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Personalized Medicine in Canada: A Survey of Adoption and Practice in Oncology, Cardiology and Family Medicine

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ABSTRACT

Canadian physicians were surveyed to understand roles, perceptions and experiences in genetic testing and personalized medicine (PM). The survey measured openness to adoption, practice, observed benefits and impacts, and barriers to adoption.

A self-administered survey was provided to Canadian oncologists, cardiologists and family physicians and responses were obtained online, by mail or by fax. The survey was designed to be exploratory. Comparisons of data were made across specialties and geography.

An overall response rate of 8.3% was obtained. Of the respondents, 43%, 30% and 27% were family physicians, cardiologists or oncologists respectively. A strong majority of respondents agreed that genetic testing and PM can have a positive impact on their practice however only 51% agreed that there is sufficient evidence to order such tests. A low percentage of respondents feel that they are sufficiently informed and confident practicing in this area, however many reported that genetic tests they have ordered have benefited their patients. Half of the respondents agreed that genetic tests that would be useful in their practice are not readily available. A lack of practice guidelines, limited provider knowledge and lack of evidence-based clinical information were cited as the main barriers to practice. Differences across provinces were observed for measures relating to access to testing and the state of practice. Differences across specialties were observed for the state of practice, reported benefits and access to testing.

Canadian physicians recognize the benefits of genetic testing and PM and are open to its adoption; however they lack the education, information and support needed to practice effectively in this area. Variability in practice and access to testing across specialties and across Canada was observed. These

results support a need for national strategies and resources to facilitate physician knowledge, training and practice in PM.

ARTICLE SUMMARY

Article Focus:

- Canadian physicians' perceptions and experience relating to genetic testing and personalized medicine (PM)
- Practice and impact of genetic testing and PM in Canada and across specialties
- Implications for continued adoption of genetic testing and PM in Canada across specialties

Key Messages:

- Family physicians, cardiologists and oncologists across Canada are practicing personalized medicine and recognize its benefits and potential impacts
- Physicians reported a number of barriers to the adoption of PM that are currently affecting medical practice in Canada
- The practice of and access to genetic testing and personalized medicine varies both across specialties and provinces that will have an impact on continued adoption in this area

AUTHORS' CONTRIBUTIONS

All authors were involved in the design of the survey, interpretation of results and drafting the article. In addition, Pun and Ashbury were involved in the implementation, data collection, and analysis. Three co-authors (Desjardins, Bonter and Currier) are employed by Cepmed. Pun and Ashbury were employed by PricewaterhouseCoopers LLP, and were commissioned by Cepmed to lead the survey project.

INTRODUCTION

"for the sweet ones [treatments] do not benefit everyone, nor do the astringent ones, nor are all the patients able to drink the same things"

(Hippocrates)

Personalized medicine (PM), the tailoring of medical treatment or prevention to the individual characteristics of each patient, has been enabled by recent advances in molecular biology (1). Research in the '-omic' sciences has resulted in improved understanding of the relationships between genes, proteins and disease, providing more tools for PM (2-5) and driving a shift in medical practice (6). Evidence of this 'shift' include a 66% increase in cancer-related genetic testing in Ontario between 2002 and 2008 (7), the fact that 10% of FDA approved drugs include pharmacogenomic information on their labels (8), and that genetic testing is recommended or required for at least 11 FDA approved drugs (9) and for 10 Health Canada approved drugs (based on a review of drug labeling using the Health Canada Drug Product Database). A number of applications of PM based on genetic testing are currently in use (10). Pharmacogenomics, the optimization of drug therapy based on genetic information, has been applied to improve clinical outcomes or reduce side effects and adverse events (11, 12). Targeted therapeutics, used in combination with companion diagnostics has been particularly successful in improving the treatment of cancer (13, 14). Finally, PM is being used to assess disease risk, facilitating prevention and early detection (15).

As a result of these developments PM has become an increasingly important topic for physicians, healthcare organizations and the public (16-17). There is widespread debate as to the intended and unintended consequences of PM on the quality and cost of healthcare, however many scientific and medical leaders expect PM to increase the quality of healthcare and reduce overall healthcare costs (13,18,19).

A few studies have assessed the adoption of genetic testing and its impact on the role and practice of physicians in Canada (20-24). These studies focused primarily on the adoption of genetic tests for diagnosis and treatment of cancer within Ontario's healthcare system, as well as the needs and recommendations for physician education, public education and improved coordination of healthcare delivery and genetic testing services. The present pan-Canadian survey of practicing oncologists, cardiologists and family doctors was designed to provide baseline data relating to genetic testing as a key element of PM in Canada with respect to openness to adoption, state of practice, and barriers to adoption.

METHODS

Ethics approval was received from IRB Services to survey a sample of Canadian physicians (oncologists, cardiologists, and family physicians) regarding their knowledge, training and practice in genetic testing and personalized medicine. Physician contact information was obtained from a 3rd party including information for 859 oncologists and 1, 165 cardiologists from across Canada. A weighted sample, based on population, of family physicians (n = 2,334) from Canadian provinces, was randomly selected from contacts with email addresses. The self-administered survey was available in French and English and distributed by mail, fax and email during the period May 26 to Sept 15, 2010. Respondents submitted their responses online, by mail or by fax. Survey candidates were contacted with up to four reminders to encourage participation. The survey questions were related to demographic information, training, practice, knowledge and education in PM based on genetic testing, nature and extent of practice in this area, and of the benefits of PM and barriers to its adoption.

Vovici software (25) was used for the online survey administration, allowing for both open-ended and close-ended questions, and menu creation for selection of pre-determined answer options for close-ended questions. All questionnaires were reviewed for completeness. The data entry protocol

included separate quality review of each survey against the entered data to ensure accuracy. Survey results were analyzed using STATA software version 11.0 (26).

This study was designed to be exploratory including analyses based on descriptive statistics and bivariate associations. Inferential analyses were not pursued. Answers to survey questions were compared according to medical specialty and region or province. Responses from the Atlantic Provinces, Saskatchewan, Manitoba and Alberta were low relative to Ontario, Quebec and British Columbia (BC). Data from the Atlantic Provinces (ATL), Nova Scotia, New Brunswick, Newfoundland and Prince Edward Island, were combined and data from Saskatchewan, Manitoba and Alberta (WST) were combined.

Due to the small sample of responses for certain questions, results with more than a 5% probability of occurring by chance were excluded. Pearson chi-squared test statistics were calculated to determine whether differences according to medical specialty, region or province were statistically significant.

RESULTS

Respondent Profile

A total of 363 physicians provided responses to the survey (8.3% overall response rate). Physicians not providing direct patient care (n=16) or not practicing in family medicine, cardiology or oncology (n=6) were excluded. Thus, the respondent group retained for the analysis comprised 341 active physicians with an adjusted response rate of 9.7%.

Of the respondents, 43%, 30% and 27% were family physicians, cardiologists and oncologists, respectively. Thirty-three percent of the respondents practiced in Ontario (ON), 20% in Quebec (QU), 24% in Manitoba, Saskatchewan and Alberta (WST), 14% in the Atlantic Provinces (ATL) and 9% in British Columbia (BC). Of the cardiologist and oncologist respondents, 73% and 79%, respectively, held academic appointments, compared to 41% of family physician respondents. One-third of survey

respondents were in the 46-55 age range. The average time since completion of training for participating oncologists was 12 years, 18 years for cardiologists, and 22 years for family physicians. Family physician respondents reported working predominately in offices or clinics, cardiologist respondents predominantly in academic health science centres, community hospitals and private office/clinic and oncologist respondents predominantly in academic health sciences centres. Respondents from all specialties were represented for each geographic area as shown in Figure 1.

Openness to Adoption

Respondents were asked a series of questions about their perceptions of the usefulness of genetic testing in the context of PM, as an indicator of physicians' openness to the adoption of PM. The majority of respondents agreed that knowing a patient's genetic profile can influence treatment decision-making (83%) and importantly, can improve patient outcomes (70%). However, only 51% of respondents agreed that there is sufficient evidence in support of ordering genetic tests. The perception of the usefulness of genetic testing was similar across specialties and provinces as no significant differences were observed (Figure 2).

State of Practice

Respondents' current levels of practice and knowledge of genetic testing and PM were also assessed. The results indicate that oncologist respondents are practicing more PM with 59% reporting having ordered a genetic test in the past month compared to only 22% of general practitioners and cardiologists. Oncologists also reported feeling more sufficiently informed, more able to interpret test results and more comfortable discussing results with patients compared to other specialties (Figure 3). Overall only 21% of respondents agreed that they are sufficiently informed about PM and 29% agreed that they are able to interpret the results of genetic tests. Thirty percent of respondents agreed that they are comfortable discussing test results with patients. These measures appear to be consistent across provinces (Figure 3). The survey also assessed physicians' perceptions of the impact of genetic

testing on their patients. Of the respondents, 40% agreed that their patients have expressed fears of discrimination based on genetic testing and 37% reported that their patients are asking them about genetic testing and PM. Similar reports of patients expressing fear of discrimination were observed across specialties (Figure 3); however, more oncologists (50%) reported that patients are asking about PM compared to 30% of cardiologists and 32% general/family physicians (Figure 3).

Impacts and Benefits

Respondents were asked a series of questions about the impact and benefits of genetic testing in their practice. Most respondents reported that genetic tests that they have ordered were for the purposes of identifying a genetic predisposition or risk factor for disorders (60% agreed vs. 20% disagreed) and that these tests influenced patient treatment plans (54% agreed vs. 18% disagreed). Many also reported that genetic tests that they have ordered increased therapeutic benefit for patients (42% agreed vs. 19% disagreed). Comparing across specialties (Figure 4, left panel), oncologist respondents were more likely to agree that tests that they had ordered had influenced treatment plans (67% agreed) compared to other specialties (Chi^2 P=0.006). Note that for the purpose of this study 'ordering' means either requisitioning a test directly or facilitating access through another healthcare professional, such as a medical geneticist or other specialist (56% of respondents reported that they are responsible for ordering genetic tests for their patients and 31% reported that a geneticist is responsible for ordering tests for their patients).

Barriers to Adoption

Respondents were asked to indicate what they perceive as the main barriers to their practice in genetic testing and PM. A list of 13 barriers (Table 1) was provided. The top 5 cited barriers were: lack of clinical practice guidelines, limited provider knowledge, attitudes and awareness of benefits, lack of evidence-based clinical information, the cost of testing and a lack of time and resources to educate patients.

Table 1: Barriers to Adoption

Barriers to physicians ordering genetic tests for PM	% of respondents who cited barrier as a 'main barrier'
Lack of clinical guidelines	60
Limited provider knowledge, awareness	57
Lack of evidence-based clinical information	53
Cost of tests is prohibitive	48
Lack of time, resources to educate patients	37
Results take too long for a treatment decision	33
Too much paperwork/bureaucracy	31
Lack of insurance coverage	28
Insufficient regulatory framework	27
Patient anxiety regarding test results	24
Lack of reimbursement	19
Approval process takes too long	14
Test results will not affect treatment	13

Access to Testing

With regards to access to appropriate genetic testing for their patients, 50% of respondents agreed that tests that they believe would be useful in their practice are not readily available, 48% indicated that the cost of genetic tests is a main barrier to the use of PM, and 33% indicated that the length of time it takes to obtain results is an important barrier to the use of PM, as the results may not be attained in adequate time to help make treatment decisions. Compared to other specialities, oncologists identified the time it takes to obtain results as a barrier to practice (59%) more often than other specialties (Figure 6). In general these measures relating to access to testing varied across provinces, possibly reflecting differences in access to genetic testing across Canada (Figure 6).

Physician Education

Most respondents reported having no formal undergraduate (92%) or graduate training (89%) in genetic testing and PM. Interestingly, 73% of respondents have attended university lectures or

engaged in self-study and 75% would like more continuing education in this area. More oncologists reported having graduate training in this area (27%) compared to other specialties (Chi^2 P=0.0001).

DISCUSSION

Openness to Adoption

The results of this study indicate that Canadian physicians are optimistic about the promise of PM, and open to its adoption. The majority of respondents agreed that genetic testing as a component of PM can influence treatment plans (83%) and improve outcomes (70%). This is consistent with a recent survey of molecular oncology testing (MOT) in Ontario where it was reported that MOT is expected to become increasingly prevalent in all areas of diagnosis, prognosis, and treatment in the foreseeable future (21). Similar findings from another Canadian survey (27) and a study of 10,000+ physicians in the United States (28) also support widespread awareness among physicians of the current value and potential impact of PM. Positive perceptions among Canadian physicians may facilitate efficient and appropriate adoption of PM into practice.

Patient engagement has been identified as a possible factor in physicians' attitudes toward adopting new practices (29, 30). Thirty-seven percent of respondents reported that patients are asking them about genetic testing and PM. Physicians also reported patients expressing fears of discrimination based on genetic testing (Figure 4). Although no existing Canadian legislation specifically prohibits genetic discrimination, a level of protection is provided through the Canadian Human Rights Act (Art. 3) and Canada's Personal Information Protection and Electronic Documents Act. Steps have been taken to strengthen these protections. In April of 2010, Bill C-508, an act to amend the Canadian Human Rights Act to specify genetic discrimination was introduced in parliament (31). Few respondents indicated that patient anxiety concerning test results is a barrier to their practice (Table 1). This is consistent

with a recent US study of more than 2,000 individuals, which found no post-test anxiety or adverse outcomes in individuals who received comprehensive genetic profiling (32).

State of Practice

This study showed that oncologists are practicing more in this area (Figures 3 and 4) and are leading the in terms of adoption of PM among the specialties surveyed. In terms of access to testing, it was found that this and other measures of the state of practice across the provinces varied (Figure 6). This variability in practice and access across Canada may be due to differences in access to testing services, funding, and the interpretation of the evidence or perception of benefits from province to province. It has been suggested that decision-making related to predictive genetic testing is ad hoc and variable across Canada and that a coordinated national approach is needed (33). Recommendations have been proposed for a coordinated approach to the adoption and funding of genetic testing in Ontario (34). Work in this area is critical to ensuring equitable access and improving parity of healthcare across Canada. A coordinated strategy and implementation across the country may be challenging given the disparate provincially funded and controlled health systems in Canada.

Barriers to Adoption

A lack of medical guidelines was identified by respondents (61%) as the predominant barrier to adoption, indicating a need for the development of best practices and guidelines to support the implementation of PM. Sharing practices as well as genetic testing and pharmacoeconomic information across provincial healthcare systems is also likely necessary to support efficient and cost-effective national implementation of PM.

Of the respondents, 62% agreed that medical informatics will be critical to delivering PM. Indeed, vast amounts of data will be generated with widespread adoption–and an IT infrastructure for collection, storage, analysis, interpretation, and reporting will be needed (35-37). Furthermore decision support

tools, including electronic medical records (EMRs), will be needed to facilitate interpretation and point-of-care decision-making. This may pose a significant barrier in Canada where IT infrastructure and EMR implementation is targeted for completion only in 2015 (38) and lags significantly behind other OECD nations.

Surveys of Canadian (21, 22) and US physicians (28) have reported the need for physician education for the successful adoption of PM. These studies found that a majority of physicians lack the education, training, and support for successful adoption. The present study supports these findings. Furthermore respondents indicated that they are actively pursuing more information with 73% engaging in self-study. These data support a need for formal and continuing physician education in this area. A 2010 survey of 90 medical schools in the US and Canada found that 80% have begun to incorporate pharmacogenomic training into their curriculum, however, approximately 60% considered this instruction at their school to be 'poor' and more than 80% were not considering increasing the level of instruction within the next 3 years (39).

Physicians' perceptions and knowledge of the evidence supporting the clinical and analytical validity of genetic tests for PM are obviously important for its adoption. Canadian and US studies have demonstrated that current physician knowledge, real-world data and guidelines relating to PM has often been insufficient for appropriate adoption (40); even where testing is recommended or publicly funded (41, 42). In the present study, 51% of respondents agreed that there is sufficient evidence to order genetic tests for PM. These results suggest either a need for better physician education or a need for additional supporting evidence for personalized medicine implementation. Most likely both factors are at play. Further supporting the need for more research was the finding that 53% of respondents cited the need for evidence-based clinical information as a main barrier to their use of genetic testing. Translational research is needed to provide more robust data for evaluating clinical

utility and best practices for adoption and implementation within Canada's healthcare system. Furthermore, resources that provide physicians with easy access to accurate and current information would certainly facilitate appropriate and efficient adoption of PM going forward.

SURVEY LIMITATIONS

The response rate to the survey was low, and, as such, we must be careful when interpreting the responses and generalizing the findings to the larger population. However, the response rates of other similar physician surveys implemented in Canada have been comparable in recent years. Physicians are asked to respond to many surveys to determine their knowledge, attitudes and practices regarding many issues. As such, it is understandable if there is "survey fatigue". Physicians will be selective when responding to surveys. Indeed the topic of this investigation is relatively new (particularly for family physicians), and may be less relevant to most practitioners. In our follow-up discussions with some physicians who participated in the survey, the opinion was offered that the subject of personalized medicine is recent and will require more education, promotion and translation into practice before physicians will have adequate understanding of and interest in responding to studies regarding this issue. In this context, our survey results can be interpreted as more "qualitative" and as a benchmark measure of family physician, oncologist and cardiologist knowledge, training and practice in personalized medicine. Also, administration of the survey over the period May 26 to Sept 15, 2010 may have negatively influenced the response rate. There may have been differences in respondents based on the medium used to complete the survey (electronic vs. paper-based). The topic of genetic testing and personalized medicine may not have been relevant to all physicians that were sent the survey, which may have negatively affected the response rate. All survey results were based on physicians' self-reports. The physician contact information was purchased through a 3rd party and some data were incomplete or inaccurate.

Conclusions

PM based on genetic testing is currently being practiced in Canada across specialties and provinces. Many physicians recognize its benefits and are open to its adoption. Patients are asking their physicians about genetic testing and PM; however, physicians are not confident in discussing genetic testing and PM with their patients. This may not be surprising considering the overall lack of formal education in the field as well as the limited time and resources available to physicians to do so. These study results also indicate variability in practice and access across Canada. National strategies and resources that facilitate healthcare provider knowledge, training, practice, and efficient adoption of beneficial practices in PM are needed.

Soaring healthcare costs across industrialized countries are not sustainable. A few PM pioneers are paving the way toward demonstrating that these new molecular tests can result in better care at lower costs. Indeed, the history of innovation across many industries such as the computer, telecommunications, higher education, transportation and many other sectors has shown that previously inaccessible and expensive products and services can be transformed into accessible and low-cost product and services through technology enablers such as personalized medicine and new business models (43). Hence, if we strive for better healthcare, PM and the new models required for its full implementation present an unavoidable challenge and opportunity to transform our healthcare system into one adapted to the 21st century.

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COMPETING INTERESTS

None

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6 - 9
		(*b*) Report category boundaries when continuous variables were categorized	6 - 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6 - 9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9 - 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12 - 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

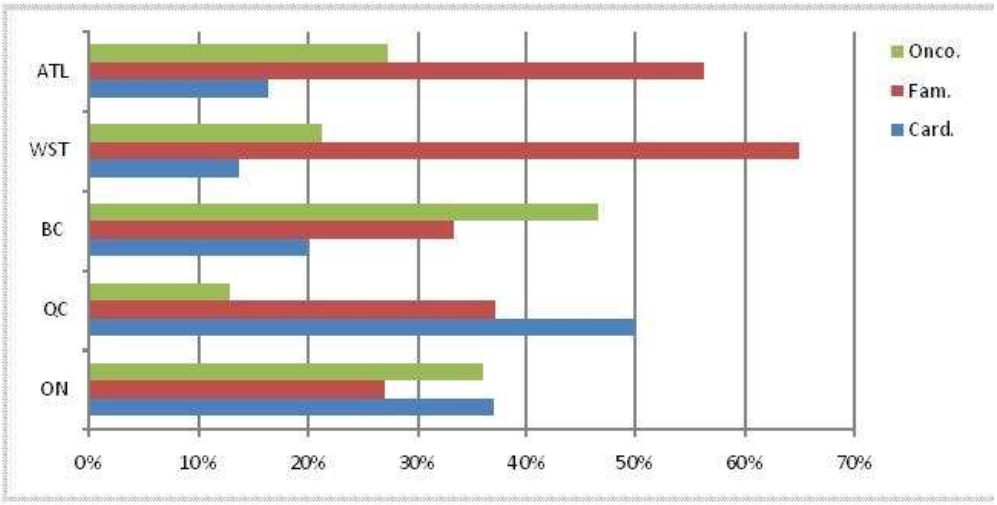

Figure 1: Distribution of respondents by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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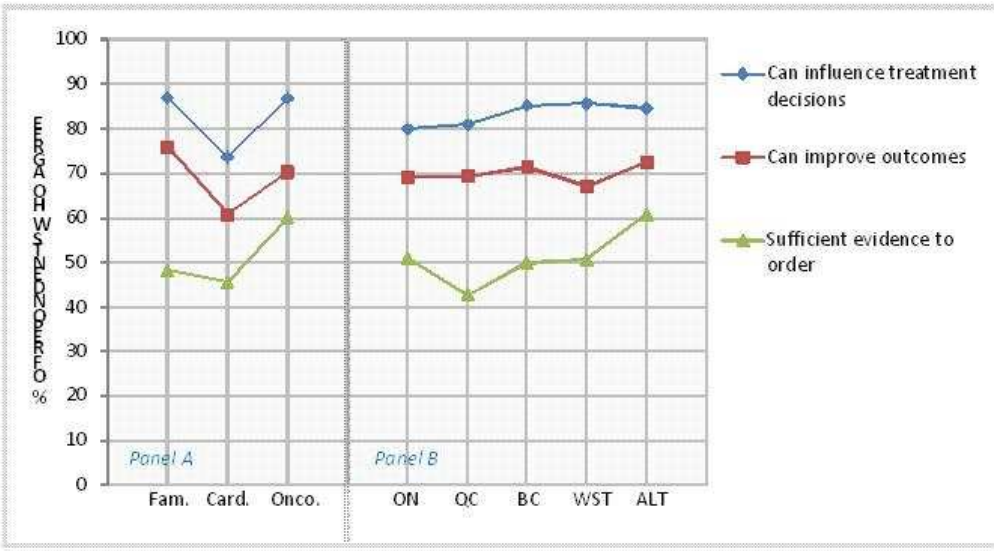

Figure 2: Respondents' perceptions of utility by specialty (panel A): family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B): Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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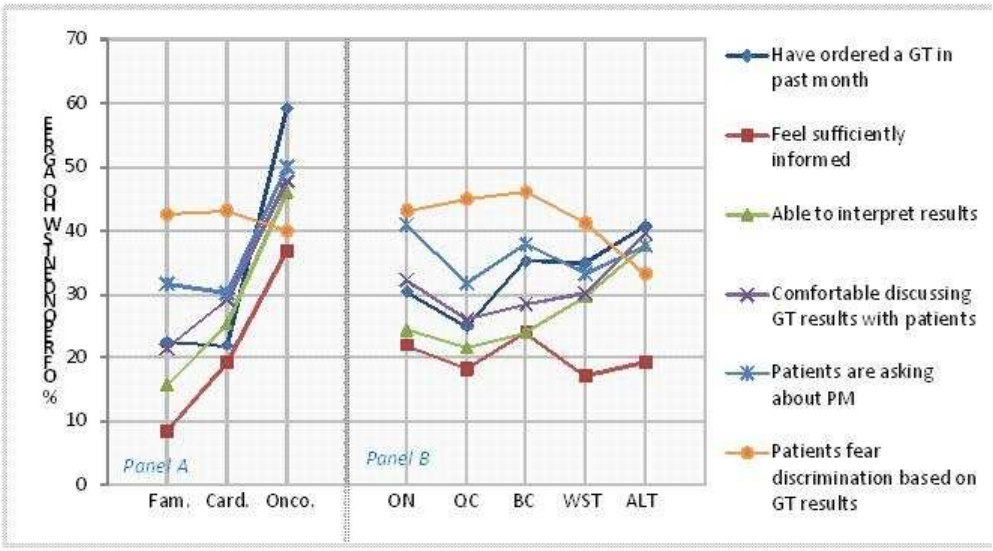

Figure 3: Measures of state of practice by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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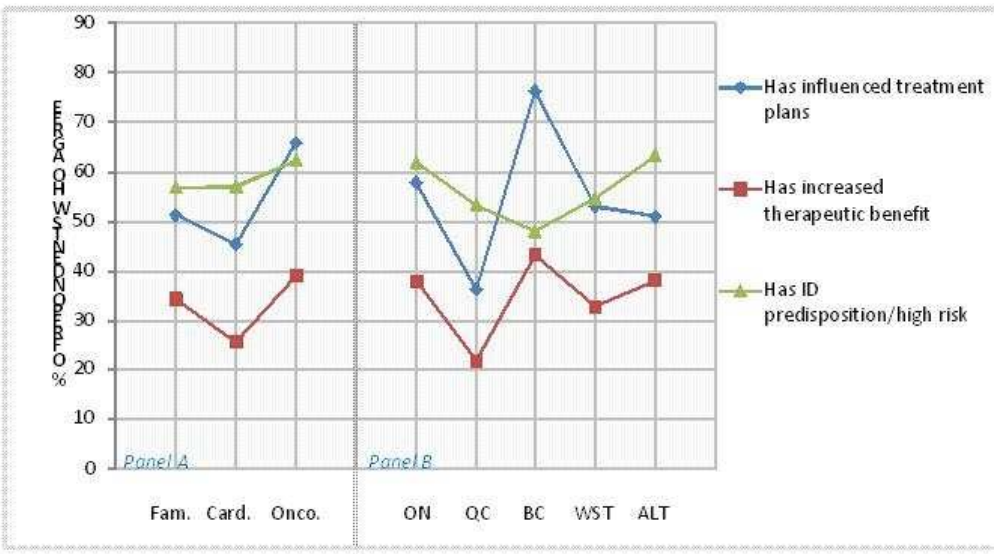

Figure 4: Comparison of reported impacts and benefits by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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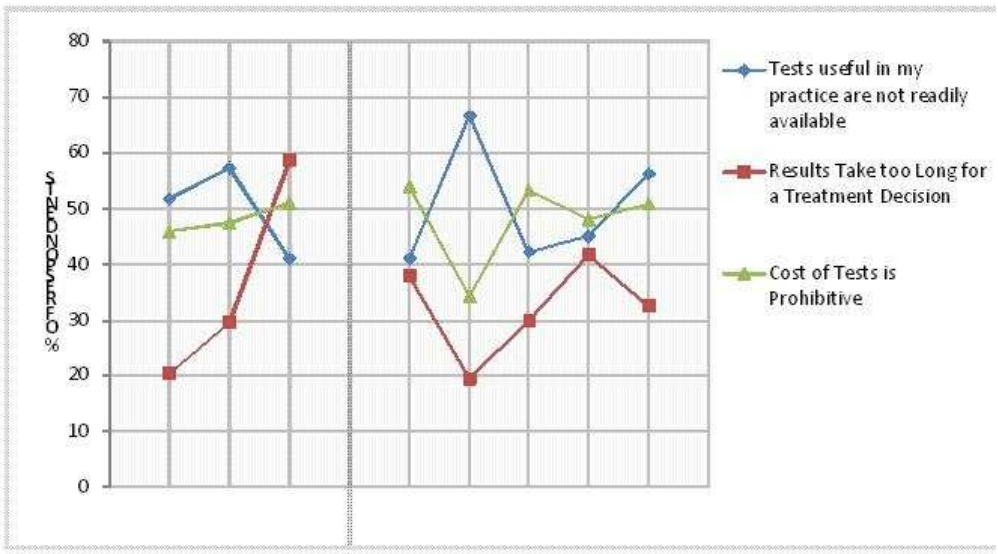

Figure 5: Measures of barriers to access by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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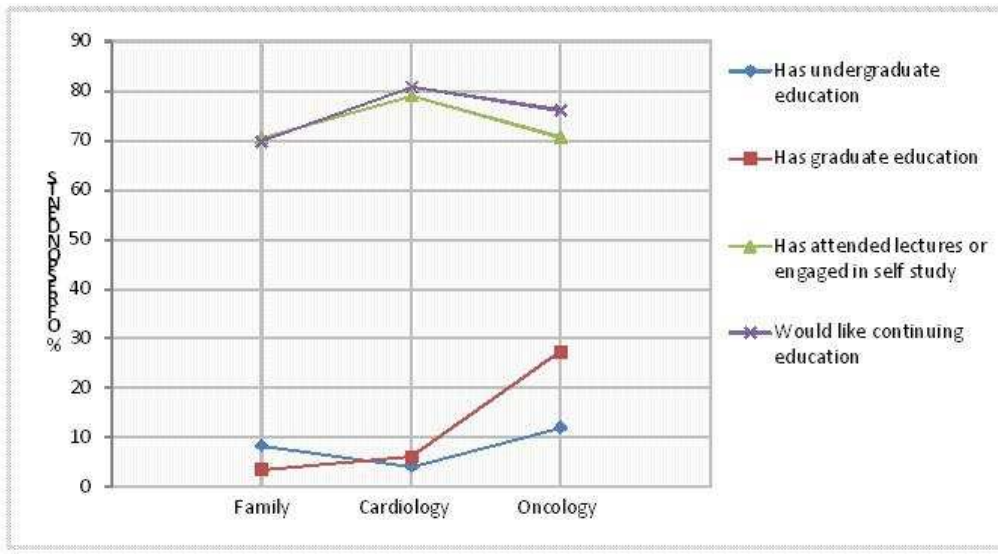

Figure 6: Measures of physician education in genetic testing and PM by specialty.

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Personalized Medicine in Canada: A Survey of Adoption and Practice in Oncology, Cardiology and Family Medicine

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Personalized Medicine in Canada: A Survey of Adoption and Practice in Oncology, Cardiology and Family Medicine

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Keywords: personalized medicine, genetic testing, survey, physician behaviour, risk assessment

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ABSTRACT

In order to provide baseline data relating to genetic testing as a key element of personalized medicine (PM), Canadian physicians were surveyed to understand roles, perceptions and experiences in this area. The survey measured attitudes practice, observed benefits and impacts, and barriers to adoption.

A self-administered survey was provided to Canadian oncologists, cardiologists and family physicians and responses were obtained online, by mail or by fax. The survey was designed to be exploratory. Comparisons of data were made across specialties and geography.

An overall response rate of 8.3% was obtained. Of the respondents, 43%, 30% and 27% were family physicians, cardiologists or oncologists respectively. A strong majority of respondents agreed that genetic testing and PM can have a positive impact on their practice however only 51% agreed that there is sufficient evidence to order such tests. A low percentage of respondents feel that they are sufficiently informed and confident practicing in this area, however many reported that genetic tests they have ordered have benefited their patients. Half of the respondents agreed that genetic tests that would be useful in their practice are not readily available. A lack of practice guidelines, limited provider knowledge and lack of evidence-based clinical information were cited as the main barriers to practice. Differences across provinces were observed for measures relating to access to testing and the state of practice. Differences across specialties were observed for the state of practice, reported benefits and access to testing.

Canadian physicians recognize the benefits of genetic testing and PM; however they lack the education, information and support needed to practice effectively in this area. Variability in practice and access to testing across specialties and across Canada was observed. These results support a need for national strategies and resources to facilitate physician knowledge, training and practice in PM.

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ARTICLE SUMMARY

Article Focus:

- Canadian physicians' perceptions and experience relating to genetic testing and personalized medicine (PM)
- Practice and impact of genetic testing and PM in Canada and across specialties
- Implications for continued adoption of genetic testing and PM in Canada across specialties

Key Messages:

- Family physicians, cardiologists and oncologists across Canada are practicing personalized medicine and recognize its benefits and potential impacts
- Physicians reported a number of barriers to the adoption of PM that are currently affecting medical practice in Canada
- The practice of and access to genetic testing and personalized medicine varies both across specialties and provinces that will have an impact on continued adoption in this area

AUTHORS' CONTRIBUTIONS

All authors were involved in the design of the survey, interpretation of results and drafting the article. In addition, Pun and Ashbury were involved in the implementation, data collection, and analysis. Three co-authors (Desjardins, Bonter and Currier) are employed by Cepmed. Pun and Ashbury were employed by PricewaterhouseCoopers LLP, and were commissioned by Cepmed to lead the survey project.

INTRODUCTION

"for the sweet ones [treatments] do not benefit everyone, nor do the astringent ones, nor are all the patients able to drink the same things"

(Hippocrates)

Personalized medicine (PM), the tailoring of medical treatment or prevention to the individual characteristics of each patient, has been enabled by recent advances in molecular biology (1). Research in the '-omic' sciences has resulted in improved understanding of the relationships between genes, proteins and disease, providing more tools for PM (2-5) and driving a shift in medical practice (6). Evidence of this 'shift' include a 66% increase in cancer-related genetic testing in Ontario between 2002 and 2008 (7), the fact that 10% of FDA approved drugs include pharmacogenomic information on their labels (8), and that genetic testing is recommended or required for at least 11 FDA approved drugs (9) and for 10 Health Canada approved drugs (based on a review of drug labeling using the Health Canada Drug Product Database). A number of applications of PM based on genetic testing are currently in use (10). Pharmacogenomics, the optimization of drug therapy based on genetic information, has been applied to improve clinical outcomes or reduce side effects and adverse events (11, 12). Targeted therapeutics, used in combination with companion diagnostics has been particularly successful in improving the treatment of cancer (13, 14). Finally, PM is being used to assess disease risk, facilitating prevention and early detection (15).

As a result of these developments PM has become an increasingly important topic for physicians, healthcare organizations and the public (16-17). There is widespread debate as to the intended and unintended consequences of PM on the quality and cost of healthcare, however many scientific and medical leaders expect PM to increase the quality of healthcare and reduce overall healthcare costs (13,18,19). A few studies have assessed the adoption of genetic testing and its impact on the role and practice of physicians in Canada (20-24). These studies focused primarily on the adoption of genetic

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tests for diagnosis and treatment of cancer within Ontario's healthcare system, as well as the needs and recommendations for physician education, public education and improved coordination of healthcare delivery and genetic testing services. In order to facilitate medical and continuing professional education in personalized medicine in Canada, it is essential to have a baseline understanding of current knowledge, attitudes, and practices.

The present pan-Canadian survey of practicing oncologists, cardiologists and family doctors was designed to provide baseline data relating to genetic testing as a key element of PM in Canada with respect to attitudes, state of practice, and barriers to adoption. There were three specialties chosen as the target audience for the survey: cardiologists and oncologists were chosen as they will experience higher volumes and needs for personalized genetic testing while family physicians are usually the first point of contact for patients, and are often involved with screening for risk of disease.

METHODS

Ethics approval was received from IRB Services to survey a sample of Canadian physicians (oncologists, cardiologists, and family physicians) regarding their knowledge, training and practice in genetic testing and personalized medicine.

Physician contact information was obtained from a 3rd party including information for 859 oncologists and 1, 165 cardiologists from across Canada. A weighted sample, based on population, of family physicians (n = 2,334) from Canadian provinces, was randomly selected from contacts with email addresses. The self-administered survey was available in French and English and distributed by mail, fax and email during the period May 26 to Sept 15, 2010. Respondents submitted their responses online, by mail or by fax. Survey candidates were contacted with up to four reminders to encourage participation. The survey questions were related to demographic information, training, practice, knowledge and education in PM based on genetic testing, nature and extent of practice in this area, and of the benefits of PM and barriers to its adoption. Questions were developed based on the authors' knowledge of genetic testing and PM. A draft of the survey questions was developed from this knowledge base and a review of the literature of previous surveys conducted in other jurisdictions (28, 29). This draft survey was subsequently reviewed by 11 physicians (5 oncologists, 3 cardiologists, 3 family physicians) and their feedback was incorporated into the final survey. The survey's design was

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informed by thinking about how new technologies or innovations are adopted in practice and a diffusion of innovations framework was considered (44). The survey solicited physicians' knowledge of, attitudes, and practice of personalized genetic testing to understand the relative advantage, compatibility, ease of implementation, and system response to understand adoption of personalized genetic testing. This is an initial application of this framework to the Canadian context.

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Vovici software (25) was used for the online survey administration, allowing for both open-ended and close-ended questions, and menu creation for selection of pre-determined answer options for close-ended questions. All questionnaires were reviewed for completeness. The data entry protocol included separate quality review of each survey against the entered data to ensure accuracy. Survey results were analyzed using STATA software version 11.0 (26).

This study was designed to be exploratory including analyses based on descriptive statistics and bivariate associations. Inferential analyses were not pursued. Answers to survey questions were compared according to medical specialty and region or province. Responses from the Atlantic Provinces, Saskatchewan, Manitoba and Alberta were low relative to Ontario, Quebec and British Columbia (BC). Data from the Atlantic Provinces (ATL), Nova Scotia, New Brunswick, Newfoundland and Prince Edward Island, were combined and data from Saskatchewan, Manitoba and Alberta (WST) were combined.

Due to the small sample of responses for certain questions, results with more than a 5% probability of occurring by chance were excluded. Pearson chi-squared test statistics were calculated to determine whether differences according to medical specialty, region or province were statistically significant.

RESULTS

Respondent Profile

A total of 363 physicians provided responses to the survey (8.3% overall response rate). Physicians not providing direct patient care (n=16) or not practicing in family medicine, cardiology or oncology (n=6)

were excluded. Thus, the respondent group retained for the analysis comprised 341 active physicians with an adjusted response rate of 9.7%.

Of the respondents, 43%, 30% and 27% were family physicians, cardiologists and oncologists, respectively. Thirty-three percent of the respondents practiced in Ontario (ON), 20% in Quebec (QU), 24% in Manitoba, Saskatchewan and Alberta (WST), 14% in the Atlantic Provinces (ATL) and 9% in British Columbia (BC). Of the cardiologist and oncologist respondents, 73% and 79%, respectively, held academic appointments, compared to 41% of family physician respondents. One-third of survey respondents were in the 46-55 age range. The average time since completion of training for participating oncologists was 12 years, 18 years for cardiologists, and 22 years for family physicians. Family physician respondents reported working predominately in offices or clinics, cardiologist respondents predominantly in academic health science centres, community hospitals and private office/clinic and oncologist respondents predominantly in academic health sciences centres. Respondents from all specialties were represented for each geographic area as shown in Figure 1.

Attitudes and Perceptions

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Respondents were asked a series of questions about their attitudes and perceptions of the usefulness of genetic testing in the context of PM, as an indicator of physicians' openness to the adoption of PM. The majority of respondents agreed that knowing a patient's genetic profile can influence treatment decision-making (83%) and importantly, can improve patient outcomes (70%). However, only 51% of respondents agreed that there is sufficient evidence in support of ordering genetic tests. The perception of the usefulness of genetic testing was similar across specialties and provinces as no significant differences were observed (Figure 2).

State of Practice

Respondents' current levels of practice and knowledge of genetic testing and PM were also assessed. The results indicate that oncologist respondents are practicing more PM with 59% reporting having ordered a genetic test in the past month compared to only 22% of general practitioners and cardiologists. Oncologists also reported feeling more sufficiently informed, more able to interpret test results and more comfortable discussing results with patients compared to other specialties (Figure 3). Overall only 21% of respondents agreed that they are sufficiently informed about PM and 29% agreed that they are able to interpret the results of genetic tests. Thirty percent of respondents agreed that they are comfortable discussing test results with patients. These measures appear to be consistent across provinces (Figure 3). The survey also assessed physicians' perceptions of the impact of genetic testing on their patients. Of the respondents, 40% agreed that their patients have expressed fears of discrimination based on genetic testing and 37% reported that their patients are asking them about genetic testing and PM. Similar reports of patients expressing fear of discrimination were observed across specialties (Figure 3); however, more oncologists (50%) reported that patients are asking about PM compared to 30% of cardiologists and 32% general/family physicians (Figure 3).

Impacts and Benefits

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Respondents were asked a series of questions about the impact and benefits of genetic testing in their practice. Most respondents reported that genetic tests that they have ordered were for the purposes of identifying a genetic predisposition or risk factor for disorders (60% agreed vs. 20% disagreed) and that these tests influenced patient treatment plans (54% agreed vs. 18% disagreed). Many also reported that genetic tests that they have ordered increased therapeutic benefit for patients (42% agreed vs. 19% disagreed). Comparing across specialties (Figure 4, left panel), oncologist respondents were more likely to agree that tests that they had ordered had influenced treatment plans (67% agreed) compared to other specialties (Chi^2 P=0.006). Note that for the purpose of this study 'ordering' means either requisitioning a test directly or facilitating access through another healthcare

professional, such as a medical geneticist or other specialist (56% of respondents reported that they are responsible for ordering genetic tests for their patients and 31% reported that a geneticist is responsible for ordering tests for their patients).

Barriers to Adoption

Respondents were asked to indicate what they perceive as the main barriers to their practice in genetic testing and PM. A list of 13 barriers (Table 1) was provided. The top 5 cited barriers were: lack of clinical practice guidelines, limited provider knowledge, attitudes and awareness of benefits, lack of evidence-based clinical information, the cost of testing and a lack of time and resources to educate patients.

Access to Testing

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With regards to access to appropriate genetic testing for their patients, 50% of respondents agreed that tests that they believe would be useful in their practice are not readily available, 48% indicated that the cost of genetic tests is a main barrier to the use of PM, and 33% indicated that the length of time it takes to obtain results is an important barrier to the use of PM, as the results may not be attained in adequate time to help make treatment decisions. Compared to other specialities, oncologists identified the time it takes to obtain results as a barrier to practice (59%) more often than other specialties (Figure 6). In general these measures relating to access to testing varied across provinces, possibly reflecting differences in access to genetic testing across Canada (Figure 6).

Physician Education

Most respondents reported having no formal undergraduate (92%) or graduate training (89%) in genetic testing and PM. Interestingly, 73% of respondents have attended university lectures or engaged in self-study and 75% would like more continuing education in this area. More oncologists reported having graduate training in this area (27%) compared to other specialties (Chi^2 P=0.0001).

DISCUSSION

Attitudes, Impacts and Benefits The results of this study indicate that Canadian physicians responding to the survey are optimistic about the promise of PM, and open to its use. The majority of respondents agreed that genetic testing as a component of PM can influence treatment plans (83%) and improve outcomes (70%). This is consistent with a recent survey of molecular oncology testing (MOT) in Ontario where it was reported that MOT is expected to become increasingly prevalent in all areas of diagnosis, prognosis, and treatment in the foreseeable future (21). Similar findings from another Canadian survey (27) and a study of 10,000+ physicians in the United States (28) also support widespread awareness among physicians of the current value and potential impact of PM. Positive perceptions among Canadian physician respondents may facilitate efficient and appropriate adoption of PM into practice.

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Patient engagement has been identified as a possible factor in physicians' attitudes toward adopting new practices (29, 30). Thirty-seven percent of respondents reported that patients are asking them about genetic testing and PM. Physicians also reported patients expressing fears of discrimination based on genetic testing (Figure 4). Although no existing Canadian legislation specifically prohibits genetic discrimination, a level of protection is provided through the Canadian Human Rights Act (Art. 3) and Canada's Personal Information Protection and Electronic Documents Act. Steps have been taken to strengthen these protections. In April of 2010, Bill C-508, an act to amend the Canadian Human Rights Act to specify genetic discrimination was introduced in parliament (31). Few respondents indicated that patient anxiety concerning test results is a barrier to their practice (Table 1). This is consistent with a recent US study of more than 2,000 individuals, which found no post-test anxiety or adverse outcomes in individuals who received comprehensive genetic profiling (32).

State of Practice

This study showed that oncologists are practicing more in this area (Figures 3 and 4) and are leading in terms of adoption of PM among the specialties surveyed. In terms of access to testing, it was found that this and other measures of the state of practice across the provinces varied (Figure 6). This variability in practice and access across Canada may be due to differences in access to testing services, funding, and the interpretation of the evidence or perception of benefits from province to province. It has been suggested that decision-making related to predictive genetic testing is ad hoc and variable across Canada and that a coordinated national approach is needed (33). Recommendations have been proposed for a coordinated approach to the adoption and funding of genetic testing in Ontario (34). Work in this area is critical to ensuring equitable access and improving parity of healthcare across Canada. A coordinated strategy and implementation across the country may be challenging given the disparate provincially funded and controlled health systems in Canada.

Barriers to Adoption

A lack of medical guidelines was identified by respondents (61%) as the predominant barrier to adoption, indicating a need for the development of best practices and guidelines to support the implementation of PM. Sharing practices as well as genetic testing and pharmacoeconomic information across provincial healthcare systems is also likely necessary to support efficient and cost-effective national implementation of PM.

Of the respondents, 62% agreed that medical informatics will be critical to delivering PM. Indeed, vast amounts of data will be generated with widespread adoption–and an IT infrastructure for collection, storage, analysis, interpretation, and reporting will be needed (35-37). Furthermore decision support tools, including electronic medical records (EMRs), will be needed to facilitate interpretation and point-of-care decision-making. This may pose a significant barrier in Canada where IT infrastructure and EMR

implementation is targeted for completion only in 2015 (38) and lags significantly behind other OECD nations.

Surveys of Canadian (21, 22) and US physicians (28) have reported the need for physician education for the successful adoption of PM. These studies found that a majority of physicians lack the education, training, and support for successful adoption. The present study supports these findings. Furthermore respondents indicated that they are actively pursuing more information with 73% engaging in self-study. These data support a need for formal and continuing physician education in this area. A 2010 survey of 90 medical schools in the US and Canada found that 80% have begun to incorporate pharmacogenomic training into their curriculum, however, approximately 60% considered this instruction at their school to be 'poor' and more than 80% were not considering increasing the level of instruction within the next 3 years (39).

Physicians' perceptions and knowledge of the evidence supporting the clinical and analytical validity of genetic tests for PM are obviously important for its adoption. Canadian and US studies have demonstrated that current physician knowledge, real-world data and guidelines relating to PM has often been insufficient for appropriate adoption (40); even where testing is recommended or publicly funded (41, 42). In the present study, 51% of respondents agreed that there is sufficient evidence to order genetic tests for PM. These results suggest either a need for better physician education or a need for additional supporting evidence for personalized medicine implementation. Most likely both factors are at play. Further supporting the need for more research was the finding that 53% of respondents cited the need for evidence-based clinical information as a main barrier to their use of genetic testing. Translational research is needed to provide more robust data for evaluating clinical utility and best practices for adoption and implementation within Canada's healthcare system.

Furthermore, resources that provide physicians with easy access to accurate and current information would certainly facilitate appropriate and efficient adoption of PM going forward.

Conclusions

PM based on genetic testing is currently being practiced in Canada across specialties and provinces. Many physician respondents recognize its benefits and are open to its adoption. Patients are asking their physicians about genetic testing and PM; however, physicians are not confident in discussing genetic testing and PM with their patients. This may not be surprising considering the overall lack of formal education in the field among surveyed physicians, as well as the limited time and resources available to physicians to do so. These study results also indicate variability in practice and access across Canada, among those surveyed, and point to the need for national strategies and resources that facilitate healthcare provider knowledge, training, and practice for efficient adoption. Soaring healthcare costs across industrialized countries are not sustainable. A few PM pioneers are paving the way toward demonstrating that these new molecular tests can result in better care at lower costs. Indeed, the history of innovation across many industries such as the computer, telecommunications, higher education, transportation and many other sectors has shown that previously inaccessible and expensive products and services can be transformed into accessible and low-cost product and services through technology enablers such as personalized medicine and new business models (43). Hence, if we strive for better healthcare, PM and the new models required for its full implementation present an unavoidable challenge and opportunity to transform our healthcare system into one adapted to the 21st century.

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ACKNOWLEDGEMENTS

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COMPETING INTERESTS

None

FUNDING STATEMENT

This study was funded by the Centre of Excellence in Personalized Medicine, a federally funded Canadian Centre of Excellence in Commercialization and Research (CECR).

SURVEY LIMITATIONS

Administration of the survey over the period May 26 to Sept 15, 2010 may have negatively influenced the response rate. There may have been differences in respondents based on the medium used to complete the survey (electronic vs. paper-based). The topic of genetic testing and personalized medicine may not have been relevant to all physicians that were sent the survey, which may have negatively affected the response rate. All survey results were based on physicians' self-reports. The physician contact information was purchased through a 3rd party and some data were incomplete or inaccurate.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6 - 9
		(*b*) Report category boundaries when continuous variables were categorized	6 - 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6 - 9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9 - 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12 - 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

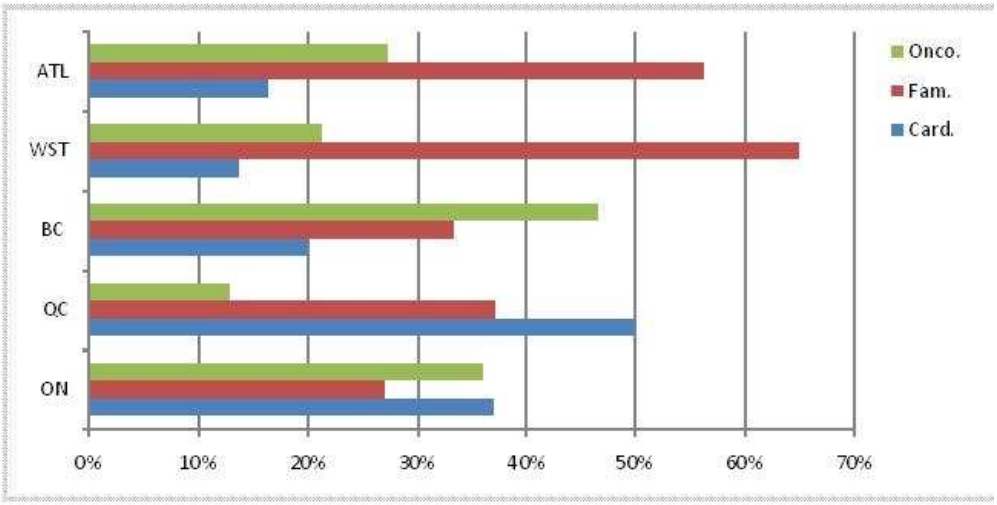

Figure 1: Distribution of respondents by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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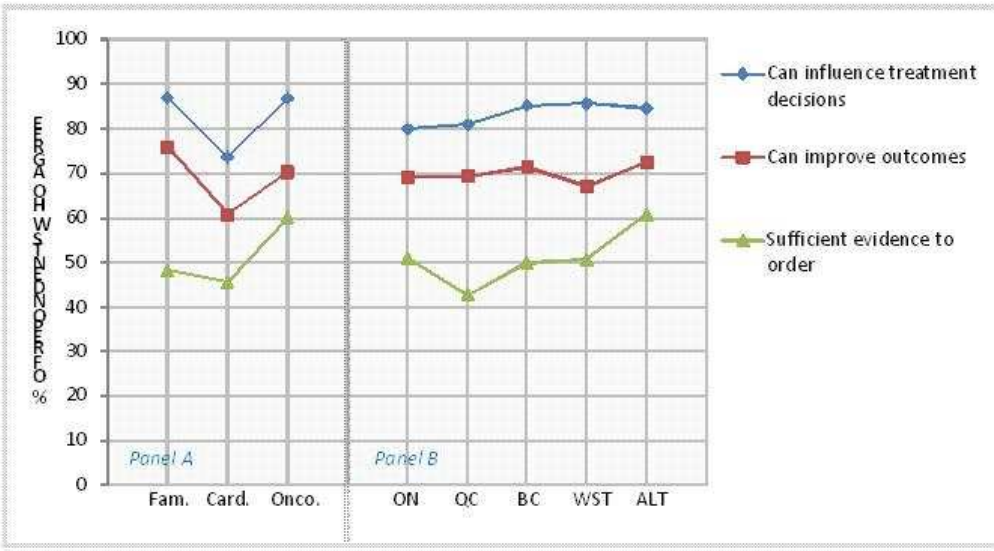

Figure 2: Respondents' perceptions of utility by specialty (panel A): family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B): Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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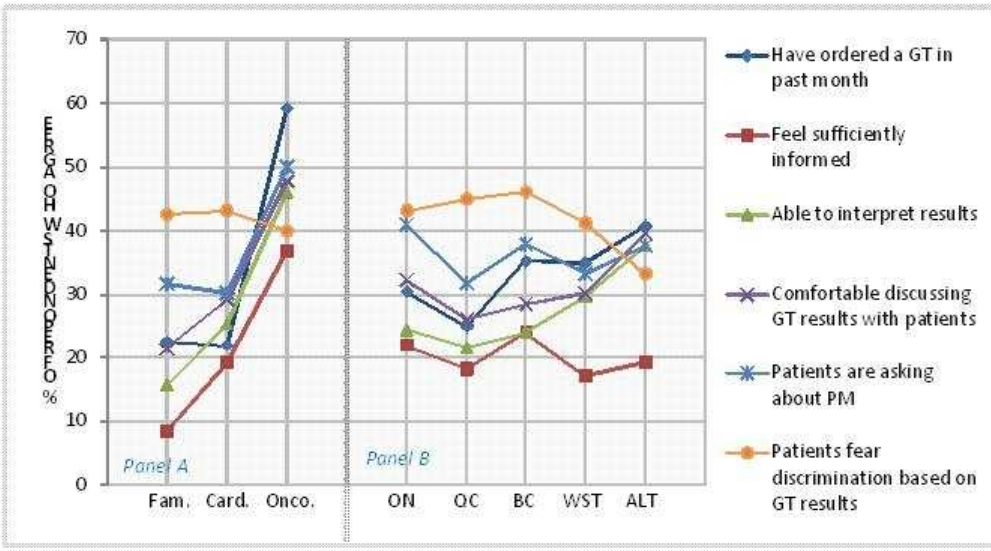

Figure 3: Measures of state of practice by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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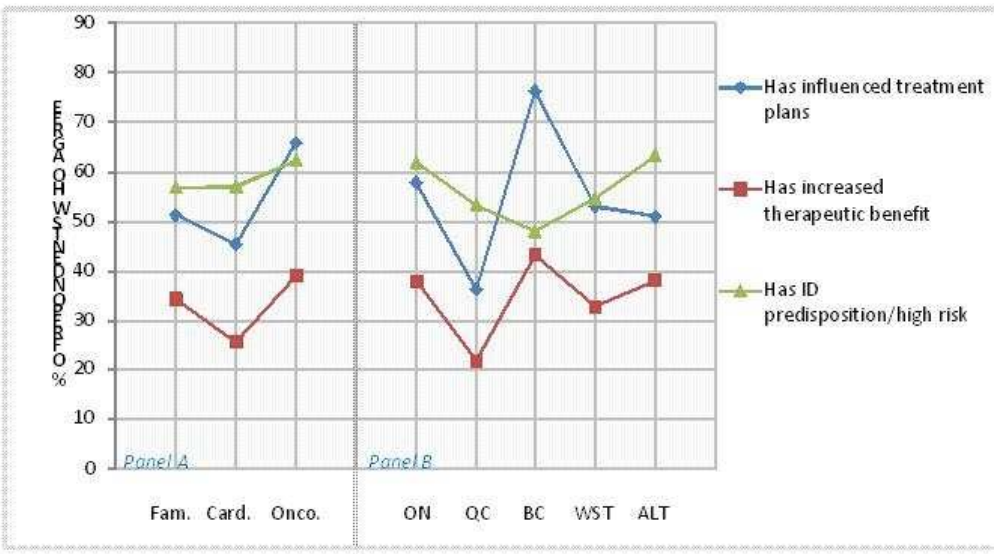

Figure 4: Comparison of reported impacts and benefits by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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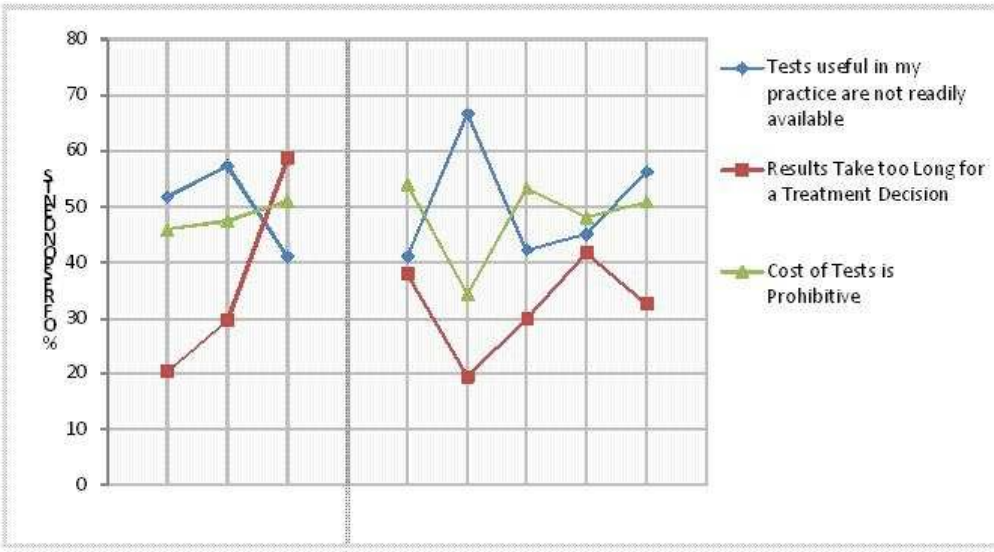

Figure 5: Measures of barriers to access by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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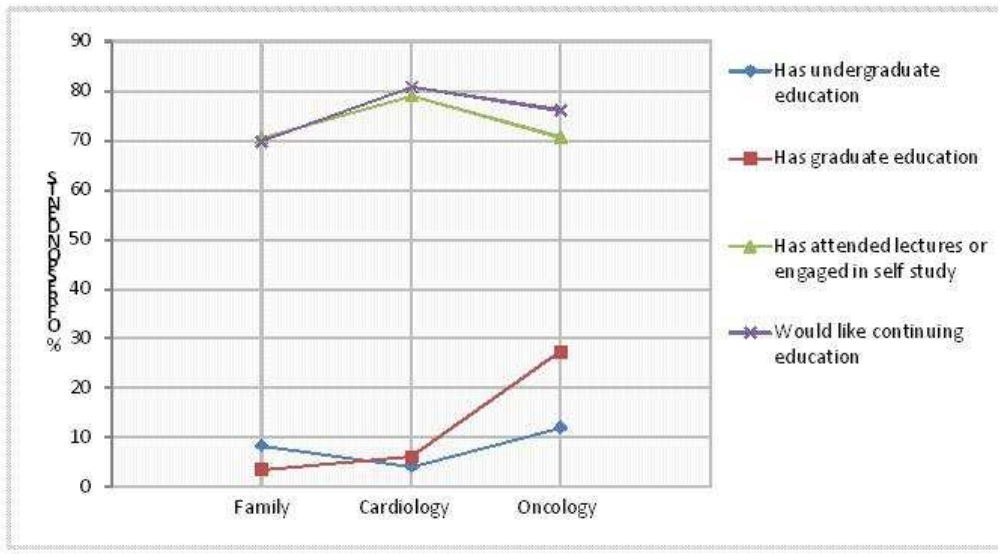

Figure 6: Measures of physician education in genetic testing and PM by specialty.

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Personalized Medicine in Canada: A Survey of Adoption and Practice in Oncology, Cardiology and Family Medicine

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Personalized Medicine in Canada: A Survey of Adoption and Practice in Oncology, Cardiology and Family Medicine

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ABSTRACT

In order to provide baseline data relating to genetic testing as a key element of personalized medicine (PM), Canadian physicians were surveyed to understand roles, perceptions and experiences in this area. The survey measured attitudes practice, observed benefits and impacts, and barriers to adoption.

A self-administered survey was provided to Canadian oncologists, cardiologists and family physicians and responses were obtained online, by mail or by fax. The survey was designed to be exploratory. Comparisons of data were made across specialties and geography.

An overall response rate of 8.3% was obtained. Of the respondents, 43%, 30% and 27% were family physicians, cardiologists or oncologists respectively. A strong majority of respondents agreed that genetic testing and PM can have a positive impact on their practice however only 51% agreed that there is sufficient evidence to order such tests. A low percentage of respondents feel that they are sufficiently informed and confident practicing in this area, however many reported that genetic tests they have ordered have benefited their patients. Half of the respondents agreed that genetic tests that would be useful in their practice are not readily available. A lack of practice guidelines, limited provider knowledge and lack of evidence-based clinical information were cited as the main barriers to practice. Differences across provinces were observed for measures relating to access to testing and the state of practice. Differences across specialties were observed for the state of practice, reported benefits and access to testing.

Canadian physicians recognize the benefits of genetic testing and PM; however they lack the education, information and support needed to practice effectively in this area. Variability in practice and access to testing across specialties and across Canada was observed. These results support a need for national strategies and resources to facilitate physician knowledge, training and practice in PM.

ARTICLE SUMMARY

Article Focus:

- Canadian physicians' perceptions and experience relating to genetic testing and personalized medicine (PM)
- Practice and impact of genetic testing and PM in Canada and across specialties
- Implications for continued adoption of genetic testing and PM in Canada across specialties

Key Messages:

- Family physicians, cardiologists and oncologists across Canada are practicing personalized medicine and recognize its benefits and potential impacts
- Physicians reported a number of barriers to the adoption of PM that are currently affecting medical practice in Canada
- The practice of and access to genetic testing and personalized medicine varies both across specialties and provinces that will have an impact on continued adoption in this area

AUTHORS' CONTRIBUTIONS

All authors were involved in the design of the survey, interpretation of results and drafting the article. In addition, Pun and Ashbury were involved in the implementation, data collection, and analysis. Three co-authors (Desjardins, Bonter and Currier) are employed by Cepmed. Pun and Ashbury were employed by PricewaterhouseCoopers LLP, and were commissioned by Cepmed to lead the survey project.

INTRODUCTION

"for the sweet ones [treatments] do not benefit everyone, nor do the astringent ones, nor are all the patients able to drink the same things"

(Hippocrates)

Personalized medicine (PM), the tailoring of medical treatment or prevention to the individual characteristics of each patient, has been enabled by recent advances in molecular biology (1). Research in the '-omic' sciences has resulted in improved understanding of the relationships between genes, proteins and disease, providing more tools for PM (2-5) and driving a shift in medical practice (6). Evidence of this 'shift' include a 66% increase in cancer-related genetic testing in Ontario between 2002 and 2008 (7), the fact that 10% of FDA approved drugs include pharmacogenomic information on their labels (8), and that genetic testing is recommended or required for at least 11 FDA approved drugs (9) and for 10 Health Canada approved drugs (based on a review of drug labeling using the Health Canada Drug Product Database). A number of applications of PM based on genetic testing are currently in use (10). Pharmacogenomics, the optimization of drug therapy based on genetic information, has been applied to improve clinical outcomes or reduce side effects and adverse events (11, 12). Targeted therapeutics, used in combination with companion diagnostics has been particularly successful in improving the treatment of cancer (13, 14). Finally, PM is being used to assess disease risk, facilitating prevention and early detection (15).

As a result of these developments PM has become an increasingly important topic for physicians, healthcare organizations and the public (16-17). There is widespread debate as to the intended and unintended consequences of PM on the quality and cost of healthcare, however many scientific and medical leaders expect PM to increase the quality of healthcare and reduce overall healthcare costs (13,18,19). A few studies have assessed the adoption of genetic testing and its impact on the role and practice of physicians in Canada (20-24). These studies focused primarily on the adoption of genetic

tests for diagnosis and treatment of cancer within Ontario's healthcare system, as well as the needs and recommendations for physician education, public education and improved coordination of healthcare delivery and genetic testing services. In order to facilitate medical and continuing professional education in personalized medicine in Canada, it is essential to have a baseline understanding of current knowledge, attitudes, and practices.

The present pan-Canadian survey of practicing oncologists, cardiologists and family doctors was designed to provide baseline data relating to genetic testing as a key element of PM in Canada with respect to attitudes, state of practice, and barriers to adoption. There were three specialties chosen as the target audience for the survey: cardiologists and oncologists were chosen as they will experience higher volumes and needs for personalized genetic testing while family physicians are usually the first point of contact for patients, and are often involved with screening for risk of disease.

METHODS

Ethics approval was received from IRB Services to survey a sample of Canadian physicians (oncologists, cardiologists, and family physicians) regarding their knowledge, training and practice in genetic testing and personalized medicine.

Physician contact information was obtained from a 3rd party including information for 859 oncologists and 1, 165 cardiologists from across Canada. A weighted sample, based on population, of family physicians (n = 2,334) from Canadian provinces, was randomly selected from contacts with email addresses. The self-administered survey was available in French and English and distributed by mail, fax and email during the period May 26 to Sept 15, 2010. Respondents submitted their responses online, by mail or by fax. Survey candidates were contacted with up to four reminders to encourage participation. The survey questions were related to demographic information, training, practice, knowledge and education in PM based on genetic testing, nature and extent of practice in this area, and of the benefits of PM and barriers to its adoption. Questions were developed based on the authors' knowledge of genetic testing and PM. A draft of the survey questions was developed from this knowledge base and a review of the literature of previous surveys conducted in other jurisdictions (28, 29). This draft survey was subsequently reviewed by 11 physicians (5 oncologists, 3 cardiologists, 3 family physicians) and their feedback was incorporated into the final survey. The survey's design was

informed by thinking about how new technologies or innovations are adopted in practice and a diffusion of innovations framework was considered (44). The survey solicited physicians' knowledge of, attitudes, and practice of personalized genetic testing to understand the relative advantage, compatibility, ease of implementation, and system response to understand adoption of personalized genetic testing. This is an initial application of this framework to the Canadian context.

Vovici software (25) was used for the online survey administration, allowing for both open-ended and close-ended questions, and menu creation for selection of pre-determined answer options for close-ended questions. All questionnaires were reviewed for completeness. The data entry protocol included separate quality review of each survey against the entered data to ensure accuracy. Survey results were analyzed using STATA software version 11.0 (26).

This study was designed to be exploratory including analyses based on descriptive statistics and bivariate associations. Inferential analyses were not pursued. Answers to survey questions were compared according to medical specialty and region or province. Responses from the Atlantic Provinces, Saskatchewan, Manitoba and Alberta were low relative to Ontario, Quebec and British Columbia (BC). Data from the Atlantic Provinces (ATL), Nova Scotia, New Brunswick, Newfoundland and Prince Edward Island, were combined and data from Saskatchewan, Manitoba and Alberta (WST) were combined.

Due to the small sample of responses for certain questions, results with more than a 5% probability of occurring by chance were excluded. Pearson chi-squared test statistics were calculated to determine whether differences according to medical specialty, region or province were statistically significant.

RESULTS

Respondent Profile

A total of 363 physicians provided responses to the survey (8.3% overall response rate). Physicians not providing direct patient care (n=16) or not practicing in family medicine, cardiology or oncology (n=6)

were excluded. Thus, the respondent group retained for the analysis comprised 341 active physicians with an adjusted response rate of 9.7%.

Of the respondents, 43%, 30% and 27% were family physicians, cardiologists and oncologists, respectively. Thirty-three percent of the respondents practiced in Ontario (ON), 20% in Quebec (QU), 24% in Manitoba, Saskatchewan and Alberta (WST), 14% in the Atlantic Provinces (ATL) and 9% in British Columbia (BC). Of the cardiologist and oncologist respondents, 73% and 79%, respectively, held academic appointments, compared to 41% of family physician respondents. One-third of survey respondents were in the 46-55 age range. The average time since completion of training for participating oncologists was 12 years, 18 years for cardiologists, and 22 years for family physicians. Family physician respondents reported working predominately in offices or clinics, cardiologist respondents predominantly in academic health science centres, community hospitals and private office/clinic and oncologist respondents predominantly in academic health sciences centres. Respondents from all specialties were represented for each geographic area as shown in Figure 1.

Attitudes and Perceptions

Respondents were asked a series of questions about their attitudes and perceptions of the usefulness of genetic testing in the context of PM, as an indicator of physicians' openness to the adoption of PM. The majority of respondents agreed that knowing a patient's genetic profile can influence treatment decision-making (83%) and importantly, can improve patient outcomes (70%). However, only 51% of respondents agreed that there is sufficient evidence in support of ordering genetic tests. The perception of the usefulness of genetic testing was similar across specialties and provinces as no significant differences were observed (Figure 2).

State of Practice

Respondents' current levels of practice and knowledge of genetic testing and PM were also assessed. The results indicate that oncologist respondents are practicing more PM with 59% reporting having ordered a genetic test in the past month compared to only 22% of general practitioners and cardiologists. Oncologists also reported feeling more sufficiently informed, more able to interpret test results and more comfortable discussing results with patients compared to other specialties (Figure 3). Overall only 21% of respondents agreed that they are sufficiently informed about PM and 29% agreed that they are able to interpret the results of genetic tests. Thirty percent of respondents agreed that they are comfortable discussing test results with patients. These measures appear to be consistent across provinces (Figure 3). The survey also assessed physicians' perceptions of the impact of genetic testing on their patients. Of the respondents, 40% agreed that their patients have expressed fears of discrimination based on genetic testing and 37% reported that their patients are asking them about genetic testing and PM. Similar reports of patients expressing fear of discrimination were observed across specialties (Figure 3); however, more oncologists (50%) reported that patients are asking about PM compared to 30% of cardiologists and 32% general/family physicians (Figure 3).

Impacts and Benefits

Respondents were asked a series of questions about the impact and benefits of genetic testing in their practice. Most respondents reported that genetic tests that they have ordered were for the purposes of identifying a genetic predisposition or risk factor for disorders (60% agreed vs. 20% disagreed) and that these tests influenced patient treatment plans (54% agreed vs. 18% disagreed). Many also reported that genetic tests that they have ordered increased therapeutic benefit for patients (42% agreed vs. 19% disagreed). Comparing across specialties (Figure 4, left panel), oncologist respondents were more likely to agree that tests that they had ordered had influenced treatment plans (67% agreed) compared to other specialties (Chi^2 P=0.006). Note that for the purpose of this study 'ordering'

means either requisitioning a test directly or facilitating access through another healthcare professional, such as a medical geneticist or other specialist (56% of respondents reported that they are responsible for ordering genetic tests for their patients and 31% reported that a geneticist is responsible for ordering tests for their patients).

Barriers to Adoption

Respondents were asked to indicate what they perceive as the main barriers to their practice in genetic testing and PM. A list of 13 barriers (Table 1) was provided. The top 5 cited barriers were: lack of clinical practice guidelines, limited provider knowledge, attitudes and awareness of benefits, lack of evidence-based clinical information, the cost of testing and a lack of time and resources to educate patients.

Access to Testing

With regards to access to appropriate genetic testing for their patients, 50% of respondents agreed that tests that they believe would be useful in their practice are not readily available, 48% indicated that the cost of genetic tests is a main barrier to the use of PM, and 33% indicated that the length of time it takes to obtain results is an important barrier to the use of PM, as the results may not be attained in adequate time to help make treatment decisions. Compared to other specialities, oncologists identified the time it takes to obtain results as a barrier to practice (59%) more often than other specialties (Figure 6). In general these measures relating to access to testing varied across provinces, possibly reflecting differences in access to genetic testing across Canada (Figure 6).

Physician Education

Most respondents reported having no formal undergraduate (92%) or graduate training (89%) in genetic testing and PM. Interestingly, 73% of respondents have attended university lectures or engaged in self-study and 75% would like more continuing education in this area. More oncologists reported having graduate training in this area (27%) compared to other specialties (Chi^2 P=0.0001).

DISCUSSION

Attitudes, Impacts and Benefits

The results of this study indicate that Canadian physicians responding to the survey are optimistic about the promise of PM, and open to its use. The majority of respondents agreed that genetic testing as a component of PM can influence treatment plans (83%) and improve outcomes (70%). This is consistent with a recent survey of molecular oncology testing (MOT) in Ontario where it was reported that MOT is expected to become increasingly prevalent in all areas of diagnosis, prognosis, and treatment in the foreseeable future (21). Similar findings from another Canadian survey (27) and a study of 10,000+ physicians in the United States (28) also support widespread awareness among physicians of the current value and potential impact of PM. Positive perceptions among Canadian physician respondents may facilitate efficient and appropriate adoption of PM into practice.

Patient engagement has been identified as a possible factor in physicians' attitudes toward adopting new practices (29, 30). Thirty-seven percent of respondents reported that patients are asking them about genetic testing and PM. Physicians also reported patients expressing fears of discrimination based on genetic testing (Figure 4). Although no existing Canadian legislation specifically prohibits genetic discrimination, a level of protection is provided through the Canadian Human Rights Act (Art. 3) and Canada's Personal Information Protection and Electronic Documents Act. Steps have been taken to strengthen these protections. In April of 2010, Bill C-508, an act to amend the Canadian Human Rights Act to specify genetic discrimination was introduced in parliament (31). Few respondents indicated that patient anxiety concerning test results is a barrier to their practice (Table 1). This is consistent with a recent US study of more than 2,000 individuals, which found no post-test anxiety or adverse outcomes in individuals who received comprehensive genetic profiling (32).

State of Practice

This study showed that oncologists are practicing more in this area (Figures 3 and 4) and are leading in terms of adoption of PM among the specialties surveyed. In terms of access to testing, it was found that this and other measures of the state of practice across the provinces varied (Figure 6). This variability in practice and access across Canada may be due to differences in access to testing services, funding, and the interpretation of the evidence or perception of benefits from province to province. It has been suggested that decision-making related to predictive genetic testing is ad hoc and variable across Canada and that a coordinated national approach is needed (33). Recommendations have been proposed for a coordinated approach to the adoption and funding of genetic testing in Ontario (34). Work in this area is critical to ensuring equitable access and improving parity of healthcare across Canada. A coordinated strategy and implementation across the country may be challenging given the disparate provincially funded and controlled health systems in Canada.

Barriers to Adoption

A lack of medical guidelines was identified by respondents (61%) as the predominant barrier to adoption, indicating a need for the development of best practices and guidelines to support the implementation of PM. Sharing practices as well as genetic testing and pharmacoeconomic information across provincial healthcare systems is also likely necessary to support efficient and cost-effective national implementation of PM.

Of the respondents, 62% agreed that medical informatics will be critical to delivering PM. Indeed, vast amounts of data will be generated with widespread adoption–and an IT infrastructure for collection, storage, analysis, interpretation, and reporting will be needed (35-37). Furthermore decision support tools, including electronic medical records (EMRs), will be needed to facilitate interpretation and point-of-care decision-making. This may pose a significant barrier in Canada where IT infrastructure and EMR

implementation is targeted for completion only in 2015 (38) and lags significantly behind other OECD nations.

Surveys of Canadian (21, 22) and US physicians (28) have reported the need for physician education for the successful adoption of PM. These studies found that a majority of physicians lack the education, training, and support for successful adoption. The present study supports these findings. Furthermore respondents indicated that they are actively pursuing more information with 73% engaging in self-study. These data support a need for formal and continuing physician education in this area. A 2010 survey of 90 medical schools in the US and Canada found that 80% have begun to incorporate pharmacogenomic training into their curriculum, however, approximately 60% considered this instruction at their school to be 'poor' and more than 80% were not considering increasing the level of instruction within the next 3 years (39).

Physicians' perceptions and knowledge of the evidence supporting the clinical and analytical validity of genetic tests for PM are obviously important for its adoption. Canadian and US studies have demonstrated that current physician knowledge, real-world data and guidelines relating to PM has often been insufficient for appropriate adoption (40); even where testing is recommended or publicly funded (41, 42). In the present study, 51% of respondents agreed that there is sufficient evidence to order genetic tests for PM. These results suggest either a need for better physician education or a need for additional supporting evidence for personalized medicine implementation. Most likely both factors are at play. Further supporting the need for more research was the finding that 53% of respondents cited the need for evidence-based clinical information as a main barrier to their use of genetic testing. Translational research is needed to provide more robust data for evaluating clinical utility and best practices for adoption and implementation within Canada's healthcare system.

Furthermore, resources that provide physicians with easy access to accurate and current information would certainly facilitate appropriate and efficient adoption of PM going forward.

Conclusions

In the absence of baseline data in provider knowledge and practice of PM in Canada, our study fills this important gap by providing a baseline upon which we can build. While other jurisdictions may have more resources in place to support PM, including those that facilitate provider and public understanding, Canada is lagging. PM based on genetic testing is currently being practiced in Canada across specialties and provinces. Many physician respondents recognize its benefits and appear to be open to its adoption. They report that patients are asking them about genetic testing and PM; however, most physician respondents are not confident in discussing genetic testing and PM with their patients. This may not be surprising considering the overall lack of formal education in the field among surveyed physicians, as well as the limited time and resources available for physicians to do so. These study results also indicate variability in practice and access to genetic tests across Canada, among those surveyed. In addition, the study results point to the need for pan-Canadian strategies and resources that facilitate healthcare provider knowledge, training, and practice at the undergraduate and graduate levels, and through targeted continuing professional education interventions.

Soaring healthcare costs across industrialized countries are not sustainable. A few PM pioneers are paving the way toward demonstrating that these new molecular tests may result in better care at lower costs. Indeed, the history of innovation across many industries such as the computer, telecommunications, higher education, transportation and many other sectors has shown that previously inaccessible and expensive products and services can be made more accessible at lower cost (43). Hence, if we strive for better healthcare, PM and the new models required for its full implementation present an unavoidable challenge and perhaps an opportunity to transform our healthcare system into one adapted to the 21st century.

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COMPETING INTERESTS

None

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SURVEY LIMITATIONS

Administration of the survey over the period May 26 to Sept 15, 2010 may have negatively influenced the response rate. There may have been differences in respondents based on the medium used to complete the survey (electronic vs. paper-based). The topic of genetic testing and personalized medicine may not have been relevant to all physicians that were sent the survey, which may have negatively affected the response rate. All survey results were based on physicians' self-reports. The physician contact information was purchased through a 3rd party and some data were incomplete or inaccurate.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	6
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6 - 9
		(*b*) Report category boundaries when continuous variables were categorized	6 - 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6 - 9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9 - 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12 - 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

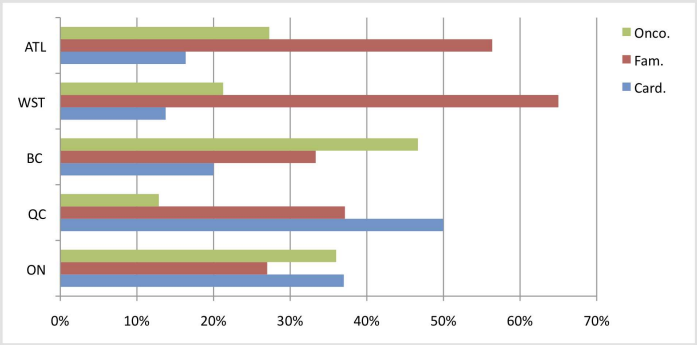

Figure 1: Distribution of respondents by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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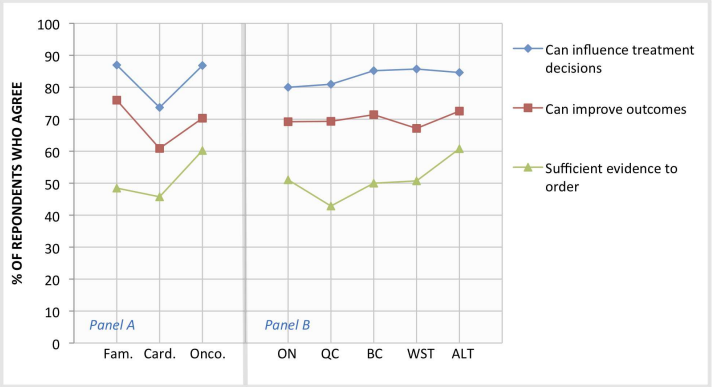

Figure 2: Respondents' perceptions of utility by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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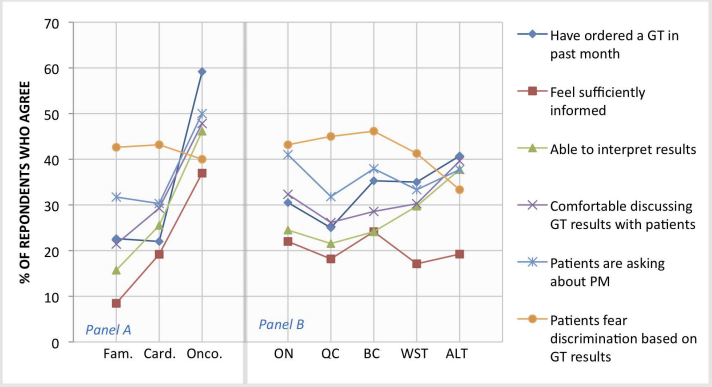

Figure 3: Measures of state of practice by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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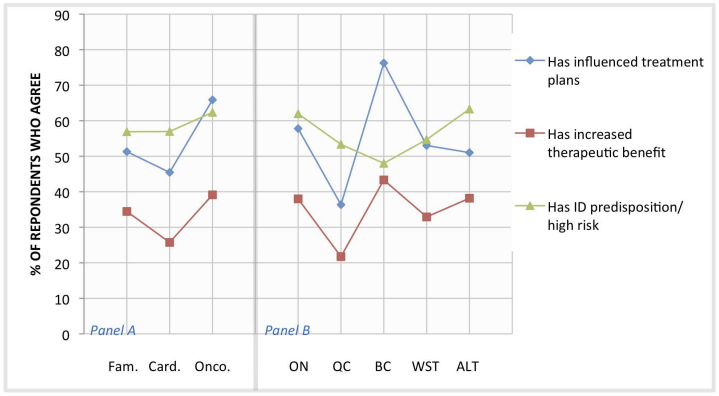

Figure 4: Comparison of reported impacts and benefits by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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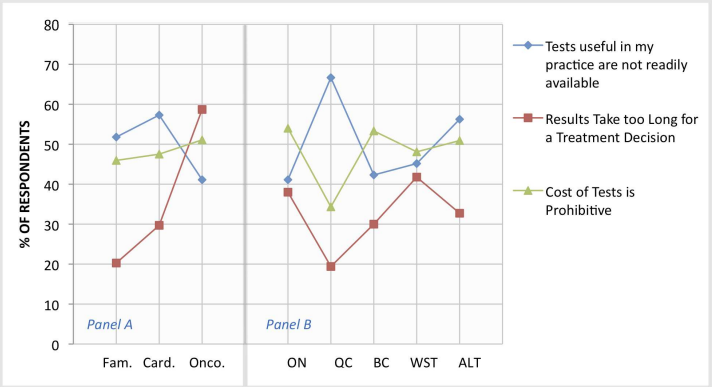

Figure 5: Measures of barriers to access by specialty (panel A); family medicine (Fam.), Cardiology (Card.) and oncology (Onco.) and by geography (panel B); Ontario (ON), Quebec (QC), British Columbia (BC), Western Provinces (WST) and Atlantic Provinces (ALT).

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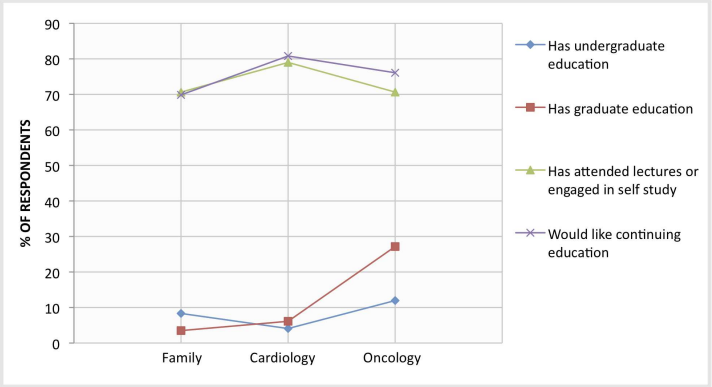

Figure 6: Measures of physician education in genetic testing and PM by specialty.

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