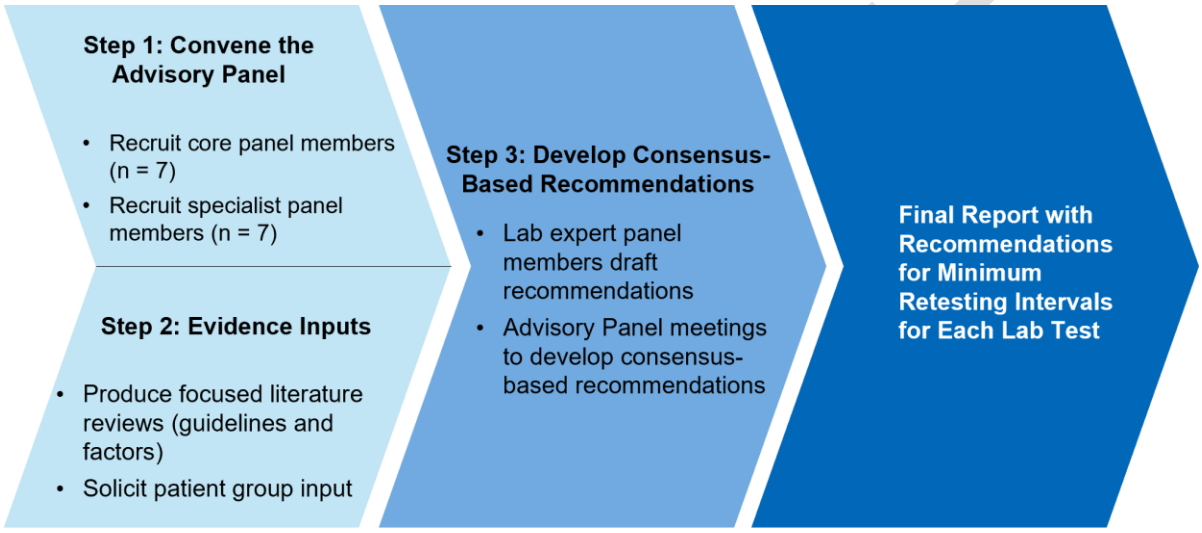
- Antinuclear antibody (ANA)
- B-type natriuretic peptide (BNP) and N-terminal pro b-type natriuretic peptide (NT-proBNP)
- Hemoglobin A1c (HbA1c)
- Lipase
- Lipid panel
- Serum protein electrophoresis (SPEP)
- Thyroid stimulating hormone (TSH)

This report includes a summary of the advisory panel discussions, the recommendations for minimum retesting intervals, and implementation advice. Appendix 1 presents the recommendations and implementation advice for all tests.

Developing the Guidance

An overview of the approach used to develop consensus-based recommendations and the guidance report is provided in Figure 1. Appendix 2 presents a detailed description of the approach we used to develop this guidance.

Figure 1. Overview of the approach used to develop the guidance



Step 1. Advisory Panel

CADTH and CWC co-convened an independent time-limited advisory panel that included specialists with expertise in clinical areas covered by each test to develop recommendations for retesting and implementation advice. The core advisory panel was comprised of 4 lab experts, one of whom was the CWC Using Labs Wisely clinical lead, 2 family doctors, and a patient member. For each test, the core advisory panel was joined by 1 or 2 specialist panel members who brought relevant clinical expertise that related to each test (i.e., endocrinology, cardiology, rheumatology, hematology oncology, gastroenterology, general internal medicine). Table 1 in Appendix 2 identifies the specialist panel members who participated in developing guidance for each test.

Step 2. Evidence Inputs

CADTH solicited input from patient groups who represent people with the prespecified main condition(s) who could receive repeat testing with the lab tests of interest. We produced focused

literature reviews for each test[7] and summarized existing guidance and evidence on factors that may impact the minimum retesting interval, including equity considerations.

Step 3. Developing Consensus-based Recommendations

The advisory panel developed consensus-based guidance on minimum retesting intervals for lab tests through a series of synchronous and asynchronous approaches.

First, the 4 lab experts independently prepared preliminary recommendations for each test. They met once (virtually) and through facilitated discussion developed a single consolidated draft recommendation for each test to be used as a starting point for the advisory panel discussions.

Next, the advisory panel composed of the core advisory panel and applicable specialists met virtually for a 1 hour facilitated structured discussion of each lab test where they generated consensus-based guidance (i.e., recommendations and implementation advice). Each discussion included considerations of the focused literature reviews, patient group input, equity considerations, and the expertise of the attending specialists to inform revision of the draft recommendations.

At the end of the discussion for each test, the advisory panel voted on accepting the recommendations as revised. The panel's recommendations were consistent with or reflected the input of patients in a majority of situations. Where they may not have been perfectly aligned it was generally because patient input was more detailed and specific than could have been incorporated into a recommendation on minimum retesting intervals. Consensus (i.e., 70% agreement or higher) was reached on the recommendations for 7 lab tests. All advisory panel members expressed agreement with the revised recommendations with the exception of lipid panels where there were dissenting opinions.

For BNP and NT-proBNP for pulmonary arterial hypertension, the advisory panel requested that the CADTH team gather additional clinical expertise prior to voting. The CADTH team, a CWC team member and the CWC Using Labs Wisely clinician lead met with 2 respirology experts to gather their clinical opinion on BNP and NT-proBNP retesting in patients with pulmonary arterial hypertension. We provided background information including a summary of the panel's discussion, patient group input, and the focused literature review in advance. After a half hour virtual consultation, we revised the recommendations for BNP and NT-proBNP for pulmonary arterial hypertension. We then circulated the revised recommendations to the advisory panel members for an electronic vote and reached consensus.

Advisory Panel Guidance

General Guidance for Implementing the Recommendations

To support the adoption of minimum retesting interval recommendations, the panel developed specific implementation advice for several included tests with the intent of providing practical advice for labs, including suggested timing for hard stops. The panel recognized the need to balance the recommendations with the workflow of the labs. For example, during their discussions they raised how different timings of hard stops would likely affect the number of override requests, which could in turn impact their effectiveness at reducing unnecessary retesting.

While recognizing that implementation will need to be tailored to the local context (e.g., care landscape, populations cared for, lab information systems), the panel developed general guidance for recommendations:

- For minimum retesting intervals to be applied effectively and for unnecessary repeat testing to be avoided, previous test results must be easily accessible for requesting physicians.
- While the recommendations cannot account for all clinical scenarios, they were designed by the panel to apply to most cases for populations covered by the recommendations. Clinicians should always be able to discuss their test order with a lab professional if they feel repeat or more frequent testing is clinically appropriate, or if there are issues with a previous test result (e.g., interference, unexpected test results for the clinical context, missing result).
- When a lab test order is automatically rejected because an order is requested within the minimum retesting interval, the requesting physician should be notified that their test was not completed, and the existing test result should be provided to them.
- When implementing these minimum retesting interval recommendations, in addition to considering local context, laboratory specialists can also explore options such as:
    - Opportunities for education can be embedded within lab information systems to support the uptake of recommendations for minimum retesting intervals and help change ordering behaviors. These can include education on what the minimum retesting interval is, reasons why a test does not need to be reordered or why it is rejected and can be included in orders and lab reports as comments or prompts, depending on the laboratory information system. For standard test panels, there

can be educational prompts that direct the ordering of individual tests as opposed to the full panel.

- Rules and algorithm suggestions for laboratory information systems: Options for implementing recommendations can, depending on the laboratory information system, include developing logic rules that account for previous test results. Labs can also consider promoting minimum retesting intervals for repeat tests based on specific levels of care, settings, or providers.

Advisory Panel Recommendations for Lab Tests

ANA

About the Test

Antinuclear antibodies (ANAs) are autoantibodies that bind to cellular components in the nucleus of cells and mediate autoimmune diseases.[8,9] The ANA test measures the quantity (i.e., the titer) and the staining pattern of the antibodies.[9] ANA testing is commonly used in the diagnosis of systemic autoimmune diseases such as systemic lupus erythematosus, systemic sclerosis, Sjogren's disease, and other rheumatic diseases.[9]

Recommendations

The clinical scenario in scope for the guidance is using ANA to monitor patients with suspected or confirmed systemic autoimmune disease. The recommendations specific to ANA are in Box 1.

Box 1. Recommendations on Repeat ANA Testing

1. If a previous ANA test is positive, do not reorder ANA for monitoring patients with suspected or confirmed systemic autoimmune disease.

   Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 5 year hard stop minimum retesting interval.

2. If a previous ANA test is negative or borderline positive, do not reorder ANA for monitoring patients with suspected or confirmed systemic autoimmune disease.

   An exception to this recommendation is if the clinical status of the patient significantly changes with newly developed symptoms, in which case ANA may be retested.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 24 month hard stop minimum retesting interval.

Developing the Guidance

The advisory panel for ANA was composed of the 7 core panel members plus a rheumatologist. They considered evidence from the ANA literature review,[7] and patient input from the Canadian Arthritis Patient Alliance, Cassie and Friends Society, Lupus Canada, and Arthritis Consumer Experts.

Key Discussion Points

Panel members discussed the following points when developing their recommendations:

- The panel discussed the clinical guidance from the literature review that supported not repeating ANA following a previously positive test result in patients with suspected or confirmed systemic autoimmune disease. They also discussed guidance from the literature review that it is only with a change in symptoms that a patient whose previous ANA test result is negative or borderline positive would warrant repeat ANA testing.
- The panel noted the importance of the titer (e.g., 1:160, 1:40) being provided alongside positive or borderline positive test results so that the results can be considered in conjunction with the patient's symptoms to help guide clinical decisions.
- Patient experiences with ANA testing were discussed, including instances where patients have newly developed symptoms following a borderline titer or test result, and the need for retesting in these situations.
- The panel discussed how more frequent testing may be warranted in pregnant patients and pediatric patients with newly developed symptoms due to heightened potential risk to the pregnant patient, the developing fetus, or the pediatric patient. The panel discussed that separate retesting intervals were not required for these populations, as the exception of retesting following newly developed symptoms applies to these populations.
- There was alignment between patient group input and the panel's concerns around equity concerns related to the impact of repeat testing on those who experience barriers to accessing care. Patient group input raised the issue of equity in terms of the impact and burden of repeat testing on patients. The panel recognized that increasing the intervals between tests or removing the need to repeat previously positive results, and thus reducing unnecessary testing and follow-up appointments, could benefit patients who

experience barriers to accessing care, such as those living in rural and remote locations or those without access to a rheumatologist or primary care provider.

- The panel reflected on the value of reducing unnecessary repeat testing for ANA, and that recommendations against reordering ANA tests in patients with suspected or confirmed autoimmune disease could contribute to reducing the time rheumatologists spend delivering low-value care and potentially increase their capacity to better serve equity-deserving populations or underserved populations.

BNP and NT-proBNP

About the Test

The hormone BNP and the inactive peptide NT-proBNP are quantitative biomarkers for cardiac stress and heart failure[10-12] and are routinely used for diagnosis and prognostication in cardiac abnormalities.[10-13] They are exclusively produced by cardiac tissue, and are primarily released from the ventricles in the heart in response to wall stress due to increased ventricular blood volumes and pressure.[11,12]

Recommendations

The clinical scenario in scope for the guidance is using BNP or NT-proBNP to monitor patients who are being treated for congestive heart failure or pulmonary arterial hypertension. The recommendations specific to BNP and NT-proBNP are in Box 2.

Box 2. Recommendations on Repeat BNP and NT-proBNP Testing

Congestive heart failure
3. Do not reorder BNP or NT-proBNP for monitoring adult patients aged 18 and older with an established diagnosis of congestive heart failure in inpatient settings. An exception to this recommendation is if the patient is being discharged. Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a hard stop minimum retesting interval of 72 hours, or no more than 2 tests in 14 days.
4. The recommended minimum retesting interval for BNP and NT-proBNP for adult patients aged 18 and older with an established diagnosis of congestive heart failure in outpatient settings is 6 months.

Pulmonary arterial hypertension
5. The recommended minimum retesting interval for BNP and NT-proBNP for monitoring adult patients aged 18 and older with established pulmonary arterial hypertension in outpatient settings is 1 month. Exceptions to this recommendation are cases with acute clinical deterioration.
6. The recommended minimum retesting interval for BNP and NT-proBNP for monitoring adult patients aged 18 and older with an established diagnosis of pulmonary arterial hypertension in inpatient settings is 72 hours. An exception to this recommendation is if the patient is being discharged.

Developing the Guidance

The advisory panel for BNP and NT-proBNP was composed of the 7 core panel members plus a cardiologist and a pediatric cardiologist. The panel considered evidence from the focused literature review,[7] and patient input from the Pulmonary Hypertension Association of Canada. For the pulmonary arterial hypertension minimum retesting interval recommendations, the panel sought additional input from 2 clinicians with expertise in treating patients with the condition.

Key Discussion Points

In the context of congestive heart failure, the panel members discussed the following when developing the recommendations:

- The panel acknowledged that there is limited evidence on the use of BNP and NT-proBNP for monitoring patients with congestive heart failure and that existing guidance is conflicting, and that both these points were reflected in the literature review.
- In inpatient settings, the panel recognized the value of BNP and NT-proBNP testing at admission to establish a diagnosis of congestive heart failure, but experts discussed that there is not strong evidence to support repeat or serial BNP or NT-proBNP testing to monitor patients aged 18 or older with an established diagnosis of congestive heart failure. This was supported by the literature review. The panel recognized that an exception to this is that providers may choose to measure BNP or NT-proBNP at discharge to help inform the patient's risk of adverse outcomes.
- To support the implementation of the recommendation and to help ensure sufficient time passes between tests to detect a clinically meaningful change, the panel suggested that labs may consider implementing a hard stop minimum retesting interval of 72 hours. To reduce serial BNP or NT-proBNP testing during admission and to encourage repeat BNP

or NT-proBNP testing only at discharge, the panel also suggested that labs may choose to limit inpatient BNP or NT-proBNP testing to no more than 2 tests in 14 days for adults with congestive heart failure.

- The panel discussed that there is not strong evidence for repeat BNP or NT-proBNP testing for adult patients aged 18 and older with congestive heart failure in outpatient settings. However, they recognized the need for clinical guidance that could reasonably reduce unnecessary BNP and NT-proBNP retesting in this clinical scenario. The panel agreed that a 6 month minimum retesting interval would be adequate for most cases.
- Experts discussed that heart failure presents differently in pediatric patients (e.g., growth failure), the importance of biomarkers for monitoring symptoms in children who cannot communicate the symptoms of heart failure, and that there is clinical nuance in how BNP and NT-proBNP are used in pediatric patients with heart failure (e.g., to help distinguish between weight gain from nutrition versus weight gain from fluid retention).
- The panel recognized that pediatric patients may require a shorter retesting interval, and based on the panel's experience that BNP and NT-proBNP are not overused in pediatric patients, the panel excluded pediatric patients from the minimum retesting interval recommendation.
- The panel discussed that there was no need to have separate BNP and NT-proBNP recommendations due to the similarities between BNP and NT-proBNP and developed 1 recommendation for both biomarkers. Whether BNP or NT-proBNP are measured will depend on the preferences of the institution and the capabilities of the lab.
- The panel considered that different drug therapies for heart failure have different impacts on BNP and NT-proBNP levels (e.g., angiotensin receptor-neprilysin inhibitors result in a small rise in overall BNP levels), but based on panel members' experiences, they felt that the difference was not substantial enough to warrant making that distinction in the recommendation.
    - The panel also reflected that it would be difficult and confusing to implement minimum retesting intervals for BNP or NT-proBNP based on which therapy (or therapies) for heart failure a patient is receiving.

In the context of pulmonary arterial hypertension, the panel members discussed the following points:

- Patient experiences with BNP and NT-proBNP testing were discussed, including that patients value the non-invasive way to gather clinical data. Patient group input raised the issue of the utility of BNP and NT-proBNP testing for monitoring pulmonary arterial

hypertension for those who may be limited in their ability to perform exercise function testing (e.g., older patients, those with comorbidities) or those who might have limited access to alternative tests (e.g., people living in rural or remote areas).

- The panel acknowledged the limited literature identified about retesting BNP and NT-proBNP for pulmonary arterial hypertension, and the need for further input from specialists in pulmonary arterial hypertension.
- The CADTH team and the CWC Using Labs Wisely clinician lead consulted with 2 respirologists who were specialists in caring for patients with pulmonary arterial hypertension. They described how BNP and NT-proBNP testing is one component of multiparameter risk assessments models used to monitor patients with pulmonary arterial hypertension. BNP is the least invasive and least expensive test for cardiac function as part of risk assessment in this population that is helpful for monitoring patients over time and guiding treatment decision-making. The specialists raised that European clinical guidelines (as identified in the literature review) recommend testing BNP every 3 to 6 months as part of multiparameter risk assessment for patients with pulmonary arterial hypertension, or more frequently with clinical worsening.
- The specialists consulted discussed how in Canada, BNP and NT-proBNP testing is critical for monitoring patients who live in rural settings as alternative cardiac function tests are harder to access in some communities. Care for patients with pulmonary arterial hypertension is centralized in a small number of expert centres in Canada, however many patients who are very sick and who are on complex medications (i.e., IV diuretics) are managed in the community.
- Patients with pulmonary arterial hypertension are a heterogenous group and some patients need more frequent testing. BNP and NT-proBNP testing can be used to help distinguish between other conditions (e.g., COVID-19) and deterioration of pulmonary arterial hypertension in this patient population. There are differences in the use of BNP and NT-proBNP testing in inpatient and outpatient settings, as some patients with severe pulmonary arterial hypertension who are admitted have long hospital stays (e.g., weeks or months) as they are adjusting to new complex medications (e.g., continuous IV pumps) that require frequent adjustment, monitoring, and training for their administration. The specialists noted that pre-discharge BNP and NT-proBNP testing is helpful to have a baseline.
- Given how centralized care is for this patient population, labs might implement minimum retesting intervals differently based on the local population or context and whether they care for patients with pulmonary arterial hypertension. For example, community-based hospitals that routinely refer patients with pulmonary arterial hypertension to a higher

acuity facility may decide to set the minimum retesting interval for BNP and NT-proBNP based on the guidance provided for congestive heart failure.

HbA1c

About the Test

The HbA1c test measures chronic glycemia and is useful for diagnosing diabetes and monitoring the overall effectiveness of treatment for diabetes.[14] HbA1c is relatively unaffected by acute changes in blood glucose levels, and is used to evaluate a person's overall level of glucose control over time.[14,15]

Recommendations

The clinical scenario in scope for the guidance was using HbA1c to monitor patients with an established diagnosis of type 1 or type 2 diabetes who are on either lifestyle modification, glucose lowering agents, or insulin. The recommendations specific to HbA1c are in Box 3.

Box 3. Recommendations on Repeat HbA1c Testing

7. The recommended minimum retesting intervals for HbA1c in patients who are being treated for diabetes are:
    - 3 months for patients who have not yet achieved stable glycemic targets.
    - 6 months for patients who have achieved stable glycemic control.

    Exceptions to this recommendation that may warrant more frequent testing include pediatric patients with type 1 diabetes, patients with diabetes who are planning to become pregnant, and patients with rapidly changing blood glucose levels due to significant recent changes to lifestyle and/or medications.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 60 to 86 day hard stop minimum retesting interval. This allows for practical considerations such as accommodating patient schedules for retesting appointments.

8. Do not reorder HbA1c tests for assessing glycemic control in patients with diabetes who have conditions that alter red blood cell turnover (e.g., iron deficiency anemia) or for pregnant patients with diabetes who are in their second or third trimester.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 60 to 86 day hard stop minimum retesting interval.

Developing the Guidance

The advisory panel for HbA1c was composed of the 7 core panel members and an endocrinologist. The panel considered evidence from the focused literature review,[7] and patient input from the Juvenile Diabetes Research Foundation and Diabetes Canada.

Key Discussion Points

Panel members discussed the following points when developing their recommendations:

- The panel discussed the clinical evidence from the literature review that supported a 3-month minimum retesting interval for adults who have not achieved glycemic control and are still adjusting their therapy for their diabetes, as it related to the life cycle of red blood cells. The panel also noted that the clinical guidance from the literature review supports a 6-month minimum retesting interval for patients with diabetes who have stable glycemic control.
- Patient experiences with HbA1c testing were discussed, including the frequency of testing reported by patients every 3 to 6 months. Patient group input raised the issue of some people requiring more frequent testing, such as those who are actively undergoing changes in their treatment for their diabetes.
- The panel recognized there are exceptions when more frequent HbA1c testing may be warranted, such as when a patient is experiencing rapid changes in their blood glucose due to changes in lifestyle or therapies, where retesting at 2 months would be appropriate.
- Experts also discussed the importance of good glycemic control in people who are trying to become pregnant and noted that evidence from the literature review supported more frequent monitoring of HbA1c in the preconception period.
- The panel considered whether there should be separate minimum retesting intervals for adult and pediatric patients, but to simplify implementation they opted to have general recommendations that apply to both adults and children, except for the specific populations listed.
- The panel considered equity issues, and recognized the importance of HbA1c testing for patients who are not able to access technologies to monitor more frequent changes in blood glucose (e.g., continuous glucose monitoring).
- The panel considered evidence from the literature review that there are several conditions (e.g., iron deficiency anemia, the second and third trimesters of pregnancy) that can result in invalid HbA1c test results (i.e., the HbA1c test result does not accurately reflect the

person's overall level of glycemic control) due to their impact on the rate of red blood cell turnover.

- Based on panel members' experiences, they felt that much of the overuse of repeat HbA1c tests happened at less than 2 months, so using a 2-month cut off would be effective in reducing the majority of unnecessary lab tests. This approach is also supported by the evidence in the literature review regarding the clinical properties of the test and the clinical recommendations. They discussed labs' experience with implementation, where labs could have a 60 to 86 day hard stop with exceptions. In particular, the panel wanted to enable access to HbA1c testing for those patients who have follow-up appointments scheduled before three months.

Lipase

About the test

Lipase is a digestive enzyme primarily produced in the pancreas to break down fats.[16] When the pancreas becomes damaged or swollen due to inflammation large amounts of lipase are released, and serum lipase testing can be used as part of the diagnostic criteria for acute pancreatitis.[16,17]

Recommendations

The clinical scenario in scope for the guidance was on using repeat lipase testing to monitor patients with acute or chronic pancreatitis. The recommendations specific to lipase are in Box 4.

Box 4. Recommendations on Repeat Lipase Testing

9. Do not reorder lipase tests for monitoring patients with an established diagnosis of acute pancreatitis.

10. Do not reorder lipase tests for monitoring patients with an established diagnosis of chronic pancreatitis.

    An exception to this recommendation is if there is clinical suspicion of acute-on-chronic pancreatitis, where lipase testing is required for diagnostic purposes.

Implementation advice: To support reductions in unnecessary retesting, in outpatient or community settings, labs may consider implementing a 6 month hard stop minimum retesting interval.

This recommendation is based on the experience of the advisory panel as no relevant information for serum lipase retesting for chronic pancreatitis was identified in the literature review.

Developing the Guidance

The advisory panel for lipase was composed of the 7 core panel members plus an internal medicine specialist and a gastroenterologist. The panel considered evidence from the focused literature review,[7] and patient input from the GI Society.

Key Discussion Points

Panel members discussed the following points when developing their recommendations:

- The panel discussed that the utility of lipase testing is for the diagnosis of acute pancreatitis, and that it does not have prognostic value in patients with acute or chronic pancreatitis, even if lipase levels are persistently elevated or if levels return to normal.
- In patients with an established diagnosis of acute pancreatitis, the consensus is that repeat lipase testing does not add clinical value, and that repeat testing in this population is unnecessary. Even in the presence of newly developed symptoms, the panel noted that repeat lipase testing does not add value once a diagnosis of acute pancreatitis is established. This is reflected in the literature review in the statements against repeat lipase testing and the consistent pattern of lipase levels after the onset of acute pancreatitis. Patient input also supports that lipase is important for diagnostic purposes but not for monitoring.
- Experts noted that the diagnostic criteria for acute pancreatitis include lipase levels that are 3 times the upper limit of normal and suggested that labs may consider restricting repeat lipase testing if the previous result was greater than or equal to 3 times the upper limit of normal.
- Experts discussed that the diagnosis of chronic pancreatitis is not based on lipase levels, and that lipase should not be retested in patients with a diagnosis of chronic pancreatitis as it has no prognostic value in patients with chronic pancreatitis. However, it was noted that acute episodes of pancreatitis can occur in patients with chronic pancreatitis (i.e., acute-on-chronic pancreatitis). Retesting lipase in patients with chronic pancreatitis is only relevant if the patient presents with symptoms of acute-on-chronic pancreatitis. In this case, panel members discussed that these patients may seek urgent care, where lipase can be used in the acute care setting to confirm the diagnosis.

- Based on panel members' experience, lipase can be mildly elevated for multiple conditions, including chronic pancreatitis and health conditions unrelated to the pancreas. However, there is no clinical utility of repeating lipase in these patients and the test results can lead to patient distress due to a lack of prognostic value. It was suggested that lipase should not be tested in the absence of pain suggestive of acute pancreatitis.
- Potential harms of repeating lipase testing in patients with an established pancreatitis diagnosis were discussed, including increased health care system costs with no added clinical value, and the potential for additional unnecessary tests being ordered for patients (e.g., imaging, endoscopy) due to persistently elevated lipase.
- The panel acknowledged that there are certain equity-deserving populations that may be at higher risk for pancreatitis (e.g., people with alcohol use disorders), but that the same guidance regarding retesting would apply to these populations.
- The panel considered that in outpatient settings some providers may repeat lipase testing to ensure lipase levels return to normal, and that education (i.e., lipase does not have prognostic value and serial lipase tests should not be ordered) is needed to help change inappropriate reordering behaviours. To support labs and care providers to reduce unnecessary retesting, the panel proposed implementing a 6 month hard stop for outpatient settings.

Lipid Panel

About the Test

The standard lipid panel (or lipid profile) measures total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides in the blood sample, from which the low-density lipoprotein (LDL) cholesterol concentration can be estimated.[18] Lipid panels can be used for screening for lipid disorders, establishing the risk of cardiovascular disease, and for monitoring the response to treatment for lipid disorders (e.g., lipid lowering therapy, lifestyle modifications).[18,19]

Recommendations

The clinical scenario in scope for the guidance is using lipid panel tests for monitoring patients who are being treated with oral lipid-lowering therapy. The recommendations specific to lipid panel are in Box 5.

Box 5. Minimum Retesting Interval Recommendations for Lipid Panel

11. The recommended minimum retesting intervals for lipid panel tests for monitoring adults who are being treated with oral lipid-lowering therapy are:
    - 3 months when assessing response to initiation or modification of therapy.
    - 12 months once targets are met on stable therapy.

    An exception to this recommendation is if the initial test is conducted in the non-fasting state and triglyceride levels are substantially elevated, then a fasting lipid panel may be reordered prior to the recommended minimum retesting interval.

Implementation advice: To support reductions in unnecessary retesting, labs may consider including an education component in their lab information system that reminds care providers that triglycerides can be ordered independently of the whole lipid panel, if more frequent monitoring of triglycerides is required. Labs may also consider implementing different rules in their lab information system based on whether the lipid panel is fasting or nonfasting (e.g., allowing for 1 reorder in fasted state following a nonfasting lipid panel). There is variation in clinical practice and guidelines about the use of repeat lipid panel testing in adult patients on oral lipid-lowering therapies. Application of minimum retesting intervals may vary by specialty and patient populations.

12. The recommended minimum retesting intervals for lipid panel tests for monitoring pediatric patients who are being treated with oral lipid-lowering therapy are:
    - 4 weeks when assessing response to initiation or modification of therapy.
    - 3 months once targets are met on stable therapy.

    An exception to this recommendation is if the initial test is conducted in the non-fasting state and triglyceride levels are substantially elevated, then a fasting lipid panel may be reordered prior to the recommended minimum retesting interval.

Implementation advice: To support reductions in unnecessary retesting, labs may consider including an education component in their lab information system that reminds care providers that triglycerides can be ordered independently of the whole lipid panel, if more frequent monitoring of triglycerides is required. Labs may also consider implementing different rules in their lab information system based on whether the lipid panel is fasting or nonfasting (e.g., allowing for 1 reorder in fasted state following a nonfasting lipid panel).

Developing the Guidance

The advisory panel for lipid panel was composed of the 7 core panel members plus an endocrinologist, a cardiologist, and a pediatric cardiologist.

CADTH solicited input on the impact of lipid panel testing frequency on patients being monitored for treatment with lipid-lowering therapy from patient groups representing relevant patient populations; however, we did not receive any. The panel considered evidence from a focused literature review.[7]

Key Discussion Points

Panel members discussed the following points when developing their recommendations:

- The panel discussed that there was disagreement between the included guidelines in the literature review about the need for lipid panel retesting and the appropriate test frequency in adult patients on oral lipid-lowering therapies. They cited differences in the recommendations between the two guidelines from Canada, the PEER group and College of Family Physicians of Canada guidelines and the Canadian Cardiovascular Society guidelines.
    - Some panel members were of the opinion that there was little-to-no value of lipid panel retesting in people on stable oral-lipid-lowing therapy. They referred to the PEER guidelines (as identified in the literature review) which recommend against repeat lipid panel testing after initiating oral lipid-lowering therapy. They follow this guidance in their clinical practice for patients who have not had a cardiovascular event. In some panel members' experience, lipid panel retesting in primary care settings can be overused as it does not add value to patient management.
    - In contrast, some panel members described that they test for lipids every 3 months when initiating oral lipid-lowering therapy, and every 12 months to monitor patients on stable therapy, particularly in those who have had a previous cardiovascular event (e.g., secondary prevention of cardiovascular disease). This approach is consistent with guidance from the Canadian Cardiovascular Society and other guidelines identified in the literature review.
    - In their discussion, panel members emphasized that the recommended minimum retesting intervals refer to the minimum time between lipid panel tests and are not a recommendation for when to repeat testing (i.e., testing frequency).
    - The panel members discussed the potential of developing different minimum retesting intervals for different patient populations (e.g., in those who have not had a cardiovascular event versus those who have). They ultimately decided on

simplified recommendations for labs that encompassed all patient populations on lipid-lowering therapies.

    - After the panel meeting, there was an asynchronous discussion with a panel member who disagreed with the minimum retesting intervals recommendation for adults. Citing the PEER guidelines, they emphasized the evidence on the benefit of statins being dose related, and that repeat testing in patients who are on stable statin therapy has not been shown to impact patient outcomes. In their opinion, there is no clinical need to repeat lipid panel tests in patients who have begun lipid-lowering therapy.

- The panel recognized that pediatric populations, especially younger children, have unique needs and therefore separate recommendations are required. They discussed that there is evidence for the use of lipid-lowering therapies in pediatric patients (as reflected in the literature review) and safety data is relatively limited when compared with that in adults, which contributes to the shorter retesting intervals in this population. They also noted that based on their experience lipid panel tests are not overused in pediatric patients.
    - Experts referenced Canadian Cardiovascular Society/Canadian Pediatric Cardiology Association clinical guidelines from the literature review that recommend a 3 to 6 month testing frequency for pediatric patients on stable therapy, and acknowledged that some patients, such as older adolescents on stable therapy, may need less frequent follow up (i.e., 6 months). Extending the retesting frequency up to every 6 months for older adolescents on stable therapy may also support preparations for transitions from pediatric to adult care.
- Experts discussed that some patients may require more frequent monitoring of triglycerides (e.g., people with hypertriglyceridemia), and the panel discussed that tests for individual lipids (e.g., triglycerides) can be ordered independently of the whole lipid panel if more frequent monitoring of specific lipids is required. Education components can be used to support providers in ordering the appropriate test.
- Based on panel member's experiences in primary care, non-fasting lipid panels are usually used as these tests are preferred by patients and providers over fasting tests, which can be very difficult for a patient. Experts discussed that if a test is initially done nonfasted and the triglyceride levels are high (i.e., greater than 4.5 mmol/L) then the whole panel should be repeated in the fasted state to eliminate the impact that the high triglyceride levels can have on calculations of LDL cholesterol.
    - The panel discussed labs' experiences with implementing different rules when ordering fasting versus nonfasting lipid panels.

- The panel considered whether there should be special considerations for specific higher risk groups, such as pregnant people, and decided that these recommendations were applicable to most patients and do not exclude any particular group.

SPEP

About the test

SPEP detects the presence or absence of monoclonal immunoglobulin (M protein) in the serum and provides a measurement of M protein concentration (or size).[20] The M protein presentation, concentration and region from the SPEP sample can support the diagnosis and subsequent monitoring of patients with suspected or confirmed plasma cell dyscrasias (e.g., multiple myeloma, monoclonal gammopathy of undetermined significance [MGUS]).[21,20,22]

Recommendations

The clinical scenario in scope for the guidance is using SPEP for monitoring patients with confirmed plasma cell dyscrasias. The recommendation specific to SPEP is in Box 6.

Box 6. Minimum Retesting Interval Recommendations for SPEP

13. The recommended minimum retesting intervals for SPEP for monitoring patients with an established diagnosis of plasma cell dyscrasias are:
    - 25 days for patients with acute or actively treated disease
    - 3 months for patients without actively treated disease

    Exceptions to this recommendation that may require more frequent testing include patients who are at high risk for plasma cell dyscrasias, those who are at high risk of poor outcomes or disease progression, those who recently completed therapy, or when there is biochemical progression that suggests impending clinical progression of the disease.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing these recommendations by specialty (e.g., hematology oncology, internal medicine, family medicine), by location of care (e.g., primary care, outpatient, oncology clinic), or by asking providers to specify the reason for ordering in the request form, based on the capabilities of their lab information system and/or which providers are monitoring patients and ordering SPEP.

Developing the Guidance

The advisory panel for SPEP was composed of the 7 core panel members plus a specialist in hematology oncology. The panel considered evidence from the focused literature review,[7] and patient input from Myeloma Canada.

Key Discussion Points

Panel members discussed the following points when developing their recommendations:

- Experts discussed that plasma cell dyscrasias are a heterogenous group of diseases which cover a spectrum of nuanced conditions that range from asymptomatic and premalignant plasma cell disorders (e.g., MGUS) to symptomatic and malignant diseases (e.g., multiple myeloma). The level of risk to the patient varies both across (e.g., smoldering myeloma versus MGUS) and within (e.g., high risk versus low risk MGUS) the different conditions.
    - The panel noted that the SPEP minimum retesting interval applies to all plasma cell dyscrasias, but that some conditions (e.g., MGUS) may require less frequent follow-up (as supported by the clinical guidance in the literature review).
- For patients with acute or actively treated disease, the panel considered that most patients have treatment regimens on a monthly cycle, and that a 1-month interval would be appropriate for most patients. The recommended minimum retesting interval of 25 days would provide flexibility to accommodate patient schedules and allow testing to align with appointments for treatment.
- Experts discussed that the disease progression varies by patient (e.g., very rapid or very slow disease progression) and that based their experiences, it is unlikely that SPEP test results would change substantially on a weekly basis in the majority of patients. It was noted that when starting therapy, there may not even be a change in SPEP after the first month of therapy, and that providers may choose to wait 2 to 3 months before making treatment adjustments based on SPEP results.
- For patients without actively treated disease, patients may not need to be monitored as frequently as those who have actively treated disease, and a 3-month minimum retesting interval was discussed as appropriate for most patients.
- The panel acknowledges that due to the variation across the disease spectrum there may be some exceptions to both recommendations, and care providers should consider the patient's specific clinical situation, such as the disease, the level of risk, biochemical changes, or the amount of time since the patient completed treatment.

- Patient group input raised the issue that some plasma cell dyscrasias disproportionately affect equity-deserving groups (e.g., Black populations, older adults). The panel acknowledged that access to testing should be equitable, including considerations for race, ethnicity, and location, and recognized that testing should aim to be patient centric and aligned with the patient's treatment cycle.
- The panel considered that the approach that labs use to operationalize the 2 different recommendations will depend on how their institution differentiates between patients with actively treated disease and without actively treated disease (e.g., by specialty, by location of care) and the capabilities of their lab information system.
- To support the implementation of the minimum retesting interval, labs can provide educational material on the different plasma cell dyscrasia conditions, including the nuances within each condition and the different levels of risk. This would assist providers with determining the SPEP retesting requirements for their patients.

TSH

About the test

Thyroid hormones T4 (thyroxine) and T3 (triiodothyronine) are regulated by pituitary Thyroid Stimulating Hormone (TSH).[23] Serum TSH testing is used to evaluate thyroid dysfunction, primarily for the detection and treatment monitoring of hyperthyroidism and hypothyroidism.[23]

Recommendations

The clinical scenario in scope for the guidance is using TSH to monitor patients who are being treated with thyroid replacement therapy for hypothyroidism and patients who are being treated for hyperthyroidism. The recommendation specific to TSH is in Box 7.

Box 7. Minimum Retesting Interval Recommendations for TSH

14. The recommended minimum retesting interval for TSH for monitoring patients with known thyroid disease who have had adjustment to their treatment (i.e., are under active investigation or management) is 6 weeks.

    Exceptions to this recommendation that may require more frequent testing include patients with overt hyperthyroidism because of the risk of life-threatening conditions (e.g., acute thyrotoxicosis), pediatric patients, and pregnant patients.

Implementation advice: Because of variation in clinical cases, labs may consider creating test codes for specific clinical exceptions to support automatic bypasses to the recommended minimum retesting interval.

Developing the Guidance

The advisory panel for TSH was composed of the 7 core panel members plus an endocrinologist. The panel considered evidence from the focused literature review,[7] and patient input from the Thyroid Foundation of Canada and Thyroid Patients Canada.

Key Discussion Points

Panel members discussed the following points when developing their recommendations:

- In non-pregnant adults with known thyroid disease who have had adjustment to their treatment (e.g., recently initiated therapy or had a dose adjustment), 6 weeks was selected as the recommended minimum retesting interval as it is appropriate for most patients (with the exception of those with overt hyperthyroidism). This is consistent with the recommendations included in the literature review.
- While the recommendation is for the minimum retesting interval for those who have had an adjustment to their treatment, the panel noted that for people with stable primary hypothyroidism (i.e., those with stable TSH levels) that the testing frequency may be longer depending on the clinical situation and could vary by patient needs.
- The panel considered whether there should be different intervals based on different clinical scenarios (e.g., hypothyroidism, hyperthyroidism, pregnancy) but noted that it may be challenging for labs to implement recommendations by condition, and that it is easier to have a single minimum retesting interval when clinically appropriate or different cut offs by age. For simplicity and to support appropriate implementation, the panel opted to recommend 1 minimum retesting interval that would apply to most situations and to specify the exceptions.
- The panel recognized that there are exceptions where retesting TSH at shorter intervals (e.g., 2 to 4 weeks) may be warranted, such as for pediatric patients, pregnant patients, and those with overt hyperthyroidism because of the risk of life-threatening conditions (e.g., acute thyrotoxicosis). This is supported by the literature review.
- Patient group input raised the issue of some people requiring more frequent TSH monitoring due to sex hormone changes, such as people in perimenopause or menopause, or those taking hormone therapy (e.g., transgender people). Experts noted

that the physiology of TSH would not be different in these populations, and that the minimum retesting interval would still apply; however, experts acknowledged that these patients may require more frequent adjustments to their therapy.

- Patient experiences with TSH testing were discussed, including the value of T3 and T4 testing. Experts discussed that TSH is the most sensitive test for monitoring patients with primary hypothyroidism, and that T3 and T4 testing may be considered when required. The panel considered that most labs have reflex testing for thyroid hormones (i.e., the lab automatically adds the T4 test to the blood sample based on an abnormal TSH result) and that there are established guidelines and testing algorithms for thyroid hormone testing.
- When considering the implementation advice for this recommendation, the panel discussed that it would be difficult to suggest hard stops for lab information systems given the variety of clinical scenarios and testing requirements for different populations that fall outside the recommended minimum retesting interval. Based on the capabilities of the lab information system and the patient populations, the panel suggested that institutions consider creating separate test codes for clinical exceptions (e.g., pregnancy) or implementing hard stops based on patient age.

Future considerations

Across their discussions of the 7 included lab tests for which they made recommendations, the advisory panel returned to common themes about the overuse of lab tests.

The importance of prior test results being available

The advisory panel noted the need to have prior test results available in the general guidance on implementing the recommendations on minimum retesting intervals. Their availability is critical to reducing unnecessary retesting and improving the efficient use of lab tests. Increased connection and coordination between labs, providers, and health care facilities alongside improvements in the ability to access and share medical information across the health system can support the availability of prior lab test results.

The importance of education

Education material can be used to support the uptake of the recommendations, to help change ordering behaviours, and to support discussions between care providers and lab professionals. Education materials can also be used to support communication between patients and care providers when discussing the value of repeat testing. When provided in combination with other

strategies, such as hard stops in lab information systems, education can help support the reduction in unnecessary repeat testing.

The value of reducing unnecessary lab testing

Unnecessary repeat testing comes at a cost to the health care system, both in terms of cost of the test and extra time to provide the low value care. It also impacts patients in terms of potential harms from unnecessary follow-up, potentially inappropriate treatments, and having to travel and take time for unnecessary repeat testing, which can be significant particularly for those patients who do not live in close proximity to laboratory testing services. Panel members also raised that unnecessary repeat testing has an environmental impact, including producing carbon emissions and environmental waste.

Reflecting on equity considerations and who is affected by minimum retesting intervals

When developing recommendations to reduce the overuse of repeat lab tests, the advisory panel reflected on whether and how different populations would be affected by their recommendations. This included subgroups who were at higher risk of a condition or worsening outcomes, but also those who had less ready access to health care, particularly specialist care, based on their location of residence. Panel members discussed how, from an equity perspective, unnecessary repeat testing takes time and other resources away from other valuable treatments or patients.

The need for guidance on screening tests

During the discussion for several tests (e.g., TSH, lipid panel) panelists raised that a likely source of overuse was by using the test under discussion for screening purposes. Although the repeat use of lab tests for screening scenarios was out of scope for this work, it highlights future opportunities to provide guidance to clinicians and labs to support appropriate use of lab testing.

The importance of communication

The panel acknowledged that these recommendations cannot account for all clinical scenarios, and that clinicians and lab professionals need to be able to communicate to discuss exceptions to the recommendations to ensure patients receive appropriate care. This is consistent with input from patient groups highlighting the importance of patient-centred care.

References

1. Naugler C, Wyonch R. What the Doctor Ordered: Improving the Use and Value of Laboratory Testing. *(Commentary No. 533)*. Toronto (ON): C.D. Howe Institute; 2019: https://www.cdhowe.org/public-policy-research/what-doctor-ordered-improving-use-and-value-laboratory-testing. Accessed 2024 Feb 05.
2. Squires JE, Cho-Young D, Aloisio LD, et al. Inappropriate use of clinical practices in Canada: a systematic review. *CMAJ.* 2022;194(8):E279-e296.
3. Identifying Overused Lab Tests in Hospital Settings: A Delphi Study. *Can J Health Technol.* 2023;3(1). https://canjhealthtechnol.ca/index.php/cjht/article/view/ES0362. Accessed 2023 Nov 09.
4. Lang T, Croal B. National minimum retesting intervals in pathology. London (GB): The Royal College of Pathologists; 2021: https://www.rcpath.org/static/253e8950-3721-4aa2-8ddd4bd94f73040e/g147_national-minimum_retesting_intervals_in_pathology.pdf. Accessed 2023 Nov 10.
5. Choosing Wisely Canada. About. [2024]; https://choosingwiselycanada.org/about/. Accessed 2024 Jan 24.
6. Choosing Wisely Canada. Using Labs Wisely. [2024]; https://choosingwiselycanada.org/hospitals/using-labs-wisely/. Accessed 2024 Jan 24.
7. Minimum Retesting Intervals for Lab Tests [in progress]. *(CADTH Heath Technology Review)*. Ottawa (ON): CADTH; 2024: https://www.cadth.ca/minimum-re-testing-intervals-lab-tests.
8. HealthLinkBC. Antinuclear Antibodies (ANA) Test. 2023; https://www.healthlinkbc.ca/tests-treatments-medications/medical-tests/antinuclear-antibodies-ana. Accessed 2023 Nov 30.
9. Bloch DB. Measurement and clinical significance of antinuclear antibodies. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2023: http://www.uptodate.com/. Accessed 2023 Nov 30.
10. Maddox TM, Januzzi JL, Jr., Allen LA, et al. 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2021;77(6):772-810.
11. Mueller C, McDonald K, de Boer RA, et al. Heart Failure Association of the European Society of Cardiology practical guidance on the use of natriuretic peptide concentrations. *Eur J Heart Fail.* 2019;21(6):715-731.
12. Colucci WS, Chen HH. Natriuretic peptide measurement in heart failure. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2023: http://www.uptodate.com/. Accessed 2023 Nov 16.
13. Chen HH, Colucci WS. Natriuretic peptide measurement in non-heart failure settings. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2023: http://www.uptodate.com/. Accessed 2023 Nov 16.
14. Selvin E. Measurements of chronic glycemia in diabetes mellitus. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate: http://www.uptodate.com/. Accessed 2023 Oct 25.
15. Eyth E, Naik R. Hemoglobin A1C. *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023: https://www.ncbi.nlm.nih.gov/books/NBK549816/. Accessed 2023 Nov 14.
16. MedlinePlus. Lipase Test. 2022; https://medlineplus.gov/lab-tests/lipase-tests/. Accessed 2023 Dec 14.
17. Beyer G, Hoffmeister A, Lorenz P, Lynen P, Lerch MM, Mayerle J. Clinical Practice Guideline-Acute and Chronic Pancreatitis. *Dtsch Arztebl Int.* 2022;119(29-30):495-501.
18. Rosenson RS. Measurement of blood lipids and lipoproteins. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2023: http://www.uptodate.com. Accessed 2023 Nov 10.
19. Cleveland Clinic. Lipid Panel: What It Is, Purpose, Preparation & Results. 2021; https://my.clevelandclinic.org/health/diagnostics/17176-lipid-panel. Accessed 2023 Nov 21.
20. Murray DL. Laboratory methods for analyzing monoclonal proteins. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2022: http://www.uptodate.com/. Accessed 2023 Dec 8.
21. Boccadoro M, Pileri A. Plasma cell dyscrasias: classification, clinical and laboratory characteristics, and differential diagnosis. *Baillieres Clin Haematol.* 1995;8(4):705-719.
22. Booth RA, McCudden CR, Balion CM, et al. Candidate recommendations for protein electrophoresis reporting from the Canadian Society of Clinical Chemists Monoclonal Gammopathy Working Group. *Clin Biochem.* 2018;51:10-20.
23. Ross DS. Laboratory assessment of thyroid function. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2023: http://www.uptodate.com/. Accessed 2023 Nov 23.

Appendix 1 - Advisory Panel Recommendations for Minimum Retesting Intervals

The Advisory Panel on Minimum Retesting Intervals for Lab Tests developed recommendations for 7 commonly repeated lab tests for monitoring patients (refer to Box 8). Minimum retesting intervals are recommendations on the minimum time before a test should be repeated, based on the biochemical properties of the test and the clinical situation in which it is used.

How a minimum retesting interval recommendation is implemented by labs will depend on the local context, for example, if the patients with the condition are cared for within their facility or catchment, and the capacity of their laboratory information system to provide educational prompts and place limits on requests. Clinicians should have the option to override a minimum retesting interval or discuss options with a laboratory professional if they feel repeat or more frequent testing is clinically appropriate, or if there are issues with a previous test result (e.g., interference, unexpected test results for the clinical context, missing result).

Box 8. Advisory Panel Recommendations for Minimum Retesting Intervals

ANA
1. If a previous ANA test is positive, do not reorder ANA for monitoring patients with suspected or confirmed systemic autoimmune disease. Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 5 year hard stop minimum retesting interval.
2. If a previous ANA test is negative or borderline positive, do not reorder ANA for monitoring patients with suspected or confirmed systemic autoimmune disease. An exception to this recommendation is if the clinical status of the patient significantly changes with newly developed symptoms, in which case ANA may be retested. Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 24 month hard stop minimum retesting interval.
BNP and NT-proBNP
3. Do not reorder BNP or NT-proBNP for monitoring adult patients aged 18 and older with an established diagnosis of congestive heart failure in the inpatient setting. An exception to this recommendation is if the patient is being discharged.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a hard stop minimum retesting interval of 72 hours, or no more than 2 tests in 14 days.

4. The recommended minimum retesting interval for BNP and NT-proBNP for adult patients aged 18 and older with an established diagnosis of congestive heart failure in outpatient settings is 6 months.

5. The recommended minimum retesting interval for BNP and NT-proBNP for monitoring adult patients aged 18 and older with established pulmonary arterial hypertension in outpatient settings is 1 month.

   Exceptions to this recommendation are cases with acute clinical deterioration.

6. The recommended minimum retesting interval for BNP and NT-proBNP for monitoring adult patients aged 18 and older with an established diagnosis of pulmonary arterial hypertension in inpatient settings is 72 hours.

   An exception to this recommendation is if the patient is being discharged.

HbA1c

7. The recommended minimum retesting intervals for HbA1c in patients who are being treated for diabetes are:

   - 3 months for patients who have not yet achieved stable glycemic targets.
   - 6 months for patients who have achieved stable glycemic control.

   Exceptions to this recommendation that may warrant more frequent testing include pediatric patients with type 1 diabetes, patients with diabetes who are planning to become pregnant, and patients with rapidly changing blood glucose levels due to significant recent changes to lifestyle and/or medications.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 60 to 86 day hard stop minimum retesting interval. This allows for practical considerations such as accommodating patient schedules for retesting appointments.

8. Do not reorder HbA1c tests for assessing glycemic control in patients with diabetes who have conditions that alter red blood cell turnover (e.g., iron deficiency anemia) or for pregnant patients with diabetes who are in their second or third trimester.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing a 60 to 86 day hard stop minimum retesting interval.

Lipase

9. Do not reorder lipase tests for monitoring patients with an established diagnosis of acute pancreatitis.

10. Do not reorder lipase tests for monitoring patients with an established diagnosis of chronic pancreatitis.

    An exception to this recommendation is if there is clinical suspicion of an episode of acute-on-chronic pancreatitis, where lipase testing is required for diagnostic purposes.

Implementation advice: To support reductions in unnecessary retesting, in outpatient or community settings, labs may consider implementing a 6 month hard stop minimum retesting interval.

This recommendation is based on the experience of the advisory panel as no relevant information for serum lipase retesting for chronic pancreatitis was identified in the literature review.

Lipid Panel

11. The recommended minimum retesting intervals for lipid panel tests for monitoring adults who are being treated with oral lipid-lowering therapy are:

    - 3 months when assessing response to initiation or modification of therapy.
    - 12 months once targets are met on stable therapy.

    An exception to this recommendation is if the initial test is conducted in the non-fasting state and triglyceride levels are substantially elevated, then a fasting lipid panel may be reordered prior to the recommended minimum retesting interval.

Implementation advice: To support reductions in unnecessary retesting, labs may consider including an education component in their lab information system that reminds care providers that triglycerides can be ordered independently of the whole lipid panel, if more frequent monitoring of triglycerides is required. Labs may also consider implementing different rules in their lab information system based on whether the lipid panel is fasting or nonfasting (e.g., allowing for 1 reorder in fasted state following a nonfasting lipid panel). There is variation in clinical practice and guidelines about the use of repeat lipid panel testing in adult patients on oral lipid-lowering therapies. Application of minimum retesting intervals may vary by specialty and patient populations.

12. The recommended minimum retesting intervals for lipid panel tests for monitoring pediatric patients who are being treated with oral lipid-lowering therapy are:

- 4 weeks when assessing response to initiation or modification of therapy.
- 3 months once targets are met on stable therapy.

An exception to this recommendation is if the initial test is conducted in the non-fasting state and triglyceride levels are substantially elevated, then a fasting lipid panel may be reordered prior to the recommended minimum retesting interval.

Implementation advice: To support reductions in unnecessary retesting, labs may consider including an education component in their lab information system that reminds care providers that triglycerides can be ordered independently of the whole lipid panel, if more frequent monitoring of triglycerides is required. Labs may also consider implementing different rules in their lab information system based on whether the lipid panel is fasting or nonfasting (e.g., allowing for 1 reorder in fasted state following a nonfasting lipid panel).

SPEP

13. The recommended minimum retesting intervals for SPEP for monitoring patients with an established diagnosis of plasma cell dyscrasias are:

    - 25 days for patients with acute or actively treated disease
    - 3 months for patients without actively treated disease

    Exceptions to this recommendation that may require more frequent testing include patients who are at high risk for plasma cell dyscrasias, those who are at high risk of poor outcomes or disease progression, those who recently completed therapy, or when there is biochemical progression that suggests impending clinical progression of the disease.

Implementation advice: To support reductions in unnecessary retesting, labs may consider implementing this recommendation by specialty (e.g., hematology oncology, internal medicine, family medicine), by location of care (e.g., primary care, outpatient, oncology clinic), or by asking providers to specify the reason for ordering in the request form, based on the capabilities of their lab information system and/or which providers are monitoring patients and ordering SPEP.

TSH

14. The recommended minimum retesting interval for TSH for monitoring patients with known thyroid disease who have had adjustment to their treatment (i.e., are under active investigation or management) is 6 weeks.

    Exceptions to this recommendation that may require more frequent testing include patients with overt hyperthyroidism because of the risk of life-threatening conditions (e.g., acute thyrotoxicosis), pediatric patients, and pregnant patients.

Implementation advice: Because of variation in clinical cases, labs may consider creating test codes for specific clinical exceptions to support automatic bypasses to the recommended minimum retesting interval.

ANA = antinuclear antibody; BNP = B-type natriuretic peptide; HbA1c = hemoglobin A1c; NT = N-terminal; SPEP = serum protein electrophoresis; TSH = thyroid stimulating hormone.

Appendix 2 – Detailed Approach

Scope

CWC identified 7 frequently used lab tests that would benefit from guidance to reduce unnecessary retesting. Our selection of tests was supported in part by a 2022 systematic review of inappropriate clinical practices in Canada that reported the percentage of overuse for TSH, HbA1c, and ANA lab tests as 3.0% to 35.1%, 22.9% to 28.1%, and 30.6%, respectively.[2] In addition, a 2023 CADTH Delphi study to support CWC's Using Labs Wisely program identified that HbA1c, TSH, lipase, BNP, and the lipid panel were highly used lab tests in Canada and potential candidates for reduction.[3] To have the greatest impact on reducing unnecessary repeat testing, we limited the scope to the main conditions or populations that are tested and retested and where minimum retesting intervals could be applied. For each lab test, CWC, CADTH, and lab experts worked together to further specify the patient populations and/or clinical situations in which these tests are regularly used. For tests with broad populations (e.g., autoimmune diseases), we identified primary populations of interest.

Out of scope for this guidance were other lab tests, conditions, patient populations, and clinical scenarios (e.g., screening).

Step 1. Forming the Advisory Panel

CADTH and CWC co-led the recruitment of the time-limited advisory panel to develop recommendations for minimum retesting intervals for the 7 included lab tests.

We formed a core advisory panel with additional specialists to bring clinical expertise appropriate for each test and prespecified patient population or clinical scenario. We recruited potential panel members and specialists through CADTH and CWC's networks (e.g., clinical societies). We consulted with CADTH's IDEA Strategic Partner and sought advice on the importance of inclusion, diversity, equity and accessibility in the panel's composition (e.g., diverse representation and geographic distribution). We consulted with CADTH's Engagement Team on developing an approach to engage patients and patient groups throughout the course of the project.

Core Advisory Panel

The core advisory panel was composed of 4 lab specialists, one of whom was a CWC Using Labs Wisely Lead, 2 family doctors, and 1 patient panel member. Panel members participated in the consensus generating discussions and provided their perspective by sharing knowledge and insight on minimum retesting intervals for the lab test(s).

Specialist Panel Members

For each lab test, the core advisory panel was joined by 1 to 3 specialist physicians for each clinical area (i.e., endocrinology, cardiology, rheumatology, hematology oncology, gastroenterology, internal medicine) to provide their expertise to the panel and participate in consensus generation (refer to Table 1).

Table 1. List of Specialist Panel Members Who Participated in Each Test Discussion

Lab Tests	Specialist(s)
ANA	Dr. Carter Thorne, Rheumatologist
BNP and NT-proBNP	Dr. Nowell Fine, Cardiologist Dr. Michael Khoury, Pediatric Cardiologist
HbA1c	Dr. Ferhan Siddiqi, Endocrinologist
Lipase	Dr. William Silverstein, General Internist Dr. Natalia Calo, Gastroenterologist
Lipid Panel	Dr. Nowell Fine, Cardiologist Dr. Ferhan Siddiqi, Endocrinologist Dr. Michael Khoury, Pediatric Cardiologist
SPEP	Dr. Matthew Cheung, Clinical Hematologist
TSH	Dr. Ferhan Siddiqi, Endocrinologist

ANA = antinuclear antibody; BNP = B-type natriuretic peptide; HbA1c = hemoglobin A1c; NT = N-terminal; SPEP = serum protein electrophoresis; TSH = thyroid stimulating hormone.

Step 2. Panel Inputs

Focused Literature Reviews

CADTH conducted focused literature reviews for each of the included lab tests to support the development of recommendations. For each test, we searched for existing recommendations on retesting in prespecified patient populations or clinical scenarios. After the initial search, a research information specialist screened the results to prioritize guidance from countries similar to Canada (e.g., US, UK, Western Europe). We also searched for evidence on biological or physiological factors that might impact the minimum retesting interval for each test. We

summarized equity considerations that may influence the minimum retesting interval when they were identified within the relevant clinical guidelines and other literature. Further details can be found in the Technology Review on Minimum Retesting Intervals for Lab Tests.[7]

Engaging Patient Groups

CADTH sought the expertise of patient groups to provide valuable insights into the impact of frequency of testing on patients when developing recommendations for minimum retesting intervals for selected lab tests. The purpose of the engagement was to broaden the patient perspectives available for the panel's consideration during their consensus generation and mitigate the risks of a small panel.

We solicited the experiences and perspectives from patient groups of each of the prespecified main conditions or populations who receive repeat testing using the lab tests of interest. These groups have expertise in clinical areas of interest and were able to share the lived experience of patients and caregivers. We reached out to 18 patient groups in total with the initial invitation sent on December 11, 2023, and subsequent reminder emails on December 19, 2023, and January 9, 2024. We received responses from 11 patient groups and recognize that some groups may not have been able to participate due to the timing of our request (i.e., over the December holidays).

We requested patients' lived experiences from patient groups through a set of survey questions which aimed to better understand the current burden of testing and gather insights on the potential impact of changing testing frequency. The survey questions also included the impact of frequency of testing on those subgroups with special considerations, such as pediatric patients and patients who are pregnant. We also consulted with CADTH's IDEA Strategic Partner on developing questions related to the impact of frequency of testing for equity-deserving groups which include but are not limited to: women, racialized groups, Indigenous Peoples, people with disabilities, and 2SLGTBQ+ community members.

We collated, summarized, and shared the patient group information with the advisory panel members in advance of meetings. The patient representative on the panel also received the complete unedited patient group feedback and their role included sharing this input during the consensus-based discussions to represent and bring to life the patient voice.

Step 3: Developing Recommendations

Draft Recommendations

Draft recommendations were prepared in advance of the full panel meetings to serve as starting points for discussion. Two lab experts from the core panel were assigned to each test, and

independently developed draft recommendations using the literature reviews, input from patient groups, and questions for consideration (including equity considerations). We consolidated the 2 independent draft recommendations for each test. The 4 lab experts from the core panel met through a 2-hour, virtual, facilitated discussion of all 7 lab tests on Jan 31, 2024. The objective of the virtual discussion was to revise the consolidated draft recommendations for clarity and so they reflected the lab experts' opinions so that they were ready for consensus generation by the full advisory panel.

Developing Consensus-based Recommendations

Prior to meeting, the advisory panel received background materials that included the draft recommendations, summaries of patient input, the literature reviews, and a discussion guide. The discussion guide included prompts for reflection and consideration, including general equity considerations and those that were raised by patient-group input or in the literature review. We consulted with CADTH's IDEA Strategic Partner to develop questions to prompt panel members to consider equity-deserving groups during their discussions and included these in the background materials.

CADTH facilitated the discussion and consensus generation, and each lab test was discussed by the panel for 1 hour. One of the lab experts who prepared the draft recommendations started the discussion by presenting their rationale. The patient panel member then shared patient group input and patients' experiences, after which the invited specialists had an opportunity to share their perspective on the draft recommendations.

Through facilitated discussion (~60 minutes), the advisory panel developed recommendations for the minimum retesting interval(s) for the lab tests in prespecified population(s). Recommendations against repeat testing for certain lab tests in specific populations were also developed when supported by the evidence and clinical expertise. We made live edits in a Word document so that advisory panel members could see suggested changes to the recommendations, as well as to implementation advice and additional considerations. The facilitator also prompted the advisory panel to ensure that equity considerations and patient groups' perspectives were discussed. Once the facilitator felt the discussion was approaching consensus, the revised draft recommendations were put to a vote. Consensus was defined as 70% agreement and was reached on the recommendations for 7 lab tests. All advisory panel members voted in agreement with the revised recommendations at the end of the discussions with the exception of lipid panels.

In our project plan, we had allowances for members to provide asynchronous contributions to the development of the draft recommendations if panel members were not able to participate in the scheduled discussions. One core panel member was not able to participate in the discussion on a test (lipid panel) due to technical difficulties. The panel member reached out to us and asked to

share their perspective, and we arranged a half hour virtual meeting to hear their perspectives. Some of their perspective was reflected in points raised by other panel members. Based on the importance of the perspective, we added detail to the discussion section for lipid panels incorporating this panel member's feedback.

Over the course of the panel meetings, the advisory panel reached consensus on recommendations on all tests except for BNP and NT-proBNP testing in adults and children being treated for pulmonary arterial hypertension. The advisory panel felt it was necessary to consult with specialists in pulmonary arterial hypertension and deferred voting on the draft recommendations for this indication. We recruited 2 specialists who treat adults with pulmonary arterial hypertension (Table 2) and shared the draft recommendations and background materials for BNP for pulmonary arterial hypertension with them. The CWC Using Labs Wisely clinical lead and CADTH team facilitated a half hour virtual discussion with the attending specialists and documented their suggestions to the recommendations and rationale. The CADTH team revised the draft recommendations, and then sent them and their rationale to the advisory panel for an asynchronous electronic vote for which consensus was reached.

We sent the revised recommendations and implementation advice developed by the advisory panel to members for optional validation prior to incorporating them into the draft guidance report.

Table 2. List of Specialists Consulted for BNP/NT-proBNP Recommendations

Specialist(s)
Dr. Jason Weatherald, respirologist with the University of Alberta Pulmonary Hypertension Program, and Associate Professor in the Department of Medicine at the University of Alberta
Dr. Doug Helmersen, respirologist with the Southern Alberta Pulmonary Hypertension Program and Clinical Associate Professor at the University of Calgary

Writing the Guidance Report

Once the consensus-based recommendations were developed, we summarized the key discussion points that arose during the development of the recommendations, including discussions of relevant information from the literature reviews, how the patient input informed the panel discussions, and clinical experience from the specialist experts.

The advisory panel had an opportunity to review the guidance report to ensure it appropriately and accurately captured their discussion and rationale for the recommendations and the implementation advice.

Opportunities for Feedback

We posted the draft guidance document on the CADTH website for a 10 day feedback period. Patient groups engaged in the project and other interested parties were notified when the draft was posted and invited to provide feedback. We reviewed feedback received and made changes to the guidance document where there were opportunities to improve clarity or accuracy.

Limitations

We aimed to reduce biases in the consensus panel by having a diverse group of clinical and expert representation and by asking for declarations of conflict of interest. We did not find any published evidence on the minimum retesting interval or testing frequency for lipase to monitor chronic pancreatitis, meaning that this recommendation was developed based on expert opinion. We worked to address equity considerations within the scope of the prespecified tests and patient populations; however, there are likely considerations that were not raised or that relate to but are outside the scope of this project. The panel's ability to comment on equity considerations was also variable, so this remains an area worth further discussion and exploration. Patient group input was intended to support decision making and address limitations in published evidence and equity considerations; however, we did not receive any input from patient groups on the impact of lipid panel testing frequency for patients being monitored for treatment with lipid-lowering therapy.

Appendix 3 –Advisory Panel Members Declarations of Conflict of Interests

The following are the declared conflicts of interests for each of the Advisory Panel members as per CADTH's Conflict of Interest Guideline:

Drs. Daniel Beriault, Dr. Natalia Calo, Dr. Manal Elnenaei, Dr. William Silverstein and Dr. Janet Simons reported no conflicts of interests.

Dr. Matthew Cheung is the Chair of Economics Committee for the Canadian Cancer Trials Group and Chair of Guidelines Subcommittee for the American Society of Hematology.

Dr. Nowell Fine received consulting honoraria from Pfizer, AstraZeneca, and Alnylan.

Dr. Michael Khoury received payment for attending an advisory board meeting from Ultragenyx.

Dr. Roseline Kraft received access to oncology drugs through clinical trials and patient access programs from BC Cancer/Canadian Cancer Trials Group/Hoffman-La Roche, BC Cancer, and Astra Zeneca's Oncology Patient Support Program. She received honoraria, waived registration fees and travel funding for her role as a patient partner in research projects and reviewing grant applications from the Canadian Cancer Society, Rethinking Breast Cancer, the Marathon of Hope Cancer Centre/TRIF, and Canadian Cancer Research Alliance. She received payment for organizing the Canadian Cancer Research Conference

Dr. Ferhan Siddiqi received travel payment from the Canadia Society for Endocrinology and Metabolism.

Dr. Carter Thorne received payment for attending advisory board meetings from Abbvie, Biogen, JAMP, Medexus, Nordic Pharma, Pfizer, Roche, Sandoz, Sanofi and grant funding from Pfizer and JAMP.

Dr. Li Wang received travel grant and speaking fees for attending the 12th Oriental Congress of Laboratory Medicine.

Dr. Yan Yu received travel funding and speaking fees from CMA Joule, Immunize.io, and the College of Family Physician of Canada. He also received payment for his work as a faculty coordinator from the Department of Medicine at the University of Calgary and for participating in an advisory board meeting from Moderna.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.