

Utilization of Renal Function & Iron Status Laboratory Test Investigations in Eastern Health

By

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## Abstract

**Introduction:** Healthcare spending in Canada reached 219.1 billion dollars in 2015. Unnecessary laboratory test investigations have been well documented in many countries, making it an area of interest in order to reduce costs, improve care and ultimately improve the performance of the health care system. The use of serum urea is unnecessary to evaluate kidney function in stable patients as serum creatinine has better specificity and no decrease in sensitivity. Therefore, we examined the use of serum urea in the community of a regional health authority. Ferritin is a good test of iron status and indicated in anemic patients, particularly when mean corpuscular volume/mean corpuscular hemoglobin levels are low. Therefore, we examined the use of iron status tests in the community to determine the degree of under-utilization in the patients likely to have iron deficient anemia and of over-utilization in patients with normal hemoglobin and blood indices.

**Methods:** We performed a retrospective analysis of Eastern Health's laboratory electronic database to investigate patterns of laboratory test utilization for two specific bundles of tests: (1) serum creatinine and serum urea; (2) hemoglobin (Hgb), ferritin and iron saturation. Laboratory tests were examined for a 6-month period in 2014 (bundle 1) and a 12-month period (bundle 2) throughout 2013-2014. Test utilization is described by age, sex, patient type (inpatient/outpatient), submitting physician specialty and test result.

**Results:** 227,092 serum creatinine and 218,289 serum urea tests were ordered for all patients within the Eastern Health Region during the 6-month period. 96.8% (n=211,279) serum urea tests were ordered in the same draw as serum creatinine. 64.6% (n=141,112) serum urea tests were ordered in the same draw as serum creatinine for outpatients. General practitioners elicited the highest rate of serum urea tests (52.5% of total), followed by the internal medicine specialty. 69.3% (n=62,274) of coupled serum creatinine and serum urea laboratory investigations ordered by general practitioners for outpatients elicited normal results for both tests. High volumes of hemoglobin (n=450,792) and iron status tests (ferritin; n=86,293, iron saturation; n=23,415) were ordered within the 12-month period. General practitioners elicited the highest ordering for all three tests for outpatients. 89.6% (n=55,595) of iron tests requested by general practitioners for non-anemic outpatients (first Hgb) produced a normal result in the 12-month period. 44.9% (n=136) of females ( $\leq 50$  years of age) with anemia did not undergo iron testing within 1-year of the first documentation of the anemia by a general practitioner.

**Conclusion:** Serum urea and iron testing may be areas of interest for the improvement of utilization of health care resources within the Eastern Health Region. Information contained in this thesis may be used as a guiding tool for decision makers in the development of interventions to improve test-ordering behaviours without compromising patient quality of care.

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## List of Abbreviations and Symbols

<b>CBC</b>	Complete Blood Count
<b>CHIA</b>	Center for Health Information and Analytics
<b>CKD</b>	Chronic Kidney Disease
<b>CP</b>	Creatinine Phosphate
<b>CWC</b>	Choosing Wisely Canada
<b>DOHCS</b>	Department of Health and Community Services
<b>GFR</b>	Glomerular Filtration Rate
<b>HgB</b>	Hemoglobin
<b>IDA</b>	Iron Deficient Anemia
<b>MCH</b>	Mean Corpuscular Hemoglobin
<b>MCV</b>	Mean Corpuscular Volume
<b>NLMA</b>	Newfoundland & Labrador Medical Association
<b>RBC</b>	Red Blood Cells

## Chapter 1: INTRODUCTION

Notable increases in health care expenditures have been reported in many countries<sup>1-4</sup>. The Government of Newfoundland & Labrador's expenditure on per person health care exceeded the Canadian average by 15.3% in 2015<sup>4</sup>. Unnecessary utilization of laboratory resources has been reported in the literature, decreasing the quality of care provided to patients<sup>5,6</sup>. Over testing may result in avoidable patient discomfort and an increase in the likelihood of false positive test results<sup>5,6</sup>. Under testing can cause delayed or missed diagnosis, creating a missed opportunity to improve patient outcomes<sup>5</sup>. Few interventions to reduce low value care undertook a laboratory resource focus<sup>7</sup>. Laboratory testing is a focal point in many clinical decisions, emphasizing the need for investigations to identify low value care in specific clinical situations and interventions to modify unnecessary testing. In a recent collaborative effort, the Quality of Care program was developed, which is an academic initiative co-funded by the Government of Newfoundland and Labrador. The purpose of the Quality of Care program is to address unnecessary utilization of health care resources through research. The Quality of Care NL program works in conjunction with Choose Wisely Canada (CWC) to reduce unnecessary care, however, it is also their intent to ensure that the right patients receives the appropriate care at the right time through NL Specific Projects<sup>8</sup>. The present study falls under the umbrella of this initiative.

## **1.1 Purpose**

This project has been undertaken as we hypothesize that there will be a large number of potentially unnecessary serum urea tests ordered by general practitioners for outpatients. Similarly, we hypothesize that there will be both under and overutilization of iron tests. The findings from this assessment will be used to design and target interventions aimed at improving the appropriateness of utilization of these tests. The purpose of this investigation is to (i) identify the patterns utilization of renal function tests (serum urea, serum creatinine) during a 6-month period in 2014 (July 1<sup>st</sup> – December 31<sup>st</sup>) and iron status (iron saturation, ferritin) and hemoglobin tests during a 12-month period (April 1<sup>st</sup>, 2013 – April 1<sup>st</sup>, 2014) in the Eastern Health Region of Newfoundland (ii) Discuss approaches supported by the literature to decrease the inappropriate utilization of these laboratory tests and increase quality of care. At the time this work was done, we did not anticipate having the results of the implemented interventions. However, following the completion of my thesis work, decision makers have implemented interventions and analyzed the outcomes to date. Therefore, we will discuss the interventions that were undertaken and present the impact within the Eastern Health Region.

## Chapter 2: LITERATURE REVIEW

### **2.1 Search Strategy**

A search was conducted through the National Library of Medicine using three databases: Medline, Embase and Cochrane Libraries with search terms pertinent to studies investigating the unnecessary utilization of health care resources, clinical laboratory tests, and the interventions undertaken to reduce the utilization of health care resources. Where applicable, inclusive initial searches were conducted to identify MeSH terms for more specific and exhaustive investigations of the literature. Bibliographies of relevant articles were also reviewed.

Restrictions of the literature search included: English articles only, abstract availability and humans only. The literature search was not restricted by date to ensure that that review would give a complete overview of the literature surrounding the unnecessary utilization of health care resources and the progress made in the effective development and implementation of interventions.

This literature review will offer background information of health care resource utilization in Canada, information on the contribution of laboratory testing to the increase in Health care expenditures and interventions undertaken to reduce the overutilization of laboratory testing. Additionally, this review will discuss the initiatives developed internationally, nationally and provincially to minimize the utilization of healthcare resources.

## **2.2 Background Information**

Healthcare spending has increased over the past several decades and is projected to continue its' rise for a variety of reasons including an ageing population and an increase in the incidence of obesity<sup>1-3</sup>. This increase has been noted in many countries and emphasizes the necessity to develop a more efficient health care system. In 2015, healthcare spending in Canada reached 219.1 billion dollars<sup>4</sup>. This expenditure represents 10.96 percent of the Gross Domestic Product (GDP) and a 4 billion dollar (1.6%) increase in comparison to 2014<sup>4</sup>. More than 60% of Canada's total health care dollars are being spent in three areas. These areas consist of hospitals (29.5%), drugs (15.7%) and physician services (15.5%)<sup>4</sup>. In 2015, the government of Newfoundland & Labrador spent \$7,036 (40% of the budget) per person on health care<sup>4</sup>. This expenditure is \$931 (15.3%) greater than the Canadian average (\$6,105)<sup>4</sup>. This is higher than any other province for per person health care expenditure in Canada, excluding the North West Territories, Nunavut & Yukon.

### **2.3 Laboratory Testing**

Laboratory testing is a prominent medical activity and is integral to many clinical decisions. It has been documented that there is a high incidence of inappropriate laboratory utilization<sup>5</sup>. This unnecessary utilization is accompanied by an increase in cost and a decrease in quality of care<sup>6</sup>. Over utilization of laboratory testing causes unnecessary blood draws and an increase in procedures associated with sample collection<sup>5</sup>. This unneeded testing increases the likelihood of generating false positive test results, elevating the risk of incorrect diagnosis which in turn can increase costs and produce adverse outcomes associated with unwarranted interventions<sup>5,6</sup>. False positive test results also have the potential to increase patient worry unnecessarily. Under testing has the potential to result in a delay or missed diagnosis, creating further implications for the patient and healthcare system downstream<sup>5,6</sup>. The result of both under and over utilization of these clinical investigations is a decrease in the quality of care provided to patients. Laboratory testing is an obvious area of interest to implement interventions to decrease inappropriate utilization; some studies have noted that the proportion of inappropriate tests range from 4.5-95%<sup>6</sup>. Identifying and rectifying inappropriate of laboratory resources is of paramount importance in order to optimize patient care and improve the performance of the health care system<sup>6</sup>.

## **2.4 Interventions to Reduce Laboratory Testing**

Recently, a systematic review was performed to investigate the effectiveness of varying types of interventions to reduce low-value care<sup>7</sup>. In this review, while complex to define, the term *low-value care* involved the use of care that was not likely to be beneficial to the patient, given the cost, available alternatives and the preferences of the patient. Colla and colleagues<sup>7</sup> strived to exclude interventions directed at reducing general utilization from efforts aimed at specific low value or inappropriate services. The authors divided all interventions into two categories: (1) Demand side interventions (patient demand for care), (2) Supply side interventions (Provider supply of care). Demand side interventions included: *Patient cost sharing, Patient education, Provider Report Cards (giving patients information on the providers use of inappropriate care with the intent of altering behaviour as a result)*. Supply-Side interventions included: *Pay-for-performance, Insurer restrictions, Risk sharing, Clinical decision support, Clinician education, Provider feedback*<sup>7</sup>. The systematic review revealed that multifaceted interventions, which address both the patient and providers roles in overuse, have the greatest potential to reduce the use of low-value care<sup>7</sup>. Performance feedback and clinical decision support were also found to be effective strategies and clinician education was also found to elicit change when coupled with other interventions<sup>7</sup>. Colla and colleagues<sup>7</sup> found that the interventions implemented to reduce low-value care were most common for medications (56%), followed by radiology (12%), procedures (10%) and labs/pathology (10%), emphasizing the need for a increase of investigations of interventions to reduce laboratory test utilization specifically for tests that provide low value care in clearly defined clinical situations.

Kobewka and colleagues<sup>9</sup> recently conducted a systematic review which specifically investigates the effectiveness of interventions to reduce laboratory test utilization by physicians.

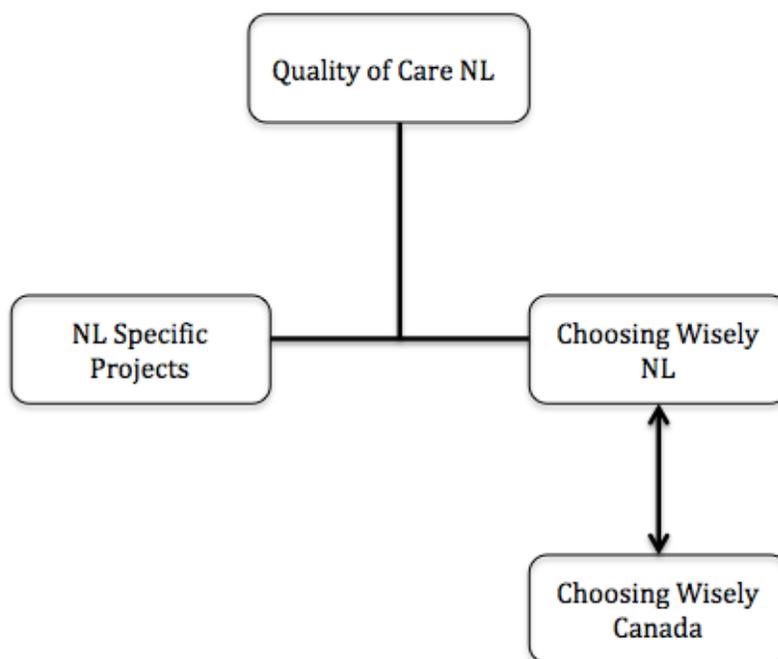
Interventions were classified into four categories: (1) Educational, (2) Audit and Feedback, (3) System-based and (4) Incentive or Penalty Interventions. Educational interventions consisted of appropriate test ordering being taught to physicians (distribution of guidelines). Audit and feedback interventions occurred when physicians were given their test utilization in comparison to their previous utilization or peer utilization (or could include total costs of their test ordering behaviour). System-based interventions consisted of a one-time, permanent change to the test ordering process (ordering form modifications, computer order entry systems with restrictions or guidelines). Finally, Incentive or Penalty interventions were defined as physicians receiving punishments or rewards for particular test ordering behaviours<sup>9</sup>. The review found that educational interventions had the highest relative reduction in laboratory test utilization, however, the sustainability of this type of intervention is questioned due to the minimal follow-up periods used throughout the literature<sup>9</sup>. In addition, it was noted that interventions with multiple strategies and interventions that targeted less than four tests were more effective<sup>9</sup>. The sample population, intervention, study design, recorded measurements and setting varied immensely across almost all studies. This high level of heterogeneity throughout the literature generates difficulty in interpreting which type of intervention is most effective and if the results are generalizable to other geographical locations and populations<sup>9</sup>.

### **2.4.1 Quality of Care NL**

The Quality of Care Newfoundland and Labrador is an initiative within Memorial University of Newfoundland that has developed a partnership with other organizations including Department of Health and Community Services (DOHCS), Newfoundland & Labrador Centre for Health Information (NLCHI), Regional Health Authorities (RHAs) and Newfoundland & Labrador Medical Association (NLMA). These together make up a working group that oversees the Quality of Care program. The primary purpose of the Quality of Care program is to identify the right patient who needs the right intervention at the right time and address unnecessary utilization of health care resources. This program is directly supported by the Center for Health Information and Analytics (CHIA). CHIA facilitates research for improving patient outcomes through the use of high-performance health informatics and data analytics hardware and will enable the integration of complex data from multiple partner sources<sup>10</sup>. The Quality of Care program is comprised of several areas of research: Laboratory Utilization, Diagnostic Imaging, Long-Term Care, Provincial Disease Management Program, Drug Utilization, Coronary Revascularization and Bariatric Surgery. The Quality of Care division is the parent program, which partakes in Newfoundland specific projects in addition to an implementation program associated with Choosing Wisely Canada (CWC) (See *Figure 1: Quality of Care Cascade*). Quality of Care NL works in close proximity to CWC in order to implement their recommendations on reducing unnecessary care. It is important to highlight that Quality of Care NL's intent is not only to reduce unnecessary care, it is also the initiative's intent to discover new ways to find who needs care, recommend the appropriate times that testing should occur and ultimately ensure that the right treatment is given to the right patient at the right time<sup>8</sup>. There are several projects that fall under the arm of this initiative, two of which are the centerpiece of this thesis: (1) Serum Urea & Serum Creatinine, (2)

Hemoglobin & Iron testing. These topics will be discussed in further detail in the sections allocated to their descriptions.

**Figure 1: Quality of Care Cascade**



### **2.4.2 Choosing Wisely**

Choosing Wisely is an initiative created by the American Board of Internal Medicine (ABIM)<sup>11</sup>. This initiative was formally launched in April 2012, with its goals oriented at promoting conversations between clinicians and patients by aiding patients to make informed choices while choosing care. The organization's mission is to facilitate care that is: (1) supported by evidence, (2) free from harm, (3) truly necessary, (4) not duplicative of other tests or procedures already received<sup>11</sup>. Initially, the organization released a "top five" list in adjunct to their campaign launch. This list consisted of five tests and treatments from nine specialty societies that were overused and did not provide meaningful benefit to their patients. Due to a positive reaction from the health care community and media coverage, 17 additional societies joined the campaign and released lists in February of 2013. Currently, there are more than 70 medical societies, comprised of over one million physicians, who are now partners with the Choosing Wisely Campaign. To date, the organization has collectively published over 450 recommendations about unnecessary tests and treatments. This campaign has developed partnerships, drawn media interest, inspired research, catalyzing the improvement of care<sup>11</sup>.

### **2.4.3 Choosing Wisely Canada (CWC)**

The Choosing Wisely Canada (CWC) campaign is modelled after the Choosing Wisely organization in the United States of America<sup>12</sup>. The CWC campaign began in Ontario and quickly sparked the interest of other provinces. To date, all provincial and territorial medical associations have endorsed the campaign and have either established or are in the process of establishing their own provincial/territorial initiative. Choosing Wisely Canada has been working with Medical schools across the country to introduce new content into undergraduate, post-graduate and

continuing medical education curricula. In addition, they have made an active effort to engage medical students by launching the STARS program (Students and Trainees Advocating for Resource Stewardship)<sup>12</sup>. Through the collaborations of various health organizations and associations, opportunities have developed to help support the implementations of physician recommendations in practice settings. They have introduced an “early adopters collaborative” to bring such groups together. The CWC campaign has invited these early adopters to participate in the 10 million challenge; a Canada wide call to action initiative to aid in the prevention of ten million unnecessary tests and treatments by the year 2020<sup>12</sup>.

#### **2.4.4 Choosing Wisely NL**

Choosing Wisely NL is the Newfoundland & Labrador provincial chapter of the Choosing Wisely Canada campaign. Choosing Wisely NL was launched October 6<sup>th</sup>, 2016. This provincial campaign is a collaborative effort between: The Translational and Personalized Medical Initiative (TPMI), The Newfoundland & Labrador Medical Association (NLMA), the provincial government, regional health authorities, patients and the Newfoundland & Labrador Centre of Health Information (NLCHI)<sup>13</sup>. The creation of Choosing Wisely NL emerged from research being conducted at the Faculty of Medicine of Memorial University<sup>14</sup>. Various stakeholders collaborated to develop a program similar to Choosing Wisely Canada (CWC)<sup>12</sup> and its American equivalent<sup>11</sup>. The desired outcome of the Choosing Wisely NL program is to be an available resource to provide recommendations to health care professionals and the public of Newfoundland and Labrador concerning the appropriate use of tests and procedures<sup>14</sup>. Choosing Wisely NL is a regional affiliate of Choosing Wisely Canada and is bound by their policies. Therefore, CWNL projects are focused on decreasing low value care while implementing recommendations of CWC.

All other projects that do not follow CWC recommendations are classified as Quality of Care projects.

#### **2.4.5 Interventions to Reduce Laboratory Testing in Primary Care settings**

This sub-category of the literature review is concerned with obtaining a complete overview of all interventions undertaken in primary care settings to reduce laboratory test utilization.

Therefore, an exhaustive search strategy was utilized. The search strategy is as follows:

The literature search was conducted using three databases: Pubmed, Embase and Cochrane Libraries. The Pubmed database was searched from 1950-2015 by combining Mesh terms of relevant articles. These Mesh search terms consisted of: *“Primary Health Care AND Clinical Laboratory Services/utilization OR Clinical Laboratory techniques/utilization OR Diagnostic Tests, Routine/utilization OR Health Services Misuse/prevention and control OR Unnecessary Procedures/utilization AND Utilization review”*. Search results were filtered to include only articles with abstracts, human subjects and restricted to the English language. The same search restrictions and key terms were applied while searching the other data sources (Embase & Cochrane Libraries). Searches were augmented and enhanced by scanning the bibliographies of included articles as well as relevant review articles. The literature search elicited nineteen articles that specifically investigated the effectiveness of interventions undertaken in a primary care setting to reduce laboratory test utilization and met the following criteria: 1.) The study had to focus on primary care (general practice physicians) or have a sub-category which focused on general practice physicians; 2.) The aim of the intervention was to modify test utilization (ordering/cost /

tests performed; 3.) A control (comparator) was required (either a no-intervention group or standard care).

Using a non-experimental, before-after study design, Larson and colleagues<sup>15</sup> investigated the effects of an education program on 63 primary care physicians at 19 primary care centres in Sweden. The intervention involved a 2-day educational series. The investigators used the physician's current practice (historical control) as a comparator. Of the 7 test ratios (e.g. Cholesterol / HDL Cholesterol) that the educational series recommended to decrease, 5 did significantly ( $p < 0.05$ )<sup>15</sup>. Additionally, 7 ratios were recommended to increase in ordering volume, 4 of which did ( $p < 0.05$ )<sup>15</sup>.

Similarly, Baricchi and colleagues<sup>16</sup> investigated the effect of an educational intervention which involved 8 training sessions for pathology specific laboratory profiles that were developed by a multidisciplinary inter-hospital team. The investigators reported that there was a 5% reduction in the number of tests requested by the intervention group ( $n=23$ ) ( $p < 0.001$ ) one year following the intervention<sup>16</sup>. The authors also highlighted there was a significant decrease in the volume of tests on each request form in the intervention district (8.73 VS. 10.77;  $p < 0.001$ ).

Rhyne and colleagues<sup>17</sup> also used a before-after study design to explore the effect of an educational intervention on all thyroid function panel tests ordered by physicians in the Duke-Watts Family Medicine Program. The authors performed an audit on all thyroid function panel tests performed during a 6-month period, then presented the results of the audit at an educational conference<sup>17</sup>. A re-audit was performed 6-months following the educational conference. The authors reported that the rate of ordering during the initial 3-months following the intervention

decreased significantly ( $p < 0.05$ ), however, the rate returned to the pre-intervention level in the final 3-months post-intervention<sup>17</sup>. As previously highlighted, the sustainability of educational interventions is brought into question due to the short follow-up periods used throughout the literature<sup>9</sup>. These investigations<sup>15-17</sup> provide support for this query.

However, Mindemarke and colleagues<sup>18</sup> conducted an extension of the trial by Larsson and colleagues<sup>15</sup> to investigate the long-term effects of an educational program on test ordering behaviours. The test ordering behaviours of 23 physicians were monitored in 2004 and compared to their ordering behaviours in 1997 (8-years post intervention follow-up)<sup>18</sup>. Eleven of the twelve investigated ratios were the same or had improved since the short- follow up period<sup>15,18</sup>. These results provide minimal evidence that continuing education intervention programs have the ability to elicit long lasting, permanent changes in test ordering.

Several trials have used multifaceted interventions, which have included an educational component<sup>19-23</sup>. Abdel-Kader and colleagues<sup>21</sup> performed a Randomized Controlled Trial on 30 Primary Care Physicians to evaluate the effectiveness of an educational & guidelines intervention to enhance the appropriateness of referrals to a specialist. The trial involved both the intervention arm (n=15) and the control arm (n=15) attending two Chronic Kidney Disease Educational sessions while the intervention group also received real time, automated, electronic medical alerts for renal referral<sup>21</sup>. The control group did not use the guideline alert system. The trial consisted of a 6-month post-intervention follow-up period and the authors reported no significant differences between groups (volume of renal referrals)<sup>21</sup>.

Thomas and colleagues<sup>23</sup> also used a Cluster Randomized Controlled trial design to implement an education and feedback intervention on 370 primary care physicians (85 primary care practices). The practices were randomly assigned to 1 of 4 arms: (1) reminder messages (n=22 practices), (2) control practices (n=20 practices), (3) enhanced feedback (n=22 practices), (4) both enhanced feedback and reminder messages (n=21 practices)<sup>23</sup>. The intervention consisted of quarterly feedback of practice requesting rates for nine laboratory tests, supplemented with educational messages and brief educational reminders<sup>23</sup>. The results showed an 11% reduction for practices receiving either feedback or reminder messages compared with the control group and a greater than 20% reduction in tests for groups that received combined interventions<sup>23</sup>. The authors suggest that these results highlight that feedback and education reminders are feasible interventions to reduce laboratory test utilization alone or in combination<sup>23</sup>.

Similarly, an investigation conducted by Bunting et colleagues<sup>22</sup> used an education and feedback intervention in an attempt to reduce laboratory test utilization. Physicians in the intervention group (n=100) were visited three times by laboratory representatives over a 2-year period<sup>22</sup>. Each visitation consisted of an educational presentation and the physicians personalized laboratory test utilization data; this personalized data was also compared to the utilization data of the physicians' peers<sup>22</sup>. The test utilization rates were measured 1-year pre-intervention, during the intervention period and 2 years after the intervention. The authors used a time series analysis and reported a significant decrease in laboratory utilization in the intervention group compared to the control group for the 2-years post intervention (-7.9%;  $p < 0.0001$ )<sup>22</sup>.

Tierney and colleagues<sup>19</sup> used a divergent approach to investigate an educational and feedback intervention. In contrast to other studies, the intervention consisted of providing information on the test ordering of the physicians based on cost. Physicians in both the intervention (n=62) and control (n=59) groups entered their orders for tests through computer workstations, the intervention group were displayed the charge of the individual test being ordered and the total charge for each patient, the control group would receive no feedback<sup>19</sup>. The intervention was undertaken for a 26-week period and during this time physicians ordered 14% fewer tests per patient visit compared to the control group ( $p < 0.005$ ). The post-intervention period endured for 19-weeks, in which the authors noted that the intervention group ordered only 7.7% fewer tests compared to the control group<sup>19</sup>.

Finally, Verstappen and colleagues<sup>20</sup> used an intervention which combined education, guidelines and feedback strategies. Their investigation involved 194 Primary Care physicians that were randomly allocated into two groups. A test ordering strategy was developed involving feedback, education on guidelines and quality improvement sessions in small groups. In these groups physicians were required to discuss each other's test ordering behaviours related to the guidelines and make individual and group plans for change<sup>20</sup>. Thirteen groups of physicians were engaged in the entire strategy whereas fourteen groups received only the feedback component of the intervention<sup>20</sup>. Verstappen and colleagues<sup>20</sup> found that the mean cost reduction in the complete intervention arm (n=13) was 144 euros larger per physician per 6-months in comparison to the physicians in the feedback only arm (n=14) ( $p=0.0048$ )<sup>20</sup>.

Studies which have used clinical guidelines and/or feedback as a crucial component of their intervention have had varied success<sup>24-27</sup>. Baker and colleagues<sup>24</sup> conducted a randomized controlled trial and implemented an intervention where physicians in one group (n=50) received guidelines and feedback on test ordering behaviours for thyroid function, rheumatoid factor testing and urine cultures. Physicians in the second group (n=38) received guidelines and feedback for their test ordering behaviours of lipid and plasma viscosity tests<sup>24</sup>. Intervention was implemented quarterly over a 12-month period with measurements being recorded at each stage<sup>24</sup>. Baker et colleagues<sup>24</sup> reported no significant change in the volume of tests per 1000 requested in either branch of the study groups, or for any individual test.

Van Wijk and colleagues<sup>25</sup> were successful at demonstrating the effectiveness of guidelines integrated into an electronic ordering system. In this randomized controlled trial two versions of BloodLink (computer-based support system) were developed: (1) BloodLink Restricted, (2) BloodLink Guidelines<sup>25</sup>. The restricted system initially displayed a reduced list of tests (15 tests found to cover most clinical scenarios seen in primary care) in addition to providing an option for physicians to select other tests. The guideline system displayed test-ordering guidelines from the Dutch College of General Practitioners to assist in decision-making and test ordering. The authors found that a decision support system based on guidelines was more effective in changing blood test ordering behaviours than a system based initially on a restricted order form<sup>25</sup>. Physicians who utilized BloodLink Guidelines on average requested 20% fewer tests compared to physicians using BloodLink Restricted<sup>25</sup>.

Similarly, Vardy and colleagues<sup>26</sup> demonstrated that a collection of laboratory routines developed by a group of experienced and certified physicians and integrated in a computerized ordering system were able to elicit a decrease in laboratory test utilization (-2%; no statistical parameters provided). However, this is a weak result and may be due to chance.

Although the literature emphasizes that effectiveness of multifaceted interventions<sup>7,9,28</sup>, Winkens and colleagues<sup>27</sup> demonstrated that an intervention composed of only feedback in the form of biannual reports of test ordering behaviours was able to elicit a significant decrease ( $p < 0.001$ ) in utilization patterns.

Interventions that are classified as system based were particularly effective at reducing laboratory test utilization in primary care settings. These system-based interventions all consisted of developing and implementing various changes to the laboratory test order form<sup>29-34</sup>. Emerson and colleagues<sup>29</sup> implemented a requisition form that was limited to Medicare approved panels. In addition, forms were also customized based on groups of specialties and patient service location with common test ordering practices. The authors reported that all specialities showed a significant reduction in laboratory utilization ( $p < 0.001$ ) excluding Neurology & AIDS (significant increase) and Urology, Orthopaedics & G.I. service (no significant change)<sup>29</sup>.

A study conducted by Kahan and colleagues<sup>31</sup> implemented a new version of a computerised order form and the volume of tests ordered in the initial month for the three target tests decreased 31-41% relative to the pre-intervention month and decreased 36 -58% the following month. Another study implemented a changing order form intervention by incorporating

the cost of 27 laboratory tests within an electronic health record<sup>30</sup>. The cost display system resulted in a significant decrease in laboratory orders per 1000 visits per month ( $p < 0.001$ )<sup>30</sup>.

Another form of a change in order form intervention throughout the literature is the implementation of restricted order forms. Shalev and colleagues<sup>33</sup> modified the regional health order form into a more restricted version, rendering the number of tests on the order form with a check box reduced from 51 to 26 tests. The authors reported that the tests that were removed elicited a 27% reduction in the first 12 months and a 19.2% reduction in the second year following the implementation of the new restricted form<sup>33</sup>.

Similarly, Zaat and colleagues<sup>34</sup> implemented a restricted order form to a group of physicians ( $n=28$ ) and compared their test ordering behaviours to a control group who used the standard ordering form ( $n=28$ ). The form was modified so that if the test was not present, the physician would write a hand-written request. The intervention elicited an 18% reduction in the number of tests ordered per general practitioner, per 1000 patients, per month during the intervention period<sup>34</sup>. An emphasized issue with restricted order forms is that they have the ability to limit appropriate test requests.

A study conducted by Meng and colleagues<sup>32</sup> took this into consideration while developing a Cardiac Troponin algorithm to limit orders from outpatient clinics while maintaining ordering abilities for emergency departments. General practitioners were still able to order troponin tests following a consultation with a clinical biochemist. This order form restriction intervention elicited a significant reduction in the number of requests for the Cardiac troponin tests

from Family medicine clinics (n=1,213(6.4% of all tests requested) to n=355 (2.7% of all tests requested), p=0.003)<sup>32</sup>.

Similar to other interventions, the sustainability of the restricted order form impact has been challenged. Meng and colleagues<sup>32</sup> and Shalev and colleagues<sup>33</sup> used relatively short follow up periods, 6 months and 24 months respectively. Zaat and colleagues<sup>34</sup> successfully reduced laboratory test utilization during the intervention period, however, the authors noted that following the removal of the restricted order form intervention the ordering behaviours returned to their pre-intervention patterns.

There have been very few studies conducted which specifically investigate the effect of interventions undertaken in primary care settings to reduce laboratory utilization and only a handful are of good quality. The majority of these studies have been conducted using an uncontrolled before-after design, which is inherently a methodologically weak study design. Another major limitation of the current literature is the generalizability of the results. The sample population, intervention, design, recorded measurements and setting varied immensely across almost all studies. This high level of heterogeneity throughout the literature generates difficulty in interpreting which type of intervention is most effective in primary care settings and if the results are generalizable to other geographical locations and populations.

**Table 1: Tabularized Overview of Interventions Undertaken in Primary Care Settings**

Study	Location	Design	Population	Method	Intervention	Control	Follow-up	Outcome
<b>Abdel-Kader et al</b>	USA	Cluster Randomized Controlled Trial	30 Primary Care Physicians	Education & Guidelines	Two Chronic Kidney Disease Educational Sessions were held for primary care physicians in both arms. Intervention Group (15 physicians) also received real time automated electronic medical record alerts for renal referral.	Control Group did not use the CDSS alert system	6- months pre-intervention & 6-months post-intervention	No significant differences between groups (Renal Referrals)
<b>Baker et al</b>	UK	Randomized Controlled Trial	33 General Practices (96 practitioners)	Guidelines & Feedback	17 practices (50 Gp's) received guidelines followed by feedback on test ordering behaviours for thyroid function, rheumatoid factor test and urine cultures they ordered (3 month intervals during a 12 month period)	16 practices (38 Gp's) received guidelines & feedback for lipid and plasma viscosity tests. Each group experimental arm was a control for the other)	Baseline - 12 months with quarterly feedback and measurements	No significant change in volume of tests per 1000 requested in either arm of the study groups or for any specific test.
<b>Baricchi et al</b>	Italy	Observational study with two retrospective audits	44 Primary Care physicians	Education	Mutidisciplinary inter-hospital team developed pathology specific laboratory profiles for more effective test requesting and provided 8 training sessions to physicians about their use (n=23 physicians)	21 General practitioners from a different district. The laboratory tests for both districts are performed at the same laboratory (current practice)	12 - Months pre- and 12 months post-intervention. Thirty days were randomly selected over the course of each period and the total number of test requests forms and the total number of ordered tests were recorded.	Number of tests requested in the trial district was significantly lower than the previous year (5%; p <0.001) -Significant decrease in the number of tests on each request form in the trial district (8.73 VS. 10.77; p <0.001)
<b>Bunting et al</b>	Canada	Time-Series Analysis	200 Primary Care Physicians	Education & Feedback	Intervention physicians (n=100) were visited up to three times by laboratory representatives over a 2-year period. At each visit the laboratory representatives presented educational material and the physicians personalized laboratory test utilization data. This personalized data was also compared to the physicians peers.	No information or personalized feedback given to the control group (n=100)	2 years post intervention	Laboratory utilization decreased significantly in the intervention group compared to the control group for the 2 years after the intervention ended. Reduced by 7.9% (p <0.0001)

**Table 1: Tabularized Overview of Interventions Undertaken in Primary Care Settings**

<b>Emerson et al</b>	USA	Non-Randomized Controlled Trial	Family physicians and residents in outpatient locations	Changing Order Form	Rquisition forms limited to Medicare approved panels. Using baseline date, requisition forms were also customized to groups of specialities and patient service locations with common ordering practices. Several cascades were implemented/emphasized in order to ensure the medical necessity of tests while decreasing diagnosis time and increasing convenience for patient/physician. The requisitions were in place for 6-months before follow-up data collection began.	Current practice: Number of all laboratory tests ordered by physicians in each outpatient location was retrieved from the laboratory information system for a period of 6-months.	7-Months post intervention	All specialties showed a significant reduction in laboratory utilization ( $p < 0.01$ ) excluding Neurology & Aids (significant increase) and G.I service, Urology & Orthopedics (No significant change)
<b>Horn et al</b>	USA	Interrupted Time Series	215 Primary Care Physicians	Changing Order Forms	Cost display of 27 laboratory tests was displayed within an electronic health record (n=153)	No cost display within health record (n=62)	12 months pre-intervention and 6-months post-intervention. In addition, surveyed physicians from both arms 6-months post intervention to assess attitudes regarding costs/cost displays.	Cost display intervention resulted in a reduction of 0.4-5.6 laboratory orders per 1000 visits per month ( $p < 0.001$ )
<b>Kahan et al</b>	Isreal	Non-Randomized Controlled Trial, Before-after design	Primary Care Physicians	Changing Order Form	A new version of a computerized order form was launched. Number of B12, folic acid and ferritin was calculated for the intervention group	Controls were the utilization patterns of laboratory tests for HgB and Iron during this period, as their presentation on the form was not affected by the new format. Current Practice.	6-months pre-intervention and 4-months post intervention	The first post-intervention month elicited a decrease of 31% - 41% relative to the pre-intervention month and a 36%-58% reduction the following month. There was a 2% - 3% change for controls

**Table 1: Tabularized Overview of Interventions Undertaken in Primary Care Settings**

<b>Larsson et al</b>	Sweden	Before - After design	63 Primary Care Physicians at 19 primary care centres.	Education	2- day educational lecture series, all recommendations were supported by references from scientific literature. These individuals were informed that their ordering habits would be monitored	Current Practice, Historical Control pre-intervention	8-months pre-intervention and 4-months post-intervention	Of the 7 ratios that were recommended to decrease in volume, 5 did significantly ( $p < 0.05$ ). Of the 7 ratios that were recommended to increase, 4 did significantly ( $p < 0.05$ )
<b>Meng et al</b>	Canada	Before - After Design	All 3 Tertiary hospitals and outpatient clinics in this region	Order form restrictions	A cardiac Troponin test algorithm was developed by a group of cardiologists, physicians and laboratory professionals. Its purpose was to limit orders from outpatient clinics and non-emergency departments while maintaining order priority for cardiac care units, intensive care units and trauma care units. Family physicians could still order the troponin tests following a consultation with a clinical biochemist.	Current practice, historical control, 6-months pre intervention	6-months post implementation of the cTnI test algorithm	Total number of test requests, the number of requests from outpatient clinics and other locations, third consecutive requests and more than 3 requests per patient reduced significantly. Specifically, the number of requests for family medicine reduced significantly from 1, 213 (6.4%) to 355 (2.7%), ( $p=0.003$ )
<b>Mindemarke et al</b>	Sweden	Before-after design	23 Primary care physicians at 16 primary health care centres	Education	No intervention, the study is a continuation of the study conducted by Larsson et al, to investigate the long-term effects of an educational programme	Historical control group, The test ordering behaviours of 23 physicians were monitored in 2004 and compared to their ordering behaviours in 1997. Subjects were told that follow-ups would take place	8-years post intervention follow-up	11/12 of the investigated ratios were the same or had improved since the time of the short follow-up period (6-months). These results suggest that continuing education programs can bring about long lasting changes in test ordering.

**Table 1: Tabularized Overview of Interventions Undertaken in Primary Care Settings**

<b>Rhyme et al</b>	USA	Before-after design	All Thyroid function panel tests ordered by physicians in the Duke-Watts Family Medicine Program	Education	Audit was performed on all Thyroid function panels performed during a 6-month period. Survey was developed from the audit to determine how "essential to good medical care" the practice members considered the TFP in the evaluation of the 10 common problems identified in the audit. To complete the education, the results of the audit, and the survey were presented at a conference. The conference focused on the process of clinical decision making, hoping physicians would gain awareness of factors that effect test ordering behavior.	Current practice, historical control	re-audit was performed 6-months post educational intervention	During the 6-month post intervention period, the rate of ordering during the first three months decreased significantly ( $p < 0.05$ ). However, the ordering rate rose to the pre-intervention level in the subsequent 3-months of the follow-up period.
<b>Shalev et al</b>	Israel	Non-experimental, descriptive study design	865 Primary Care Physicians	Change in ordering form	Altering the order form into a more restricted version. The volume of tests on order form available using a check box reduced from 51 to 26	Current practice (form) prior to intervention	12 months pre-intervention and 24 months post-intervention	The tests that were removed elicited a 27% reduction in the first year and 19.2% reduction in the second year following the implementation of the restricted order form
<b>Thomas et al</b>	UK	Randomized Controlled Trial	370 Primary Care Physicians (33 practices)	Education and Feedback	Quarterly feedback of practice requesting rates for nine laboratory tests, enhanced with educational messages and brief educational reminders. The practices were assigned to 1 of 4 arms: reminder messages (22 practices), control (20 practices), enhanced feedback (22 practices), both enhanced feedback and reminder messages (21 practices)	Control group consisting of 20 practices, current practice	12-months pre-intervention and 12-months post-intervention	11% reduction in requests for practices receiving feedback or reminder messages compared with control group. Both in combination or alone are feasible methods for reducing test requesting in primary care settings.

**Table 1: Tabularized Overview of Interventions Undertaken in Primary Care Settings**

<b>Tierney et al</b>	USA	Randomized Controlled Trial	121 primary care physicians (4 practices) in the Regenstrief Health Center	Education and Feedback	The intervention group (n=62), the charge of the test being ordered and the total charge of tests for that patient on that day were displayed. The intervention period was undertaken for a 26 week period.	Control Group (n=59) no feedback given	14 weeks pre-intervention and 19 week post-intervention	During the intervention period, the physicians ordered 14% fewer tests per patient visit compared to the control group ( p <0.005). During the post-intervention period, the intervention group ordered 7.7% fewer tests compared to the control group.
<b>Van Wijk et al</b>	Netherlands	Randomized Controlled Trial	60 Primary Care Physicians from 44 practices	Guidelines using electronic ordering system	Two versions of BloodLink, which is a computer based support system were developed. BloodLink Restricted initially displays a reduced list of tests and BloodLink-Guideline is based on guidelines of the Dutch College of General Practitioners	Each group acted as a control for the other	Study Period: July 1, 1994 - June 1995	Decision support based on guidelines is more effective in changing blood test-ordering behavior than decision support that is based on initially displaying a restricted number of tests. General practitioners who used BloodLink Guidelines requested 20% fewer tests on average compared to physicians using BloodLink Restricted
<b>Vardy et al</b>	Israel	Non-Randomized Controlled Trial	380 Primary Care Physicians	Guidelines	Consensus group of experienced and certified physicians was formed in order to develop a compendium of laboratory routines. The computerized laboratory routines were organized into tests for screening, tests to assess the extent of the problem and full evaluation.	Historical control group	3-months post intervention	2% decrease in laboratory tests ordered in 2004 (1,792,221) compared to 2003 (1,834,366)

**Table 1: Tabularized Overview of Interventions Undertaken in Primary Care Settings**

<b>Verstappen et al</b>	Netherlands	Randomized Controlled Trial	194 Primary Care Physicians	Education, Guidelines and feedback	Test ordering strategy was developed systematically and it combined feedback, education on guidelines and quality improvement sessions in small groups. In these groups physicians discussed eachothers test ordering behaviors, realted to guidelines and made individual/group plans for change.13 groups engaged in th entire strategy whereas 14 groups received feedback only.	Current Practice	6-months pre intervention and 6 months post intervention	Mean cost reduction in complete intervention arm was 144 euro larger per physician per 6-months compared to the physicians in the feedback arm (p=0.048)
<b>Winkens et al</b>	Netherlands	Non-Randomized Controlled Trial	85 Primary Care Physicians	Feedback	Feedback on test ordering behaviour of general practitioner in biannual reports between 1985-1995	Control group consisted of General Practitioners in another region of the Netherlands that did not receive feedback (Laboratory A)	5 years (1985-1990)	For the 46 available tests, the intervention group ordered 101 983 tests in 1983 and 83 062 in 1989. The control group ordered 182 283 in 1983 and 276 401 in 1989. The effect of feedback elicited a significant decrease (p< 0.001)
<b>Zaat et al</b>	Netherlands	Non-randomized controlled trial	75 Primary Care Physicians	Education & Change in Order Form	Order form restriction. If test was not present on the form physicians would have to write a hand written request (n=47 physicians)	Control group used the standard form (n=28 physicians)	12-months post intervention	18% reduction in the number of tests ordered per general practitioner, per 1,000 patients, per month during the intervention period. Following the re-introduction of the standard order form the ordering practices returned to their old patterns

## **2.5 Serum Urea & Serum Creatinine**

Serum urea and serum creatinine are nitrogenous end products of metabolism and are used as screening tests for renal function<sup>35-39</sup>. Due to their distinct physiological properties their production and serum levels have distinct differences and implications<sup>35</sup>. Creatine is formed in the liver, where it enters circulation and is predominantly absorbed and stored in muscle tissue<sup>38</sup>. The majority of this stored creatine is phosphorylated into creatine phosphate in a reaction that is catalyzed by the enzyme creatine phosphokinase (CPK); a small portion of these stores are transformed into creatinine through a non-enzymatic reaction<sup>38</sup>. Due to this relationship, creatinine production is closely related to lean muscle mass, it is relatively constant and minimally impacted by physical activity, protein intake and protein catabolism<sup>35,38,39</sup>. Upon release, creatinine gains access to the plasma and it is exclusively excreted from the body by the kidney<sup>35</sup>. Owing to the fact that creatinine is largely dependent on filtration at the glomerulus for excretion, the Glomerular Filtration Rate (GFR) is inversely related to the serum creatinine level. Therefore, serum creatinine level can be used to estimate GFR and thereby kidney function. Similarly, serum urea is the principal end product of protein and amino acid catabolism. It is produced when toxic ammonia from protein catabolism is converted to non-toxic urea through a process known as the Urea cycle<sup>37</sup>. Divergent to serum creatinine, serum urea is a poor indicator of glomerular filtration rate (GFR) as its' production levels depends on several non-renal factors. In addition, urea is variably reabsorbed by the renal tubule after filtration, a process that is influenced by factors such as dehydration. Factors that can cause an increase in urea include: dehydration, congestive heart failure, shock, bleeding in the gastrointestinal tract, ingestion of large quantities of protein (diet) and illnesses that cause protein catabolism<sup>35,37-39</sup>. When compared to serum urea, serum creatinine is a more specific test of renal function and is no less sensitive<sup>37</sup>. Serum

creatinine is the preferred test to monitor kidney function and the progression of chronic kidney disease (CKD)<sup>40</sup>. Assessing the clinical value of tests requires the consideration of test validity, convenience and expense. As tests of renal function, serum urea and serum creatinine are considered to be: low cost, requiring minimal resources, low risk and convenient<sup>35</sup>. Although accompanied with limitations, serum urea may be useful in the diagnosis of acute kidney injury and in combination with serum creatinine may be useful in identifying: Azotemia, liver disease, nutritional requirements, and rhabdomyolysis<sup>38,39</sup>. The use of these tests will be discussed further as it comprises a main feature of this paper.

## **2.6 Hemoglobin and Iron Tests**

Anemia is characterized by a decrease in the total amount of haemoglobin (Hgb) or the number of red blood cells (RBC) throughout the body<sup>41,42</sup>. A reduction in this constituent of blood will result in the decreased ability of the circulatory system to transport adequate oxygen to the tissues<sup>43</sup>. Hgb is the iron-containing protein in red blood cells that binds oxygen and carries it throughout the body<sup>43</sup>. A low Hgb blood test result may indicate anemia<sup>43,44</sup>. Emphasized causes of anemia include: sickle cell disease, thalassemias, iron deficient anemia (IDA), malaria, schistosomiasis and hookworm<sup>42</sup>. Iron deficient anemia is one of the most critical and serious nutritional deficiencies globally to date<sup>42,45</sup>. IDA is characterized by hypochromic and microcytic red blood cells in addition to low iron stores<sup>41,44,46,47</sup>. Causes of IDA may include: Increased iron loss, increased iron demand, insufficient iron intake and inadequate iron absorption<sup>43</sup>. Pre-Menopausal women represent a large population of individuals who fulfill the criteria of IDA, reasons include: pregnancy, menstruation, breast feeding<sup>44</sup>. Complete blood count (CBC) is useful for determining the mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH)<sup>46</sup>. MCV is the measure of the average RBC volume<sup>46</sup>. MCH is a measure of concentration of haemoglobin in a given volume of RBC's<sup>46</sup>. A serum ferritin test should be performed in individuals with anemia; it reflects stored iron and is the most accurate test for diagnosing IDA<sup>44,46,47</sup>. It is important to note that ferritin levels may be deceptive while accompanied by acute or chronic inflammation<sup>48</sup>. Similarly, Iron saturation is another indicator of iron stores in the body. This test takes into consideration two indices: (1) Serum Iron, (2) Total Iron binding capacity<sup>49</sup>. The utilization of these tests forms the centerpiece of this paper and will be discussed further in the proceeding chapter

## Summary of Literature Review

Healthcare spending has increased over the last several decades for a variety of reasons<sup>1-3</sup>. In addition, frequency of laboratory test utilization has increased over time. The literature suggests that often utilization is inappropriate<sup>5</sup>. Inappropriate utilization is accompanied by increased financial costs and decreased quality of care<sup>6</sup>. Systematic investigations have been undertaken to investigate the effect of interventions to reduce the unnecessary utilization of laboratory resources<sup>7,9</sup>. Authors found that multifaceted, educational interventions had the greatest degree of success; however, their sustainability is questioned<sup>7,9</sup>. Interventions undertaken in primary care settings have had varied success<sup>15-34</sup>. The high level of heterogeneity throughout the literature jeopardizes the generalizability and validity of the results. Similarly, the majority of the literature uses weak uncontrolled pre-post designs, short follow up periods and small sample sizes, decreasing the quality and validity of the investigations. Several initiatives have recently been launched, internationally<sup>11</sup>, nationally<sup>12</sup> and provincially<sup>8,13,14</sup>, with the objective of reducing the unnecessary utilization of health care resources and improving care. Through these initiatives problem areas have been identified in Newfoundland Eastern Health Care Region particularly in primary care settings. Areas of interest identified include: serum urea, serum Creatinine, HgB and iron testing.

## **Chapter 3: METHODS**

### **3.1 Ethical Considerations**

A complete ethics application was prepared and submitted (reference number: 2016.183) to the Health Research Ethics Board (HREB) for the secondary use of data approval (Appendix A). Following approval, data was de-identified and encrypted to ensure anonymity of all identifying information. All research conducted complied with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans<sup>50</sup>. All members of the research team were required to sign an oath of confidentiality through the Centre of Health Informatics and Analytics (CHIA). Presently, the study has been closed with HREB due to the fact that once data collection is completed the study does not have to remain open (Appendix A).

The intent of these data is for internal use for assessment, management and improvement purposes, therefore, this investigation is classified as program evaluation/quality improvement based on article 2.5 of TCPS guidelines<sup>51</sup>. For these reasons, no informed consent is required. An Institutional Review Board (IRB) is allowed to waive the requirements for obtaining informed consent of the subjects when: (1) The risks to the subjects are minimal; (2) Conducting the research with the use of informed consent is not practicable<sup>51</sup>

### **3.2 Participant Protection and Data Storage**

As previously mentioned, all personal identifiers were removed from the data to ensure the privacy and confidentiality of those included in the data set. Only individuals with the required ethical approval and permission are able to view the identifiable data.

A data custodian will retain all collected data for 5 years following submission date of this paper. The data will remain restricted and de-identified. The data set is electronic; therefore, it will be kept on an encrypted computer and/or encrypted flash drive with the necessary security requirements in place.

### **3.3 Participants and Research Settings**

This investigation takes place in the Eastern Health region of Newfoundland and Labrador. Eastern Health is the largest health organization in Newfoundland and Labrador. This organization provides many health services to a regional population of greater than 300,000. Eastern Health extends from St. John's to Port Blandford and includes all of the communities on the Avalon, Burin and Bonavista peninsulas. The regional range of Eastern Health is included within a total of 21,000 km<sup>2</sup> <sup>52</sup> (See Figure 2). The participants in this investigation include all patients in the Eastern Health Region who received tests for Blood Urea Nitrogen, serum creatinine, hemoglobin, ferritin and iron saturation and the physicians who requested these laboratory examinations.



Figure 2

**Figure 2: The Geographic Boundaries of Eastern Health**

Image of the Eastern Health Region with site locations depicted. Retrieved from: <http://www.easternhealth.ca/AboutEH.aspx?d=1&id=1095&p=73>

### **3.4 Data Sources**

Data concerning test-ordering behaviour was obtained from Eastern Health's Meditech system through the Center for Health Informatics and Analytics (CHIA). Variables provided through this system includes: specimen ID, patient identifying code (encrypted), patients age, patients sex, patient status (inpatient V.s. outpatient) test being ordered, laboratory location used, submitting physician code, attending physician code, submitting physician specialty, attending physician specialty, test collection date, time, test result. Data for the blood urea nitrogen and serum creatinine was obtained for a 6-month period in 2014 (July 1<sup>st</sup>-December 31<sup>st</sup>). Data for the haemoglobin, ferritin and iron saturation tests were obtained for a 12 –month period (April 1<sup>st</sup>, 2013 – April 1<sup>st</sup>, 2014).

### **3.5 Laboratory Test Reference Ranges**

All reference ranges were obtained from the Chief of Clinical Biochemistry with Eastern Health<sup>53</sup>. The April 2016 version of adult reference ranges was used for this paper. The following ranges represent the normal values for each test.

<b>Serum Urea:</b>	3.0 – 7.0 mmol/L (Male/Female)
<b>Serum Creatinine:</b>	37 – 91 µmol/L (Female) 54 – 113 µmol/L (Male)
<b>Hemoglobin:</b>	120 – 160 g/L (Female) 140 – 180 g/L (Male)
<b>MCV:</b>	80 – 99 fL (Male/Female)
<b>MCH:</b>	27 – 32 pg (Male/Female)
<b>Ferritin:</b>	30 – 160 µg/L (Female 18-49 years of age) 30 – 300 µg/L (Male) 30 – 300 µg/L (Female 50+ years of age)
<b>Iron Saturation:</b>	0.2 – 0.55 (Male/Female)

### **3.6 Data Analysis**

All data were obtained in the form of Microsoft Excel files. Initially, files were organized into individual sheets for each test and preliminary data cleaning and analysis occurred at this stage. The initial stage of this analysis was comprised of interpreting the data set, cleaning and recoding variables in order to investigate the topic of interest and perform an efficient analysis. Initial data cleaning consisted of the removal of patients less than 18 years of age. Submitting physician specialty was recoded in order to create two separate variables: (1) submitting physician code (numerical), (2) submitting physician specialty (string). The patient type variable was recoded so that every patient type that ended in “IN” or “INx” was classified as inpatient; the remainders were coded as outpatients. Patients with missing values that were required for analysis (e.g. test result) were removed from the data set; the impact is believed to be negligible, however, this is discussed in sections allocated to limitations. The analysis for this project only used descriptive statistics; no statistical parameters are provided. Following initial assessment, the analysis was moderately divergent for the two separate bundles of tests: (1) serum urea and serum creatinine, (2) hemoglobin, ferritin, iron saturation. The differing processes are as follows:

#### **3.6.1 Serum urea & Serum Creatinine**

The data set was initially analyzed using descriptive statistics of variables of interest. Test results for both tests were coded as normal or above normal. All tests that elicited a result that was less than the reference range were included in the normal category; for the purposes of this project our only interest was those tests results that were high and their associated clinical implications. All individuals who were less than eighteen years of age were removed from the data set; for the

purposes of this project we were only interested in adults. Serum creatinine and serum urea datasets were then linked using IBM SPSS Modeler<sup>54</sup>. The data was linked by specimen I.D, age, sex, patient I.D, collection date and time, creating an inner join merge of the datasets. This allowed for the investigation of tests that were ordered in combination at the same time. Following data linkage, the data was stratified by specialties with the highest utilization and by test result. All data is presented using graphs, generated by the Microsoft excel program<sup>55</sup>.

### **3.6.2 Hemoglobin, Ferritin, Iron Saturation**

Similarly, the initial analysis consisted of investigating the data set by using descriptive statistics on variables of interest. In contrast to the previous test bundle, all test results that elicited a result that was higher than the reference range were included in the normal category; for this project we are only interested in results that were normal or low and their associated clinical implications. Once again, this data set contained only adults (all individuals less than 18 years of age removed). The process undertaken to link the data sets was slightly different for the potential over-utilization and under-utilization analysis. The number of *tests* ordered for the over-utilization analysis was obtained by merging the iron status tests data sets to the Hgb dataset, creating a semi outer join or left join. The iron status tests were linked to the patients' first Hgb test using the unique patient code and collection date. The number of *patients* for the under-utilization analysis was obtained by first filtering the Hgb data set for unique patients only. This process allowed for the removal of repeating patient codes, allowing for an accurate representation of the number of patients who underwent testing. Patients were then linked with their unique patient code to their first Hgb test using the collection date variable. The Hgb data set was then linked to the iron status data set using the unique patient code variable, creating a semi-outer join of the datasets. The data merges were achieved using IBM SPSS Modeler<sup>54</sup>. Age was not used in the link due to the fact

that this bundle of tests contains the test ordering behaviours during a 12-month period; therefore, there is a possibility that someone's age changed during this time period. The data was spot checked by comparing unique patient I.Ds between the original and linked data files to ensure the number of iron tests performed for each patient was accurate. The data was then categorized and analyzed by test result, number of iron tests performed in a specified date range, sex, specialty type and patient type. All data are presented using graphs, generated by Microsoft excel<sup>55</sup>.

## **Chapter 4: RESULTS**

### **4.1 Serum Urea & Serum Creatinine**

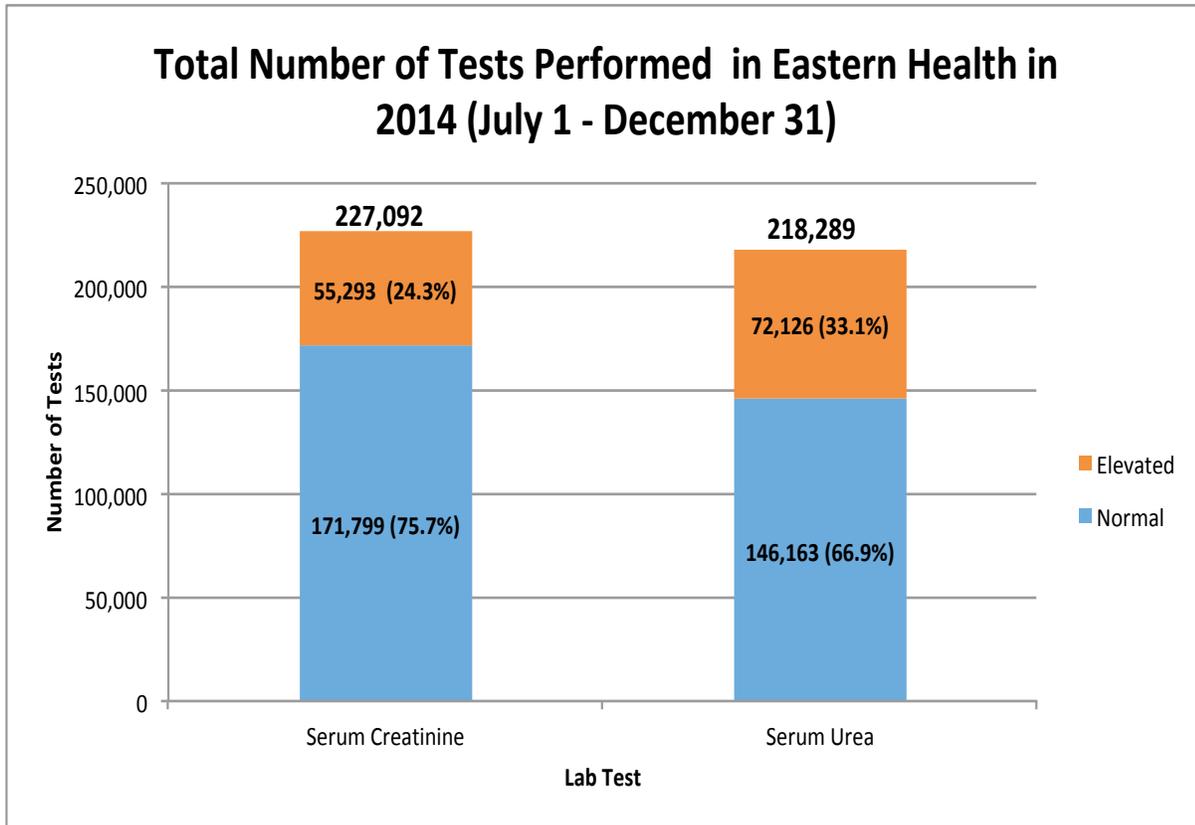
#### **4.1.1 Volume of Tests**

227,092 serum creatinine and 218,289 serum urea tests were ordered during the time period of July 1<sup>st</sup>, 2014 – December 31<sup>st</sup>, 2014. Of these laboratory investigations, 24.3% of serum creatinine tests and 33.1% of serum urea tests elicited elevated results (Figure 3).

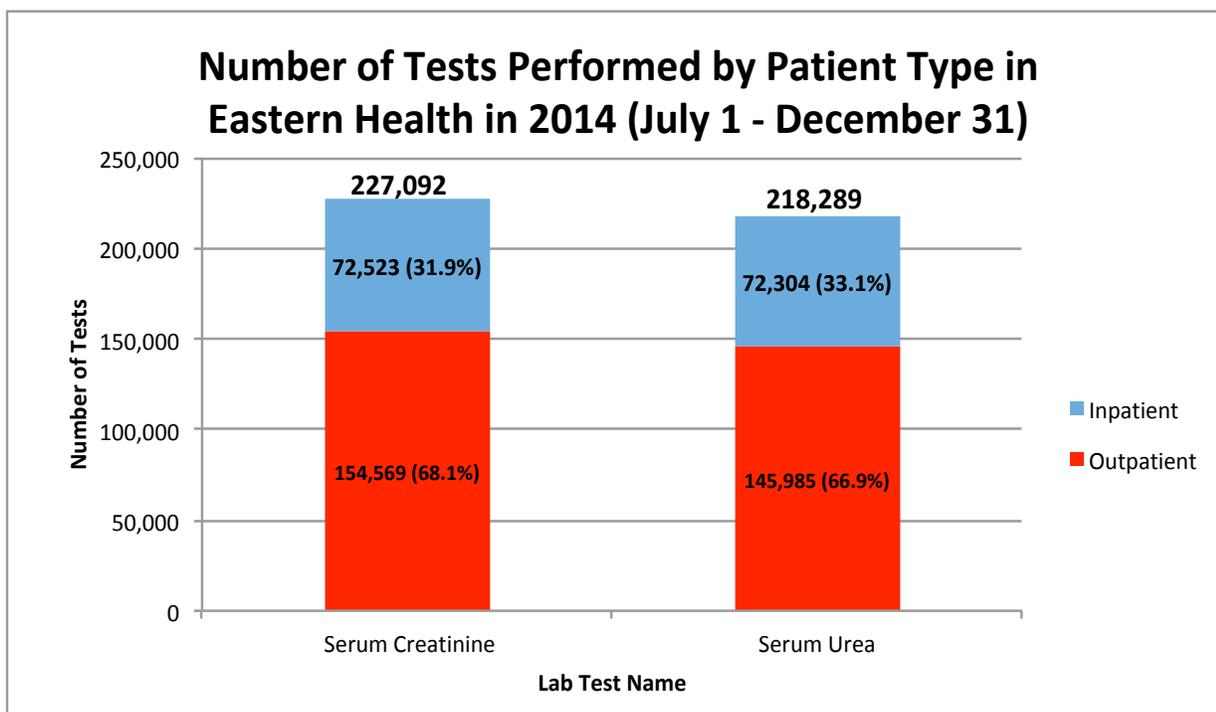
68.1% of all serum creatinine tests and 66.9% of all serum urea tests were ordered for outpatients (Figure 4).

Figure 5 describes the number of serum urea and serum creatinine ordered each month. The pattern of test ordering remained relatively stable throughout the 6-month period with slight increases during the months of September and October. Serum creatinine was ordered at a slightly higher volume each month.

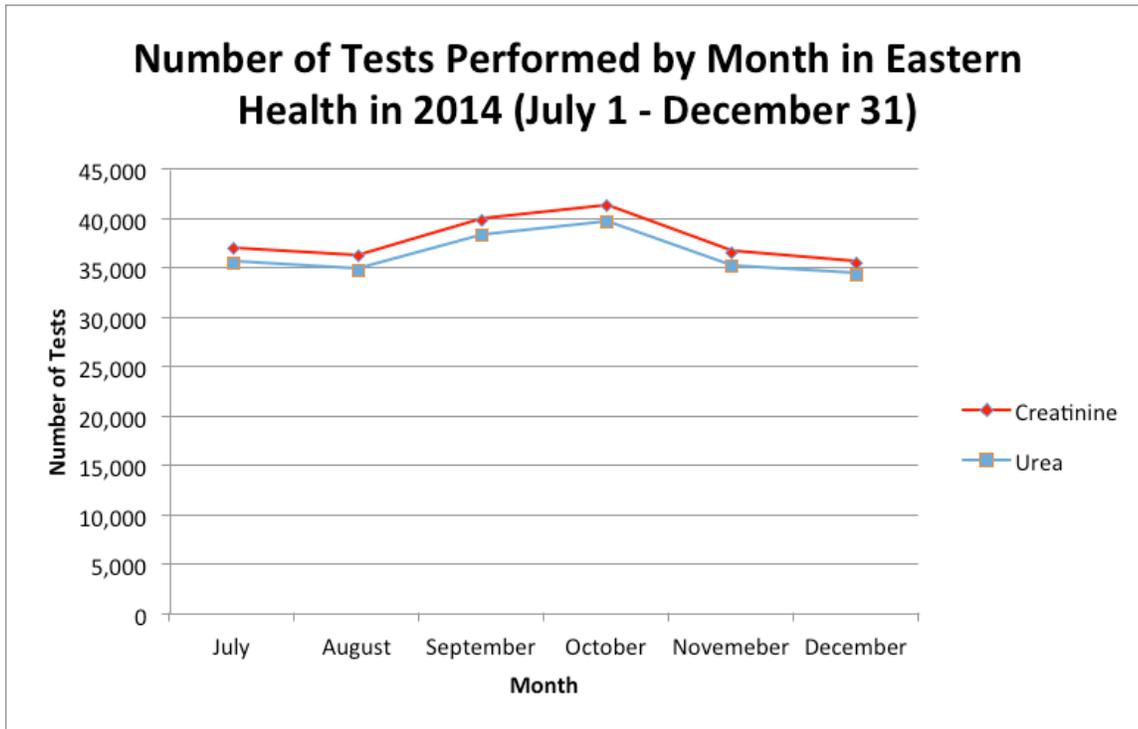
**Figure 3. Total Number of Tests Performed in Eastern Health in 2014.** A high volume of serum creatinine and serum urea tests were ordered in the regional health authority within the 6-month period. A large proportion of both laboratory investigations elicited a normal test result.



**Figure 4. Number of Tests Performed by Patient Type in Eastern Health in 2014.** The majority of serum creatinine (68.1%) and serum urea (66.9%) laboratory tests were ordered for outpatients within the Eastern Health Region.



**Figure 5. Number of Tests Performed by Month in Eastern Health in 2014.** Ordering of renal function tests in Eastern Health was relatively consistent during the 6-month period in 2014 with urea tests ordered at a slightly smaller volume each month.



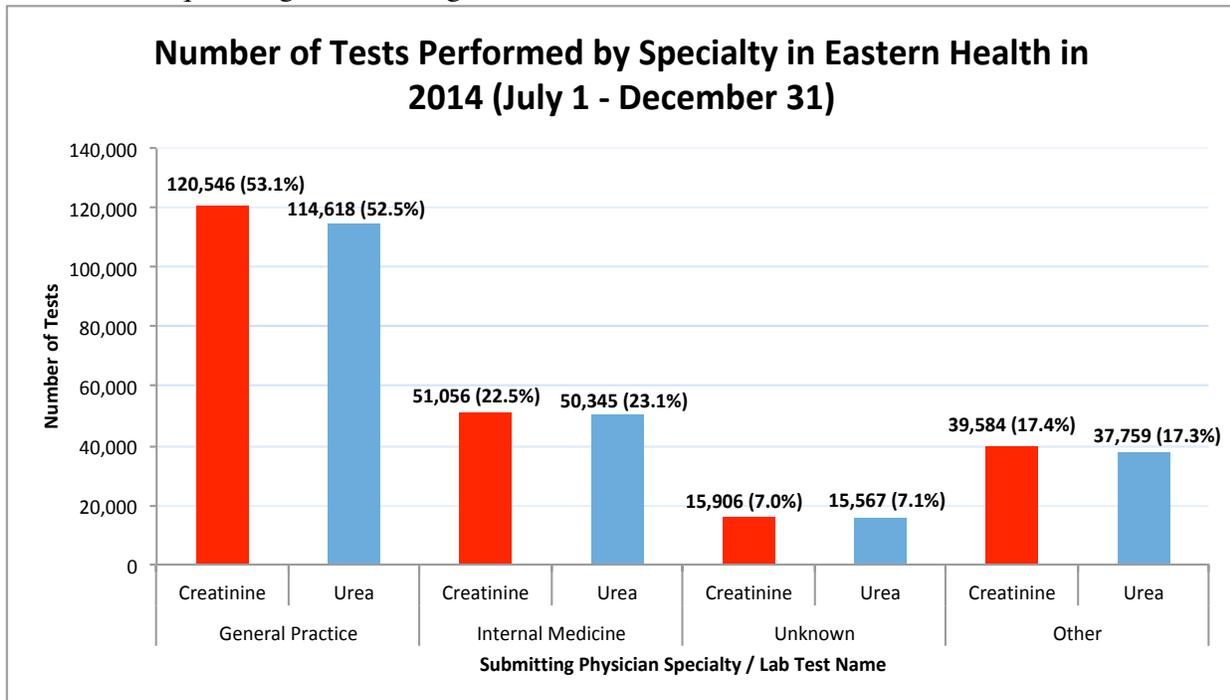
#### **4.1.2 Volume of Tests Ordered by General Practitioners**

Figure 6 demonstrates the number of serum urea and serum creatinine tests ordered by practicing specialties within the Eastern Health Region. General Practitioners had the highest rates with 53.1% of serum creatinine and 52.5% of serum urea tests being ordered by this discipline. Internal Medicine had the subsequent highest ordering rates with 22.5% and 23.1% for creatinine and urea, respectively. A large proportion of serum urea (89.6%) and serum creatinine (90.1%) tests ordered by general practitioners were done so for outpatients (Figure 7 & Figure 8).

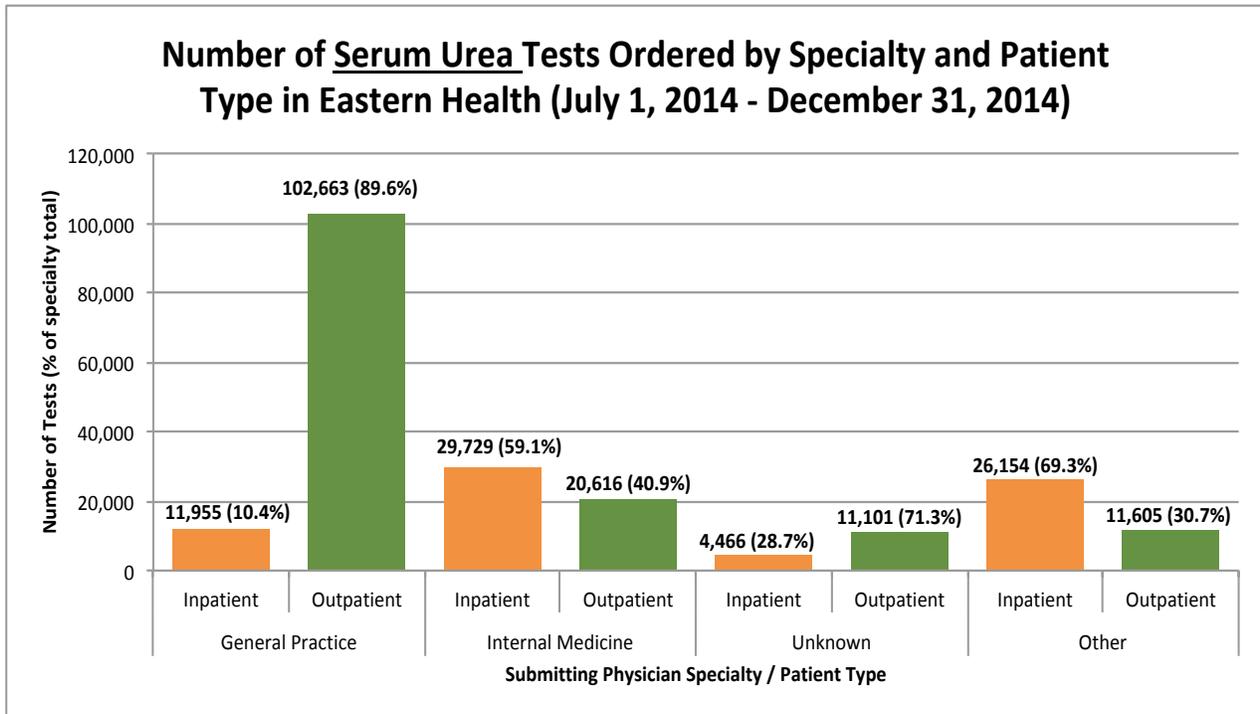
Of the laboratory investigations requested by general practitioners, 24.3% of serum creatinine tests and 33.6% of serum urea tests elicited elevated results (Figure 9). 34,411 (33.5%) of serum urea investigations ordered by a general practitioner for outpatients resulted in an elevated test outcome (Figure 10).

There is a high variability for the number of serum urea tests being ordered between general practitioners, with the top physician ordering 1,622 tests in a 6-month period (Figure 12 & Figure 13).

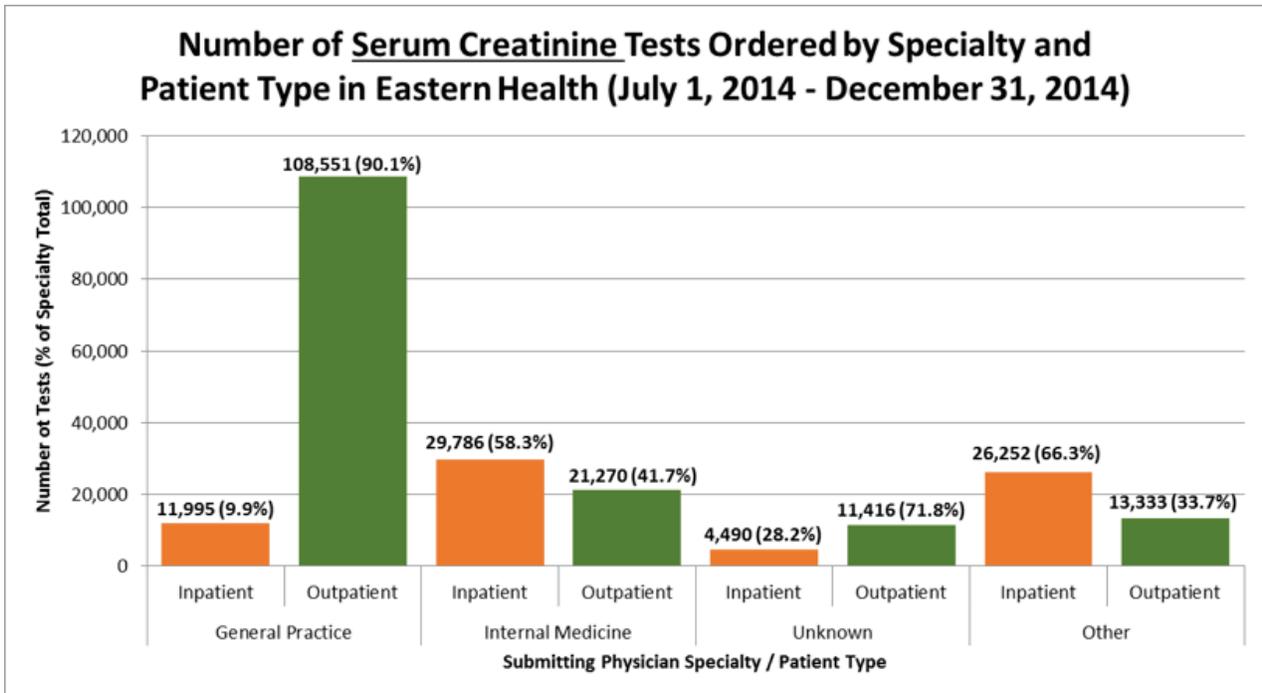
**Figure 6. Number of Tests Performed by Specialty in Eastern Health in 2014.** General Practitioners ordered the highest volume of serum creatinine (53.1% of total) and serum urea (52.5% of total) tests during the 6-month period in Eastern Health. The internal medicine specialty had the subsequent highest ordering rates for both tests.



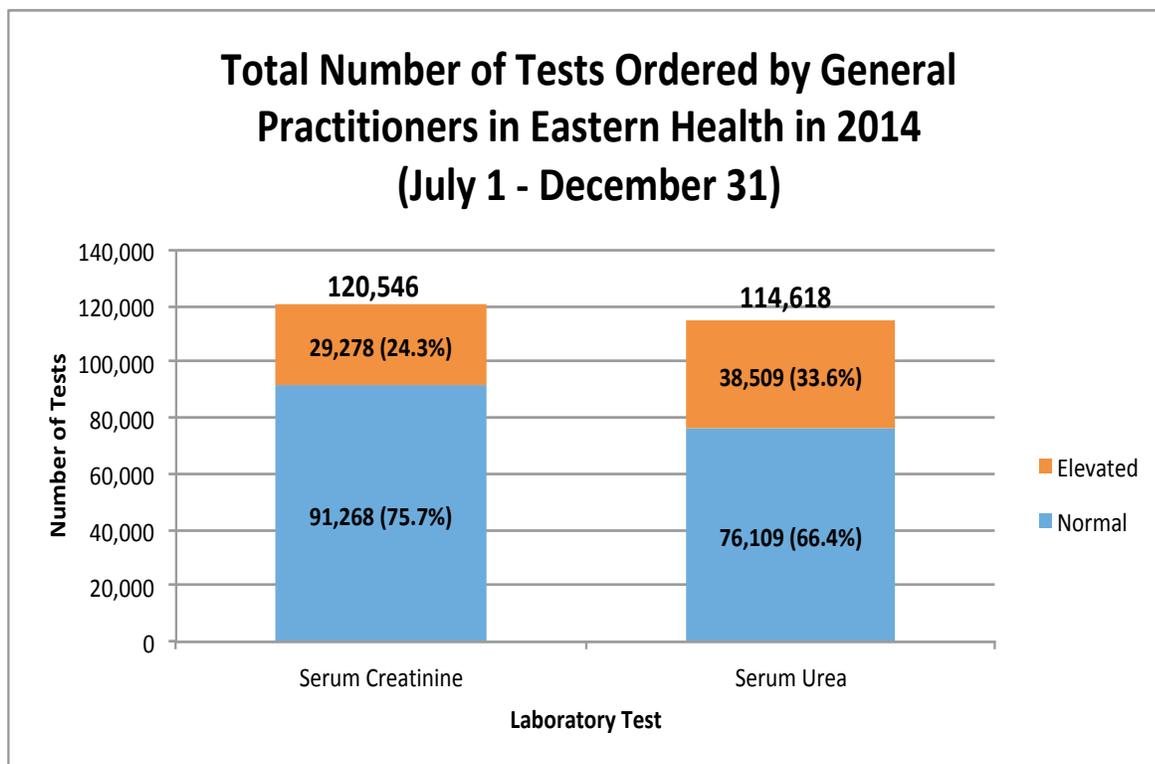
**Figure 7. Number of Urea Tests Ordered by Specialty and Patient Type in Eastern Health in 2014.** The highest volume of serum urea tests ordered for outpatients were requested by general practitioners. The highest number of urea tests ordered for inpatients were requested by the internal medicine specialty.



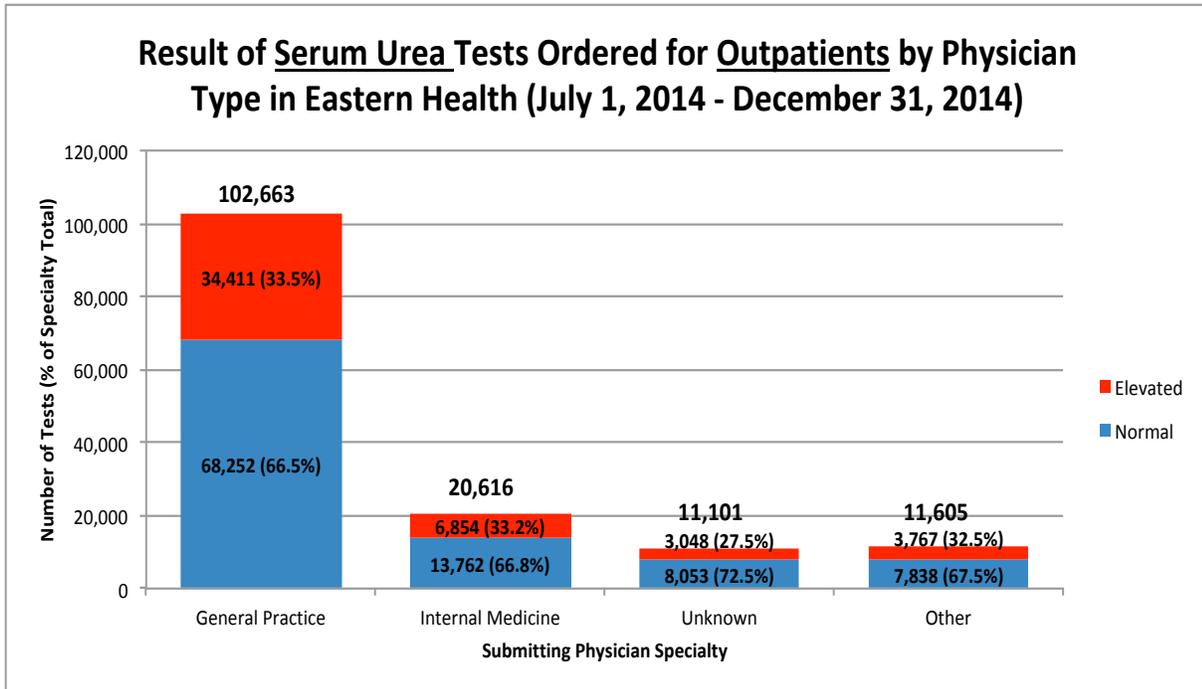
**Figure 8. Number of Serum Creatinine Tests Ordered by Specialty and Patient Type in Eastern Health in 2014.** The highest volume of serum creatinine tests ordered for outpatients were requested by general practitioners. The highest number of serum creatinine tests ordered for inpatients were requested by the internal medicine specialty.



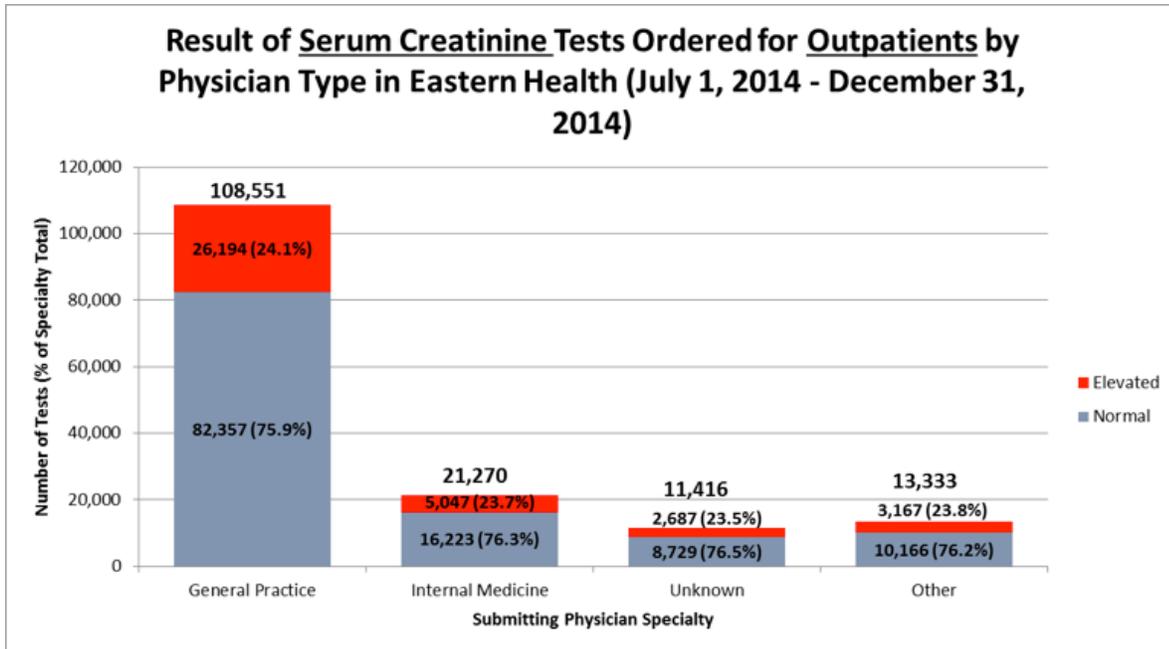
**Figure 9. Total Number of Tests Ordered by General Practitioners in Eastern Health in 2014.** A large proportion of serum creatinine (75.7%) and serum urea (66.4%) tests ordered within the 6-month period by general practitioners elicited a normal result.



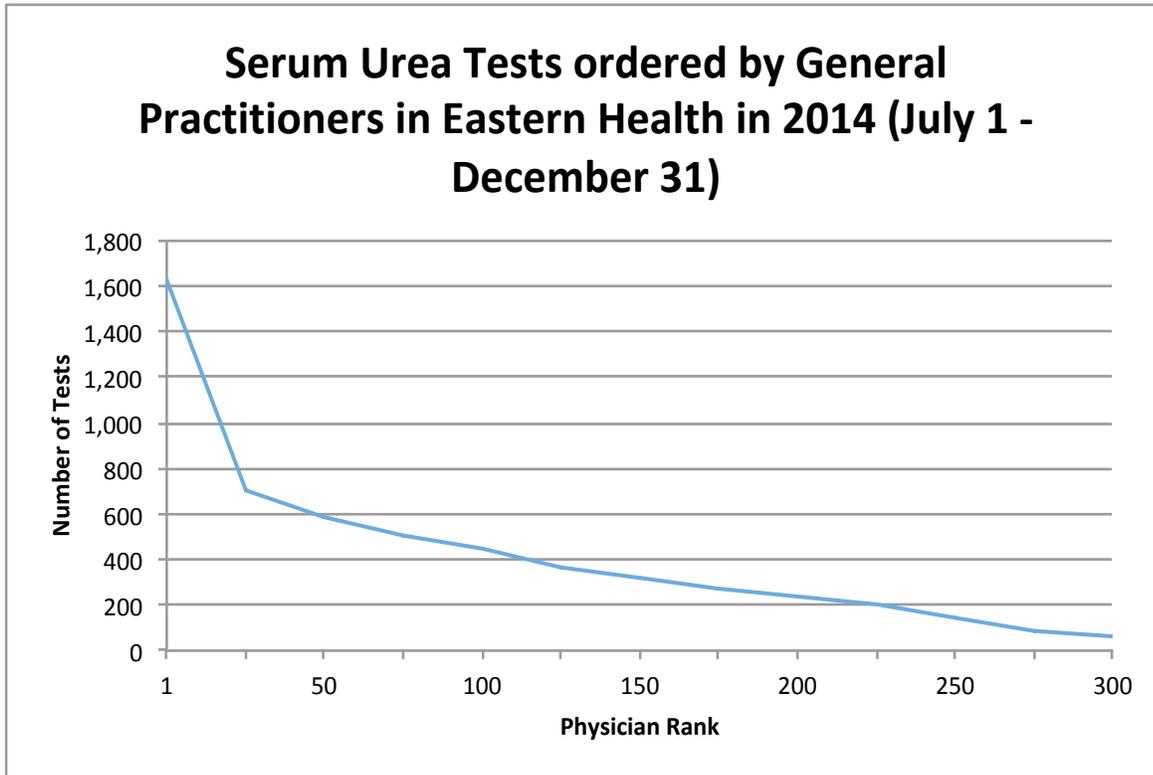
**Figure 10. Result of Serum Urea Tests Ordered for Outpatients by Physician Type in Eastern Health in 2014.** The majority of urea tests performed for outpatients were requested by general practitioners and elicited a normal result.



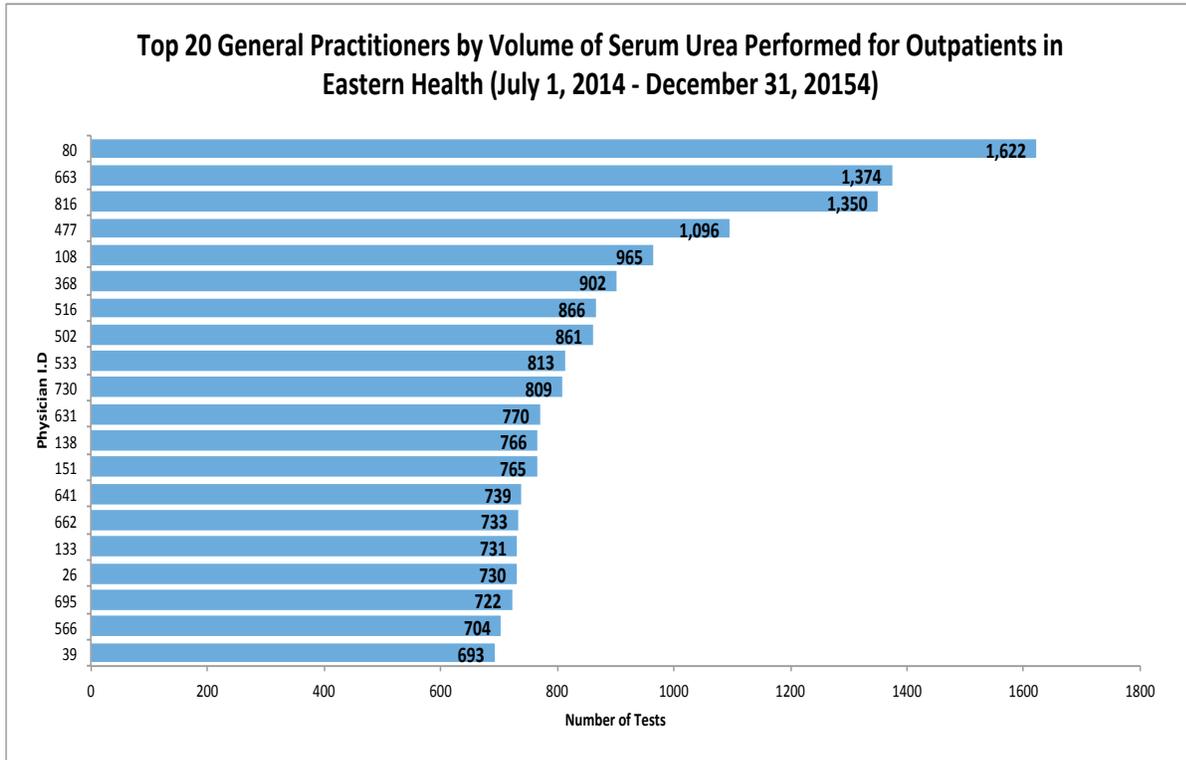
**Figure 11. Result of Serum Creatinine Tests Ordered for Outpatients by Physician Type in Eastern Health in 2014.** The majority of serum creatinine tests performed for outpatients were requested by general practitioners and elicited a normal result.



**Figure 12. Serum Urea Tests Ordered by General Practitioners in Eastern Health in 2014.** There is a great deal of variability in the test ordering behaviors of general practitioners for the serum urea laboratory investigation. A small proportion of the general practitioners within the Eastern Health Region may be responsible for a large proportion of ordered tests.



**Figure 13. Top 20 General Practitioners by Volume of Serum Urea Performed for Outpatients in the Eastern Health Region during a 6-month period in 2014.** There is a great deal of variability in the test ordering behaviors of general practitioners for the serum urea laboratory investigation. A small proportion of the general practitioners within the Eastern Health Region may be responsible for a large proportion of ordered tests.



#### **4.1.3 Serum Urea & Serum Creatinine Coupled**

Table 2 compares the number of serum urea and serum creatinine tests ordered in the same draw based on the ordering physicians specialty for outpatients. 141, 112 serum urea (96.7% of total for outpatients) and serum creatinine (91.3% of total for outpatients) were ordered together. General practitioners ordered the highest quantity of tests in combination for outpatients (70.9%) with Internal Medicine following, accounting for 14.5% of all coupled tests. These findings highlight the key point that these tests are almost always ordered together, rendering the urea test redundant. These two tests are likely being ordered for the same purpose, therefore the redundancy is that serum creatinine is the more specific test to assess renal function and monitor the progress of chronic kidney disease.

**Table 2:** Number of Serum Urea and Serum Creatinine Tests Ordered Together by Specialty in Eastern Health for Outpatients (July 1, 2014 – December 31, 2014)

Submitting Physician Specialty/Laboratory Test Count	Number of Serum Creatine and Serum Urea Ordered in Same Draw	
	n (%)	Combined Total N
General Practice	100, 028 (70.9)	200, 056
Internal Medicine	20, 447 (14.5)	40, 894
Other	10, 704 (7.6)	21, 408
Unknown	9, 933 (7.0)	19, 866
Total	141, 112	282, 224

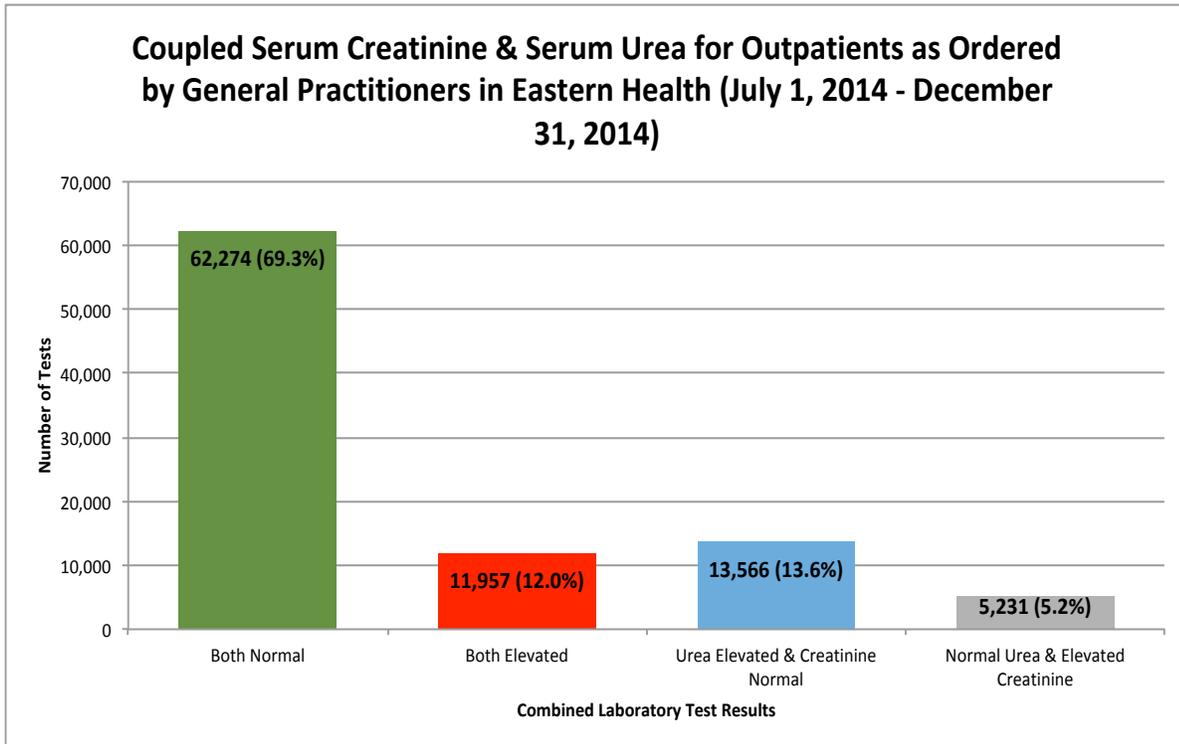
#### **4.1.4 Test Results of Coupled Serum Urea & Serum Creatinine**

Figure 14 demonstrates the independent test results for serum urea and serum creatinine laboratory investigations ordered together by general practitioners for outpatients only. The largest volume of tests, 69,274 (69.3%), elicited both normal serum urea and serum creatinine results. 13,566 (13.6%) were found to have an elevated urea and a normal creatinine result. Tests that elicited elevated levels of both serum urea and serum creatinine totaled 11,957 (12.0%). Normal serum urea and elevated serum creatinine test results accounted for 5,231 (5.2%), the smallest volume of all test result categories.

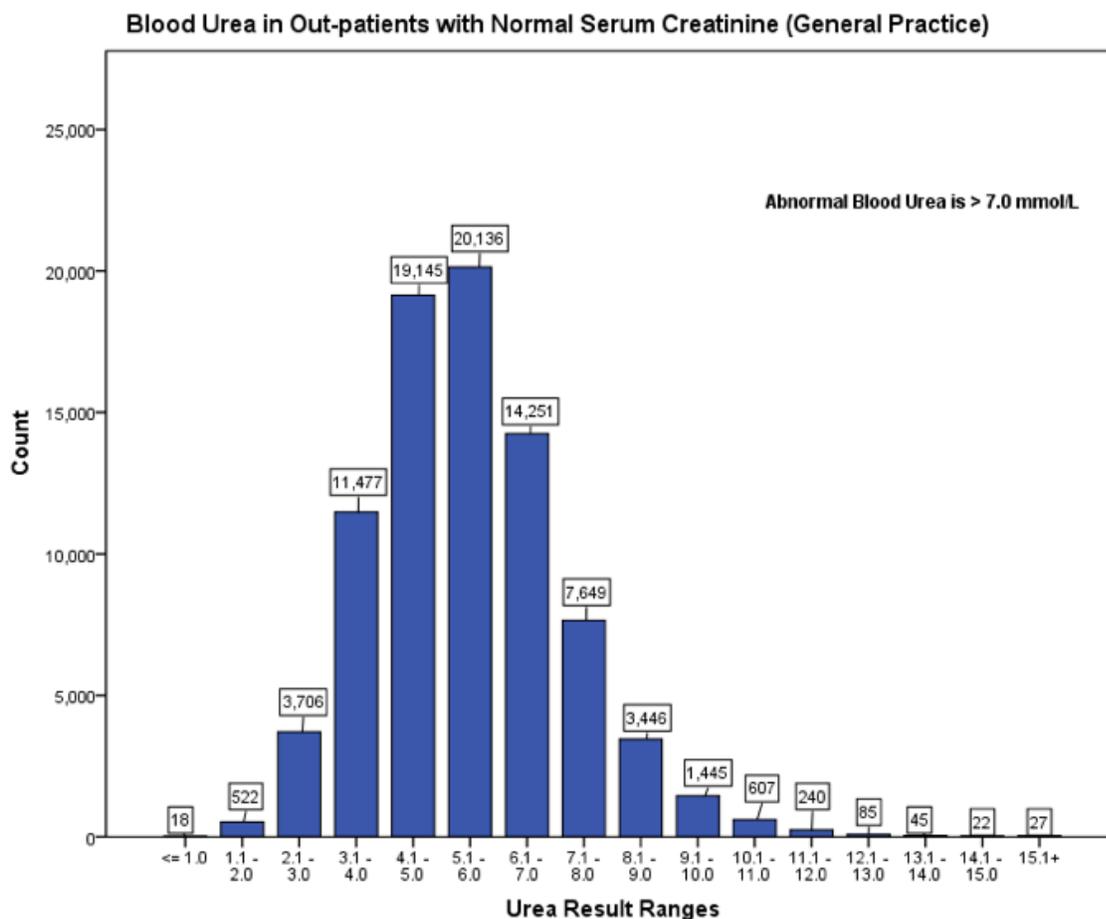
Figure 15 portrays the distribution of serum urea results that were ordered by general practitioners in combination with a normal serum creatinine result for outpatients only. 13,566 (16.4%) of serum urea tests ordered with a normal serum creatinine produced an elevated result. 7,649 (56.4%) of these abnormal serum urea tests have a result between 7.1 – 8.0 mmol/L. 11,095 (81.8%) between 7.1 – 9.0 mmol/L. 12,540 (92.4%) between 7.1 – 10.0 mmol/L.

**Figure 14. Serum Creatinine and Serum Urea Laboratory Investigations Ordered at the Same Time by General Practitioners during a 6-month period in the Eastern Health Region.**

This figure shows the volume of tests ordered in combination and their corresponding results. A considerable proportion of the coupled serum creatinine and serum urea tests (69.3%) had a normal outcome for both tests.



**Figure 15. The distribution of Serum Urea tests results in outpatients with a normal serum creatinine test outcome as ordered by a general practitioner.** The urea laboratory investigation is considered to be abnormal when the outcome is greater than 7.0 mmol/L. A large proportion of the abnormal urea tests results in outpatients with a normal serum creatinine are only elevated within 3.0 mmol/L (92.4%). This abnormal result caused by a small elevation may not provide any clinical value.



## **4.2 Hemoglobin (Hgb), Ferritin & Iron Saturation**

### **4.2.1 Volume of Testing**

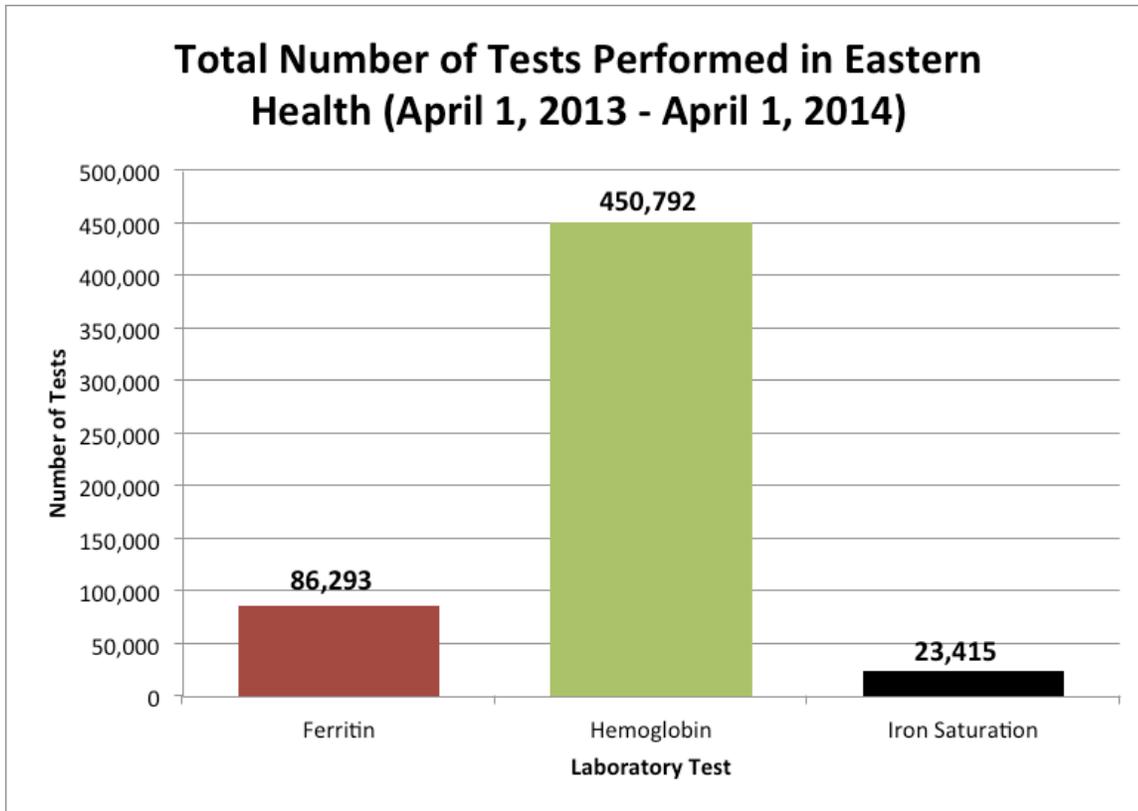
During the time period of April 1<sup>st</sup>, 2013 – April 1<sup>st</sup>, 2014, the Hemoglobin laboratory test was ordered more frequently in comparison to Ferritin and Iron saturation tests. During this 12-month period Hemoglobin was ordered 450, 792 times, Ferritin was performed 86, 293 times and iron saturation laboratory investigations were performed 23, 415 times (Figure 16).

Hemoglobin, ferritin and iron saturation were performed in larger quantities for females as compared to males within the Eastern Health Region: 55.5%, 63.4% and 56.0%, respectively (Figure 17).

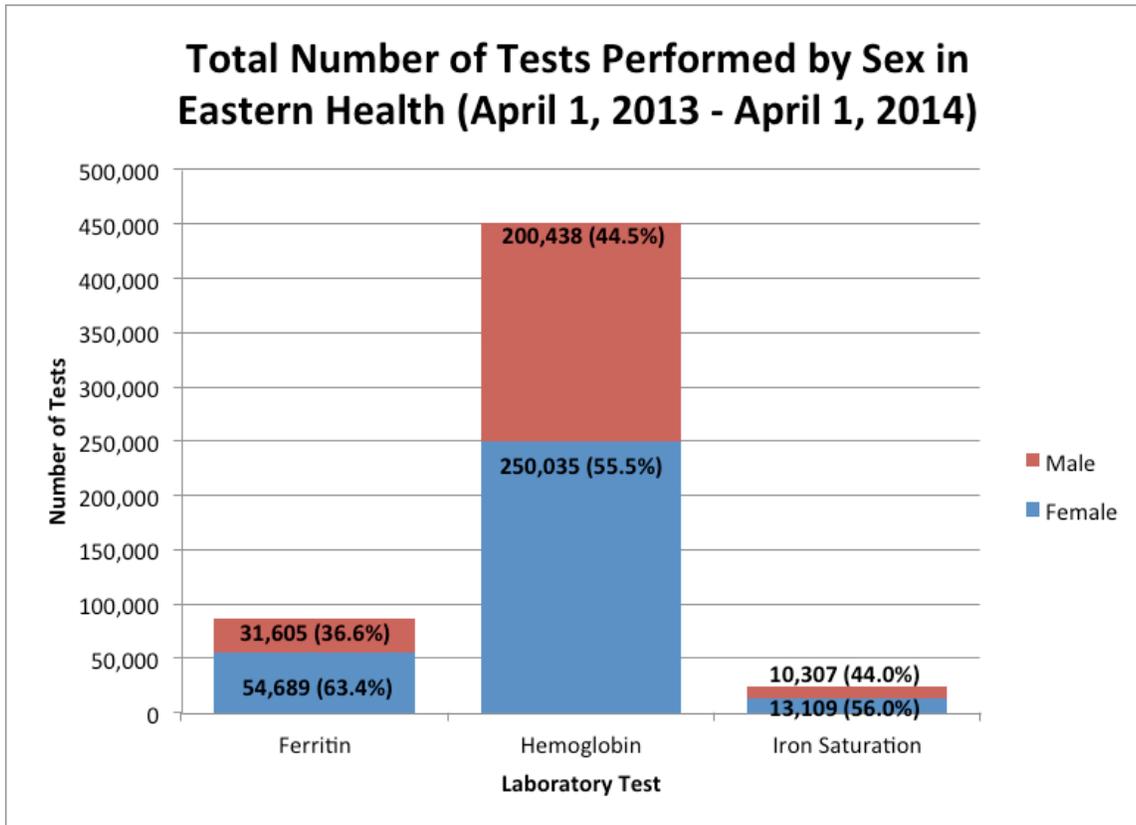
320, 121 (71.1%) of all Hgb tests were ordered for outpatients. The Majority of ferritin and iron saturation tests were also ordered for outpatients, 84, 670 (98.1%) and 22, 212 (94.9%), respectively (Figure 18).

Individual Test ordering behavior was relatively consistent throughout the 12-month period, with Hgb being ordered in a substantially greater volume per month (Figure 19).

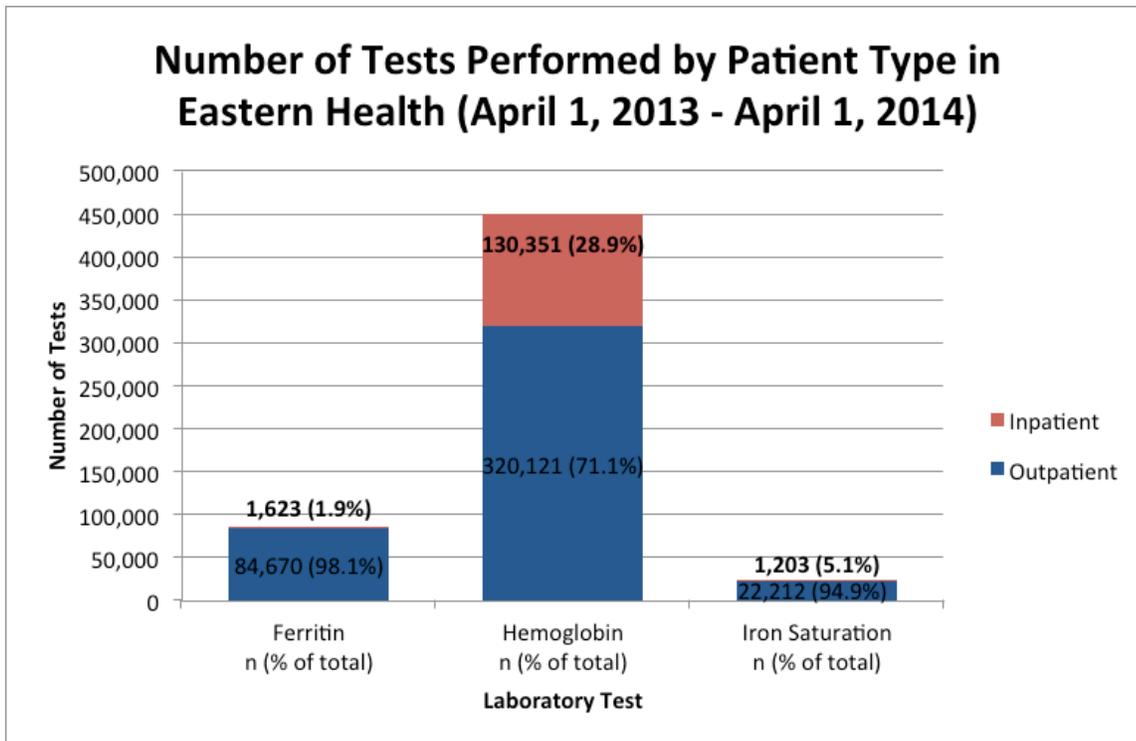
**Figure 16. Total Number of Ferritin, Hemoglobin and Iron Saturation Tests Performed in Eastern Health within a 12-month.** A high volume of iron status and hemoglobin tests were ordered during the 12-month period. Of particular interest is the number of hemoglobin tests that were requested (n= 450, 792). This is a large volume of tests when taking into consideration that the Eastern Health Regional Authority has approximately 300,000 patients.



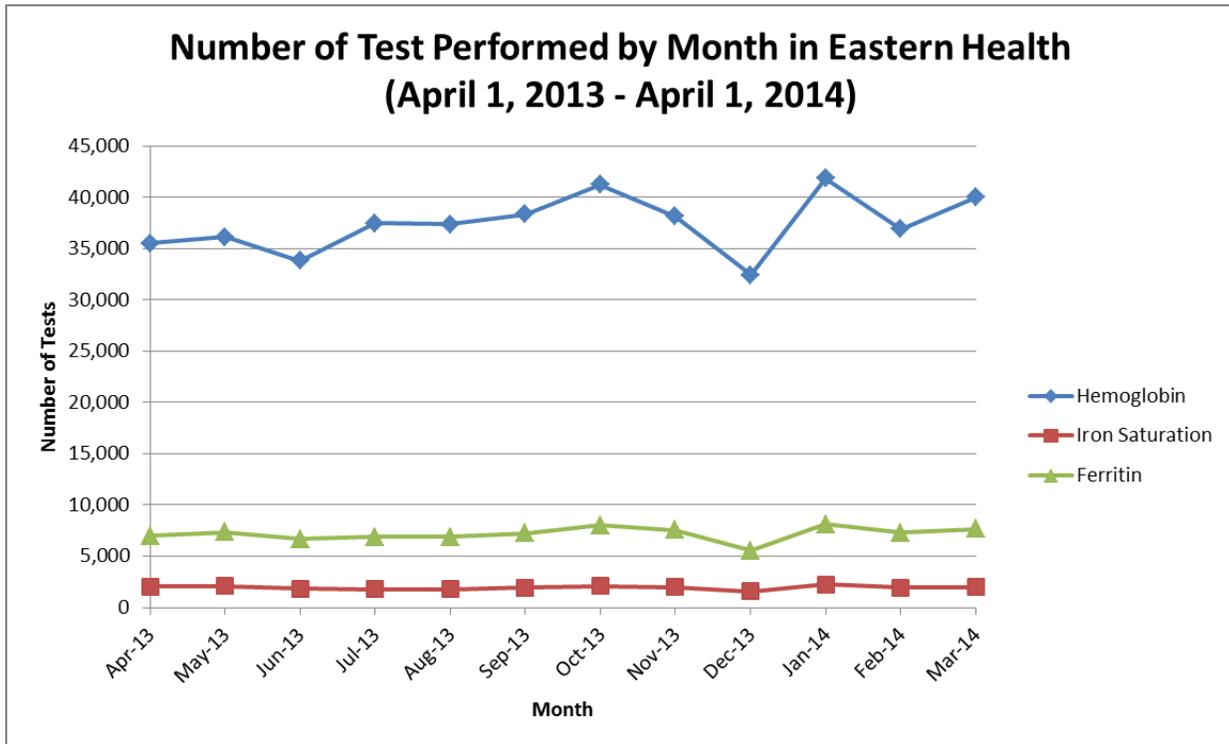
**Figure 17. Total Number of Ferritin, Hemoglobin and Iron Saturation Tests Performed by Gender in Eastern Health within a 12-month period.** The iron status and hemoglobin laboratory investigations were ordered more often for female patients.



**Figure 18. Number of Tests Performed by Patient Type in Eastern Health within a 12-month period.** The majority of hemoglobin (71.1%), ferritin (98.1%) and iron saturation (94.9%) tests were ordered for outpatients compared to inpatients.



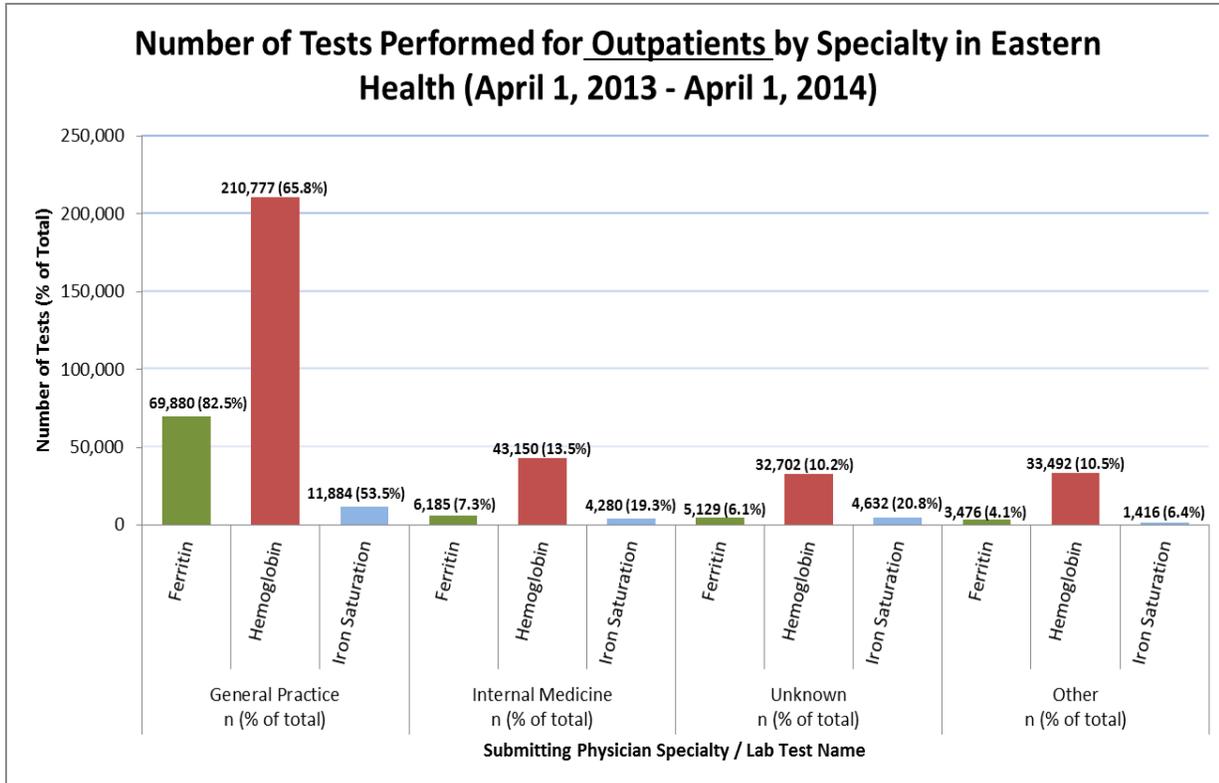
**Figure 19. Number of Tests Performed by Month in Eastern Health during a 12-month period.** Test ordering behaviours were relatively consistent each month for the three tests with hemoglobin tests being ordered at a substantially greater volume.



#### **4.2.2 Volume of Testing by General Practitioners**

During the 12- month period, general practitioners ordered all three tests in a higher volume for outpatients compared to other specialties within the Eastern Health Region. Ferritin laboratory investigations had the highest proportion of tests ordered by general practitioners (82.5%). General practitioners ordered 65.8% and 53.5% of all Hgb and iron saturation tests, respectively. Internal medicine practitioners were the following specialty for the highest ordering rates with considerably less tests requested for Hgb, ferritin and iron saturation as compared to general practitioners: 13.5%, 7.3% and 19.3%, respectively (Figure 20).

**Figure 20. Number of Tests Performed for Outpatients by Specialty in Eastern Health during a 12-month period.** General practitioners had the highest ordering rates for ferritin (82.5% of total), hemoglobin (65.8% of total) and iron saturation (53.5% of total) tests.



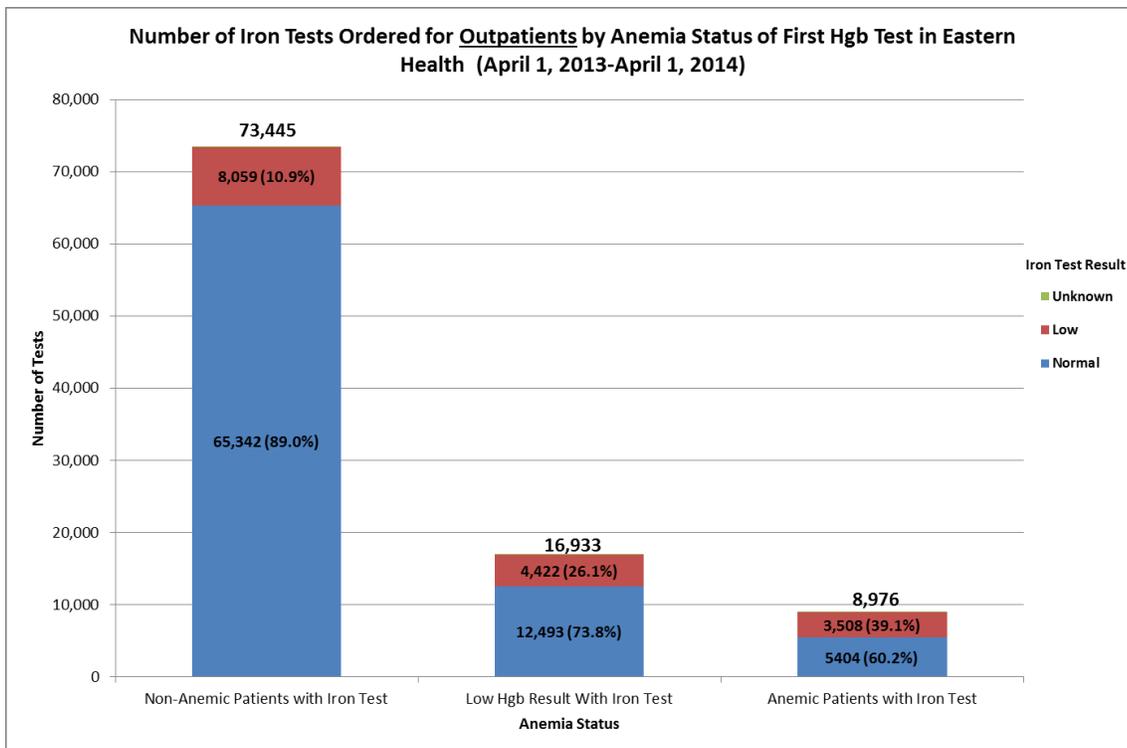
#### **4.2.3.1 Overutilization Overview**

For the purposes of this analysis, patients were considered to be non-anemic if their hemoglobin laboratory test result was within the normal range for their gender (male = 140 – 180 g/L; female = 120 – 160 g/L). A test result below 110 g/L for both males and females was considered to be anemic. This cut off was chosen as it falls below the normal range of both genders and likely reflective of a true anemia.

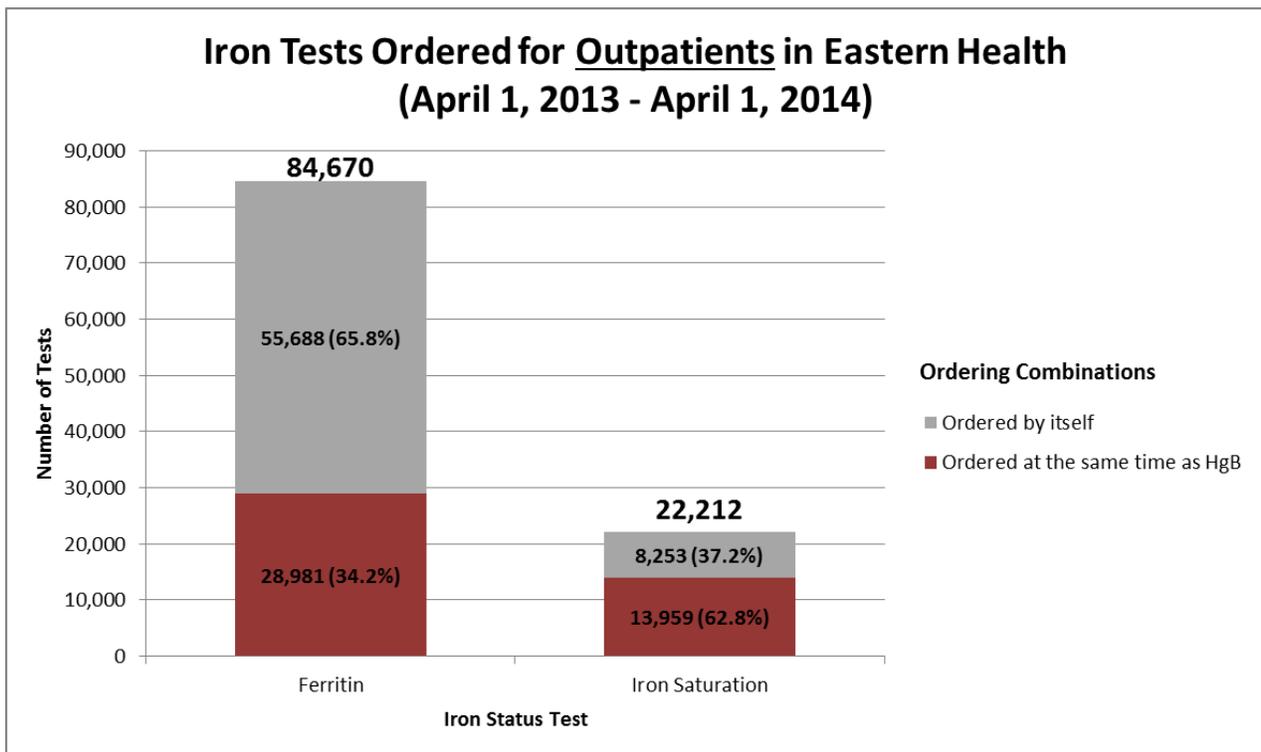
Figure 21 describes the number of iron tests ordered in the Eastern Health region for outpatients during the 12-month period by the patient's result of their first hemoglobin test. 8,976 iron tests were ordered in patients with an anemic (<110 g/L) result for their first Hgb test. 16,933 and 73,445 iron tests were ordered for patients with a low Hgb and non-anemic result, respectively. 89.0% of the iron tests ordered for non-anemic (first Hgb) outpatients elicited a normal iron status result.

34.2% of all ferritin tests and 62.8% of all iron saturation tests ordered for outpatients were requested in the same draw as an Hgb test during the 12-month period in Eastern Health (Figure 22).

**Figure 21. Number of Iron Tests Ordered for outpatients by Anemia Result of the Patients First Hemoglobin test in Eastern Health during a 12-month Period.** A large proportion of iron status tests were ordered for patients with a non-anemic first Hgb test result (n=73,445). The majority of these investigations resulted in a normal outcome (89.0%).



**Figure 22. Iron Tests Ordered for Outpatients in the Eastern Health Region during a 12-month period.** 34.2 % of all ferritin and 62.8% of all iron saturation laboratory investigations ordered for outpatients were requested in the same draw as a hemoglobin test.



#### **4.2.3.2 Overutilization by General Practitioners**

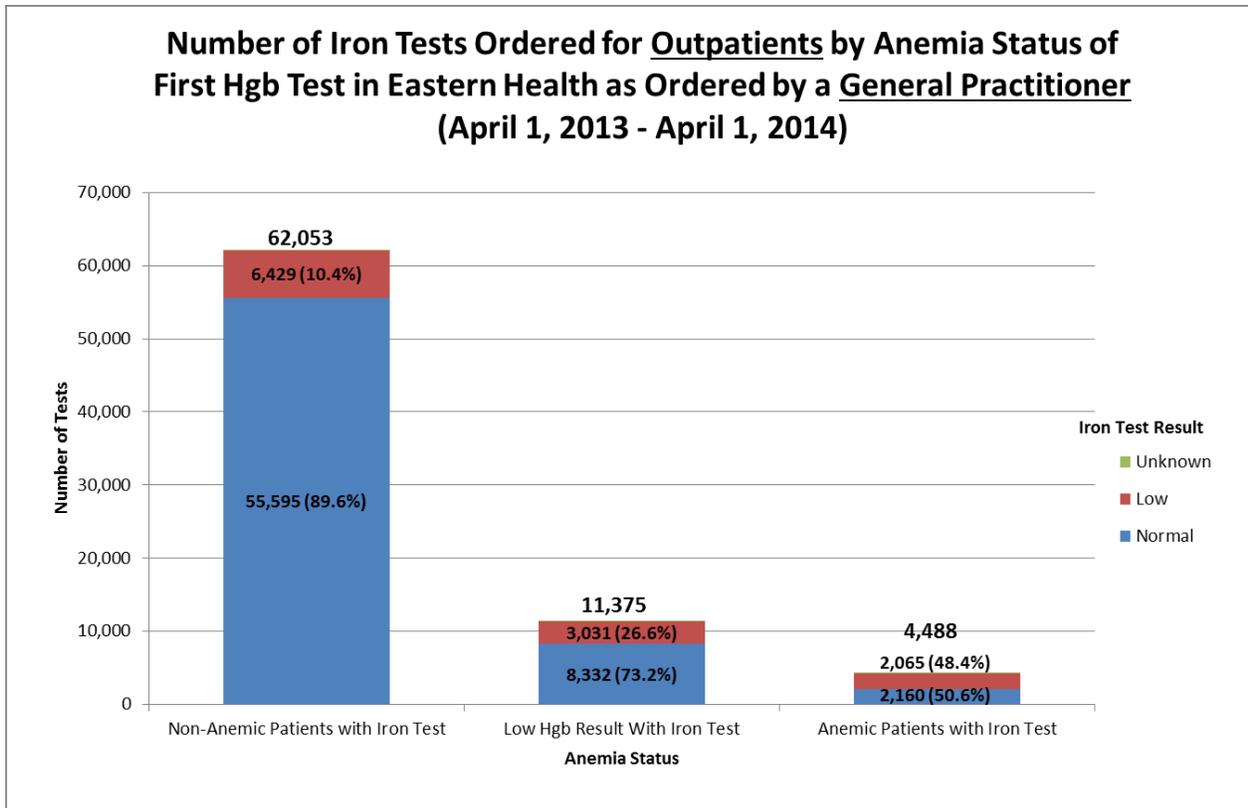
Figure 23 describes the number of iron tests ordered for outpatients by general practitioners based on the patient's anemia status derived from their first Hgb test between the time period of April 1<sup>st</sup>, 2013-April 1<sup>st</sup>, 2014. 62,053 iron tests were requested by general practitioners for outpatients with a non-anemic (normal) first Hgb test result within the 12-month period. 89.6% of those iron status tests produced a normal result.

29.9% of all ferritin tests and 70.2% of all iron saturation tests ordered by general practitioners for outpatients were requested at the same time as an Hgb test (Figure 24).

General practitioners requested 66,904 iron tests within 90 days (+/-) of an outpatient's first Hgb test within the 12-month period. 54,905 of the iron tests were requested for patients with a non-anemic (normal) result for their first Hgb test; 90.1% of them eliciting a normal iron status result (Figure 25).

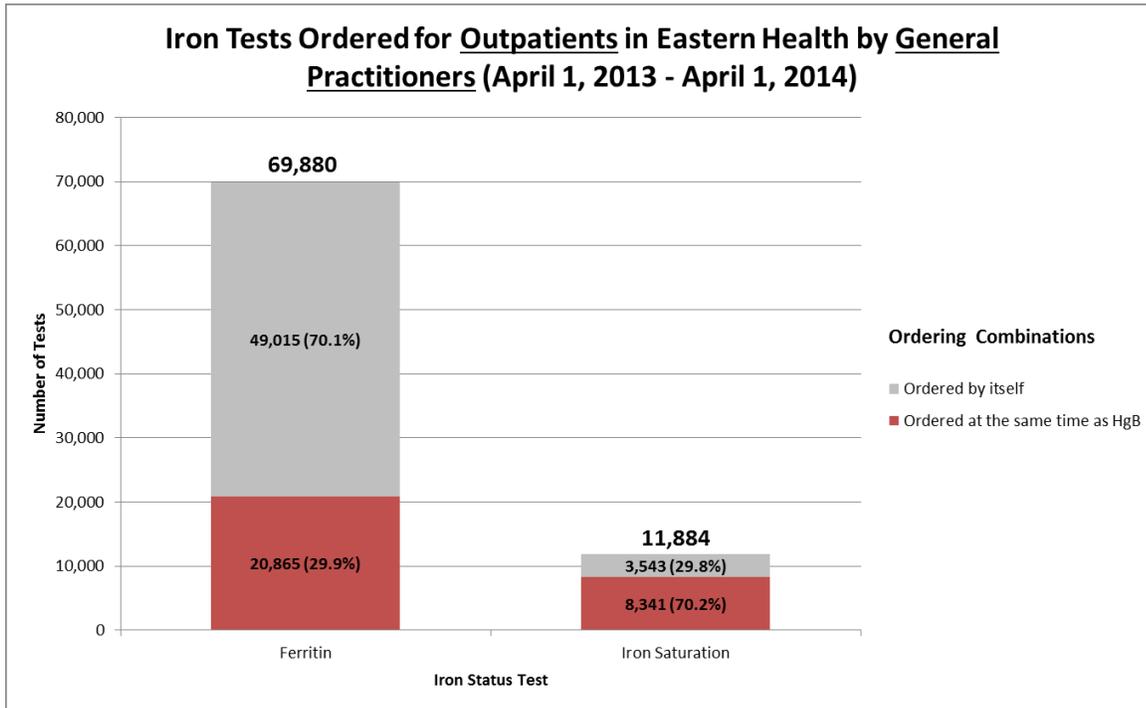
General practitioners requested 10,786 iron tests more than 90 days (+/-) of an outpatient's first Hgb test. 7,147 tests were ordered for patients whose first Hgb test produced a non-anemic result. 6,126 (85.3%) of iron tests ordered for this patient population elicited a normal iron status result (Figure 26).

**Figure 23. Number of Iron Tests Ordered by General Practitioners for Outpatients by the Result of the Patients First Hemoglobin Test Requested During the 12-month Period in the Eastern Health Region.** A large volume of iron status tests were ordered by general practitioners for outpatients whose first hemoglobin test elicited a non-anemic (normal) result (n=62,053).

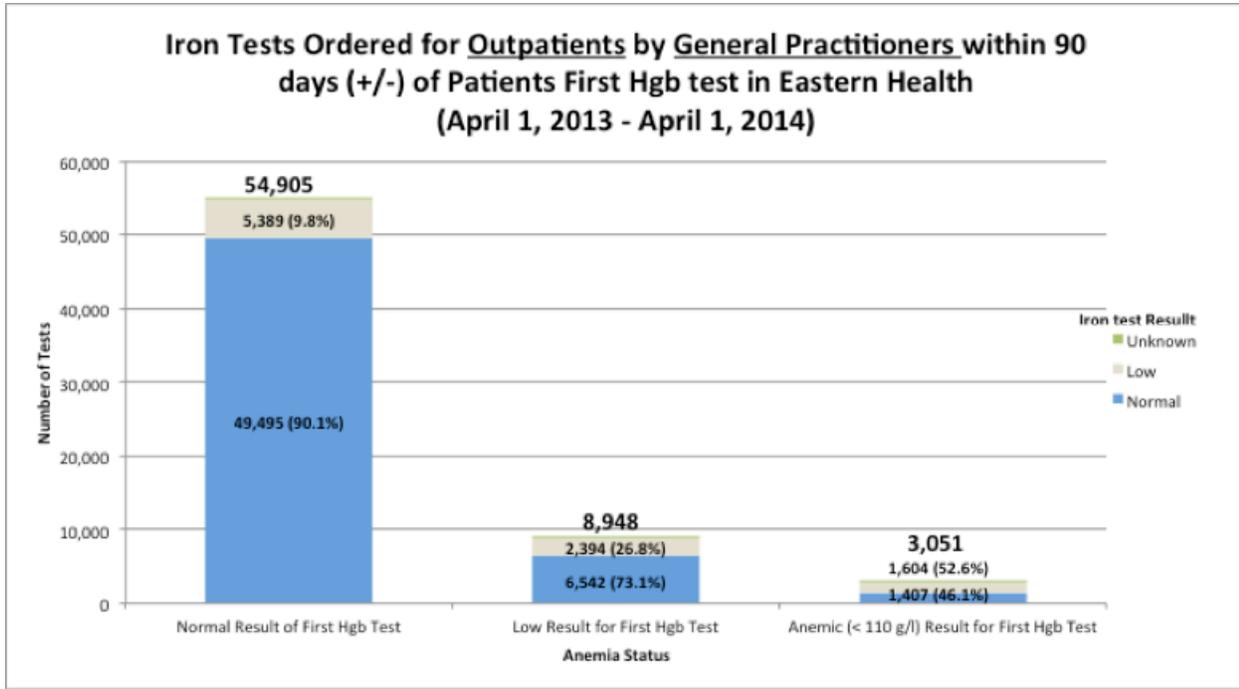


**Figure 24. Iron Tests Ordered for Outpatients in Eastern Health by General Practitioners.**

This figure describes the iron tests that were ordered for outpatients by general practitioners in the same draw as a hemoglobin test or independently during the 12-month period in the Eastern Health Region. 70.2% of iron saturation tests ordered by general practitioners for outpatients were ordered in the same draw as a hemoglobin test. 29.9% of ferritin tests ordered by a general practitioner for outpatients were ordered in the same draw as a hemoglobin test.



**Figure 25. Iron Tests Ordered for Outpatients by General Practitioners within 90 days of the Patients First Hemoglobin test during the 12-month period in the Eastern Health Region. 54,905 iron status tests were ordered within 90 days of a first hemoglobin test that produced a normal (non-anemic) outcome. 90.1% of these iron status investigations elicited a normal result.**



**Figure 26. Iron Tests Ordered for Outpatients by General Practitioners Greater than 90 days of the Patients First Hemoglobin test during the 12-month period in the Eastern Health Region.** 7, 147 iron status tests were ordered greater than 90 days of a first hemoglobin test that produced a normal (non-anemic) outcome. 85.3% of these iron status investigations elicited a normal result.

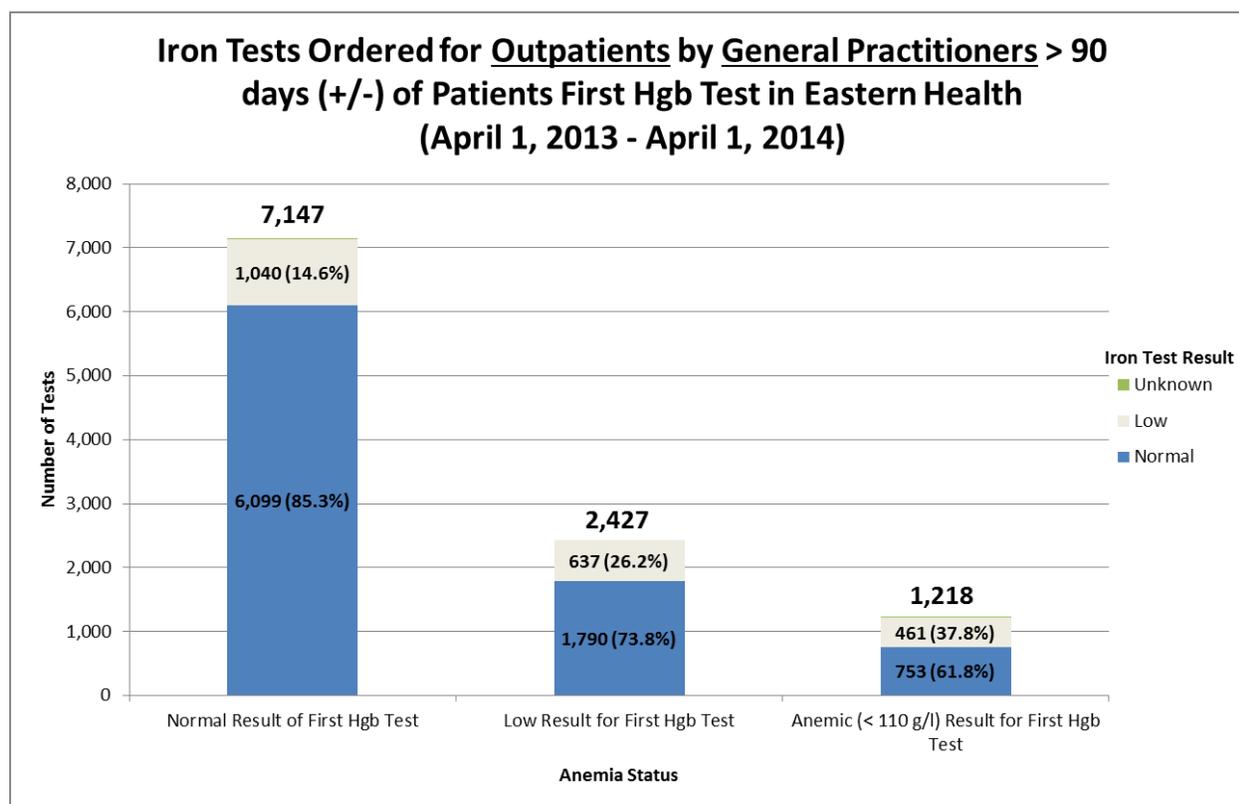


Table 3 describes the number of iron tests ordered within 90 days (+/-) of outpatients ( $\leq 50$  years of age) first Hgb test, stratified by gender.

Table 4 describes the number of iron status tests requested within 90 days (+/-) of outpatients ( $> 50$  years of age) first Hgb test, stratified by gender.

General practitioners requested 27, 689 iron status tests in outpatients ( $\leq 50$  years of age) within 90 days (+/-) of their first Hgb test within the 12-month period in Eastern Health. 17, 854 iron tests were ordered for females aged 50 years or younger who had an associated non-anemic (normal) first Hgb test result. 84.4% of those iron investigations elicited a normal result. 6, 796

iron investigations were requested for males aged 50 years or younger whose first Hgb test resulted in a non-anemic outcome. 97.1% of those ordered iron laboratory investigation produced a normal result (Table 5).

General practitioners requested 39,215 iron tests in outpatients (> 50 years of age) within 90 days (+/-) of their first Hgb Test during the April 1<sup>st</sup>, 2013-April 1<sup>st</sup>, 2014 time period. 19,337 iron investigations were requested for females who had an associated non-anemic first Hgb test result and were older than 50 years of age. 90.4% of those iron status tests elicited a normal result. 10,913 iron tests were ordered in men with a normal first Hgb test result and were older than 50 years of age. 94.6% of those iron investigations produced a normal result (Table 6).

79.6% of iron tests were ordered by general practitioners, for outpatients with a non-anemic (first Hgb) test result within the 12-month period. 54,905 of these investigations were requested within +/- 90 days of the patients first Hgb and 90.1% of the tests elicited a normal iron status result. 95.9% (n=52,699) of these patients were never anemic within the 12-month period (none of the patients' subsequent tests were anemic). These findings indicate that a large proportion of iron status tests are being ordered for patients who do not have an Hgb test indicating that they are anemic. The vast majority of the iron status tests elicited a normal result, further supporting that these tests may be being used in an inappropriate clinical scenario, supporting potential overutilization by general practitioners.

**Table 3:** Number of Iron Tests Ordered for Outpatients  $\leq 50$  years of age within 90 days (+/-) of their First Hgb Test Stratified by Gender (Eastern Health: April 1, 2013 - April 1, 2014)

First Hgb Result	Gender	Iron Test Result			Total N
		Normal n (%total)	Low n (%total)	Unknown n(%total)	
Non-Anemic	Female	17,324 (83.9%)	3,321 (16.0%)	11 (0.1%)	20,656
	Male	7,742 (96.8%)	260 (3.2%)	0	8,002
Low	Female	871 (47.7%)	950 (51.9%)	7 (0.4%)	1,829
	Male	911 (80.7%)	217 (19.2%)	1 (0.1%)	1,129
Anemic	Female	299 (27.0%)	771 (69.6%)	38 (3.4%)	1,108
	Male	139 (61.2%)	85 (37.4%)	3 (1.4%)	227

**Table 4:** Number of Iron Tests Ordered for Outpatients  $> 50$  years of age within 90 days (+/-) of their First Hgb Test Stratified by Gender (Eastern Health: April 1, 2013 - April 1, 2014)

First Hgb Result	Gender	Iron Test Result			Total N
		Normal n (%total)	Low n (%total)	Unknown n(%total)	
Non-Anemic	Female	20,031 (89.7%)	2,294 (10.2%)	10 (0.1%)	22,335
	Male	12,068 (94.2%)	729 (5.7%)	8 (0.1%)	12,805
Low	Female	1,960 (68.4%)	898 (31.4%)	6 (0.2%)	2,864
	Male	5,147 (81.2%)	1,187 (18.7%)	1 (0.1%)	6,335
Anemic	Female	1,455 (56.8%)	1098 (42.8%)	11 (0.4%)	2,564
	Male	975 (65.7%)	506 (34.1%)	3 (0.2%)	1,484

**Table 5:** Number of Iron Tests Ordered by General Practitioners for Outpatients ≤ 50 years of age within 90 days (+/-) of their First Hgb Test Stratified by Gender (Eastern Health: April 1, 2013 - April 1, 2014)

First Hgb Result	Gender	Iron Test Result			Total N
		Normal n (%total)	Low n (%total)	Unknown n(%total)	
Non-Anemic					
	Female	15,067 (84.4%)	2,781 (15.6%)	6 (0.03%)	17, 854
	Male	6,602 (97.1%)	194 (2.9%)	0	6,796
Low					
	Female	673 (47.0%)	752 (52.6%)	6 (0.4%)	1,431
	Male	633 (82.9%)	130 (17.0%)	1 (0.1%)	764
Anemic					
	Female	168 (21.4%)	587 (74.8%)	30 (3.8%)	785
	Male	23 (39.0%)	35 (59.3%)	1 (1.7%)	59

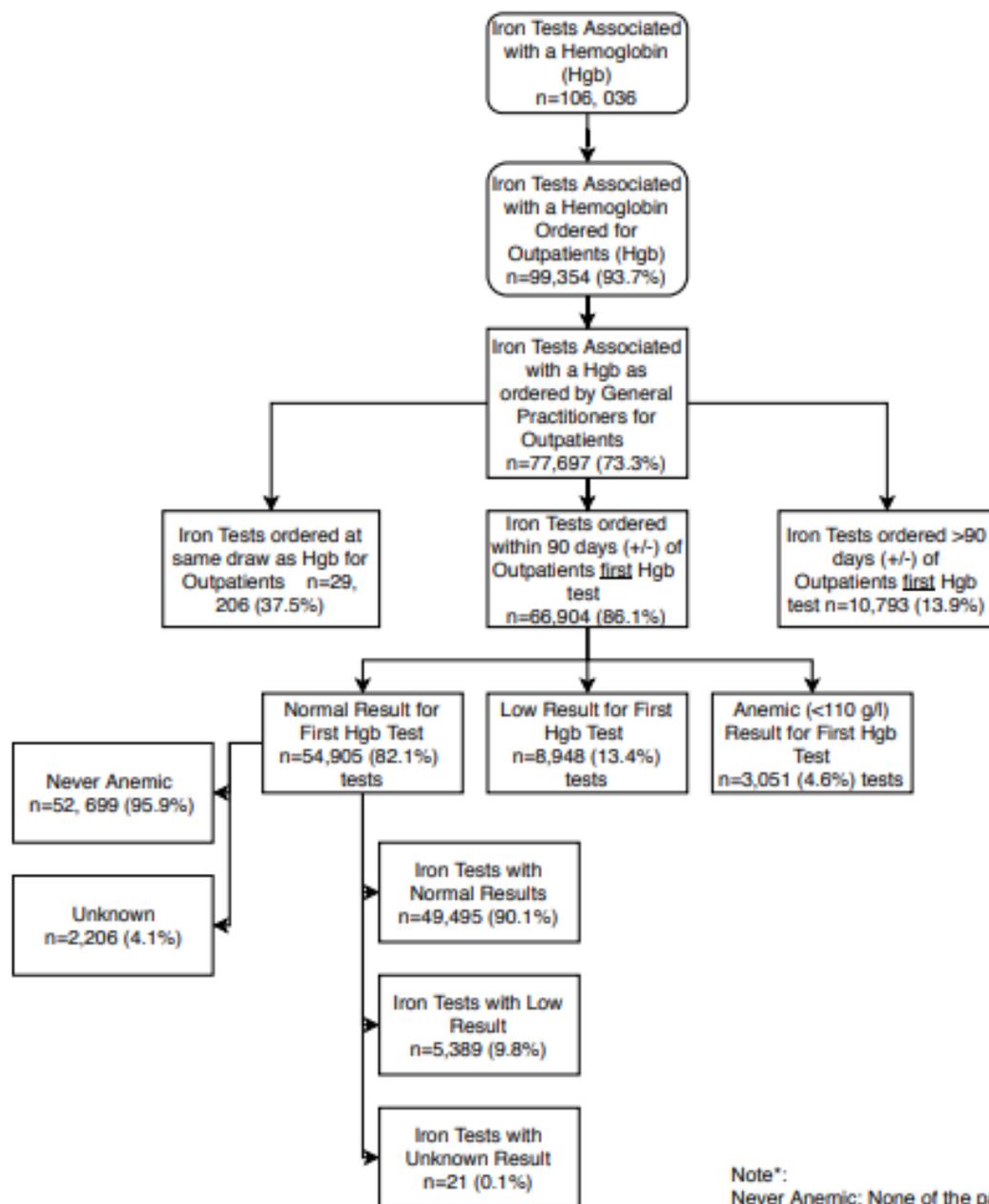
**Table 6:** Number of Iron Tests Ordered by General Practitioners for Outpatients > 50 years of age within 90 days (+/-) of their First Hgb Test Stratified by Gender (Eastern Health: April 1, 2013 - April 1, 2014)

First Hgb Result	Gender	Iron Test Result			Total N
		Normal n (%total)	Low n (%total)	Unknown n(%total)	
Non-Anemic					
	Female	17,489 (90.4%)	1,840 (9.5%)	8 (0.1%)	19,337
	Male	10,332 (94.6%)	574 (5.3%)	7 (0.1%)	10,913
Low					
	Female	1,484 (68.1%)	689 (31.6%)	5 (0.3%)	2,178
	Male	3,756 (82.0%)	824 (18.0%)	0	4,580
Anemic					
	Female	878 (54.4%)	726 (45.0%)	9 (0.6%)	1,613
	Male	338 (56.9%)	256 (43.1%)	0	594

### **4.2.3 Potential Test Overutilization**

Figure 27 provides a streamlined collection of the data presented in the previous figures which may support potential test overutilization.

**Figure 27: Cascade of Potential Overutilization.** This cascade highlights the points of interest that may support potential test overutilization of the iron status and hemoglobin tests in the Eastern Health Region during a 12-month period.



Note\*:  
**Never Anemic:** None of the patients subsequent Hgb tests were anemic  
**Unknown:** The patients first Hgb test was normal but the results of the subsequent tests changed

#### **4.2.4.1 Underutilization Overview**

Figure 28 describes the number of outpatients by the anemia status of their associated first Hgb test and if they underwent iron status laboratory investigations during the 12-month period in the Eastern Health Region.

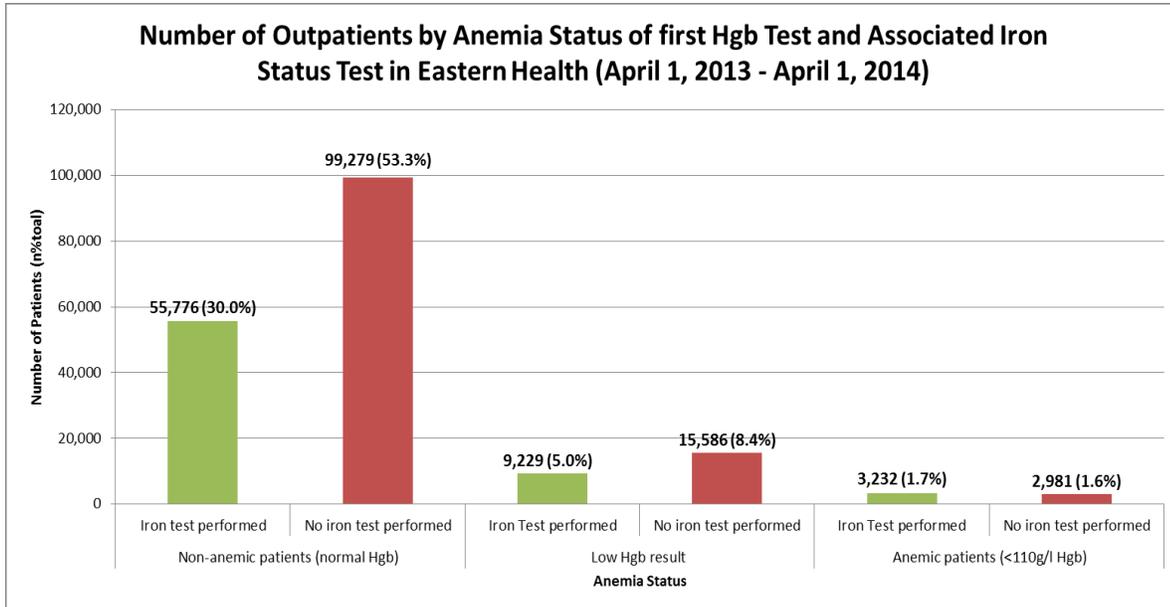
There are 206,864 unique patients within the Hgb data set (Figure 28). 75.0% of all outpatients first Hgb test resulted in a normal outcome. 12.0% of outpatients had a low first test result. 3.9% elicited an Anemic (110 g/L) first Hgb test result. 3.0 % of all outpatients were anemic and underwent iron testing. 2,981 (1.6%) of outpatients with an anemic first Hgb test outcome did not have iron laboratory investigations undertaken (Figure 28).

10.1% of all outpatients with an anemic result and a low MCH and/or MCV were not ordered iron test investigations during the 12-month period (Figure 29).

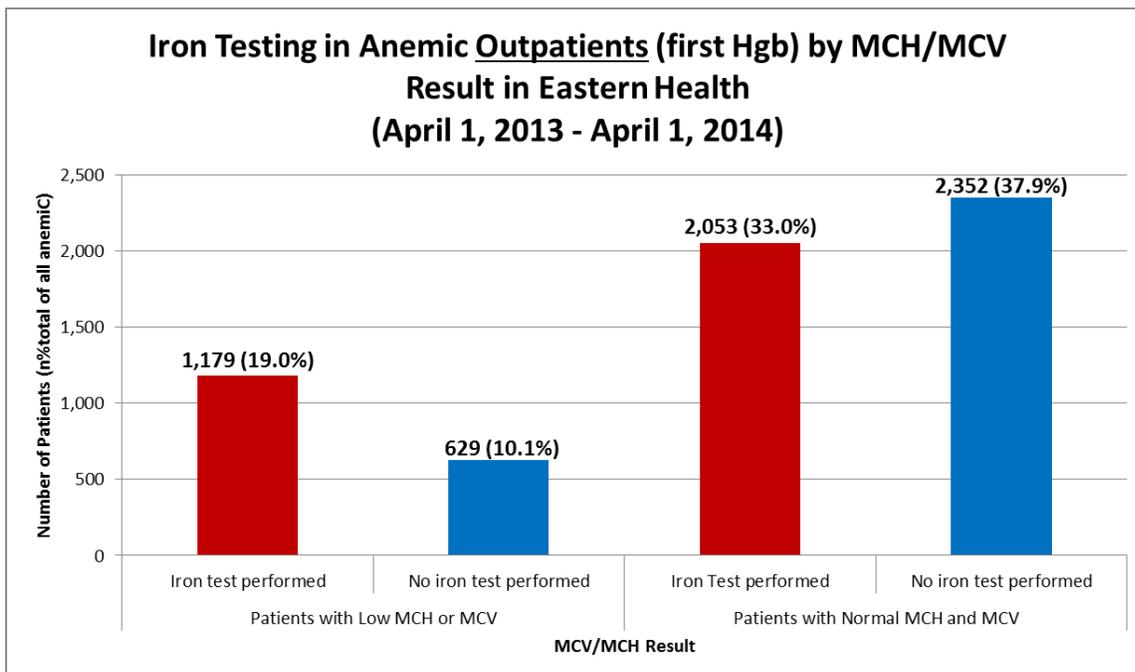
32.6 % of anemic (first Hgb) females and 25.0% of anemic males (first Hgb) 50 years of age or younger with an associated low MCH and/or MCV did not have an iron test performed within 1-year of their first Hgb (Table 7).

35.0% of anemic (first Hgb) females and 41.8% of anemic males (first Hgb) older than 50 years of age with an associated low MCH and/or MCV did not have an iron test requested within the 12-month period (Table 8).

**Figure 28. Number of Outpatients by Anemia Status of Patients First Hemoglobin Tests and their Associated Iron Status Tests in the Eastern Health Region during a 12-month period.** 2,981 outpatients had an anemic first hemoglobin test result and did not undergo iron testing during the 12-month period. Representing a potential missed opportunity for testing.



**Figure 29. Iron Testing in Anemic (first Hgb) Outpatients by MCH/MCV result in the Eastern Health Region during a 12-month period.** 629 anemic outpatients with an associated low MCH or MCV did not undergo iron testing during a 12-month period in Eastern Health



**Table 7:** Number of Anemic Outpatients (first Hgb)  $\leq$  50 years of age with Low MCV and/or MCH by Iron testing in Eastern Health (April 1, 2013 - April 1, 2014)

Gender/Testing	Total	Date Range	Iron Testing	
	n		Yes	No
Female	709			
		Within 1-month of First Hgb	403 (56.8%)	306 (43.2%)
		Within 3-months of First Hgb	443 (62.5%)	266 (37.5%)
		Within 1-year of First Hgb	478 (67.4%)	231 (32.6%)
Male	64			
		Within 1-month of First Hgb	39 (60.9%)	25 (39.1%)
		Within 3-months of First Hgb	44 (68.8%)	20 (31.3%)
		Within 1-year of First Hgb	48 (75.0%)	16 (25.0%)

**Table 8:** Number of Anemic Outpatients (first Hgb)  $>$  50 years of age with Low MCV and/or MCH by Iron testing in Eastern Health (April 1, 2013 - April 1, 2014)

Gender/Testing	Total	Date Range	Iron Testing	
	n		Yes	No
Female	741			
		Within 1-month of First Hgb	377 (50.9%)	364 (49.1%)
		Within 3-months of First Hgb	435 (58.7%)	306 (41.3%)
		Within 1-year of First Hgb	482 (65.0%)	259 (35.0%)
Male	294			
		Within 1-month of First Hgb	127 (43.2%)	167 (56.8%)
		Within 3-months of First Hgb	157 (53.4%)	137 (46.6%)
		Within 1-year of First Hgb	171 (58.2%)	123 (41.8%)

259 anemic females less than fifty years of age did not undergo iron testing within 1-year of their first Hgb. Similarly, 259 females and 123 males over the age of fifty did not undergo iron status testing within 1-year of their first Hgb. These patients should have had iron status testing investigations in order to determine the cause of their anemia. These findings represent a missed

opportunity for testing and potential underutilization of these laboratory resources.

#### **4.2.4.2 Underutilization by General Practitioners**

Figure 30 describes the number of outpatients by the anemia status of their associated first Hgb test as requested by a general practitioner and if they underwent iron status laboratory investigations during the 12-month period in the Eastern Health Region.

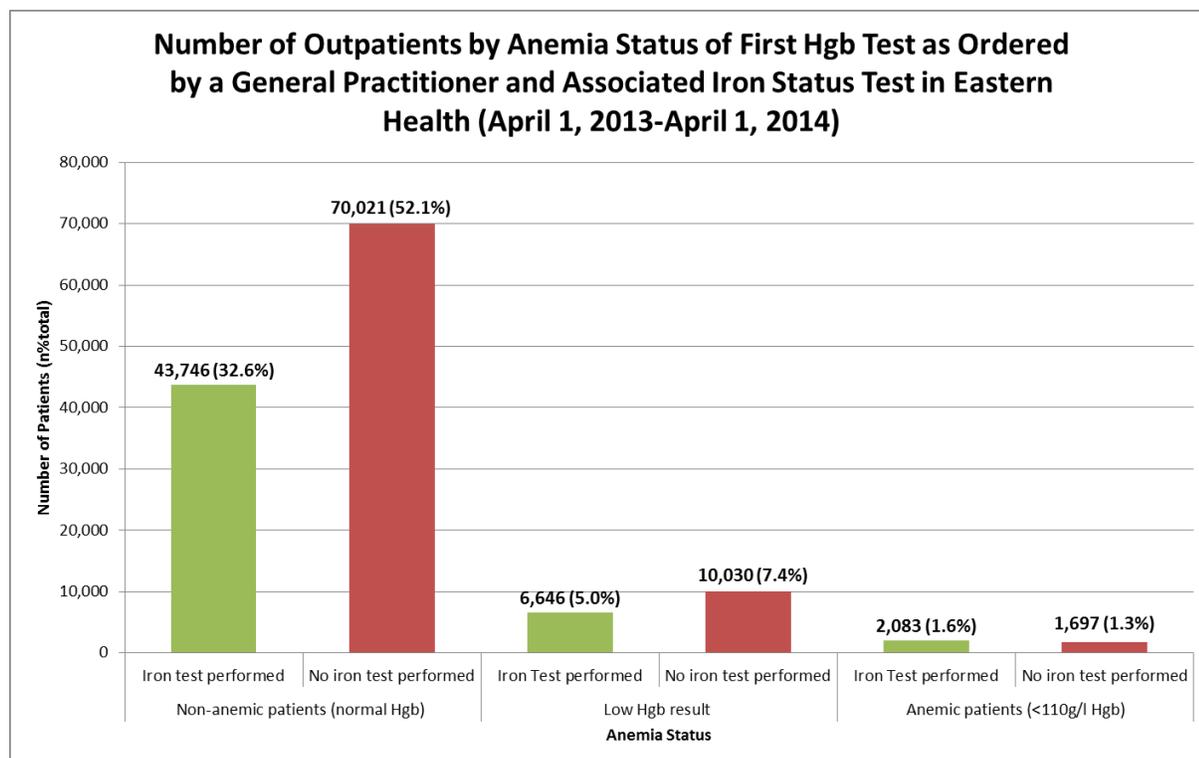
139, 223 unique outpatients had their first Hgb test requested by a general practitioner. 84.7% of all unique outpatients first Hgb test requested by a general practitioner resulted in a normal outcome. 12.4% elicited a low and 2.9% an anemic (< 110 g/L) first Hgb test result within the 12- month period. 52.1% of outpatients with a normal first Hgb test result as requested by a general practitioner did not undergo iron-testing investigations. 1, 697 (1.3%) anemic outpatients (first Hgb) as ordered by a general practitioner did not have an iron test performed (Figure 30).

34.8% of all anemic outpatients (first Hgb test) as requested by general practitioners with an associated normal MCH and MCV result did not have an iron test performed. 10.1% of all outpatients with an anemic Hgb and a low MCH and/or MCV test result as ordered by a general practitioner were not ordered further iron test investigations during the 12-month period (Figure 31).

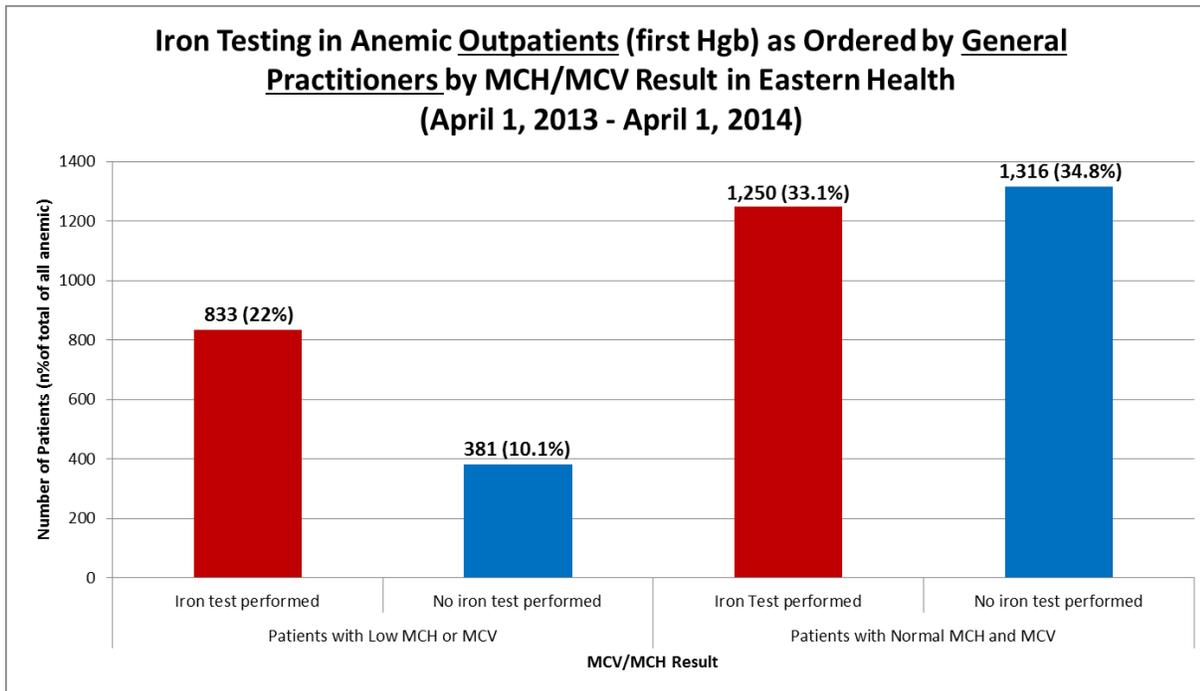
28.3 % of anemic (first Hgb) females and 13.9% of anemic males (first Hgb ordered by general practitioner) 50 years of age or younger with an associated low MCH and/or MCV did not have an iron test performed within 1-year of their first Hgb (Table 9).

32.6% of anemic (first Hgb ordered by general practitioner) females and 39.5% of anemic males (first Hgb) older than 50 years of age with an associated low MCH and/or MCV did not have an iron test requested within the 12-month period (Table 10).

**Figure 30. Number of Outpatients by Anemia Status of First Hgb Test as Ordered by a General Practitioner and Associated Iron Status test during a 12-month Period in Eastern Health.** 1, 697 anemic patients (first hemoglobin ordered by a general practitioner) did not undergo iron testing within the 12-month period. Representing a potential missed opportunity of testing.



**Figure 31. Iron Testing in Anemic Outpatients (first Hgb) as Ordered by a General Practitioner by MCH/MCV result in Eastern Health during a 12-month period.** 381 anemic outpatients with an associated low MCH or MCV did not undergo iron testing within the 12-month period. Representing a potential missed opportunity for testing.



**Table 9:** Number of Anemic Outpatients (first Hgb)  $\leq$  50 years of age with Low MCV and/or MCH by Iron testing in Eastern Health (April 1, 2013 - April 1, 2014) as Ordered by General Practitioners

Gender/Testing	Total	Date Range	Iron Testing	
	n		Yes	No
Female	481	Within 1-month of First Hgb	307 (63.8%)	174 (36.2%)
		Within 3-months of First Hgb	329 (68.4%)	152 (31.6%)
		Within 1-year of First Hgb	345 (71.7%)	136 (28.3%)
Male	36	Within 1-month of First Hgb	27 (75.0%)	9 (25.0%)
		Within 3-months of First Hgb	30 (83.3%)	6 (16.7%)
		Within 1-year of First Hgb	31 (86.1%)	5 (13.9%)

**Table 10:** Number of Anemic Outpatients (first Hgb)  $>$  50 years of age with Low MCV and/or MCH by Iron testing in Eastern Health (April 1, 2013 - April 1, 2014) as Ordered by General Practitioners

Gender/Testing	Total	Date Range	Iron Testing	
	n		Yes	No
Female	512	Within 1-month of First Hgb	278 (54.8%)	234 (45.2%)
		Within 3-months of First Hgb	320 (62.5%)	192 (37.5%)
		Within 1-year of First Hgb	345 (67.4%)	167 (32.6%)
Male	185	Within 1-month of First Hgb	90 (48.6%)	95 (51.4%)
		Within 3-months of First Hgb	101 (55.0%)	84 (45.0%)
		Within 1-year of First Hgb	112 (60.5%)	73 (39.5%)

136 anemic females less than fifty years of age did not undergo iron testing within 1-year of their first Hgb. Similarly, 167 females and 73 males over the age of fifty did not undergo iron

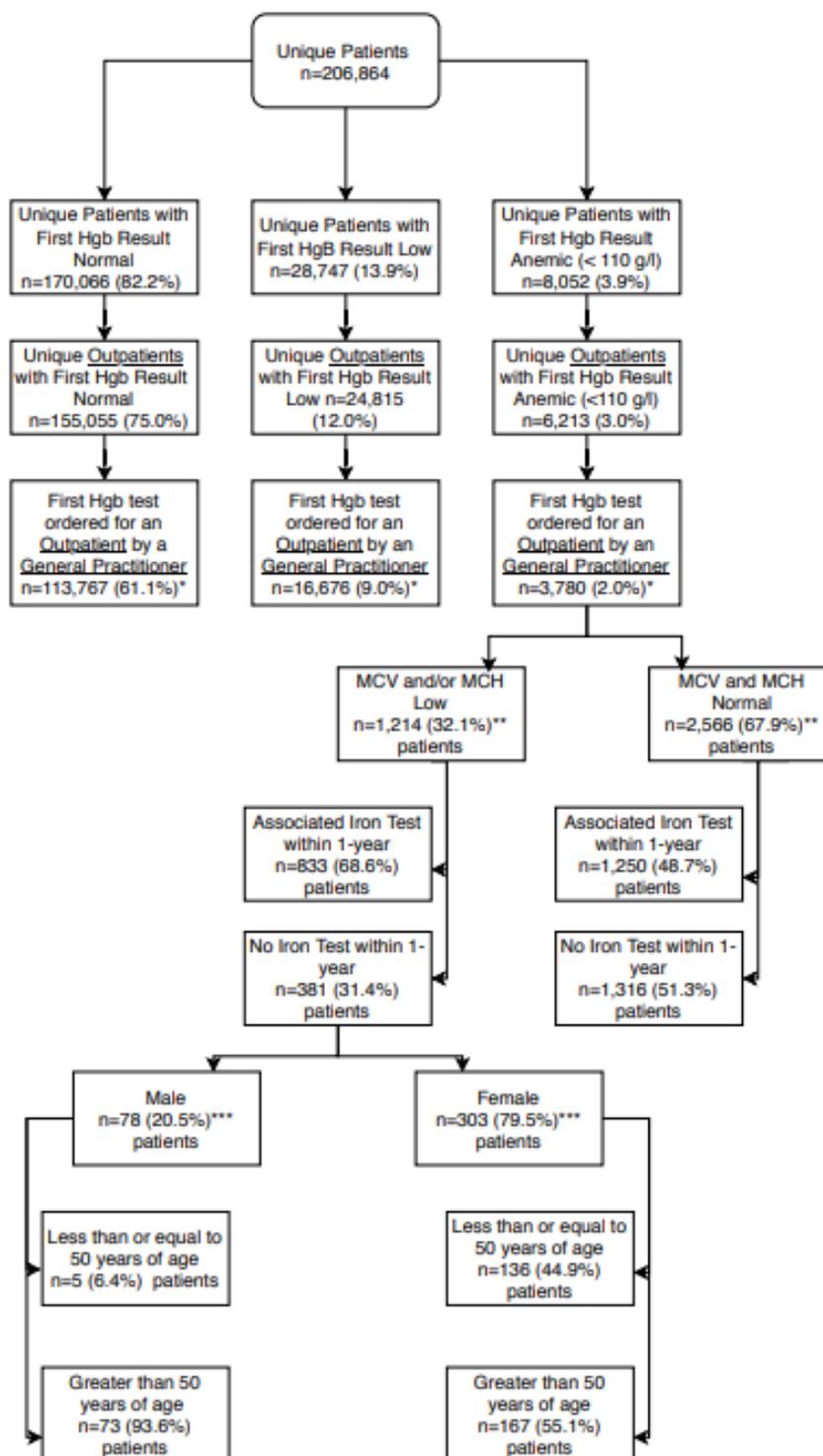
status testing within 1-year of their first Hgb. These patients should have had iron status testing investigations in order to determine the cause of their anemic result. These findings may represent a missed opportunity for testing and potential underutilization of these laboratory resources. Under testing has the potential to result in a delay or missed diagnosis of illness, potentially creating further implications for the patient and healthcare system downstream. It is, however, important to take into consideration that the failure to follow up with iron testing in these anemic cases may have been due to other factors (e.g. patient mortality).

In terms of our investigations of interest, missing an opportunity for testing in younger women may mean not treating an iron deficiency. In an older individual, it might represent a missed opportunity to investigate the cause of the anemia (diagnosing a bowel cancer for example). Ultimately, under testing in individuals where it may be indicated will decrease the quality of care provided for patient populations. It is important to take into consideration that the failure to follow up with iron testing in these anemic cases may have been due to other factors (e.g. patient mortality).

#### **4.2.4 Potential Test Underutilization**

Figure 32 provides a streamlined collection of the data presented in the previous figures which may support potential test underutilization.

**Figure 32: Cascade of Potential Underutilization.** This cascade highlights the points of interest that may support potential test underutilization of the iron status and hemoglobin tests in the Eastern Health Region during a 12-month period.



## NOTE:

\* = Percentage of the total of unique Out-patients

\*\* = Percentage of the total of unique patients with an anemic first Hgb test result as ordered by a General Practitioner

\*\*\* = Percentage of the total of unique patients with an anemic first Hgb test and associated low MCH/MCV result as ordered by a General Practitioner, who did not have iron testing undertaken

## Chapter 5: DISCUSSION

We examined the utilization of renal function tests (serum urea & serum creatinine), iron status tests (ferritin, iron saturation) and hemoglobin. These tests were analyzed individually and in combination with the other tests included within their specified bundle. Variables of interest assessed include: submitting physician specialty, patient age, patient sex, laboratory test result and patient type (inpatient vs. outpatient). Additionally, interventions undertaken to modify test-ordering behaviours are discussed in order to recommend an approach to any issues identified in the laboratory test utilization analysis.

Following analysis of the renal function tests we concluded that serum urea is commonly coupled with serum creatinine and is ordered in large numbers by general practitioners. This is likely unnecessary as the majority of test results are normal and there is a high degree of concordance between the information gained from creatinine and urea levels. Additionally, there is a great deal of variability in serum urea laboratory test ordering amongst general practitioners. However, a portion of this variability may be explained by taking into consideration that general practitioners included within this data set are not seeing the same patient numbers or profile.

We concluded that there is a large number of iron status tests being performed, particularly in general practice. The minority of iron status tests performed were iron saturation investigations, which are likely, unnecessary when ferritin is available. Large numbers of these tests were performed in non-anemic patients, which may be only indicated in particular subsets of patients. Underutilization was found to be small in volume, however, may have considerable clinical implications in specific patient populations.

## **5.1 Serum Urea & Serum Creatinine**

227,092 serum creatinine and 218,289 serum urea (Figure 3) tests were ordered in the Eastern Health Region during the 6-month period. The number of tests ordered during this time period emphasizes the substantial utilization of both kidney function tests when taking into consideration that the Eastern Health Authority services a regional population of approximately 300,000 people<sup>54</sup>. Serum creatinine is the preferred test to monitor kidney function and the progression of chronic kidney disease (CKD); serum should not be used to evaluate kidney function in stable patients, as it is the less specific test<sup>37</sup>. However, the data indicates that the majority of serum urea tests (96.8% of total) are coupled with serum creatinine tests.

General practitioners ordered the largest number of serum urea tests (52.5% of total; Figure 6). Similarly, the greatest quantities of serum urea tests coupled with serum creatinine were requested by general practitioners (52.9%; Table 2). This may be expected as general practitioners are considered to be the front-line investigators of the health care system<sup>58</sup>, however, requesting serum urea in these large numbers and in combination with serum creatinine is likely unnecessary. Serum urea may be useful in the diagnosis of acute kidney injury and the assessment of its origin<sup>38,39</sup> and therefore may be useful in specific clinical situations. As a physician, particularly from a community oriented general practitioner perspective, it is pertinent that the appropriate services are made available to each patient in order to identify health problems and monitor the impact of changes. The use of these tests in large numbers and in combination may be indicative of potential over-utilization in clinical screening investigations that are not indicated based on the clinical scenario. General practitioners play an extensive role in the monitoring of chronic conditions of

patients within the health care system; a population in which serum urea can be a non-specific indicator of pre-renal factors effecting its' levels <sup>37,39-41</sup>. A large proportion of coupled serum creatinine and serum urea tests elicited normal results for both tests (69.3%; Figure 14), supporting potential over-utilization while performing clinical investigations. Additionally, a noteworthy proportion (13.6%; Figure 14) of these tests produced an elevated serum urea result accompanied by a normal serum creatinine result. This combination of results while evaluating kidney function in stable patients has the potential to cause undesired diagnostic uncertainty. A possible response to uncertainty would be to order the test again, doubling up on unnecessary testing. This is further supported by the data, which demonstrates that 92.4% of patients with laboratory investigations that elicited an increased serum urea and a normal serum creatinine are elevated only within 3 mmol/L of the classified normal range (3 – 7 mmol/L) (Figure 15). This elevation in serum urea may be of minimal clinical significance.

There is a great deal of variability in the number of serum urea tests ordered by general practitioners throughout the Eastern Health Region. Albeit a proportion of the variability may be explained by differences in geographical location (rural vs. urban) and discrepancies in population demographics throughout the region. Understanding the large variability may require a shift in focus from the patient population to the general practitioners themselves. The pattern of test ordering may be reflective of the physician's year of graduation as medical school curriculum teachings are constantly being modified.

## **5.2 Iron Testing**

Analysis of laboratory investigations over a 12-month period in the Eastern Health Region exhibits a high volume of iron testing. As expected, due to their primary care role in the health care system<sup>56</sup>, general practitioners were found to have the highest ordering rate for these tests. Iron saturation tests were the minority of iron status investigations ordered, with 12,094 requested by general practitioners. This measure of iron status is likely unnecessary when ferritin is available as a serum ferritin test reflects stored iron and is the most accurate test for diagnosing Iron Deficient Anemia (IDA)<sup>44,46,47</sup>.

There is a large of patients who underwent iron testing as ordered by general practitioners, despite not being anaemic (79.6% of total; Figure 23). Furthermore, a large proportion of these patients' subsequent Hgb tests did not identify any anemia (95.8%; Figure 27). 38.3% (Figure 27) of these patients had an iron test ordered in the same draw as an Hgb. The high volume of iron status tests ordered in patients with a non-anemic result (normal Hgb, MCV, MCH) is likely unnecessary and provides support for potential test over-utilization. Iron testing is not clinically indicated in patients who present with normal hemoglobin, MCV and MCH and are not experiencing symptoms of iron deficiency<sup>57</sup>.

However, the literature suggests that iron testing may be beneficial in particular populations even when found to be non-anemic. Pre-menopausal women represent a large population of patients who may be at risk of IDA<sup>44</sup>, therefore, iron testing may be acceptable in symptomatic young women of reproductive age due to the loss of iron during menstruation and the increased demand for iron during pregnancy<sup>57</sup>. Ordering a serum ferritin in pre-menopausal, non-anemic women is likely justified as it aids in identifying patients who may benefit from iron

therapy. The evidence shows that in non-anemic women of reproductive age with a low serum ferritin level, oral<sup>58,59</sup> and intravenous<sup>60</sup> iron supplementation produces improvements in fatigue<sup>58,60</sup>, maximal and submaximal<sup>59</sup> exercise performance. However, the data indicates that there is a large volume of iron status investigations performed in older (> 50 years old) males and females; particularly patients whose first Hgb test result produced a normal result, further supporting potential test overutilization.

Underutilization of iron testing is small in volume; however, it is important to take into consideration as it may have clinical importance and impact outcomes in specific patient populations. 44.9% (Table 9) of females who were less than 50 years of age did not undergo iron testing within 1-year of their first anemic Hgb test result (Hgb <110 g/L, low MCH and/or MCV). This underutilization of the indicated clinical test produces a potential missed opportunity to mitigate factors that may affect pregnancy and treat IDA associated symptoms. Iron therapy may be valuable for this population as their IDA may be associated with decreased iron absorption, increased iron demand and insufficient dietary intake<sup>57</sup>. Furthermore, 93.6% (n=73) (Table 10) of male outpatients and 55.1 % of female outpatients (n=167) (Table 10) over the age of 50 did not undergo iron testing within 1- year of their first Hgb test, which produced an anemic result (Hgb <110 g/L, low MCH and/or MCV). Older populations should also be considered as an important group where a missed opportunity for testing may have a significant impact on health outcomes. Occult bleeding originating from the gastrointestinal tract is one of the leading sources of IDA in post-menopausal women and men<sup>61</sup>. Patients who are greater than 65 years of age with IDA should be screened for occult gastrointestinal cancers<sup>57</sup>. There is evidence to suggest that older

adults with anemia have gastrointestinal cancer 31 times more frequently than adults without anemia<sup>62</sup>

### **5.3 Potential Approaches to Improve Utilization of Laboratory Test Bundles in Eastern**

#### **Health**

Improving test-ordering behaviours, particularly in a primary care setting may be an intricate task. There are a number of factors to take into consideration in the development of interventions to improve laboratory test utilization including but not limited to: patient expectations of their physician, physician training, feasibility of the intervention and the extent in which patient-practitioner priorities coincide. Primary care physicians have often completed their training and have already developed individual heuristics for test ordering, creating further difficulty in eliciting behaviour change<sup>9</sup>. Investigations have found that a high proportion of patients would like to undergo more laboratory testing in order to diagnose their illness<sup>63</sup>. This highlights the importance of physician education to improve test utilization, improve quality of care and provide physicians with the necessary knowledge to explain to patients the impracticality of unnecessary testing.

While developing approaches to improve the utilization of these test bundles it is important to consider that there is a small body of literature, which specifically investigates the impact of interventions in the primary care setting. Many of these studies are considered to be of low methodological quality, impacting the external validity of the results<sup>28</sup>. Additionally, these inquiries do not specifically investigate the effects of these actions on the two bundles of tests

analyzed in this thesis, introducing the notion that these interventions may not be appropriate for these specific tests <sup>28</sup>.

The literature suggests that interventions involving restricted computerised ordering systems <sup>31</sup>, computerised ordering systems with integrated cost display <sup>19</sup> or integrated decision-making <sup>25,26</sup> may be effective in improving test ordering behaviours. However, general practitioners working within the Eastern Health region do not have a standardized computer ordering system, rendering these types of interventions impractical at this time.

System based, order form restriction interventions were successful in altering test ordering behaviours, however their sustainability is challenged as they may only elicit superficial behaviour change <sup>29,32-34</sup>. Restricted order forms may not be the ideal intervention for altering test-ordering behaviours as they may limit appropriate test requests. The main focus of only reducing test ordering does not correspond to the purpose of the Quality of Care NL's initiative, which is to ensure the right treatment is provided to the right patient at the right time<sup>4</sup>. However, this category of intervention may be practical for tests that may be considerably over-utilized (e.g. blood urea). Meng and colleagues <sup>32</sup> bypassed the risk of not providing the necessary care to patients due to a restricted order form by allowing general practitioners to order restricted tests following consultation with a clinical biochemist.

Based on the literature, an educational intervention would theoretically be the most effective in altering test-ordering behaviours for primary care settings in the Eastern Health Region while simultaneously preserving the goals of the Quality of Care NL's initiative. Education-based

strategies have been found to be effective in improving test-ordering behaviours in primary care physicians<sup>28</sup>. Moreover, there is evidence in the literature to suggest that providing physicians with educational guidelines is relatively inexpensive and practical for a comprehensive implementation<sup>64</sup>. The feasibility of intervention distribution is important, particularly in the Eastern Health Region due to its large geographical area<sup>52</sup>. The sustainability of these interventions is scrutinized throughout the literature, however, Mindemark and colleagues<sup>18</sup> provide evidence, although minimal, that test ordering behaviours remained improved 8-years post educational intervention. Educational-based interventions should incorporate multiple strategies (i.e. education and personalized performance feedback) and only target less than four tests for ordering behaviour modification<sup>9</sup>. Educational feedback programs should be designed systematically while incorporating guidance from the literature<sup>65</sup>. Implementing interventions to educate physicians to deliver high-value care is a difficult task and may be facilitated by providing effective knowledge translation, encouraging reflective practices and providing a supportive environment<sup>66</sup>.

#### **5.4 Undertaken Interventions to Improve Utilization in Eastern Health**

As a result of these investigations, interventions have been implemented throughout the Eastern Health Region to improve the utilization of tests described in this thesis.

Methods implemented within the region to reduce test utilization consisted of: (1) Audit & feedback to physicians through personalized report cards, (2) Academic detailing with knowledge translation, (3) system-based order form restriction. In addition to data analyzed in this thesis, more recent test ordering behaviours were taken into consideration and personalized report cards demonstrating physicians test-ordering behaviours compared to his/her peers were provided to all physicians through email. Academic detailing through knowledge translation consisted of a clinical specialist visiting physician's practices and discussing test ordering behaviours and reviewing clinical scenarios where each test are indicated. The system-based intervention consisted of a restricted ordering form where blood urea was removed. As previously mentioned, a restricted order form may directly contradict Quality of Care NL's initiative to ensure the right patient receives the right treatment at the right time. However, similar to Meng and colleagues<sup>32</sup>, a clinical specialist who implemented the process change allowed physicians to request the test manually in a separate hand written request box to mitigate the risk of not providing the necessary care to patients when felt to be clinically indicated. The same solution was applied in Eastern Health. All three interventions were used to improve test ordering of the urea kidney function test.

Audit and personalized report cards and academic detailing through knowledge translation were used to improve ordering behaviour of iron status tests (serum ferritin).

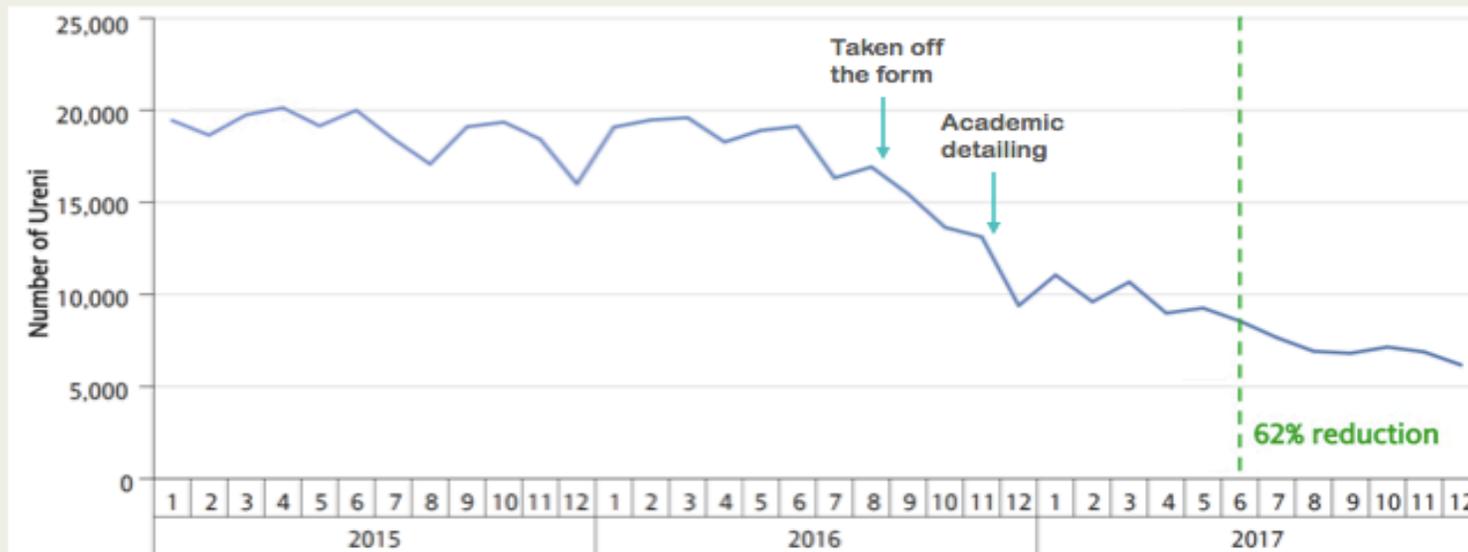
As of June 2017, data would suggest that following the implementation of the three interventions to reduce serum urea ordering there has been a 62% reduction in the volume of urea clinical investigations being requested for outpatients within the Eastern Health Region since January 2015. This decrease has produced an estimated annual cost avoidance in Eastern Health of \$267, 220<sup>67</sup> (*See figure 33*). Furthermore, following implementation of the discussed intervention serum ferritin test ordering has undergone a 20% reduction, eliciting an estimated annual cost avoidance in Eastern Health of \$159, 280<sup>67</sup> (*See Figure 34*).

**Figure 33: Quality of Care NL Blood Urea Practice Point.** This figure highlights that there has been a 62% reduction in urea testing ordered by general practitioners following the test being removed from the order form and academic detailing. The estimated cost avoidance is \$267,220

## Practice Point:

Blood urea is not a necessary test to measure kidney function in stable patients

Monthly volume of Urea over three years

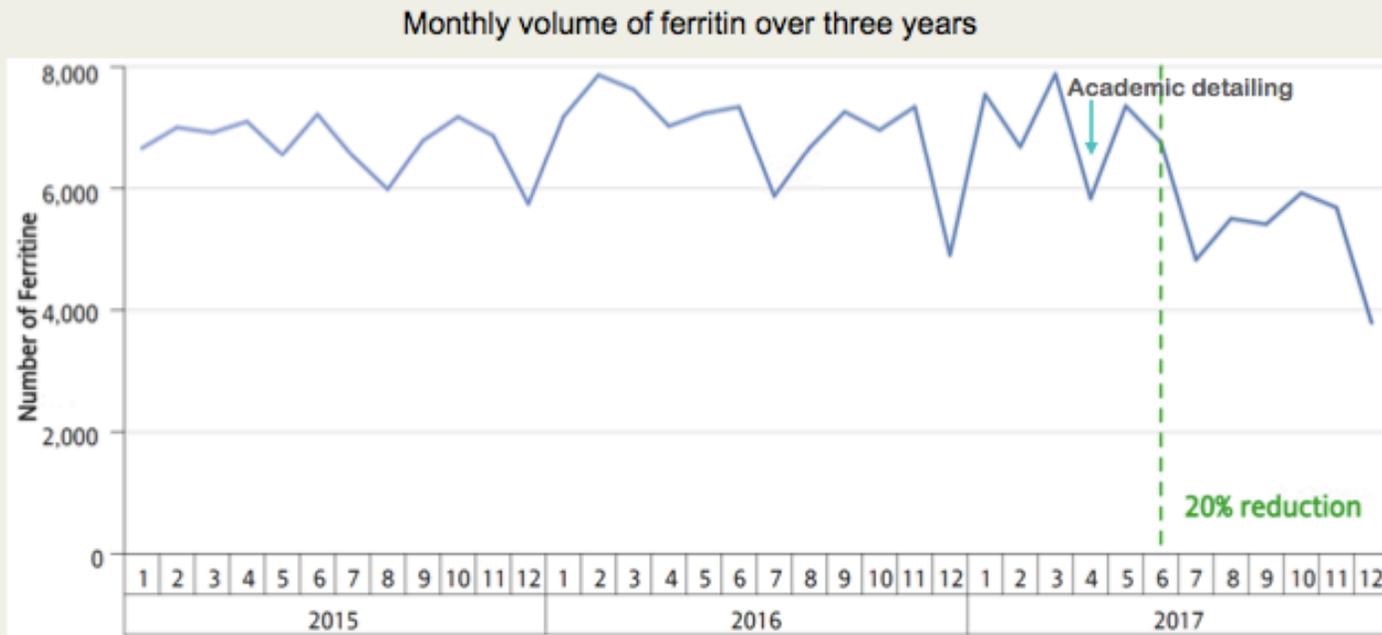


Estimated annual cost avoidance in Eastern Health: \$267,220

**Figure 34: Quality of Care NL Iron Testing Practice Point.** This figure highlights that there has been a 20% reduction in ferritin testing ordered by general practitioners following academic detailing. The estimated cost avoidance is \$159,280

## Practice Point:

Serum ferritin is a useful iron status test particularly in the diagnosis of iron deficiency. It is likely not useful in patients with normal hemoglobin and normal MCV/MCH, except maybe in symptomatic menstruating females where oral iron may be prescribed



Estimated annual cost avoidance in Eastern Health: \$159,280

## **5.5 Limitations**

In an attempt to minimize bias and to maintain the validity of the analysis, the initial total for tests ordered during the previously specified time period did not undergo data cleansing. This allowed for an accurate representation of the crude number of laboratory investigations being performed. Following this initial analysis, data cleansing required the removal of all tests that provided either no test result or a result that was believed to be inaccurate. Removed or edited test results typically occur when there is a sample quality problem or if there is an insufficient amount of the sample to complete the test.. This data cleaning process may have introduced bias into this investigation through the removal of data points due to absent or inconsistent values. The noteworthy numbers of removed tests during this process are as follows: 20, 239 (4.3% of total) Hgb, 3, 853 (4.5% of total) ferritin and 971 (4.1% of total) iron saturation tests. Taking this into consideration, it is believed that the impact of this limitation is minimal. The risk of bias is greatly mitigated by the large data set. The small alterations would have minimal impact on the pattern of test utilization portrayed by the data.

The foremost limitation of this investigation is that it does not take into consideration the specific clinical situation in which tests were ordered. Patient history, symptoms and test indication data pertaining to each ordered laboratory investigation were not included in this analysis. For this reason, the interpretation of the results is more difficult. Taking this into consideration, this investigation has the capacity to identify patterns of utilization and provide information to deduce areas of the health care system that may require further investigations to undergo improvement in terms of test ordering behaviour. However, it does not provide certain evidence of inappropriate utilization for these bundles of tests.

## **5.6 Implications**

Our findings suggest that serum urea may be over-utilized independently and in combination with serum creatinine. It is also indicated that iron testing is potentially over and under used. General practitioners elicited the highest ordering rates for both tests and based on the literature an educational-based intervention in conjunction with personalized physician ordering feedback may be the most effective method for improving ordering behaviour for both bundles of tests. Serum urea ordering patterns may benefit from the implementation of a system-based, order form restriction.

The information reported is useful for decision makers as it provides areas of concern for test ordering patterns. Additionally, the qualitative synthesis of the literature describes the appropriate clinical scenario that is indicated for the use of each test and methods used to improve laboratory test utilization in primary care settings. This information could serve as a tool for decision makers to guide the development of future interventions. This would ensure that the modification of test ordering behaviour would not be associated with a decrease in the quality of care provided by general practitioners, thereby maintaining the overarching goals of the Quality of Care NL's initiative. It is important for decision makers to consider the impact of interventions on the clinical outcomes of patients, as there are minimal data available that consider the subsequent effects of test ordering<sup>28</sup>.

One novel aspect of this investigation is that it takes into consideration the result of the laboratory requests. The majority of the literature, which investigates the utilization of laboratory investigations, focuses on the physician, with minimal consideration from the patients' perspective

28. Enhanced appropriateness of test ordering behaviours should be associated with improved clinical outcomes for patients<sup>68</sup>.

As previously acknowledged, a major limitation of this investigation is that it does not include data that pertains to the clinical situation in which the tests were ordered. There is a possibility that laboratory tests were indicated based on presenting patient symptoms and history.

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## **Appendix A**



Ethics Office  
Suite 200, Eastern Trust Building  
95 Bonaventure Avenue  
St. John's, NL  
A1B 2X5

June 28, 2016

Faculty of Medicine

Dear Mr. Thorburn:

**Researcher Portal File # 20170423**  
**Reference # 2016.183**

**RE: "Utilization of Laboratory Tests at Eastern Health"**

Your application received an expedited review by a sub-committee of the Health Research Ethics Board (HREB). **Full approval** of this research study is granted for one year effective **June 28, 2016**.

**This is your ethics approval only. Organizational approval may also be required.** It is your responsibility to seek the necessary organizational approval from the Regional Health Authority (RHA) or other organization as appropriate. You can refer to the HREA website for further guidance on organizational approvals.

This is to confirm that the HREB reviewed and approved or acknowledged the following documents (as indicated):

- Application, approved
- Letter to data custodian, approved

**MARK THE DATE**

**This approval will lapse on June 28, 2017.** It is your responsibility to ensure that the Ethics Renewal form is submitted prior to the renewal date; you may not receive a reminder. The Ethics Renewal form can be found on the Researcher Portal as an Event form.

*If you do not return the completed Ethics Renewal form prior to date of renewal:*

- **You will no longer have ethics approval**
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*
- *Lapse in ethics approval **may result in interruption or termination of funding***

**You are solely responsible for providing a copy of this letter**, along with your approved HREB application form; to **Research Grant and Contract Services** should your research depend on funding administered through that office.

Modifications of the protocol/consent are not permitted without prior approval from the

HREB. **Implementing changes without HREB approval may result in your ethics approval being revoked, meaning your research must stop.** Request for modification to the protocol/consent must be outlined on an amendment form (available on the Researcher Portal website as an Event form) and submitted to the HREB for review.

The HREB operates according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2), the Health Research Ethics Authority Act (HREA Act) and applicable laws and regulations.

**You are responsible** for the ethical conduct of this research, notwithstanding the approval of the HREB.

We wish you every success with your study.

Sincerely,



Dr Fern Brunger (Chair, Non-Clinical Trials Health Research Ethics Board)  
Ms. Patricia Grainger (Vice-Chair, Non-Clinical Trials Health Research Ethics Board)

CC: Patrick Parfrey  
E. Dicks





