



**Windsor Regional**  
**Vascular Health and Research Institute**  
**Kidney and Dialysis Research Institute**



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Dr. Albert Kadri, MD, FRCPC  
Nephrology and Internal Medicine  
Medical Director and Clinical Research Lead  
Windsor Regional Vascular Health and Research Institute



JULY 2015  
WINDSOR ESSEX COUNTY, ONTARIO  
A vision since 2011



**Windsor Regional**  
**Vascular Health and Research Institute**  
**Kidney and Dialysis Research Institute**



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Perhaps the greatest impact healthcare providers can have on patient outcomes is to successfully promote adoption of and adherence to therapies in high-risk patients that have been proven to reduce morbidity and mortality from cardiovascular and kidney disease. **The most important and trusted healthcare provider for a majority of patients, is their primary care practitioner.** They will likely have the greatest success in ensuring adoption and compliance to evidence based therapies suggested by qualified specialists. Enhancing coordination of multispecialty care to provide primary care practitioners with comprehensive and timely care plans for the high-risk cardiovascular and renal patient will likely be beneficial in helping to reinforce and follow through on suggested therapies. Specialists would benefit from a coordinated model if they were provided with the tools and resources to more seamlessly manage complex patients effectively while participating in a change process leading to higher levels of patient satisfaction and outcomes. Ultimately the main goal of this novel model is to transfer the greatest benefit to patients that we all serve.

**Our Objectives:**

1. To better support the central role of primary care practitioners, who have the greatest influence on affecting positive health care changes in patients to reduce the incidence of cardiovascular and renal disease.
2. To improve coordination of and access to specialty services to better meet the needs of patients and primary care practitioners.
3. To research the impact of a novel integrated model of specialty care with respect to health care outcomes and cost effectiveness in an academic research setting in order to lower CVD and CKD morbidity and mortality in Windsor and Essex County.

*Supported by: **Erie St. Clair Local Health Integration Network** and the **Ontario Renal Network***



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July 2015

An Innovative Specialty Care Model for Vascular Health and Wellness
An Evidenced-Based Model of Community Centred Specialty Care to Optimize Cardiovascular and Renal Outcomes

Albert Kadri, MD, Maher El-Masri, PhD, Nicole Dziamarski, HBSc, C. Pharm. Asst.

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Erie St. Clair LHIN  
 RLISS d'Érié St. Clair  
 www.eriesclairlhin.on.ca

180 Riverview Drive 180, Riverview Drive  
 Chatham ON N7M 5Z8 Chatham ON N7M 5Z8  
 Tel: 1-866-231-5446 Tél: 1-866-231-5446  
 519-351-5677 519-351-5677  
 Fax: 519-351-9672 Téléc: 519-351-9672

**Via email**

April 7, 2015

Dr. Albert Kadri, MD, FRCPC  
 Dr. A. Kadri Medicine Professional Corporation  
 1106 Ouellette Avenue Suite 104  
 Windsor, ON N9A 1C9

Dear Dr. Kadri:


**Re: Business Case for the Erie St. Clair Local Health Integration Network  
 - Regional Hypertension and Vascular Health Clinic**

The Erie St. Clair Local Health Integration Network (LHIN) is in alignment with the principles and overall goals of your proposal for a Regional Hypertension and Vascular Health Clinic. Clearly your business case, employing a coordinated community multidisciplinary approach to treatment, is consistent with the LHIN's goals to improve patient satisfaction, reduce visits to the emergency department, reduce re-admission rates, and reduce the burden of acute end-organ complications such as heart disease, stroke and renal failure.

The one-stop vascular centre that you have envisioned with coordinated multidisciplinary supports, a single electronic medical record (EMR), pharmacy, and laboratory has great potential for improving access, cost effectiveness and information sharing across disciplines and generally enhancing patient satisfaction and outcomes. We look forward to continue working with you in the future to improve chronic disease management and prevention in our communities closer to home.

Sincerely,

*Let's Make It Happen !*

  
 Gary Switzer,  
 Chief Executive Officer

AA:am

cc: Ralph Ganter, Senior Director, Health System Design and Implementation, Erie St. Clair LHIN  
 Alec Anderson, Director of Chronic Disease Prevention and Management, Erie St. Clair LHIN

 Ontario  
 Erie St. Clair Local Health  
 Integration Network  
 Réseau local d'intégration  
 des services de santé  
 d'Érié St. Clair

# Ontario Renal Network

## Réseau Rénal de L'Ontario

525 University Avenue, Toronto ON, M5G 2L7  
 tel: 416.971.9800 fax: 416.971.6888  
 www.renalnetwork.on.ca

September 29<sup>th</sup>, 2014

Dr. Albert Kadri, MD, FRCPC  
 Dr. A. Kadri Medicine Professional Corporation  
 1106 Ouellette Avenue Suite 104  
 Windsor, ON N9A 1C9

**Re: Business Case for the Erie St. Clair Local Health Integration Network (LHIN) Regional Hypertension and Vascular Health Clinic**

Dear Dr. Albert Kadri:

The Ontario Renal Network (ORN) supports the principles behind the Erie St. Clair LHIN's proposal for a Regional Hypertension and Vascular Health Clinic. The proposed model in the business case aims to improve coordination of, and access to, chronic disease prevention and management services, such as hypertension, diabetes, cardiovascular and kidney care in a community setting.

This initiative aligns with one of the ORN's strategic priorities: to reduce the impact of chronic kidney disease (CKD) by improving early detection and prevention of progression. As such, we anticipate that this work will address the following desired outcomes:

- Improved management of CKD and related comorbid conditions in a community setting;
- Delay or prevent the progression of CKD, where possible;
- Decreased emergent dialysis starts for persons with CKD.

We look forward to hearing more from you in regards to the the proposed Hypertension and Vascular Health Clinic.

Sincerely,



Rebecca Harvey  
 Vice President  
 Ontario Renal Network



Dr. Peter Blake  
 Provincial Medical Director  
 Ontario Renal Network



## *Abstract*

The changing dynamics of our aging population and the escalating costs of acute care services mandate a change to our current model of health care delivery. The complex nature of the high-risk cardiovascular and renal patient necessitates a collaborative multispecialty and multidisciplinary approach to patient care and a shift away from a traditionally siloed and reactive acute care model. A shift towards a more coordinated, proactive and preventative patient-centred wellness model, will almost certainly translate into improved patient outcomes and significant savings in direct and indirect costs for our patients and the taxpaying community.

A single site, *community based*, academic research institute providing coordinated, collaborative care - utilizing a single electronic medical record and database - would enhance the ability to optimize care and promote adherence to clinically proven therapeutic strategies. A one-stop centre of excellence has great potential for improving cost effectiveness by reducing duplication of tests and investigations, and by increasing information sharing across specialties and disciplines it will consequentially enhance patient care and reduce the risk of error. Multiple specialists and healthcare team members interacting around complex cases in a coordinated fashion can only improve quality of care and outcomes for patients. The enhanced coordination of care and single site access to multispecialty service will lead to improved collaboration with primary care practitioners and increased patient satisfaction translating to increased attendance to both primary and specialty care visits that are necessary for promoting health and wellness in this high risk patient population. This in turn will hopefully create an atmosphere fostering greater compliance to strategies known to positively affect patient outcomes and reduce reliance on emergency room departments and inpatient acute care services.

The **Windsor Regional Vascular Health and Research Institute** proposes to serve the high-risk *cardiovascular and renal patient* using a novel *5 Pillar Model of Care* in order to promote patient-centred, evidence-based and cost-effective strategies to reduce the burden of illness in Windsor-Essex County. These goals align with the Ontario Chronic Disease Prevention model and are supported by both the Ontario Renal Network and by the Erie St. Clair Local Health Integration Network as well as the Integrated Vascular Health Blueprint for Ontario. The next step in this research protocol is to perform a needs assessment with local primary care practitioners, relevant specialists, and funding agencies.

## **Introduction**

**T**he field of medicine is constantly evolving as a result of new information and technology. In fact, a great deal of what I learned in medical school over 20 years ago is no longer applicable. We must constantly adjust the way we do things to enhance the quality of care for our patients, as well as the cost-effectiveness for our healthcare system. After completing my medical training, I returned to practice internal medicine and nephrology in the community that I was raised in. I have been a direct witness to the outstanding care that our front-line healthcare professionals provide to patients in our community. I've also seen the challenges, as well as the opportunities, within our health care system in

trying to reduce patient morbidity and mortality in a meaningful, cost effective and evidence-based manner. As a medical community, we have traditionally been very focused and effective at treating established disease but our efforts on preventing cardiovascular and renal disease are far less systematic and developed. Numerous studies across many different high-risk populations have proven that strategies that help prevent acute illness and vital organ damage are far more effective than treating established disease, however the uptake of these strategies remains sub-optimal, **Table 1**.

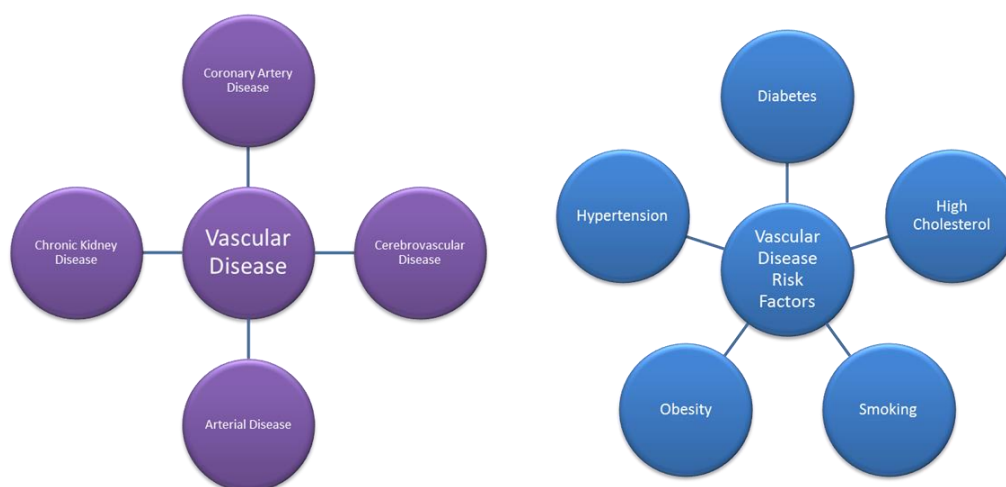
**Table 1** Select examples of the disconnect between the evidence for preventing cardiovascular events and their clinical uptake.

Intervention	Studies showing importance of preventative management in at risk populations	Studies showing poor uptake of evidence based measures
<b>BP control</b>	<p><b>SOLVD</b><sup>1</sup> Patients on enalapril in prevention trial with no history of HF showed a significant reduction in death or development of CHF than patients in the treatment trial entering the study with clinical evidence of CHF.</p> <p><b>IDNT</b><sup>2</sup> Hypertensive Type II diabetic patients on irbesartan showed delayed progression of renal disease and lower mortality.</p>	<p><b>REACH</b><sup>3</sup> Classic risk factors for cardiovascular disease were common and undertreated in many regions of the world. There was evidence for under treatment with statins, antiplatelets and other risk reduction therapies.</p> <p><b>ADA Survey</b><sup>4</sup> Inadequate achievement of American Diabetes Association prevention and clinical practice recommendations in US diabetics.</p> <p><b>EUROASPIRE III</b><sup>5</sup> Poor lifestyle intervention and inadequate control of BP, lipids and glucose for primary prevention in high risk asymptomatic patients.</p> <p><b>EURIKA</b><sup>6</sup> Among patients with varied risk, less than ½ of hypertensive and dyslipidemia patients attained treatment goals according to 2007 European guidelines on CVD prevention. Less than 1/3 achieved desired Hb1Ac levels. Lifestyle interventions were generally not well-implemented, especially with regards to smoking cessation (less than 1/3) and weight loss.</p> <p><b>CORIMA</b><sup>7</sup> Even for high-risk German patients, majority have not achieved treatment goals. If these were achieved, it is predicted that high risk patients could reduce from 20% to &lt;5%</p>
<b>Lipids control</b>	<p><b>SPARCL</b><sup>9</sup> Daily high dose of atorvastatin reduced the incidence of stroke and cardiovascular events in patients with recent TIA without known CAD (with slight increase in hemorrhagic strokes)</p> <p><b>HPS</b><sup>10</sup> Regardless of initial cholesterol concentrations, simvastatin reduced rates of MI, stroke, revascularization and all-cause mortality in high cardiovascular risk patients.</p>	
<b>HbA1C control</b>	<p><b>DCCT</b><sup>11</sup> intensive blood sugar control delays onset of diabetic retinopathy, neuropathy, nephropathy in IDDM</p>	
<b>Lifestyle and smoking cessation</b>	<p><b>LHS</b><sup>12</sup> Smoking cessation programs significantly reduced all-cause mortality and mortality due to cardiovascular disease even when successful in minority of patients.</p>	
<b>Anti-platelet therapy</b>	<p><b>JPAD</b><sup>13</sup> Low dose Aspirin in DM2 patients with mild (but not severe) renal dysfunction was useful in primary prevention of atherosclerotic events of IHD, stroke and PAD.</p>	<p><b>Maio et al.</b> showed only 2/3 of eligible patients following MI were initiated on B-blocker therapy despite evidence of substantial reductions in mortality and morbidity. This is similar to rates in other countries, including Canada.<sup>8</sup></p>

**Table 1** shows a few of the many examples of evidence based measures to reduce cardiovascular and kidney disease. Clinical uptake of these measures depend on a variety of factors, many of which are not under the control of health care practitioners. Suboptimal uptake of evidence-based therapies can include factors related to providers, patients and the health care system in general. Our goal is to better address systematic issues that can reduce uptake of proven therapies.

Vascular or cardiovascular disease (CVD) affects virtually every organ system across numerous medical specialties (cardiology, neurology, nephrology, endocrinology, vascular surgery and internal medicine) and it encompasses any disease involving the blood vessels. Thus many chronic conditions fall within this category including: coronary artery disease (CAD), cerebrovascular disease (CBVD), peripheral

arterial disease (PAD) and chronic kidney disease (CKD), shown in **Figure 1a**. All of these conditions have very similar risk factors (including diabetes, hypertension, dyslipidemia, established atherosclerotic disease, obesity and smoking) and often co-exist together.<sup>14</sup> Therefore it is our position that the full spectrum of cardiovascular disease should include heart disease, stroke, peripheral vascular disease and kidney disease as a single system of disorders with virtually identical risk factors, **Figure 1b**. Early intervention strategies to prevent and manage these risk factors including early chronic kidney disease can have a profound impact on patient outcomes, see **Table 2**.



**Figure 1 a** (Image left) Forms of vascular disease, **b** (image right) risk factors for vascular disease.

In 2011, I presented and began advocating for a novel community-based approach to the high-risk *cardiovascular and renal patient* to promote a coordinated, patient-centred, evidence-based and cost-effective strategies to reduce the burden of the illness in our region. These strategies focused on increasing access and coordination of care as a means of increasing the uptake of scientifically proven therapies known to prevent acute illness, hospitalization and vital organ damage.

*“An ounce of prevention is worth a pound of cure.”*

- Benjamin Franklin

### Rationale and Need for Innovation

Over many years of medical practice, I have been a witness to a rapidly changing dynamic within our patient population and our healthcare system, which necessitates a change from the ‘business as usual’ approach to managing chronic illnesses that lead to *cardiovascular and renal disease*. Cardiovascular disease remains the leading cause of hospitalization and death in Canada.<sup>15,16</sup> The risk factors for cardiovascular disease such as diabetes and hypertension are increasing as the population ages.<sup>17,18</sup> Correspondingly, the major cause of cause of death by circulatory diseases increases dramatically with age, with a mortality rate of 11% for people aged 20-44, 21% for people 45-64, 28% for 65-79 and 38% for people aged 80 and over.<sup>19</sup> The vast majority of chronic kidney disease cases are due to diabetes, hypertension and vascular disease.<sup>20,21,22</sup> In high risk CKD patients the statistics show that approximately 80% of these patients will die of cardiovascular disease, often before they even need dialysis.<sup>23,24</sup>



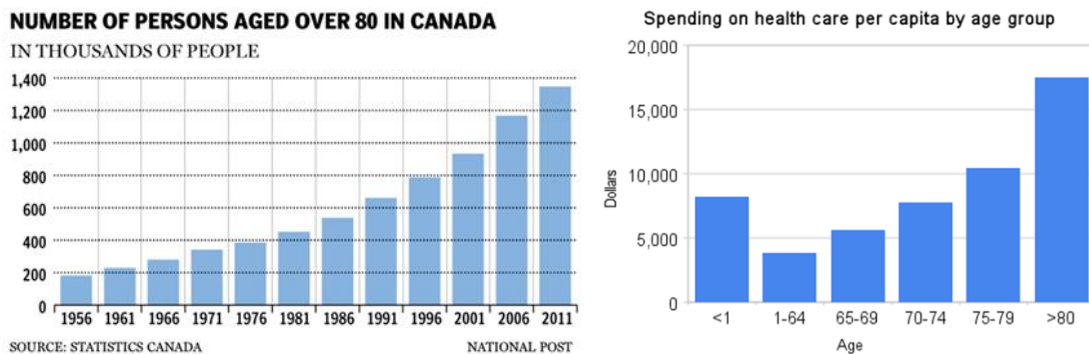
Windsor and Essex county has one of the highest rates of cardiovascular and kidney disease in the province. In our region the number of patients on dialysis within the last 15 years has roughly quadrupled while we have maintained a relatively constant population. Between 2007 and 2011, circulatory diseases accounted for a mortality rate of 33.2% in Windsor-Essex County.<sup>25</sup> Thus there is an increasing urgency to lower the incidence of cardiovascular and kidney disease and consequently to lower the overall morbidity and mortality rates within our region in this at risk population.

*“Necessity is the mother of invention.”*

- Plato

## The Epidemic of an Aging Population

Globally, good health is most valued in people’s lives.<sup>26</sup> Our population demographics are changing and we have an ever-expanding elderly population, **Figure 2a**. Between 1956 and 2011, our elderly population has increased by over 700%. As our population ages, the risk of significant illness increases correspondingly, as does the expense of health care, **Figure 2b**. In fact, the cost of health care spending on a senior over the age of 80 is 400% higher than the cost of healthcare for someone between the ages of 1 and 64. As a result, we must come up with strategies to reduce the incidence of acute illness and prevent vital organ damage in order to lessen the burdens of chronic disease. In addition to reducing patient quality-of-life, acute illness also increases emergency room visits and hospitalizations, which are tremendously costly to our healthcare system.



**Figure 2a** (image left) Increasing trend of aging population<sup>27</sup>, **b** (image right) consequential high cost of an aging population.<sup>28</sup>

The leading cause of hospital based healthcare expenditure in Canada is the treatment of acute cardiovascular disease.<sup>29</sup> In 1998, CVD was responsible for over \$21.2 billion in expenditures.<sup>15</sup> From 2004-2005 acute care inpatient costs for diseases of the circulatory system cost over \$3.29 billion; the most expensive clinical health care sector.<sup>29</sup> In Canada, the public sector carries roughly 70% of the cost of health care.<sup>30</sup> Thus, these expenditures become the burden of taxpayers within our healthcare system. Finding ways to keep our population healthier and avoid emergency room visits and hospitalizations not only benefits patients and their families but also all of those responsible for maintaining our healthcare system. By examining these statistics, it becomes indisputable that decreasing the health care burdens of chronic disease would be a tremendous benefit to the entire populace.

## Co-morbidity Leading to Cardiovascular Disease

Co-morbidity is a significant problem as it leads to more complex clinical management which can be extremely challenging when many different specialists are involved without the tools needed to effectively coordinate patient care, leading to worse outcomes and increased costs.<sup>31</sup> There are a multitude of risk factors for progressive cardiovascular disease. An escalating proportion of patients have multiple co-existing chronic conditions, which can significantly elevate their risk of cardiovascular disease.<sup>14</sup> The high prevalence rates for hypertension, diabetes, high cholesterol levels, obesity and renal impairment as we age result in a significant portion of the population managing many if not all of these conditions simultaneously.

A patient with CKD may also have to manage diabetes, hypertension, cardiovascular disease, cerebrovascular disease, coronary artery disease, and peripheral vascular disease. Managing multiple chronic illnesses at the same time, numerous prescriptions and at times conflicting approaches to management can be immensely challenging and confusing to patients seeing several health care specialists in isolation. For instance, being able to balance the conflicting dietary restrictions between a diabetic and renal diet can be quite onerous to patients. Conflicting fluid intake recommendations for patients managing both kidney and cardiac disease can be confusing. Making the most optimal medication choices, knowing when to dose adjust certain medications, managing contraindications and side effects in patients that are on multiple different medications with different indications can be difficult. For example, in most high-risk diabetic patients with hypertension, 3 to 4 medications are often required just to manage their blood pressure,<sup>32</sup> not to mention medications to manage their other conditions. Consequently, polypharmacy remains a significant issue and an ongoing source of morbidity and mortality.<sup>33</sup> Also from a practical perspective, juggling multiple medical visits to different specialists, numerous different laboratory investigations attached to each of these visits, additional investigations and imaging tests (often with significant duplication), can be tremendously daunting for a patient. Medical visit fatigue combined with non-attendance and non-compliance are often results of this.

Issues of timely access to multi-system management when needed remain, prompting a high

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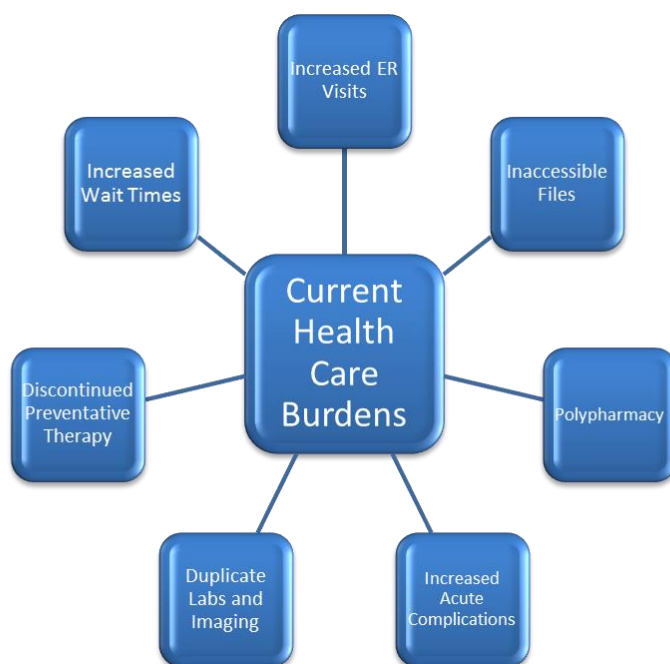
*“Many of my high risk vascular patients report that they spend all of their time going to medical appointments: physician visits, specialty appointments, lab work, and so on. It is often disheartening to see that many do not attend their primary care practitioner’s office as often as they should; missing opportunities for routine preventative health care and maintenance. As a medical community we know the immense importance of these preventative strategies for preventing disease progression and further comorbidities. Their nonattendance can lead to detrimental health care implications. For instance, missing important preventative screening strategies (cancer screenings, etc) might mean the progression of disease states in additional systems thereby worsening the patient’s overall health.*

*In addition, high risk patients experiencing medical visit fatigue will miss important specialist appointments, citing their escalating frustrations with the overwhelming number of medical visits that they must attend. I have heard this time and time again. We owe it to our patients to lessen the burdens they are faced with when dealing with their chronic illnesses.”*

- Dr. A. Kadri, Internal Medicine and Nephrology Specialist

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rate of usage of the emergency room as a last resort. The traditional health care model is not geared to optimally manage an aging population with multiple chronic conditions as it *does not* optimize community based treatment coordination among various specialties, and many burdens are left on the shoulders of the acute healthcare system. These include: increased acute complications and increased ER visits, increased wait times, inaccessible files, discontinued preventative therapies, polypharmacy and duplicate investigations **Figure 3**. All of these burdens increase the cost and consequences to the health care system and to the patient. Undoubtedly, there is a need for a new model of care to alleviate the burdens the current system is faced with. By increasing coordination of services for patients with chronic disease the overall financial cost to taxpayers would be significantly decreased, while simultaneously increasing patient quality of life; a highly desired outcome.



**Figure 3** A variety of examples of the health care burdens resulting from our current model of care.

### Our Siloed Health Care System

Within our health care system we have highly trained professionals in both primary and specialty care. Their skills can benefit patients in our community tremendously; however our community-based systems of care need to adapt to maximize the effectiveness of these professionals in order to optimize outcomes for patients. We have a very segmented or ‘*siloed*’ health care system, with health care providers often working in isolation rather than in collaboration with other health care professionals, leading to significant issues of coordination and access. A siloed system may lead to suboptimal outcomes for patients and escalating health care costs.<sup>34</sup> The silo symptom of our traditional health care model leads to an array of health care burdens to both patients and the community, as was shown in **Figure 3**.

Traditionally, our health care system tends to focus on disease or condition specific interventions, often in isolation of the efforts of other healthcare practitioners and with very little real time communication. This can inadvertently lead to adverse outcomes due to suboptimal coordination

and timeliness of care.<sup>34</sup> For instance, in most pre-dialysis clinics, the focus for advanced chronic kidney disease care is often on managing and limiting renal-related complications such as anemia, altered bone metabolism, fluid balance issues as well as dialysis preparation and modality selection.<sup>35</sup> What may at times get lost in the process is that optimally managing cardiovascular risk factors is of even greater importance in reducing morbidity and mortality in CKD patients.<sup>23,36</sup> Providing integrated, comprehensive and evidence based care would certainly enhance patient outcomes while reducing burdens on the health care system. Utilizing an integrated network of *multispecialty* care professionals that have access to the same electronic medical record (EMR) and database of information would limit many of the current problems and allow for a timely and more cohesive and comprehensive treatment plan for the patient. Eliminating extended waits (sometimes even several months) to see specialists necessary to their care and limiting the need to travel (which may be several hours of travel time) for these appointments would be a huge benefit of a one-stop community vascular health centre for high risk patients. Specialists would benefit from a coordinated model if they were provided with the tools and resources to more seamlessly manage complex patients effectively while participating in a change process leading to higher levels of patient satisfaction and outcomes.

Primary care practitioners are central to this model and would be provided with support from the entire specialty care team, from multidisciplinary specialists to allied health care professionals, see **Figure 4**. The most important and trusted healthcare provider for a majority of patients is their primary care practitioner. They will likely have the greatest success in ensuring adoption and compliance to evidence based therapies suggested by qualified specialists and have the greatest influence on affecting positive health care changes in patients in order to reduce the incidence of cardiovascular and renal disease. Enhancing coordination of multispecialty care in order to provide comprehensive and timely care plans to primary care practitioners for their high-risk cardiovascular and renal patients will be beneficial in helping to reinforce and follow through on suggested therapies. In addition, reducing the number of medical visits that high risk cardiovascular and renal patients must attend allows for more time with their primary care practitioners. In order to reinforce recommendations and therapies after visiting the specialty centre there must be a mandatory visit to the patient's primary care practitioner in order to review the comprehensive care plan provided, thereby enhancing patient adherence and education.



**Figure 4** The Integrated Multispecialty Patient Care Team

This model fosters mutually beneficial outcomes for the patient and the entire health care team. It provides primary care practitioners with the tools they need to effectively manage their patients and an environment for specialists to work cooperatively to improve patient outcomes. Reduced therapeutic inertia in interventions would be seen due to the immediate opportunity to discuss complex cases with other specialists. A greater accountability for managing each cardiovascular issue through case management would also improve patient outcomes. An integrated specialty centre would provide better follow up on interventions through comprehensive case management, particularly restarting medications that have been held for acute conditions that may have resolved quickly. For instance, transient hyperkalemia on ACE therapy leading to discontinuation, temporary cessation of statin therapy due to perceived side effects, or ASA or anticoagulant withdrawal due to temporary side effects. Often these medications are discontinued for transient reasons and never restarted due to uncertainty about reasons for discontinuation, safety of use, or lack of availability of close follow-up. The opportunities for improved health care services are significant and illustrate the need for health care reform.

### **The Benefits of Wellness Focused Preventative Care**

Care delivered within the community can help patients and practitioners foster a culture of wellness. This is in contrast to hospital-based care which tends to give patients a perception of illness. Thus, for patients with chronic disease obtaining care in a community setting provides a sociological benefit. Promoting a focus on wellness can improve patient state of mind which helps to enhance their adherence and outcomes. Care provided in a community setting also strengthens the link with their primary health care team which is significant in patient outcomes.<sup>37</sup> A wellness model must shift the focus of patient care away from an acute care ‘treatment’ model to one that focuses on disease ‘prevention’. A model that focuses on preventative care will certainly provide improved patient outcomes. For instance, limitations of CKD treatments and the high rates of morbidity illustrate the critical importance of instituting a preventative model to slow or prevent progression of the disease.<sup>38</sup> Once diseased states and organ damage progress, treatments become far less effective.

Care that begins before the onset of disease is termed ‘primary intervention’, once the diseased state is confirmed onset of care is ‘secondary intervention’ and following the onset of disease – in order to prevent further co-morbidities - is ‘tertiary/late intervention’.<sup>39</sup> Preventative strategies have been shown to reduce risk of *cardiovascular and renal disease* progression in both primary and secondary disease settings. Interventions are much more effective when instituted earlier when the burdens of established disease are lower and they become less effective as organ damage increases and diseased states progress. The benefits of optimizing these therapies are established in well-conducted scientific studies and have benefits across many different disease states,<sup>40,41</sup> as shown in **Table 2**.

**Table 2** Studies highlighting primary, secondary and late interventions in various disease states.

Condition	Studies Supporting Effectiveness of Primary and Secondary Interventions	Studies Confirming Late Intervention Ineffective
<b>DM</b>	<p><b>Diabetes Care</b><sup>42</sup> Appropriate lifestyle and medical interventions reduce the risk of CVD in diabetics.</p> <p><b>MedDiets</b><sup>43</sup> A Mediterranean diet without calorie restriction is effective in reducing the incidence of DM in those with high CVD risk.</p> <p><b>CARDS</b><sup>44</sup> The effectiveness of lipid lowering treatment (atorvastatin) was evaluated in patients with type 2 diabetes without high LDL cholesterol in primary prevention of CV events and reduced mortality by 27%.</p> <p><b>JPAD</b><sup>43</sup> Low dose Aspirin in DM 2 patients with mild (but not severe or slight) renal dysfunction was useful in primary prevention of atherosclerotic events of IHD, stroke and PAD.</p> <p><b>DCCT</b><sup>41</sup> intensive blood sugar control delays onset of diabetic retinopathy, neuropathy, nephropathy in IDDM</p> <p><b>UKPDS</b><sup>45</sup> Metformin monotherapy reduces mortality and cardiovascular morbidity and mortality, and is favourable in most patients with newly diagnosed type 2 diabetes when dietary measures insufficient.</p> <p><b>STENO-2</b><sup>46</sup> Multifactorial intervention when done early reduces vascular complications and rates of death from any cause and CV causes</p> <p><b>ADVANCE</b><sup>47</sup> A 20% decrease in nephropathy shown with tight blood sugar and blood pressure control but has no significant effect in reducing macrovascular disease, less burden of CVD at onset of trial</p> <p><b>ABCD</b><sup>48,49</sup> In patients with type 2 diabetes and HTN nisoldipine group showed significantly higher rate of MI than in the enalapril group.</p> <p><b>BENEDICT</b><sup>50</sup> Patients with type 2 diabetes, HTN had the lowest incidence of persistent microalbuminuria (5.7%) on trandolapril plus verapamil compared to other treatment groups.</p>	<p><b>ACCORD</b><sup>51</sup> Patients with pre-existing DM for 10 years and established CVD showed no reduction in CV events with BP and lipid therapies.</p> <p><b>Look AHEAD</b><sup>52</sup> Intensive lifestyle intervention focusing on weight loss did not reduce cardiovascular events in DM2 overweight or obese patients (DM pre-existing for median of 5 years)</p> <p><b>VADT</b><sup>53</sup> Intensive glucose control had no significant effect on rates of major cardiovascular events, death or microvascular complications in patients with long-standing poorly controlled DM2 (also found increased rates of adverse hypoglycemia).</p> <p><b>FIELD</b><sup>54</sup> DM2 patients (median duration = 5 yrs) without previous statin administration did not benefit from fenofibrate through reduced risk of coronary events</p> <p><b>TREAT</b><sup>55</sup> Patients with DM2 + CKD + anemia did not benefit from darbepoetin. Treatment group had increased risk of stroke with no difference in CV event, renal event or death as compared to placebo</p>
<b>HTN</b>	<p><b>DASH</b><sup>56</sup> Benefits of lifestyle interventions in reducing need for meds (diet rich in fruits, vegetables, and low-fat dairy foods and with reduced saturated and total fat can substantially lower blood pressure), offers an additional approach to preventing and treating hypertension.</p> <p><b>ACCOMPLISH</b><sup>57</sup> and <b>ALLHAT</b><sup>58</sup> Studies in high risk but less established CVD resulted in less CVD and HF with HTN therapies</p> <p><b>LIFE</b><sup>59</sup> Losartan treatment resulted in a reduction in CV morbidity in patients with left ventricular hypertrophy documented by ECG.</p> <p><b>PROGRESS</b><sup>60</sup> Reduction in stroke observed in both hypertensive and non-hypertensive patients with history of stroke or TIA</p> <p><b>SHEP</b><sup>61</sup> Patients with systolic hypertension showed a reduction in major adverse cardiovascular events at 5 year follow-up when treated with chlorthalidone.</p> <p><b>HOT</b><sup>62</sup> Hypertensive patients taking felodipine as initial therapy and following a subsequent 5 step regime experienced a reduction in blood pressure as well as a reduction in all major CV events.</p> <p><b>SYMPPLICITY-HTN 2</b><sup>63</sup> Catheter-based renal denervation substantially reduced blood pressure in treatment-resistant hypertensive patients.</p> <p><b>SYST-Eur</b><sup>64</sup> The primary endpoint of fatal and nonfatal stroke was reduced by 42%.</p>	<p><b>VALUE</b><sup>65</sup> The comparative statin study does not show a significant difference between the treatment groups with regard to the primary end point in patients with hypertension AND coronary disease, cerebrovascular disease, peripheral arterial disease or left ventricular hypertrophy (high risk patients).</p> <p><b>DRASTIC</b><sup>66,67,68</sup> In patients with HTN and renal artery stenosis no significant differences between the angioplasty and drug-therapy groups in systolic and diastolic blood pressures, daily drug doses, or renal function.</p>

Condition	Studies Supporting Effectiveness of Primary and Secondary Interventions	Studies Confirming Late Intervention Ineffective
HTN <sub>cont'd</sub>	<p><b>HYVET</b><sup>69</sup> Treatment of patients over 80 years old with diuretic indapamide (and perindopril if necessary) resulted in 23% reduction in death from CV causes and 21% reduction in all-cause mortality.</p> <p><b>STOP-Hypertension 2</b><sup>70</sup> Reduction in CV events and mortality in elderly hypertensives on both classical and newer antihypertensive agents (Lisinopril, enalapril, isradipine and felodipine).</p> <p>Aerobic exercise reduces BP in both hypertensive and normotensive patients and should be considered an important component of primary prevention<sup>71</sup></p>	<p><b>4D</b><sup>85</sup> &amp; <b>Aurora</b><sup>86</sup> No benefits in CV event reduction with statins for patients on hemodialysis or stage 4 CKD.</p> <p><b>ALERT</b><sup>87</sup> Although fluvastatin lowered LDL, there was no significant benefit in risk reduction of coronary intervention or mortality in hemodialysis patients</p>
Lipids	<p>Weight reduction by dieting increases HDL-C and decreases other blood lipids and is a viable approach to normalize lipid levels in overweight patients.<sup>72</sup></p> <p><b>HPS</b><sup>10</sup> Regardless of initial cholesterol concentrations, simvastatin reduced rates of MI, stroke, revascularization and all-cause mortality in high cardiovascular risk patients</p> <p><b>ASCOT-LLA</b><sup>73</sup> Atorvastatin in hypertensive patients with risk factors for CHD and up to average cholesterol reduced major CV events (non-fatal MI, fatal CAD, stroke) but not all-cause mortality.</p> <p><b>SHARP</b><sup>74</sup> Patients on simvastatin and ezetimibe therapy with CKD experienced decreased atherosclerotic CVD, findings emphasize need to treat early in disease.</p> <p><b>ASTEROID</b><sup>75</sup> Patients with evidence of CAD and indication of coronary catheterization received intensive statin therapy which resulted in significant regression of atherosclerosis.</p> <p><b>CARDS</b><sup>44,76</sup> Patients with type 2 diabetes and one other risk factor for CHD experienced 5.8% acute coronary heart disease events compared to 9.0% for placebo group.</p> <p><b>JUPITER</b><sup>77,78</sup> In high risk patients with elevated hsCRP but normal LDL levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.</p> <p><b>4S</b><sup>79</sup> Patients with CAD and serum total cholesterol levels between 5.5 and 8.0mmol on simvastatin experienced a risk reduction of 30% and a 42% reduction in the risk of coronary death.</p> <p><b>WOSCOPS</b><sup>80</sup> Pravastatin administered to men with hypercholesterolemia without previous history of MI reduced incidence of non-fatal MI and cardiovascular death by about 30%</p> <p><b>LIPID</b><sup>81</sup> Pravastatin therapy reduced mortality from CAD, overall mortality and incidence of CV events in high risk patients with MI or UA with a broad range of initial cholesterol levels.</p> <p><b>HHS</b><sup>82</sup> Gemfibrozil decreased the incidence of coronary heart disease (no difference in overall mortality) in asymptomatic patients with primary dyslipidemia.</p> <p><b>MEGA</b><sup>83</sup> In patients with mild or moderate hyperlipidemia, low dose pravastatin reduced the risk of CVD by 30%-40% in all age groups and both genders.</p> <p><b>Brown et al.</b>,<sup>84</sup> showed in high risk men with increased ApoB levels, intensive lipid-lowering therapy decreased progression to coronary disease, increased regression of atherosclerosis and reduced the frequency of CV events.</p>	

Condition	Studies Supporting Effectiveness of Primary and Secondary Interventions	Studies Confirming Late Intervention Ineffective
CKD	<p><b>MICRO-HOPE</b><sup>88</sup> Patients with diabetes and microalbuminuria given ramipril. For patients without microalbuminuria there was a reduction in risk for new onset microalbuminuria (relative risk 9%, p=0.17). Ramipril also reduced the risk of combined microvascular outcomes in patients by 16% (p=0.036).</p> <p><b>IRMA-2</b><sup>89</sup> Patients that were hypertensive with Type II diabetes and microalbuminuria on irbesartan therapy resulted in a reduction of development of nephropathy.</p> <p><b>IDNT</b><sup>2</sup> Hypertensive Type II diabetic patients on irbesartan showed delayed progression of renal disease and lower mortality.</p> <p><b>The Collaborative Study</b><sup>90</sup> Captopril slows progression of diabetic nephropathy in patients with DM for over 7 years.</p> <p><b>AASK</b><sup>91,92</sup> Ramipril reduced the risk of end stage renal disease and death by 22% (p=0.04) and 38% (p=0.004) compared to amlodipine and metoprolol groups in patients with HTN and GFR 20-65ml/min per 1.73m<sup>2</sup>.</p> <p><b>RENAAL</b><sup>93</sup> In patients with type 2 diabetes and nephropathy, losartan reduced incidence of end-stage renal disease (28%, p=0.02) but did not influence mortality rates.</p> <p><b>Benazepril Study</b><sup>94</sup> Benazepril showed significant benefit to CKD patients with 23% reduction in the rate of decline in renal function.</p>	<p><b>4D</b><sup>85</sup> &amp; <b>Aurora</b><sup>86</sup> No benefits in CV event reduction with statins for patients on hemodialysis or stage 4 CKD.</p> <p><b>OCTOPUS</b><sup>95</sup> BP-lowering ARB olmesartan did not reduce the risk of major cardiovascular event or mortality in hypertensive patients undergoing chronic hemodialysis.</p> <p><b>Chan et al.</b>,<sup>96</sup> showed combined ARB and ACEi in hemodialysis patients was associated with increased risk of cardiovascular death.</p> <p><b>TREAT</b><sup>97</sup> Patients with DM2 + CKD + anemia did not benefit from darbepoetin vs. placebo. Treatment group had increased risk of stroke with no difference in CV event, renal event or death.</p> <p>CKD patients who had access to early nephrology referral showed reduced mortality, hospitalization, earlier placement of AV fistula and better uptake of peritoneal dialysis compared to late referral patients.<sup>98</sup></p>
CAD	<p>Most MIs in women may be preventable by a combination of healthy diet and lifestyle factors such as healthy diet, moderate alcohol, physical activity and a healthy weight.<sup>99</sup></p> <p><b>LHS</b><sup>12</sup> Smoking cessation programs significantly reduced all-cause mortality and mortality due to cardiovascular disease even when successful in minority of patients.</p> <p><b>CURE</b><sup>100</sup> Patients with ACS without ST segment elevation benefit from clopidogrel in prevention of cardiovascular outcomes (with increased risk of bleeding).</p> <p><b>CARE</b><sup>101</sup> Pravastatin reduced MI recurrence and stroke in patients with previous MI and average cholesterol.</p> <p><b>PrediMED</b><sup>102</sup> A Mediterranean diet with olive oil or nuts reduced the incidence of major cardiovascular events in high risk patients (MI, stroke, cardiovascular death).</p> <p><b>MRFIT</b><sup>103,104</sup> A primary prevention trial to examine the multifactorial intervention program's effect in mortality for CHD determined significant reduction in fatal and nonfatal CHD and CVD rates.</p> <p><b>AIRE</b><sup>105</sup> Ramipril reduced the risk of sudden death by roughly 30% but did not alter the rate of stroke in patients with evidence of HF and surviving AMI.</p> <p><b>EUROPA</b><sup>106</sup> ACEi perindopril reduced cardiovascular death, MI, cardiac arrest, ACS and development of heart failure in patients with stable CAD without HF.</p>	<p><b>PEACE</b><sup>107</sup> Patients with CAD on trandolapril showed no benefit against CV or MI events.</p> <p><b>TRANSCEND</b><sup>108</sup> ACEi intolerant patients with CAD, CVD, PVD or end-organ DM on telmisartan (ARB) showed no benefit over placebo against composite outcome of cardiovascular death, MI, stroke or hospitalization from heart failure.</p>



Condition	Studies Supporting Effectiveness of Primary and Secondary Interventions	Studies Confirming Late Intervention Ineffective
CAD <sub>cont'd</sub>	<p>Simvastatin + niacin show angiographically measurable benefits and lower frequency of cardiovascular endpoint (death, MI, stroke or revascularization) in patients with coronary disease and low plasma HDL but normal LDL.<sup>109</sup></p> <p>Gemfibrozil therapy significantly reduces risk of major cardiovascular events by raising HDL in CAD patients.<sup>110</sup></p> <p><b>BHAT</b><sup>111</sup> In patients with acute MI daily administration of propranolol resulted in a mortality rate reduction of 26%. Use of beta blockers in high risk patients reduced the mortality rate by 43%.</p> <p><b>GREACE</b><sup>112</sup> Total mortality was 2.9% in patients taking atorvastatin versus 5% with standard care in patients with CHD with similar reductions in coronary morbidity and mortality.</p> <p><b>ONTARGET</b><sup>113</sup> Patients with vascular disease or high-risk diabetes without HF were treated with either telmisartan, ramipril or both. Telmisartan and Ramipril were considered equivalent and were associated with less angioedema whereas no benefits of combined therapies were discovered (and more adverse events).</p> <p><b>PCI-CURE</b><sup>114</sup> Patients with symptoms of acute coronary syndrome undergoing percutaneous coronary intervention on long term clopidogrel after stenting had a lower rate of CV death or MI (31% reduction).</p> <p><b>PROVE IT-TIMI 22</b><sup>115</sup> In patients who had acute coronary syndrome atorvastatin reduced all-cause mortality over pravastatin.</p> <p><b>VALIANT</b><sup>116,117</sup> In patients with HF and/or LVSD after MI, valsartan was as effective as captopril in reducing CV events.</p> <p>Dietary and non-dietary intake of n-3 polyunsaturated fatty acids decreased overall mortality, death due to MI and sudden death in CAD patients.<sup>118</sup></p>	<p><b>QUIET</b><sup>119</sup> Quinapril did not reduce incidence of ischemic events, the progression of atherosclerosis and all-cause mortality in patients with IHD that had already undergone angioplasty or atherectomy.</p>
CHF	<p><b>SOLVD</b><sup>1</sup> Patients on enalapril in prevention trial with no history of HF showed a significant reduction in death or development of CHF than patients in treatment trial entering study with clinical evidence of CHF.</p> <p><b>SAVE</b><sup>120</sup> Reduction in morbidity and mortality with captopril in patients who with left ventricular dysfunction and a history of MI.</p> <p><b>RALES</b><sup>121</sup> Patients with CHF taking spironolactone experienced largest benefits in reduction of morbidity and mortality relative to highest pretreatment levels</p> <p><b>EPHESUS</b><sup>122</sup> Patients with MI complicated by left ventricular dysfunction and heart failure on eplerenone showed a reduction in morbidity and mortality.</p> <p><b>HOPE</b><sup>123</sup> The rate of death and CV events was reduced in high-risk patients on ramipril.</p> <p><b>CONSENSUS</b><sup>124</sup> Enalapril in CHF patients reduced mortality by progressive heart failure (rather than sudden cardiac death) and also showed greater improvement in NYHA classification along with decreased need for other medications. Implies that benefit is due to reduced progression of HF</p> <p><b>AIREX</b><sup>125</sup> In the long term follow up of patients with clinical HF after acute MI, there was relative RR of over 35% in all-cause mortality for patients with ramipril</p> <p><b>CORONA + GISSI-HF</b><sup>126</sup> Statistically decreased risk of MI in patients with ischemic heart disease on rosuvastatin</p>	<p><b>HFPEF</b><sup>127</sup> Data seems to suggest ACEi are successful only in HF patients with reduced EF rather than preserved EF.</p> <p><b>I-PRESERVE</b><sup>128</sup> In patients with CHF but normal LVEF, iversartan did not improve mortality or morbidity.</p>

Condition	Studies Supporting Effectiveness of Primary and Secondary Interventions	Studies Confirming Late Intervention Ineffective
CHF <sup>cont'd</sup>	<p><b>CHARM-OVERALL</b><sup>129</sup> In patients with CHF a reduction of CV related deaths was seen with patients on candesartan therapy.</p> <p><b>CHARM-ADDED</b><sup>130</sup> In patients with CHF candesartan added to ACE therapies led to clinically important reduction in CV events.</p> <p><b>VALHEFT</b><sup>131</sup> Patients with NYHA class II-IV HF taking valsartan had a reduced rate of morbidity and mortality from HF and improved NYHA class.</p> <p><b>COPERNICUS</b><sup>132,133</sup> Patients with symptoms of heart failure on carvedilol experienced a 35% reduction in the risk of death.</p> <p><b>MERIT-HF</b><sup>134</sup> Treatment of patients with NYDA class II-IV HF metoprolol significantly reduced all-cause mortality when added to standard therapies.</p> <p><b>RESOLVD</b><sup>135,136</sup> Patients with stage I and II CHF the use of metoprolol CR improves ventricular function and results in lower morbidity.</p>	
CVD	<p><b>SPARCL</b><sup>137</sup> Daily high dose of atorvastatin reduced the incidence of stroke and cardiovascular events in patients with recent TIA without known CVD (with slight increase in hemorrhagic strokes).</p> <p><b>PROGRESS</b><sup>138</sup> Patients (with or without HTN) with history of TIA or stroke with CBVD showed reduction in risk of stroke, coronary and vascular events on perindopril and indapamide.</p> <p>Statin use early during stroke hospitalization is associated with improved post-stroke survival and withdrawal is associated with worsened survival.<sup>139</sup></p> <p><b>PROspective</b> In high risk DM2 patients with previous stroke, pioglitazone reduced the recurrence of stroke (no effect in patients without previous stroke).<sup>140</sup></p> <p><b>HPS</b><sup>141</sup> Simvastatin reduced ischemic strokes, TIA and need for carotid intervention in individuals that were high risk for vascular disease. It reduced vascular events in those that already had CVD.</p> <p><b>MOSES</b><sup>142</sup> The incidence of all-cause mortality, cardiovascular or cerebrovascular events was reduced in hypertensive stroke patients (high-risk patients) was reduced and a high percentage of patients reached target blood pressures. Protective effects of eposartan were seen over nitrendipine in high risk patients.</p> <p><b>STT</b><sup>143</sup> Alteplase significantly improves outcomes in stroke patients when administered under 4.5h, with emphasis on earlier treatment leading to bigger benefits.</p>	
PVD	<p>Role of Aspirin unclear in primary prevention as one needs to weight the risk of bleeding with the benefits of vascular prevention (ATT)</p> <p><b>CAPRIE</b><sup>144</sup> In patients at risk of vascular events with atherosclerosis plavix was more effective than aspirin in reducing CV events.</p> <p><b>ATT</b><sup>145</sup> Aspirin resulted in reduction of serious vascular events, stroke and coronary events in secondary prevention trials of vascular disease. In patients with Stage I or II PAD including those with DM2, low dose Aspirin reduces major vascular events (death, MI, stroke) and critical leg ischemia.<sup>146</sup></p> <p><b>STIMS</b><sup>147</sup> Ticlopidine reduces cardiovascular and cerebrovascular morbidity and mortality in patients with intermittent claudication.</p>	

Condition	Studies Supporting Effectiveness of Primary and Secondary Interventions	Studies Confirming Late Intervention Ineffective
<b>AFib</b>	<p>In patients with non-valvular AF without history of stroke or TIA, dose-adjusted warfarin significantly reduces stroke and embolic events vs. ASA (but carries a risk for intracranial hemorrhages).<sup>148</sup></p> <p><b>SPAF</b><sup>149</sup> Warfarin and aspirin showed a reduction in ischemic stroke and systemic embolism in patients with atrial fibrillation.</p> <p><b>ROCKET AF</b><sup>150</sup> Xarelto was non-inferior to warfarin in patients with AF and both experienced reduction in stroke events.</p> <p><b>RE-LY</b><sup>151</sup> Patients on dabigatran and warfarin at increased risk of stroke with AF had similar reductions in rates of stroke on both of these therapies.</p> <p><b>AFFIRM</b><sup>152</sup> In patients with AFib at risk of stroke there was no significant advantage between heart rate control over rhythm control therapies in preventing mortality.</p> <p><b>CTAF</b><sup>153</sup> Patients with at least one episode of symptomatic AFib taking amiodarone experienced 35% recurrence of AFib and patients on sotalol and/or propafenone experienced 63% recurrence.</p>	No late intervention data available for dialysis patients with atrial fibrillation.

From the multitude of studies presented in the preceding table, it is clear that early primary and secondary intervention treatments are more effective and show more favourable patient outcomes than late interventions. Treatments after significant disease burdens have been repeatedly shown to be much less effective in reducing morbidity and mortality. Instituting and optimizing these therapies according to available data can dramatically improve patient outcomes.

### The Patient Impact and Costs of Acute Health Care

In medicine, our primary focus for research and innovation should be on improving patient outcomes in a cost-effective manner in order to allow for potential broader applications. When considering systematic changes to our healthcare system, we must first understand the challenges patients face as end-users within our current framework. To a patient with multiple chronic illnesses, navigating through our current healthcare system can be quite onerous. In particular, a high-risk vascular patient is often seeing three or four different specialists (endocrinologist, cardiologist, nephrologist, vascular specialist, neurologist, internist, etc.) regularly while still trying to maintain routine contact with their primary care practitioner. In fact, an advanced CKD patient is recommended to see their nephrologist at pre-dialysis clinic visits up to 6 times per year.<sup>35,154</sup> Multiple medical visits to different specialists, numerous different laboratory investigations attached to each of these visits, additional investigations and imaging tests, often with significant duplication, may translate into well over 20 different medical visits per year. This does not consider any other medical conditions they may be trying to manage as well. This can be quite time-consuming and overwhelming to patients and family members who often have to take time away from work and home to attend these appointments, leading to medical visit fatigue and subsequently a lack of attendance. If high risk patient care is not optimally coordinated and attended, there is potential for suboptimal patient outcomes, disease progression and an increase in morbidity and mortality.<sup>155,156</sup>

In addition, in subacute situations, care is not readily accessible, and may lead to the need for emergency room visits and potentially for hospital admissions. In our current system, access to semi-urgent specialty care is usually through the emergency room. The rising cost of delivering services in an acute care setting is putting a strain on our healthcare system.<sup>29,157</sup> It is extremely important to build the

appropriate capacity and services within the community to prevent acute illness and the progression of chronic disease to limit vital organ damage and the need for emergency room visits, hospital admissions and acute care services. In addition, the cost of delivering certain services in hospital settings has been shown by the Ministry of Health to be approximately 30% higher than in community based settings.<sup>158</sup>

As healthcare professionals, doctors and nurses alike, our most important role within the healthcare system is to act as patient advocates. I routinely see the significant impact on patients and families that acute illness can cause. The reduction in quality of life to patients, stress on families and the economic impact of lost wages are significant side effects and deserve quality improvement measures. As a nephrologist, it is often disheartening to see the constant turnover of patients in dialysis units with new patients needing dialysis services on a regular basis. As a medical community, we should be using the available evidence to guide our decision-making and adjusting healthcare system delivery strategies to try and optimize outcomes for patients in the most cost-effective manner.

*“Insanity: doing the same thing over and over again and expecting different results.”*

- Albert Einstein

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## **Windsor *Regional Vascular Health and Research Institute***

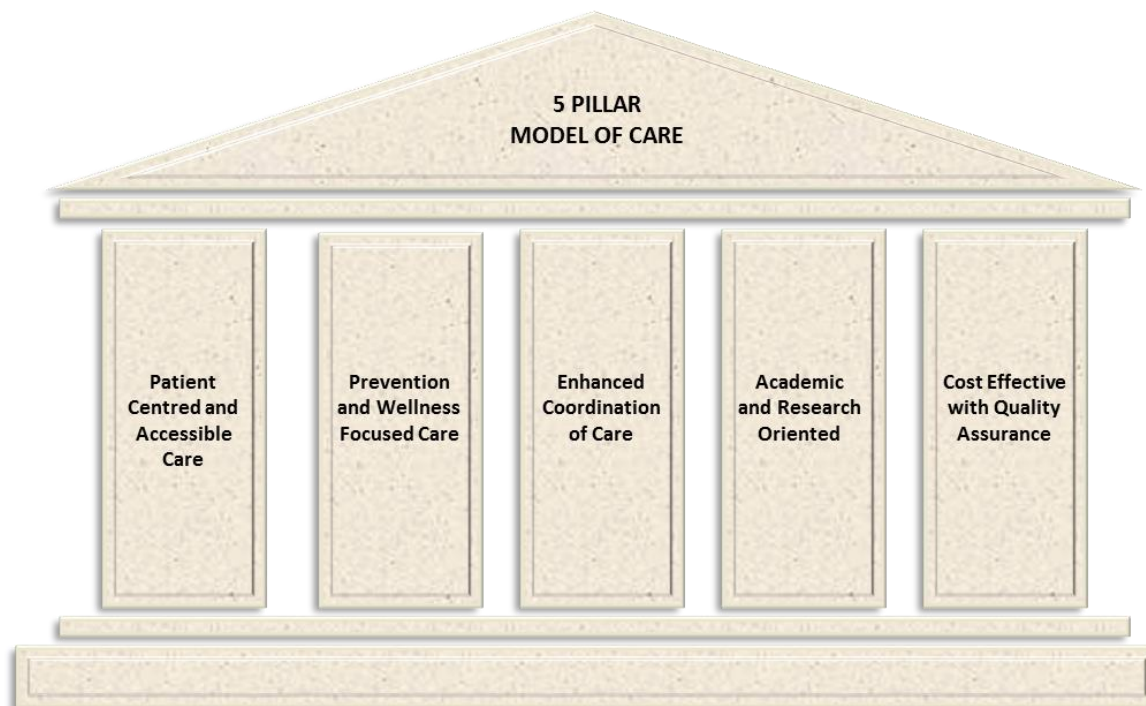
### **Target Population and General Objectives**

The high-risk cardiovascular and chronic kidney disease patient would be ideally served in a single site multi-specialty and multidisciplinary centre of excellence with a common EMR and enhanced coordination of care between specialists and primary care practitioners. This patient population would consist of those that require ongoing input and collaboration between multiple specialists and primary care practitioners to improve health, avoid emergency room visits, the need for acute care services and for hospital admissions. This includes patients with established:

- Cardiovascular disease
- Advanced chronic kidney disease
- Cerebrovascular disease
- Peripheral Vascular disease or Wound Care needs
- Difficult to control risk factors such as hypertension, diabetes or dyslipidemia
- Significant complications of therapy or significant polypharmacy
- High risk of requiring sub-acute or emergency services or hospital admission

The primary focus is to study and critically analyze how to effectively reduce cardiovascular and kidney disease in high risk patients in a community based academic research setting in order to reduce morbidity and mortality. The secondary focus would be to reduce the need for emergency room services, hospitalizations and prevent progressive vital organ damage in a cost effective manner. Additional goals would include enhancing patient satisfaction, access to care and adherence to proven therapies known to have benefits in reducing the incidence of cardiovascular and renal disease.

## Vascular Health and Research Institute - Five Pillar Model of Care



### 1. Patient Centred and Accessible Care

Models of health care delivery must become more patient centred in order to be successful in achieving desired outcomes. We must realize that the challenges that patients face are real and meaningful and unless addressed can limit our ability to deliver cost-effective care. Simple measures such as increased hours of operation of a clinic and free parking can dramatically improve attendance and ensure that fewer patients are lost to follow up. Once a patient is lost to follow up, they would be more likely to experience disease progression and require the use of emergency services. Reducing the total burden of visits for care (less lab work and testing duplication and multi service visits) while enhancing interaction with specialty services and primary care will likely lead to greater adherence to therapies and attendance to visits. In addition to expanded hours, the availability of subacute care and reduced wait times to see specialists can reduce the need for emergency room visits and hospital admissions by addressing issues proactively to prevent acute illness from developing. Using technology such as videoconferencing to reduce travel time for patients can also be incorporated to improve access to care. Having multispecialty (cardiology, nephrology, endocrinology, neurology, internal medicine, vascular and wound care, etc) and multidisciplinary services (nurse practitioners, physician assistants, social workers, dieticians, clinical pharmacy specialists, lab technicians) coordinated at a single site community-based centre will ensure that patients who need services will have ease of access. Comprehensive and coordinated patient care that is made easier and more accessible to patients - as well as continuous follow-up with primary care will almost certainly enhance patient satisfaction which usually translates into greater uptake of proven preventative therapies and improved patient outcomes.

## 2. Prevention and Wellness Focused Care

As a healthcare system we must shift our focus and resources from treating established acute illness to promoting health, wellness and disease prevention. This will not only help keep our population healthier and living longer with a higher quality of life but will also reduce acute care expenditures that account for a significant proportion of overall health care costs.<sup>29</sup> These efforts should be community-based, coordinated and focused on instituting evidence-based preventative health care strategies. Increasing education among affected populations in conjunction with enhancing public awareness is a key component of promoting health and wellness strategies. Using available technology and web-based approaches for education and awareness will help patients and family members engage more actively in their care. Promoting self-management strategies has been shown to improve achievement of target quality indicators.<sup>159,160</sup>

## 3. Enhanced Coordination of Care

A comprehensive team approach to care of the high risk patient will almost certainly have multiple quantifiable benefits to patients and to the healthcare system.<sup>161</sup> Enhancing coordination of care has the potential to dramatically improve uptake of proven preventative therapies to reduce the incidence of cardiovascular and kidney disease. In addition to this, enhanced coordination of care can reduce polypharmacy and potential medication errors that can lead to adverse events and emergency room admissions.<sup>32,33</sup> Multiple specialists and healthcare team members interacting around complex cases in a coordinated fashion can only improve quality of care and outcomes. Using a single electronic medical record can help various healthcare team members easily access information that is vital to preventing errors and ensuring that each patient has the most optimal plan of care. Using case managers (nursing specialists, clinical pharmacy specialists etc) within the specialty clinic that can reach out to primary care practitioners and local pharmacies and continually update them on therapeutic interventions and care plans will help coordinate care to maximize involvement of primary care practitioners to help carry out and reinforce optimal care plans. Using technology to provide patients with access to their own records through a web-based portal will help communication with other healthcare practitioners both within the community and abroad. This will allow 24 hour access to records when needed by any acute care facility or emergency room anywhere in the world. Too often, due to the lack of coordination of care and information sharing, important proven preventative therapies for cardiovascular and kidney disease are discontinued and never restarted or never initiated in the first place. Studies show that the uptake of these proven therapies may be as low as 50%.<sup>162</sup> Improving this uptake can have a dramatic effect on reducing acute illness and organ damage that can increase patient morbidity and mortality.<sup>36,41,162</sup> On an outpatient basis, there are often significant wait times to see specialists. This leaves opportunities for patients to fall through the cracks when subacute management issues arise. In a coordinated model, where multi-specialty assessment is immediately available when necessary, there will almost certainly be higher success rates in avoiding rapid clinical deterioration, which prompts the use of the emergency room for access to needed urgent specialty care.

## 4. Academic and Research Oriented

A high functioning team of healthcare specialists is likely to accomplish much more than any single individual could in improving patient outcomes. Opportunities to collaborate, information share and transfer knowledge and practice patterns in an academic research setting can only lead to benefits for

our patients. Promoting academic research and teaching in a community based setting would be an exciting and intellectually stimulating opportunity for aspiring physicians and healthcare personnel that would ultimately enhance recruitment of elite professionals. The use of a single database will enhance research opportunities in cardiovascular and kidney disease management in order to reduce the rates of morbidity and mortality in our region. The opportunity to provide regular teaching and educational lectures to medical and nursing trainees within the community about chronic disease prevention will enhance the experience of the younger generations of healthcare professionals. Hopefully, this will help to shift traditional models of healthcare education, which have historically focused on treating acute illness to a model focused on promoting wellness and disease prevention.

#### 5. Cost-Effective with Quality Assurance

Any novel model of healthcare delivery must focus on improving the quality of patient care while maintaining or reducing costs to the overall health care system. A single site community-based coordinated specialty centre for cardiovascular and renal care has the potential to be a more cost-effective solution than traditional models of care.<sup>158</sup> Enhanced coordination and access to specialty care will likely lead to less duplication, increased patient attendance, increased adherence to therapies, and reduced emergency room use and hospitalization. Over time, this may translate into significantly reduced incidence of end-stage renal failure, coronary artery disease, PVD, congestive heart failure and stroke rates. If this indeed is the case, it would translate into tremendous savings to our healthcare system. In addition to this, currently, for hospitalized patients with multiple chronic illnesses, they are often kept in the hospital longer than needed solely because of a lack of coordinated multi-specialty care within the community to allow a safe discharge. This type of clinic has the potential to reduce the length of stay of an admitted hospital patient with multiple chronic issues that needs close comprehensive attention post discharge. Continuous improvement and quality assurance measures would be easier to identify and implement in a single site facility. This type of model also aligns closely with funding agency reforms and the stated direction of promoting community-based care in a patient centred fashion.<sup>16</sup>

#### **What we have accomplished since 2011:**

- Presented CDPM in Vascular Health to Erie St. Clair Local Health Integration Network – July 2011
- Engaged local and provincial funding agencies, 2011-2015
- Secured a centrally located community-based site - 2011
- Established a local non-profit charitable foundation, Care For Kidneys Foundation - 2012
- Implemented a single electronic medical record - 2013
- Coordinated a multidisciplinary team - 2013
- Developed a university-affiliated academic and productive research team - 2013
- Established a community based Chronic Kidney Disease Clinic – 2013
- Established Canada's first ASH accredited Specialty Hypertension Clinic – Jan 2014
- Proposed Business Case Outline to Erie St. Clair Local Health Integration Network – Apr 2014
- Awarded prestigious grant to conduct first ever Windsor Based Clinical Trial (RCT) – 2014
- Developed patient education resources for distribution within the community - 2014
- Obtained letter of support from Ontario Renal Network – 2014
- Obtained letter of support from Erie St. Clair Local Health Integration Network – 2015

## Summary of the Goals of the 5 Pillar Model and Outcome Measures

There are numerous potential benefits of a coordinated community-based cardiovascular and renal specialty centre of excellence:

1. Enhanced patient satisfaction
2. Increased patient safety
3. Increased attendance to health care visits both in specialty and primary care setting
4. Enhanced use of multi-specialty algorithms and care maps aimed at cardiovascular and renal disease therapy adherence
5. Enhanced uptake of preventative therapies proven to reduce cardiovascular and renal disease - compliance
6. Increased satisfaction of primary care practitioners with specialty care services
7. Enhanced wellness promotion – adoption of self-management strategies and home-based therapies
8. Reduced emergency room visits
9. Reduced length of stay in hospital
10. Reduced crash starts on to dialysis
11. Reduction in incidence of end-stage renal failure requiring dialysis
12. Reduction in costs related to acute care management of cardiovascular and renal disease
13. Reduction in cardiovascular events such as myocardial infarction, stroke, need for amputation and heart failure and death rates from CVD and renal disease
14. Increased academic activity with enhanced research opportunities
15. Enhanced quality and coordination of outpatient medical and nursing teaching programs

## Governance Model

A clinical advisory and quality assurance committee would be utilized to ensure the needs of patients and health care providers are being met to a high level of satisfaction, to continually improve patient outcomes and provide quality control.



**Figure 5** Windsor Regional Vascular Health and Research Institute Governance Model



## Research and Innovation Needed

Research is an essential element within the field of medicine and in analyzing healthcare systems, which allows for continuous quality improvement. Our research group has been progressively implementing components of this model over the last several years. We plan to actively study the model for key measures as described above. We have been working collaboratively with various health care agencies in advancing the implementation of this model of care. It will be extremely important to determine the true cost of delivering this type of care in a community based setting as historical funding models are based on costs within acute care facilities.

We are extremely excited about the opportunities that can arise from increased collaboration of local specialists in a teaching and academic environment, stimulating innovative ideas and fostering research. Ultimately, this can only enhance the drive to improve patient care and outcomes. In the process, the training of our future physicians can begin to shift towards an increased focus on prevention and not just on acute management of illness. In order for this to be effective, our medical and nursing learners must have significant exposure to this philosophy as part of their training.

## Change Management

This model of care aligns with the principles of our provincial Ministry of Health and Long Term Care objectives,<sup>16</sup> as well as the philosophy of our local healthcare agencies: Erie St. Clair LIHN and Ontario Renal Network. Traditional models of care must adapt to our changing population and their healthcare needs while demonstrating cost-effectiveness and long-term sustainability. Embracing the philosophical need for change is understandable to the vast majority who work within our healthcare system. Nonetheless changing existing healthcare systems and traditional practices is not an easy task. It requires buy-in from key stakeholders including funding agencies, healthcare providers as well as patients as end-users.<sup>160</sup> Any proposed systematic changes must incorporate the following key principles to enhance adoption:

1. Patient-centred focus
2. Evidence-based decision making
3. High likelihood of improved cost-effectiveness
4. Measurable outcomes of value to patients, providers and healthcare agencies
5. Minimize disruption to existing practices

The process of change management can be difficult to navigate through when you are disturbing the status quo.<sup>163</sup> It must be clear to those involved and affected by the change that change is indeed necessary to achieve desired outcomes with the ultimate goal of improving patient care in the most cost-effective manner. What must also be clear are the consequences of maintaining the status quo. In the case of meeting the needs of an aging population from a cardiovascular and renal perspective, the escalating costs of providing acute care services are not likely to be sustainable. In the absence of increased public taxation, this may translate into a reduction in services to patients, resources to frontline healthcare workers and funding to acute care facilities. It is also important to remember that making only small incremental improvements in key outcome measures can have dramatic effects on the healthcare system in terms of improving morbidity and mortality as well as significantly reducing healthcare costs.

## Conclusion

Health system reform is needed to address the changing needs of our population. We must use patient-centred strategies with supportive evidence to guide our decision making and to positively engage funding agencies, health care providers, and the general public that we serve. This is essential to aid in countering the inertia associated with maintaining the status quo and resisting change. It is important to create innovative, cost-effective solutions to increase patient access and quality of care with the goal of improving quality of life and reducing acute care utilization with subsequent research to validate these hypotheses. Strategies aimed at chronic illness management reform in the United States acknowledge that a significant challenge to change was in convincing highly trained healthcare professionals - who felt that they were already doing a good job - to buy into the concept of trying to improve the achievement of quality targets.<sup>160</sup> The real question is not whether we are doing a good job currently but rather, whether or not we can do better.

Data suggests that optimizing proven therapies can reduce the high risk cardiovascular population from 20% down to less than 5%.<sup>7</sup> On a broad scale, even decreasing rates of congestive heart failure, dialysis, heart attacks and stroke rates by only 5% can translate into hundreds of millions of dollars in savings to our health care system, not to mention the direct benefits of preventing these illnesses on patients and families. The potential savings associated with implementing more cost-effective health care strategies can be re-invested in supporting our frontline healthcare professionals with better staffing, resources and technology to make available the highest quality acute care services when needed.

The Cardiac Care Network, Heart and Stroke Foundation and Ontario Stroke Network collaborated to produce “An Integrated Vascular Blueprint for Ontario” in August 2012. They reached similar conclusions about the benefits of an improved, patient centred and integrated system to improve services, continuity through transitions, health outcomes and quality of life for patients and caregivers.<sup>164</sup> Improving the patient experience by establishing a single-site, team approach to comprehensive, coordinated and accessible care can only enhance adherence to proven therapies, reduce the burden of acute illness and the costs associated with it and increase patient satisfaction with the healthcare system. **It is important to note that engaging and supporting the role of primary care provider is key to the success of this model.** The primary care physician is the quarterback in this system that can re-inforce and promote adherence and compliance to therapy most effectively. Too often, patients state they spend so much time on specialist appointments, that they don't frequently see their primary care practitioners. In order for chronic disease management to be successful, the role of the primary care practitioner must be bolstered and supported. In the complex, high risk patient it can be challenging for primary care providers to significantly improve adherence to preventative strategies without highly specialized supportive care that is well coordinated amongst the specialty care team. Providing primary care practitioners with timely, comprehensive and well-communicated multi-disciplinary and multi-specialty support for patients in their practice that are at highest risk for acute cardiovascular and renal illness will help provide them with more clarity on care plans to follow through on. This coordination and reduced total burden of isolated visits to specialists can help return the lead in a patient's care back to the primary care practitioner, improving ongoing preventative health maintenance for a broader array of conditions.

Supporting cardiovascular and renal care specialists within the facility and armed with the resources they need to effectively intervene in a timely, coordinated fashion when caring for high risk patients will undoubtedly reduce the risk of emergency room utilization, hospital admissions and the need for acute care interventions in these patients. A team of specialists with comprehensive support

services working in an academic research environment and in collaboration with primary care can only help enhance care delivered, which is ultimately the main goal for patients and practitioners.

*“Excellence is the gradual result of always striving to do better.”*

- Pat Riley

### About the Authors

Dr. Albert Kadri specializes in internal medicine and nephrology. He has completed the specialty certification from the American Society of Hypertension as a hypertension clinical specialist. He has served as the Chief of Medicine at Windsor Regional Hospital - Ouellette Campus and the Medical Director of the Renal Program. He is an adjunct professor at the Schulich School of Medicine and Dentistry–Windsor campus.



Dr. Maher M. El-Masri, PhD, RN is a Professor and Research Chair in the Faculty of Nursing, at the University of Windsor. He is an Adjunct Research Professor in the Dept. of Biostatistics and Epidemiology at the Schulich School of Medicine, for Western University. Dr. El-Masri is a visiting Scholar at the University of North Dakota and Editor of Canadian Journal of Nursing Research.



Nicole Dziemarski completed the St. Clair College Pharmacy Technician program and subsequently completed an Honours Degree in Biochemistry with a Thesis in Chemistry at the University of Windsor. She has been involved with volunteering and research with the nephrology department at Windsor Regional Hospital - Ouellette Campus for many years, and has previously co-authored a paper<sup>165</sup> alongside Dr. Kadri and other esteemed nephrology colleagues.



### Acknowledgements

With appreciation to Ontario Renal Network and Erie St. Clair Local Health Integration Network for their support of our vision to bring Windsor and Essex County the first regional Vascular Health and Research Institute, centre of excellence in cardiovascular and renal disease prevention.

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**Abbreviations**

<b>ACE</b>	angiotensin converting enzyme
<b>ACEi</b>	inhibitor therapy for ACE
<b>ARB</b>	angiotensin II receptor blocker
<b>AF/AFib</b>	atrial fibrillation
<b>ASA</b>	acetyl-salicylic acid, Aspirin
<b>BP</b>	blood pressure
<b>BS</b>	blood sugar
<b>CAD</b>	coronary artery disease
<b>CBVD</b>	cerebrovascular disease
<b>CKD</b>	chronic kidney disease
<b>CV</b>	cardiovascular
<b>CVD</b>	cardiovascular disease
<b>DM</b>	diabetes mellitus,
<b>DM2</b>	Type II diabetes mellitus
<b>EF</b>	ejection fraction
<b>LVEF</b>	left ventricular ejection fraction
<b>HbA1C</b>	glycated hemoglobin
<b>HDL</b>	high density lipoprotein, one of the cholesterol measurements
<b>HF</b>	heart failure
<b>CHF</b>	congestive heart failure
<b>hsCRP</b>	high sensitivity C-reactive protein
<b>HTN</b>	hypertension

<b>IDDM</b>	insulin-dependent diabetes mellitus
<b>IHD</b>	ischemic heart disease
<b>LDL</b>	low-density lipoprotein, one of the cholesterol measurements
<b>LVSD</b>	left ventricular systolic dysfunction
<b>MI</b>	myocardial infarction
<b>NYHA</b>	New York Heart Association
<b>PAD</b>	peripheral artery disease
<b>PVD</b>	peripheral vascular disease
<b>TIA</b>	transient ischemic attack
<b>UA</b>	unstable angina
<b>WRVHRI</b>	Windsor Regional Vascular Health and Research Institute

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## HEALTH CARE



Dr. Albert Kadri's hypertension clinic is the first in Canada to receive accreditation from the American Society of Hypertension.

### New Windsor hypertension clinic keeps patients close to home

DAVE BATTAGELL  
The Windsor Star

Patients suffering from high blood pressure leading to hypertension — potentially a life-threatening precursor to heart attack or stroke — often had to travel to London to see a specialist.

But those days are gone thanks to a Windsor nephrologist.

Dr. Albert Kadri, chief of medicine and medical director of the renal program at Windsor Regional Hospital's Ouellette Campus, established the city's first hypertension clinic about six months ago after recently earning specialty certification.

"There was no hypertension centre in Windsor and Essex County," he said. "We took on the project to establish the centre with cardiovascular disease on the rise — especially in Windsor-Essex.

"Complex cases that used to go to London are being treated locally."

The clinic has become the first in Canada to receive accreditation from the American Society of Hypertension — and one of only a dozen to date across North America to be so honoured since the program began in 2009.

"This is a first for our community, and for Canada," Kadri said.

"We are doing something in this community to reduce incidents of end-stage stroke, heart attack and heart-related fatalities. It's an important preventative health measure. This recognizes what we are doing in a formal way."

Accreditation is given through an on-site visit by the society to check protocol and equipment. They toured Kadri's clinic in November and accreditation was granted in recent days, he said.

Kadri treats about 100 patients per week as a specialist, with 40 per cent of those related to hypertension. The Ouellette Avenue clinic has a half-dozen employees: a couple of pharmacists, a nurse and three physicians.

Instead of patients travelling to London to see a specialist for hypertension, some of those same physicians are now travelling to Windsor to work at the clinic, Kadri said.

"My colleagues from London are now coming to our clinic," he said.

One of the clinic's patients is Ed Michael of LaSalle, who was referred to Kadri last year by his family physician.

"My physician gave me high-blood pressure medication," he said.

"He was telling me I could stay on the pills basically forever or I can send you to (Kadri)."

At the clinic, Michael was checked for an enlarged adrenal gland.

"He sent me for a bunch of tests and my left adrenal gland was overactive," he said. "That was causing my high blood pressure. If it was removed there would be no more medication."

Without having the local clinic open last year, Michael knew he was faced with travelling to

London to see a specialist.

"My job is busy and running to London I would have had to take a whole day off," he said. "Dr. Kadri opens at 7 a.m. I'm usually done at 7:30 a.m. and back at work."

Michael has had the adrenal gland surgery and his blood pressure is close to normal levels.

"My blood pressure was out of control," he said. "This was very convenient and fit into my schedule. They diagnosed the problem and fixed it — that's the most important thing."

Patients interested in treatment at the hypertension clinic should consult with their physician, Kadri said.

"It's been very well-received," he said. "It's really been going great."



Dr. Albert Kadri

1106 Ouellette Avenue, Suite 104, Windsor, Ontario, N9A 1C9

Phone 519.946.0103 Fax 519.977.6690 Email [windsor.nephrology@careforkidneys.org](mailto:windsor.nephrology@careforkidneys.org)

[www.careforkidneys.com](http://www.careforkidneys.com)

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## HEALTH CARE

NEWS / Health Care

### New machine, procedure helps reduce amputations in dialysis patients



Doctors Carman Iannicello, left, Albert Kadri and Jack Speirs visit with dialysis patient Raymond Vaillancourt on Monday, March 24, 2014, at the Windsor Regional Hospital downtown campus. They will soon be able to reduce the number of amputations in patients undergoing dialysis thanks to a new piece of surgical equipment. (DAN JANSISSE/The Windsor Star)

### Kidney dialysis in Windsor-Essex

The number of people starting dialysis in Windsor-Essex grows each year, said Dr. Albert Kadri, and it will only go up as the population grows older and the of heart disease, diabetes and high blood pressure increases.

The local dialysis population is growing by between seven and 10 per cent each year, he said. Compare that to the Greater Toronto Area, where the rate is between one and two per cent.

These health conditions can lead to kidney disease and the eventual need for dialysis, where a machine filters out the toxins from the bloodstream.

Patients typically undergo dialysis three times per week at a local dialysis centre, and the procedure takes 3-4 hours.

A new surgical procedure coming to Windsor will help decrease the risk of amputation among patients who rely on kidney dialysis.

"Once you start amputating things then the overall prognosis drops dramatically," said Dr. Albert Kadri, the director of the renal program at Windsor Regional Hospital. "It's kind of the beginning of the end."

The new procedure, which requires a special machine expected to arrive at the hospital by mid-April, will reduce the number of costly amputations among dialysis patients while improving their quality of life and prolonging their lifespan, too.

Kadri said Windsor Regional will be one of the few hospitals in Canada – and possibly the first in Ontario – to offer the service, known as the MILLER banding procedure.

Of the roughly 350 dialysis patients in Windsor-Essex, about 35 will face complications that could lead to the amputation of their fingers or hand.

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Patients who rely on dialysis to clean out the toxins from their blood have a special port of access inserted either into their arm, called an arteriovenous (or AV) fistula, or in their chest leading straight to their heart, called a permacath.

The AV fistula is considered the best way of accessing the arteries and veins. It works by diverting part of the blood flow from the artery in the arm to the vein, sort of like a short circuit, said Dr. Carman Iannicello, a vascular surgeon at the hospital who performs AV fistula surgeries.

Iannicello said what he and his colleagues have noticed is that, as the number of patients requiring dialysis grows, so do the cases of hand ischemia, where a lack of blood flow to the hand leads to infection and gangrene and eventually to amputation. It turns out that the vein, over time, grows bigger and diverts more and more blood from the artery back up to the heart and less and less blood down to the hand and fingers.

"Up until now, we haven't had a very good strategy to deal with it," Kadri said. In some cases, they could remove the AV fistula and insert a permacath, but that's not an ideal solution because a permacath can become infected.

But the new machine, which uses a special sensor and catheter, will allow Iannicello and his colleague, Dr. Jack Speirs, an interventional radiologist, to measure the blood flow and regulate the opening of the AV fistula to divert more blood to the hand by placing a tiny band around it.

"We kind of measure and adjust and get it just right," said Speirs, the head of interventional radiology at Windsor Regional, whose job it is to fix AV fistulas when there's a problem.

The machine costs about \$15,000. Kadri said it is paid for exclusively by funds raised through the local Care for Kidneys Foundation. Speirs said the cost to run the machine each year is just a few thousand dollars and the procedure, which takes about 20 minutes, can be done on an outpatient basis.

In contrast, the hospitalization and followup costs for amputation surgery can run as high as \$100,000, to say nothing of the devastating effects it has on the patient's quality of life, Kadri said.

1106 Ouellette Avenue, Suite 104, Windsor, Ontario, N9A 1C9

Phone 519.946.0103 Fax 519.977.6690 Email [windsor.nephrology@careforkidneys.org](mailto:windsor.nephrology@careforkidneys.org)

[www.careforkidneys.com](http://www.careforkidneys.com)

# Hotel-Dieu dialysis study breaks ground

BEATRICE FANTONI  
The Windsor Star

A study by Windsor doctors and pharmacists published recently in an international dialysis journal shows the city can punch above its weight when it comes to conducting medical studies all while helping kidney doctors find the most cost-effective way of preventing blood clots in their patients.

The study led by doctors and pharmacists from Hotel-Dieu Grace Hospital's kidney program, is the first major study to tackle the question of what is the ideal dose of alteplase, a common blood clot-dissolving drug for patients with dialysis catheters.

It is also the first time Hotel-Dieu's kidney program has undertaken a major study and had it published.

The team hopes this will help put Windsor on the medical research map, showing that the city has the infrastructure to conduct studies and opening up more research opportunities and funding for the city's health care professionals and medical students.

The retrospective study, which was published online in November in the journal Hemodialysis International, looked at whether kidney dialysis patients who use a catheter to have blood drawn require fewer catheter replacements and cleaning procedures when they receive a two milligram dose of alteplase.

"It is an important question that's never been answered," said Dr. Al Kadri, a kidney specialist and chief of medicine at Hotel-Dieu who worked on the study. "Nobody knows which (dosage) is best."

The catheter, which is inserted into the jugular vein and threaded to the right side of the heart, can sometimes develop blood clots which, if untreated, can result in insufficient dialysis, infections and hospital stays.

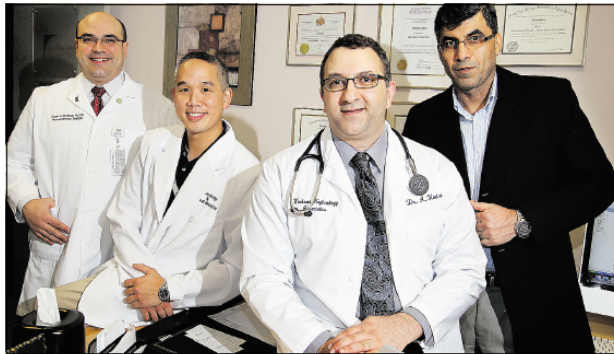
Dialysis is a blood-cleaning procedure used in patients whose kidneys stop working and cannot flush out toxins from the blood independently.

Even though Hotel-Dieu is not categorized as a research hospital and even though the majority of the team is made up of full-time doctors and pharmacists, not full-time researchers, that didn't stop Kadri and his colleagues.

They had no outside funding and worked on weekends and after hours to collect and analyze the data, write the paper and pitch it for publication.

The group reviewed six years' worth of medical records of roughly 240 local dialysis patients with dialysis catheters who took alteplase to prevent clotting, comparing the outcomes of those patients who received one milligram doses with the outcomes of those who received two milligram doses.

The general sense in the medical community was that, based on some small studies, the one milligram dose



Dialysis medicine research team leader Dr. Albert Kadri, centre right, with colleagues Dr. Wasim El Nekidy, left, Dr. Derrick Soong and Dr. Maher El-Masri, right, conducted a recently published study done at Hotel-Dieu Grace Hospital.

was as effective — and more affordable for the hospital — as the larger dose, Kadri said.

Instead, what they found was that using the double dose yielded "far superior" results than the single dose.

A patient taking the one milligram dose only was almost three times as likely to require a procedure than the patient who took the two milligram dose of the clot medication.

Patients who were on the double dose required fewer catheter replacements or cleanings.

Hotel-Dieu, which runs the region's dialysis program, has about 375 kidney dialysis patients, and about half of them use a catheter to draw out blood and clean it. These patients might make use of alteplase weekly or monthly.

Alteplase is a costly drug — it runs between \$90 and \$75 per dose — and takes up a large portion of Hotel-Dieu's annual medication budget,

said Derrick Soong, a pharmacist in the kidney program who worked on the paper. Along with dialysis patients, the anti-clotting drug is used in sudden heart attacks and strokes. The hospital goes through roughly 500 doses of alteplase in a year, Soong estimated.

But based on the group's findings, it looks as if the benefits of using the double dose outweigh the costs, said Wasim El Nekidy, another pharmacist in the group. While alteplase is expensive, it can save the hospital money in terms of radiologist fees and catheter cleanings and replacements — invasive procedures that can be risky for the patient.

Replacing the catheter is much more expensive and invasive than preventing the blood clot in the first place, El Nekidy said.

Now the group wants to take the research even further and conduct what's known as a prospective ran-

domized clinical trial to generate more accurate results. A randomized control trial could take from two to three years and would require funding, so the team is putting in more volunteer hours, writing up grant applications.

"It's an interesting result," said Dr. Louise Moist, a kidney specialist at London Health Sciences Centre, commenting on the paper, adding that the process should definitely be repeated in a randomized clinical trial.

Moist also said it's also great to see research coming out of a community dialysis program in Windsor, where the patients represent the general population.

Soong said that after the findings were published, a dialysis unit in Toronto called to ask for advice because the doctors there were thinking of switching to the one milligram dose until they saw the Windsor study.

## References

- 1 The SOLVD Investigators. Effect of Enalapril on Survival in Patients with Reduced Left Ventricular Ejection Fractions and Congestive Heart Failure. *N Engl J Med* 1991; 325:293-302.
- 2 Rodby, R.A. et al. The Irbesartan type II diabetic nephropathy trial: study design and baseline patient characteristics. For the Collaborative Study Group. *Nephrol Dial Transplant*. 2000 Apr; 15(4): 487-97.
- 3 Bhatt, D. L., et al. "International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis." *Jama* 295.2 (2006): 180-189.
- 4 Resnick, H. E., et al. "Achievement of American Diabetes Association Clinical Practice Recommendations Among US Adults With Diabetes, 1999–2002 The National Health and Nutrition Examination Survey." *Diabetes care* 29.3 (2006): 531-537.
- 5 Kotseva, K. et al. "EUROASPIRE III. Management of cardiovascular risk factors in asymptomatic high-risk patients in general practice: cross-sectional survey in 12 European countries." *European Journal of Cardiovascular Prevention & Rehabilitation* 17.5 (2010): 530-540.
- 6 Banegas, J. R. et al. Achievement of treatment goals for primary prevention of cardiovascular disease in clinical practice across europe: The EURIKA study. *European Heart Journal*, 2011; 32(17), 2143-2152. doi:10.1093/eurheartj/ehr080
- 7 Geller, J.C. et al. Achievement of guideline-defined treatment goals in primary care: the German Coronary Risk Management (CoRiMa) study. *Eur Heart J*. 2007 Dec; 28(24):3051-8.
- 8 Maio, V. et al. Beta-blocker initiation and adherence after hospitalization for acute myocardial infarction. *Eur J Cardiovasc Prev Rehabil*. 2011 Jun;18(3):438-45.

1106 Ouellette Avenue, Suite 104, Windsor, Ontario, N9A 1C9

Phone 519.946.0103 Fax 519.977.6690 Email [windsor.nephrology@careforkidneys.org](mailto:windsor.nephrology@careforkidneys.org)

[www.careforkidneys.com](http://www.careforkidneys.com)



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- <sup>9</sup> The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med* 2006; 355: 549-559.
- <sup>10</sup> Heart Protection Study Collaborative Group. MRC/BHF heart protection study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomized placebo-controlled trial. *Lancet*. 2002 Jul 6; 360(9326):7-22.
- <sup>11</sup> The Diabetes Control and Complications Trial Research Group. The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus. *N Engl J Med* 1993; 329:977-986.
- <sup>12</sup> Anthonisen, N.R. et al. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med*. 2005 Feb 15;142(4):233-9.
- <sup>13</sup> Saito, Y. et al. Low-Dose Aspirin Therapy in Patients With Type 2 Diabetes and Reduced Glomerular Filtration Rate Subanalysis from the JPAD trial. *Diabetes Care* 34.2 (2011): 280-285.
- <sup>14</sup> Canadian Institute for Health Information. Seniors and the Health Care System: What Is the Impact of Multiple Chronic Conditions. Jan 2011.
- <sup>15</sup> Tarride, J.E. et al. A review of the cost of cardiovascular disease. *Can J Cardiol* 2009; 25(6):e195-e202.
- <sup>16</sup> Preventing and Managing Chronic Disease: Ontario's Framework. Ministry of Health and Long Term Care. May 2007.
- <sup>17</sup> Public Health Agency of Canada (July 2011); Using 2008/09 data from the Canadian Chronic Disease Surveillance System (Public Health Agency of Canada).
- <sup>18</sup> Statistics Canada, CANSIM, Table 105-0501 and Catalogue no. 82-221-X. Last modified: 2014-06-12.
- <sup>19</sup> Mortality by major causes and age groups, Canada, 2006 Statistics Canada. Obtained from: <http://www.phac-aspc.gc.ca/cphorsphc-respcacsp/2010/fr-rc/longdesc/3-3-eng.ph>.
- <sup>20</sup> Proportion of Incident Dialysis Patients by Comorbid Conditions in Ontario Patients with One or More Identified Comorbid Conditions, FY13/14. Ontario Renal Reporting System. Reported Feb 2015.
- <sup>21</sup> Sarraf, M., Masoumi, A. and Schrier, R. W. Cardiorenal Syndrome in Acute Decompensated Heart Failure. *Clin J Am Soc Nephrol* 4: 2013–2026, 2009.
- <sup>22</sup> Foley, R.N. et al. Chronic Kidney Disease and the Risk for Cardiovascular Disease, Renal Replacement, and Death in the United States Medicare Population, 1998 to 1999. *J Am Soc Nephrol* 16: 489-495, 2005.
- <sup>23</sup> Go, et al. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events and Hospitalization. *N Engl J Med* 2004; 351:1296-305.
- <sup>24</sup> Vanholder, R. et al. Chronic kidney disease as cause of cardiovascular morbidity and mortality. *Nephrol Dial Transplant* (2005) 20: 1048–1056.
- <sup>25</sup> Vital Statistics, IntelliHealth Ontario, MOHLTC. Cause of Death in Windsor-Essex 2007-2011. Obtained June 2015. Obtained from: <https://www.wechu.org/about-us/reports-and-statistics/cause-death-windsor-essex-2007-2011>.
- <sup>26</sup> PEW Research Centre. Globally, Good Health Most Important. Spring Global Attitudes Survey 1Q14a-I.
- <sup>27</sup> Statistics Canada. Number of Persons Aged Over 80 in Canada. 2011.
- <sup>28</sup> Canadian Institute for Health Information. Spending on health care per capita by age group. 2011.
- <sup>29</sup> Canadian Institute for Health Information. The Cost of Acute Care Hospital Stays by Medical Condition in Canada, 2004-2005. (Ottawa: CHI, 2008).
- <sup>30</sup> Canadian Institute for Health Information, National Health Expenditure Trends, 1975 to 2009. Ottawa, Ont., CIHI, 2009.
- <sup>31</sup> Valderas, J.M. et al. Defining Comorbidity: Implications for Understanding Health and Health Services. *Ann Fam Med* 2009 Jul; 7(4): 357–363.
-

- 
- <sup>32</sup> McPherson, M. et al. Medication Use among Canadian Seniors. *Healthcare Quarterly* Vol.15 No.4 2012.
- <sup>33</sup> Terner, M. et al. The impact of polypharmacy on the health of Canadian seniors. *Family Practice* 2012; 29 (4): 427-432.
- <sup>34</sup> Ogilvie, K. K. The Silo Syndrome in Canadian Health Care. Jan/Feb 2014. (verbatim speech)
- <sup>35</sup> Ministry of Health and Long-Term Care. Quality-Based Procedures Clinical Handbook for Chronic Kidney Disease. March 2013.
- <sup>36</sup> Osterberg, L. and Blaschke, T. Adherence to Medication. *N Engl J Med.* 353, 487-497, 2005.
- <sup>37</sup> Ministry of Health and Long Term Care. A policy guide for creating community based specialty clinics. Ontario. Dec 2013.
- <sup>38</sup> Alebiosu, C.O., and Ayodele, O.E. The global burden of chronic kidney disease and the way forward. *Ethn Dis.* 2005 Summer; 15(3):418-23.
- <sup>39</sup> Novotny, T. Preventing Chronic Disease: Everybody's Business, In: Nolte E & McKee M, eds. *Caring for People With Chronic Conditions.* Maidenhead, U.K.: Open University Press, 2008, pp. 92-115.
- <sup>40</sup> Naderi, S.H., Bestwick, J.P. and Wald, D.S. Adherence to drugs that prevent cardiovascular disease. *Am J Med.* 2012 Sep;125(9):882-7.e1.
- <sup>41</sup> World Health Organization. Adherence to long term therapies. Switzerland, 2003.
- <sup>42</sup> Buse, J.B. et al. Primary Prevention of Cardiovascular Diseases in People with Diabetes Mellitus: A scientific statement from the American Heart Association and the American Diabetes Association. *Diabetes Care.* 2007 Jan;30(1):162-72.
- <sup>43</sup> Salas-Salvadó, J. et al. Reduction in the Incidence of Type 2 Diabetes With the Mediterranean Diet Results of the PREDIMED-Reus nutrition intervention randomized trial. *Diabetes Care.* 2011 Jan; 34(1): 14-9.
- <sup>44</sup> Colhoun, H.M. et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet.* 2004 Aug 21-27; 364(9435):685-96.
- <sup>45</sup> Type 2 diabetes and metformin. First choice for monotherapy: weak evidence of efficacy but well-known and acceptable adverse effects. *Prescrire Int.* 2014 Nov;23(154):269-72.
- <sup>46</sup> Gaede et al. Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes. *N Engl J Med* 2008;358:580-91.
- <sup>47</sup> Heller, S. R. and on behalf of the ADVANCE Collaborative Group. A Summary of the ADVANCE Trial. *Diabetes Care.* 2009 Nov; 32(Suppl 2): S357-S361.
- <sup>48</sup> Savage S. et al. The ABCD (Appropriate Blood Pressure Control in Diabetes) trial. Rationale and design of a trial of hypertension control (moderate or intensive) in type II diabetes. *Online J Curr Clin Trials.* 1993 Nov 24;Doc No 104.
- <sup>49</sup> Raymond O. E. et al. The Effect of Nisoldipine as Compared with Enalapril on Cardiovascular Outcomes in Patients with Non-Insulin-Dependent Diabetes and Hypertension. *N Engl J Med* 1998; 338: 645-52.
- <sup>50</sup> Jiten, V. BENEDICT: primary prevention of microalbuminuria in hypertensive type 2 diabetes. Bergamo Nephrologic Diabetes Complication Trial (BENEDICT). *N Engl J Med* 2004;351:1941-5.
- <sup>51</sup> Papademetriou, V. et al. Chronic kidney disease and intensive glycemic control increase cardiovascular risk in patients with type 2 diabetes. *Kidney Int.* 2015 Mar; 87(3):649-59.
- <sup>52</sup> Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013; 369.2: 145.
- <sup>53</sup> Duckworth, William, et al. Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med.* 2009 Jan 8;360(2):129-39.
-

- 
- <sup>54</sup> FIELD Study Investigators. "Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial." *The Lancet* 366.9500 (2005): 1849-1861.
- <sup>55</sup> Pfeffer, Marc A., et al. "A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease." *New England Journal of Medicine* 361.21 (2009): 2019-2032.
- <sup>56</sup> Appel, L.J. et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med.* 1997 Apr 17;336(16):1117-24.
- <sup>57</sup> Jamerson, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N Engl J Med.* 2008 Dec 4; 359(23):2417-28.
- <sup>58</sup> The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial *JAMA.* 2002; 288(23):2981-2997.
- <sup>59</sup> Dahlöf, B et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet.* 2002 Mar 23;359(9311):995-1003.
- <sup>60</sup> PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet.* 2001 Sep 29; 358(9287):1033-41.
- <sup>61</sup> Kostis, J.B. et al. Long-term effect of diuretic-based therapy on fatal outcomes in subjects with isolated systolic hypertension with and without diabetes. *Am J Cardiol.* 2005 Jan 1;95(1):29-35.
- <sup>62</sup> Hansson, L. The Hypertension Optimal Treatment study and the importance of lowering blood pressure. *J Hypertens Suppl.* 1999 Feb;17(1):S9-13.
- <sup>63</sup> Esler, M. et al. Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. *Lancet.* 2010 Dec 4;376(9756):1903-9
- <sup>64</sup> Staessen, J.A. et al. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. Systolic Hypertension in Europe Trial Investigators. *JAMA.* 1999 Aug 11; 282(6):539-46.
- <sup>65</sup> Nicholls, S.J. Effect of two intensive statin regimens on progression of coronary disease. *N Engl J Med.* 2011 Dec 1;365(22):2078-87.
- <sup>66</sup> Van Jaarsveld, B.C. et al. The Dutch Renal Artery Stenosis Intervention Cooperative (DRASTIC) study: rationale, design and inclusion data. *J Hypertens* 1998; 16 Suppl 6:S21-7.
- <sup>67</sup> Van Jaarsveld, B.C. et al. The effect of balloon angioplasty on hypertension in atherosclerotic renal-artery stenosis. Dutch Renal Artery Stenosis Intervention Cooperative Study Group. *N Engl J Med.* 2000 Apr 6;342(14):1007-14.
- <sup>68</sup> Van Jaarsveld, B.C. et al. Resistance to Antihypertensive Medication as a Predictor of Renal Artery Stenosis: Comparison of Two Drug Regimes. *J Hum Hypertens* 2001; 15: 669-76.
- <sup>69</sup> Beckett, N. S. et al. Treatment of Hypertension in Patients 80 Years of Age or Older. *N Engl J Med* 2008; 358:1887-1898.
- <sup>70</sup> Dahlöf, B. et al. STOP-Hypertension 2: A Prospective Intervention Trial of "Newer" versus "Older" Treatment Alternatives in Old Patients with Hypertension. *Blood Press* 1993; 2: 136-141.
- <sup>71</sup> Whelton, S. P. et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann Intern Med.* 2002 Apr 2;136(7):493-503.
- <sup>72</sup> Dattilo, A. M. and Kris-Etherton, P.M. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am J Clin Nutr.* 1992 Aug;56(2):320-8.
-

- 
- <sup>73</sup> Sever, P. S. et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet*. 2003 Apr 5;361(9364):1149-58.
- <sup>74</sup> Baigent, C. et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomized placebo-controlled trial. *Lancet* 2011; 377: 2181–92.
- <sup>75</sup> Nissen, S.E. et al. Effect of very high-intensity statin therapy on regression of coronary atherosclerosis: the ASTEROID trial. *JAMA*. 2006 Apr 5;295(13):1556-65. Epub 2006 Mar 13.
- <sup>76</sup> Colhoun, H. M. et al. Design of the Collaborative Atorvastatin Diabetes Study (CARDS) in patients with Type 2 Diabetes. *Diabet Med* 2002; 19:201-11.
- <sup>77</sup> Ridker, P. M. et al. Rosuvastatin in the Primary Prevention of the Cardiovascular Disease Among Patients with Low Levels of Low-density Lipoprotein Cholesterol and Elevated High Sensitivity C-Reactive Protein. Rationale and design of the JUPITER trial. *Circulation* 2003; 108: 2292-2297.
- <sup>78</sup> Ridiker, P. M. et al. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. *N Engl J Med* 2008; 359:2195-2207.
- <sup>79</sup> The Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994 Nov 19;344(8934):1383-9.
- <sup>80</sup> Shepherd, J. et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995; 333:1301-1308.
- <sup>81</sup> The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med* 1998; 339: 1349-135.
- <sup>82</sup> Frick, M.H. et al. Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. *N Engl J Med*. 1987 Nov 12;317(20):1237-45.
- <sup>83</sup> Nakaya, N. et al. Low-Dose Pravastatin and Age-Related Differences in Risk Factors for Cardiovascular Disease in Hypercholesterolaemic Japanese: analysis of the management of elevated cholesterol in the primary prevention group of adult Japanese (MEGA study). *Drugs Aging*. 2011 Sep 1;28(9):681-92.
- <sup>84</sup> Brown, G. et al. Regression of coronary artery disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B. *N Engl J Med* 1990; 323:1289-1298.
- <sup>85</sup> Wanner, C. Atorvastatin in Patients with Type 2 Diabetes Mellitus Undergoing Hemodialysis. *N Engl J Med* 2005; 353:238-248.
- <sup>86</sup> Fellstrom B.C. et al. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis (AURORA). *N Engl J Med* 2009; 360:1395-1407.
- <sup>87</sup> Holdaas, H. et al. Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial. *Lancet*. 2003 Jun 14;361(9374):2024-31.
- <sup>88</sup> Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. *Lancet*. 2000 Jan 22; 355(9200):253-9.
- <sup>89</sup> Parving, H.H. et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med*. 2001 Sep 20; 345(12):870-8.
- <sup>90</sup> Lewis, E.J. et al. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. *N Engl J Med*. 1993 Nov 11; 329(20):1456-62.
-

- 
- <sup>91</sup> Agodoa L.Y. et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. *JAMA*. 2001 Jun 6;285(21):2719-28.
- <sup>92</sup> Wright J.T. Jr. et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA* 2002;288:2421-31.
- <sup>93</sup> Brenner, B. M. et al. Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy. *N Engl J Med* 2001; 345:861-869.
- <sup>94</sup> Hou, F. et al. Efficacy and Safety of Benazepril for Advanced Chronic Renal Insufficiency. *N Engl J Med* 2006; 354:131-140.
- <sup>95</sup> OCTOPUS Group. Effects of angiotensin receptor blockade (ARB) on mortality and cardiovascular outcomes in patients with long-term haemodialysis: a randomized controlled trial. *Nephrol. Dial. Transplant.* (2013) 28 (6): 1579-1589.
- <sup>96</sup> Chan, K. E. et al. Combined angiotensin-converting enzyme inhibition and receptor blockade associate with increased risk of cardiovascular death in hemodialysis patients. *Kidney Int.* 2011 Nov;80(9):978-85.
- <sup>97</sup> Pfeffer, M.A. A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease. *N Engl J Med* 2009; 361:2019-2032.
- <sup>98</sup> Smart, N. A., and Titus, T.T. Outcomes of early versus late nephrology referral in chronic kidney disease: a systematic review. *Am J Med.* 2011 Nov;124(11):1073-80.e2.
- <sup>99</sup> Åkesson, A. et al. Combined effect of low-risk dietary and lifestyle behaviors in primary prevention of myocardial infarction in women. *Arch Intern Med.* 2007; 167(19):2122-2127.
- <sup>100</sup> Yusuf, Salim, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; 345:494-502.
- <sup>101</sup> Plehn, J. F. et al. Reduction of stroke incidence after myocardial infarction with pravastatin The Cholesterol and Recurrent Events (CARE) Study. *Circulation.* 1999 Jan 19;99(2):216-23.
- <sup>102</sup> Estruch, R. et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med* 2013; 368:1279-1290.
- <sup>103</sup> MRFIT Research Group. Multiple Risk Factor Intervention Trial: Risk Factor Changes and Mortality Results. *JAMA.* 1982;248(12):1465-1477.
- <sup>104</sup> Stamler, J. Multiple Risk Factor Intervention Trial Revisited: A New Perspective Based on Nonfatal and Fatal Composite Endpoints, Coronary and Cardiovascular, During the Trial. *J Am Heart Assoc.* 2012; 1.
- <sup>105</sup> Ball, S.G. et al. ACE inhibition, atherosclerosis and myocardial infarction--the AIRE Study in practice. Acute Infarction Ramipril Efficacy Study. *Eur Heart J.* 1994 May;15 Suppl B:20-5; Discussion 26-30.
- <sup>106</sup> Fox, K.M. and the EUROPA Investigators. 2003. Efficacy of Perindopril in Reduction of Cardiovascular Events among Patients with Stable Coronary Artery Disease: Randomised, Double-Blind, Placebo-Controlled, Multicentre Trial (the EUROPA Study). *Lancet.* 2003 Sep 6;362(9386):782-8.
- <sup>107</sup> The PEACE Trial Investigators. Angiotensin-Converting-Enzyme Inhibition in Stable Coronary Artery Disease. *N Engl J Med* 2004; 351: 2058-2068.
- <sup>108</sup> The TRANSCEND Investigators. Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial. *Lancet.* 2008 Sep 27;372(9644):1174-83.
- <sup>109</sup> Brown, B. G. et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. *N Engl J Med* 2001; 345:1583-1592.
- <sup>110</sup> Rubins, H. B. et al. "Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. *N Engl J Med.* 1999 Aug 5;341(6):410-8.
-

- 
- <sup>111</sup> A Randomized Trial of Propranolol in Patients with Acute Myocardial Infarction: I. Mortality Results JAMA. 1982; 247(12):1707-1714.
- <sup>112</sup> Athyros, V. G. et al. Treatment with Atorvastatin to the National Cholesterol Education Program Goal versus 'Usual' Care in Secondary Coronary Heart Disease Prevention. *Curr Med Res Opin* 2002; 18:220-8.
- <sup>113</sup> The ONTARGET Investigators. Telmisartan, Ramipril, or Both in Patients at High Risk for Vascular Events. *N Engl J Med* 2008; 358:1547-1559.
- <sup>114</sup> Mehta, S.R., et al. Effects of Pretreatment with Clopidogrel and Aspirin Followed by Long-Term Therapy in Patients Undergoing Percutaneous Coronary Intervention: the PCI-CURE Study. *Lancet* 2001; 358:527-533.
- <sup>115</sup> Murphy, S.A. et al. Reduction in recurrent cardiovascular events with intensive lipid-lowering statin therapy compared with moderate lipid-lowering statin therapy after acute coronary syndromes from the PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) trial. *J Am Coll Cardiol.* 2009 Dec 15;54(25):2358-62.
- <sup>116</sup> Pfeffer, M.A. et al. Valsartan in acute myocardial infarction trial (VALIANT): rationale and design. *Am Heart J.* 2000 Nov; 140(5):727-50.
- <sup>117</sup> Pfeffer M.A. et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med.* 2003 Nov 13;349(20):1893-906.
- <sup>118</sup> Bucher, H. C. et al. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. *Am J Med.* 2002 Mar;112(4):298-304.
- <sup>119</sup> Pitt, B. et al. The QUinapril Ischemic Event Trial (QUIET): evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. *Am J Cardiol.* 2001 May 1;87(9):1058-63.
- <sup>120</sup> Pfeffer, M.A. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *N Engl J Med.* 1992 Sep 3;327(10):669-77.
- <sup>121</sup> Zannad, F. et al. Limitation of Excessive Extracellular Matrix Turnover May Contribute to Survival Benefit of Spironolactone Therapy in Patients With Congestive Heart Failure Insights From the Randomized Aldactone Evaluation Study (RALES). *Circulation.* 2000 Nov 28; 102(22):2700-6.
- <sup>122</sup> Pitt, B. et al. Eplerenone, a Selective Aldosterone Blocker, in Patients with Left Ventricular Dysfunction after Myocardial Infarction. *N Engl J Med* 2003; 348:1309-1321.
- <sup>123</sup> Yusuf, S. et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med.* 2000 Jan 20; 342(3):145-53.
- <sup>124</sup> CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure: results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med.* 1987 Jun 4;316(23):1429-35.
- <sup>125</sup> Hall, A. S., et al. and the AIREX Study Investigators. (1997). Follow-up study of patients randomly allocated ramipril or placebo for heart failure after acute myocardial infarction: AIRE Extension (AIREX) Study. *Lancet.* 1997 May 24;349(9064):1493-7.
- <sup>126</sup> Feinstein, M. J. et al. Do statins reduce the risk of myocardial infarction in patients with heart failure? A pooled individual-level reanalysis of CORONA and GISSI-HF. *Eur J Heart Fail.* 2015 Apr;17(4):434-41.
- <sup>127</sup> Kitzman, D.W. et al. A Randomized Double-Blind Trial of Enalapril in Older Patients with Heart Failure and Preserved Ejection Fraction effects on exercise tolerance and arterial distensibility. *Circ Heart Fail.* 2010 Jul; 3(4):477-85.
-

- <sup>128</sup> McMurray, John JV, et al. "Heart failure with preserved ejection fraction: Clinical characteristics of 4133 patients enrolled in the I-PRESERVE trial." *European journal of heart failure* 10.2 (2008): 149-156.
- <sup>129</sup> Swedberg, K. et al. Candesartan in Heart Failure – Assessment of Reduction in Mortality and morbidity (CHARM): rationale and design. *J Card Fail* 1999; 5: 276-82.
- <sup>130</sup> McMurray, J.J. et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet*. 2003 Sep 6; 362(9386):767-71.
- <sup>131</sup> Cohn, J.N. et al. Rationale and design of the Valsartan Heart Failure Trial: a large multinational trial to assess the effects of valsartan, an angiotensin-receptor blocker, on morbidity and mortality in congestive heart failure. *J Card Fail* 1999; 5:155-160.
- <sup>132</sup> Packer, M. et al. COPERNICUS (Carvedilol Prospective Randomized Cumulative Survival Trial). A multicenter randomized double-blind, placebo-controlled study to determine the effect of carvedilol on mortality in severe congestive heart failure. *Cardiovasc Drugs Ther* 1999; 13:24.
- <sup>133</sup> Packer, M. et al. Effect of Carvedilol on Survival in Severe Chronic Heart Failure. *N Engl J Med* 2001; 344:1651-1658.
- <sup>134</sup> Hjalmarson, A. Effects of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure: the Metoprolol CR/XL Randomized Intervention Trial in congestive heart failure (MERIT-HF). MERIT-HF Study Group. *JAMA*. 2000 Mar 8; 283(10):1295-302.
- <sup>135</sup> McKelvie, R.S. Comparison of candesartan, enalapril, and their combination in congestive heart failure: randomized evaluation of strategies for left ventricular dysfunction (RESOLVD) pilot study. The RESOLVD Pilot Study Investigators. *Circulation*. 1999 Sep 7;100 (10):1056-64.
- <sup>136</sup> The RESOLVD Investigators. Effects of metoprolol CR in patients with ischemic and dilated cardiomyopathy : the randomized evaluation of strategies for left ventricular dysfunction pilot study. *Circulation*. 2000 Feb 1;101(4):378-84.
- <sup>137</sup> The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med* 2006; 355:549-559.
- <sup>138</sup> PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet*. 2001 Sep 29; 358(9287):1033-41.
- <sup>139</sup> Flint, A. C. et al. Statin use during ischemic stroke hospitalization is strongly associated with improved poststroke survival. *Stroke*. 2012; 43: 147-154.
- <sup>140</sup> Wilcox, R. et al. Effects of Pioglitazone in Patients With Type 2 Diabetes With or Without Previous Stroke Results From PROactive (PROspective pioglitAzone Clinical Trial In macroVascular Events 04). *Stroke*. 2007 Mar; 38(3):865-73.
- <sup>141</sup> Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20 536 people with cerebrovascular disease or other high-risk conditions. *Lancet*. 2004 Mar 6; 363(9411):757-67.
- <sup>142</sup> Schrader, J. et al. Morbidity and Mortality after Stroke, Eprosartan Compared with Nitrendipine for secondary Prevention. *Stroke* 2005; 36:1218-1226.
- <sup>143</sup> Emberson, J. et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. *Lancet*. 2014 Nov 29; 384(9958):1929-35.
- <sup>144</sup> Creager, M. A. Results of the CAPRIE trial: efficacy and safety of Clopidogrel. *Vasc Med*. 1998; 3(3):257-60.

- 
- <sup>145</sup> Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002; 324:71.
- <sup>146</sup> Catalano, M., G. Born, and Peto, R. Prevention of serious vascular events by aspirin amongst patients with peripheral arterial disease: randomized, double-blind trial. *J Intern Med.* 2007 Mar; 261(3):276-84.
- <sup>147</sup> Janzon, L., et al. Prevention of myocardial infarction and stroke in patients with intermittent claudication; effects of ticlopidine. Results from STIMS, the Swedish Ticlopidine Multicentre Study. *J Intern Med.* 1990 May;227(5):301-8.
- <sup>148</sup> Aguilar, M.I., Hart, R. and Pearce, L.A. Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no history of stroke or transient ischemic attacks. *Cochrane Database Syst Rev.* 2007 Jul 18; (3):CD006186.
- <sup>149</sup> Stroke Prevention in Atrial Fibrillation Investigators. Stroke Prevention in Atrial Fibrillation Study Final Results. *Circulation.* 1991 Aug;84(2):527-39.
- <sup>150</sup> Patel, M.R. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *N Engl J Med* 2011; 365: 883-891.
- <sup>151</sup> Connolly, S. J. et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. *N Engl J Med* 2009; 361:1139-1151.
- <sup>152</sup> Wyse, D.G. et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med.* 2002 Dec 5; 347(23):1825-33.
- <sup>153</sup> Roy, D. et al. Amiodarone to Prevent Recurrence of Atrial Fibrillation. *N Engl J Med* 2000; 342:913-920.
- <sup>154</sup> Ontario Renal Network. Ontario Renal Plan II 2015-2019. Toronto, 2015.
- <sup>155</sup> Canadian Institute for Health Information. Adverse Drug Reaction-Related Hospitalizations Among Seniors, 2006-2011. Ottawa: CHI, March 2013.
- <sup>156</sup> Canadian Institute for Health Information. All-Cause Readmission to Acute Care and Return to the Emergency Department. Ottawa: CHI, 2012.
- <sup>157</sup> Dawson, H. and Zinck, G. The Financial Cost to Emergency Departments of Patients Waiting for Access to an In-Patient Bed. *Healthcare Quarterly*, Vol 12, No 1, 2009.
- <sup>158</sup> 2012 Annual Report of the Office of the Auditor General of Ontario. Independent Health Facilities. Ministry of Health and Long-Term Care.
- <sup>159</sup> Wagner et al. Quality Improvement in Chronic Illness Care: A Collaborative Approach. *Journal on Quality Improvement.* Vol 27, No 2, 2001.
- <sup>160</sup> Wagner et al. Improving Chronic Illness Care: Translating Evidence into Action. *Health Aff (Millwood).* 2001 Nov-Dec;20(6):64-78.
- <sup>161</sup> Bayliss et al. Multidisciplinary Renal Care, *Clin J Am Soc Nephrol* 6: 704–710, 2011.
- <sup>162</sup> B.A. Briesacher et al. "Comparison of Drug Adherence Rates Among Patients with Seven Different Medical Conditions." *Pharmacotherapy*, June 2008.
- <sup>163</sup> Golden, B.R., Edmonson, Amy C., and Young, G.J. Turnaround at the Veterans Health Administration. Harvard Business School. June 19, 2007.
- <sup>164</sup> An Integrated Vascular Health Blueprint for Ontario. August 2012; Toronto: Cardiac Care Network of Ontario, Heart and Stroke Foundation and Ontario Stroke Network.
- <sup>165</sup> El Nekidy, W. et al. Cloxacillin-induced seizure in a hemodialysis patient. *Hemodial Int.* 2015 Jan 12.
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