PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Personalized Medicine in Canada: A Survey of Adoption and Practice in Oncology, Cardiology and Family Medicine
AUTHORS	Bonter, Katherine; Desjardins, Clarissa; Currier, Nathan; Pun, Jason; Ashbury, Fredrick

VERSION 1 - REVIEW

REVIEWER	***Colleen M. McBride, Ph.D.*** Chief, Senior Investigator National Human Genome Research Institute National Institutes of Health 31 Center Dr., Bldg 31, B1B54b Bethesda, MD 20892 I have no competing interests to report
REVIEW RETURNED	11-Mar-2011

THE STUDY	This is a descriptive study and hence a formal research question is not necessary. However, in this case it is unclear what gap in knowledge is filled by this descriptive study. The rationale for the design of the study, the sampling strategy by specialty is unclear. Moreover, the response rate is low and it is unclear whether the response rate varied by specialty group which would be germane to interpreting the findings.
RESULTS & CONCLUSIONS	Again, the research question is not entirely clear with respect to why a survey of physicians is needed and what the implications of the results are for the field. Interpretation and conclusions are weak in that they reflect the current state of affairs in a highly self-selected group of providers. this makes it very difficult to discern how these results might be applied. Moreover, the results echo the results of many other physician surveys and thus add little to the field
REPORTING & ETHICS	Some of the rationale for the study and the sampling strategy are not explained.

REVIEWER	***Prof Don Iverson*** Pro Vice-Chancellor (Health) and Executive Director, Illawarra Health & Medical Research Institute University of Wollongong Australia
REVIEW RETURNED	19-Mar-2011

THE STUDY	The sampling approach is acceptable but with an 8.3% response rate it is not reasonable to assume that the respondents are representative of participants in the sample frame. The authors comment on why the response rate may be lower than usual with physician surveys.

	The methods section does not include a description of how the survey items were developed or selected; there is also no indication of the theoretical underpinning, if any, of the survey sections - this is most relevant for the 'openness to adoption' survey section. The supplemental documents should not be reported in the manuscript - they are appropriate in the form of supplemental documents.
RESULTS & CONCLUSIONS	The results are credible for the 363 respondents but cannot be considered credible for the categories of respondents given the 8.3% response rate. Within each of the three survey sections the responses seem credible, eg, that the greatest barrier to physicians ordering genetic tests is the lack of guidelines and that oncologists are the most likely of the three physician groups to have ordered genetic tests in the last month. In the Discussion section the authors state, for example, that "...Canadian physicians are optimisti about the promise of PM, and open to its adoption". This is a rather definitive statement given the 8.3% response rate and the authors' comments in the Survey Limitations section where they state "...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". It would be appropriate for the discussion to be more cautious in commenting on views and practices of Canadian physicians as opposed to those held by the survey respondents.
GENERAL COMMENTS	Two major issues should be addressed in the revision - a description of how the survey was developed including the theoretical underpinnings, if any that guided selection/development of items in the three survey sections; and the need to take a more cautious approach in the Discussion section given the low response rate.

REVIEWER	***Christopher-Paul Milne, DVM, MPH, JD*** Associate Director Tufts University Medical School Center for the Study of Drug Development Boston, MA, USA
REVIEW RETURNED	21-Mar-2011

THE STUDY	Patients - study does not involve patients (at least directly) Supplemental Documents - there are not any that need to be reported in manuscript
RESULTS & CONCLUSIONS	The research question is open-ended, i.e., collecting baseline data on an evolving field of practice. The response rate is low, ~10%, so whether baseline data is representative of the broader population of practitioners intended as the target sample frame will be established by the accumulation of surveys similar to the one reported here over time. Authors acknowledge this as a limitation of the study (but in this context such a response rate is normal).

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

"...it is unclear what gap in knowledge is filled by this descriptive study."

• We agree that it is important to outline the gap in knowledge, and believe the following statement in the introduction sufficiently describes this gap (because the other two reviewers did not express a similar concern):

“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 personalized medicine in Canada…”

• For added clarity, we have added this statement to the Abstract to highlight the rationale:

“In order to provide baseline data relating to genetic testing as a key element of personalized medicine (PM) in Canada, physicians were surveyed to understand roles, perceptions and experiences in this area.”

“...not entirely clear with respect to why a survey of physicians is needed, and what the implications of the results are for the field.”

• A major driver of this research was the fact that there is very limited literature on physician practice of genetic testing and personalized medicine in Canada. Secondly, to facilitate medical and continuing professional education and personalized medicine, it is essential to have a baseline understanding of current knowledge, attitudes, and practices (particularly among the three disciplines investigated in this study who are expected to play an increasing role in personalized genetic testing as new technologies emerge). For increased clarity, we have added the following statement to the introduction:

“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.

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.”

• While we agree the response rate was low, we believe the descriptive results do provide implications for the field for educators, policy makers, and health care providers, as already outlined in the conclusion of the paper.

“The rationale for the design of the study, the sampling strategy by specialty is unclear.”

• Oncology and cardiology were chosen because these are specialties with increased roles in genetic testing and personalized medicine, and both specialities have specific genetic tests with predictive and prognostic value. Our revision, to the introduction, noted above, we hope serves also to satisfy the reviewers concern.

“Cardiologists and oncologists will experience higher volumes and needs for personalized genetic testing…”

• We have also added, a clearer rationale for the inclusion of family physicians in our study, by adding the following sentence in the same section of the introduction:

"…family physicians are usually the first point of contact for patients, and are often involved with screening for risk of disease."

"…the results echo the results of many other physician surveys and thus add little to the field."

• We are not aware of any publication of similar scope and size with regards to genetic testing and personalized medicine in oncology, cardiology, and family medicine in Canada, and believe the local (national) perspective is valuable to the field. We have cited relevant physician surveys in other jurisdictions and commented how they compare or not to our own findings. As clarified above, we have emphasized how this work is specific to our Canadian jurisdiction.

Reviewer 2
"The methods section does not include a description of how the survey items were developed or selected; there is no indication of the theoretical underpinning, if any, of the survey sections – this is most relevant for the 'openness to adoption' survey section."

• We accept the reviewer comment that a theoretical basis for the questions were not provided, especially in the 'openness to adoption' section. We have revised the methods section of the manuscript to include:

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. 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. 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.

• We have revised the results and discussion sections previously entitled 'Openness to Adoption' to 'attitudes and perceptions,' and revised text throughout the manuscript to reflect this concept rather than drawing conclusions to overall adoption of PM by physicians in Canada.

"It would be appropriate for the discussion to be more cautious in commenting on views and practices of Canadian physicians as opposed to those held by the survey respondents."

• We accept the reviewers comments, and have revised text in the discussion and conclusion accordingly.

Reviewer 3
"The response rate is low, ~10%, so whether baseline data is representative of the broader population of practitioners intended as the target sample frame will be established by the accumulation of surveys of similar to the one reported here over time."

• We agree with the reviewer that the current study had a low response rate (as acknowledged in our limitations), and have revised the discussion and conclusion text to eliminate any generalizations to physicians in Canada.

VERSION 2 - REVIEW

REVIEWER	***Don Iverson***
REVIEW RETURNED	25-Apr-2011

THE STUDY	No information from the supplemental documents need be included in the manuscript.
RESULTS & CONCLUSIONS	While the results are credible for the responding sample they are likely not credible for the three study populations given the low response rate. However, the authors have been more cautious in the revised manuscript in noting the results only extend to the responding samples of the three study populations. In terms of the final message the authors note the variability in practice and access to genetic testing and PM across Canada, and the lack of comfort many physicians have in discussing genetic testing and PM with their patients. If the overriding message is that significant education efforts are required, it is more implicit than explicit in the manuscript.

REVIEWER	***Colleen M. McBride***
REVIEW RETURNED	10-May-2011

THE STUDY	The conclusions to the manuscript tend to be valenced towards the high end of positive rather than taking a more balanced approach given that few of the tests currently have any established clinical utility. Also seems that there are limits to the study findings that warrant some mention.
RESULTS & CONCLUSIONS	As mentioned above, the authors inadvertently extend some of the hype of future potential that has yet to be established. It would be better to stay closer to the objective of the manuscript and tell us what gaps are filled by these findings and why that is important. Instead the conclusions read a bit like an advert for new genetic technologies.
GENERAL COMMENTS	This is a revised manuscript and the authors were quite responsive to the prior review. My ongoing concern, however, with this manuscript is that it doesn't add much to the literature and echoes some of the same recommendations about "provider knowledge, training and practice for efficient adoption." The authors seem to assume that these new technologies will benefit health care even when there is as yet no evidence to support this supposition.

VERSION 2 – AUTHOR RESPONSE

Dear Mr. Sands,
Thank-you for the comments from the reviewers and the opportunity to respond. We have revised the conclusion to clarify that this study's goal was to establish a baseline of knowledge and practice of personalized medicine in Canada. We continue to disagree with the reviewer that indicated it does not contribute to the literature, as no baseline study of this topic area has been done to date in Canada. There are factors in Canada, such as a smaller population and the public nature of our health care system, that warrants independent analyses, which can and has often yielded different results to the

US. We have also revised the language of the conclusion, to reflect the reviewers comment that that in some cases there is not yet evidence to support the benefit of personalized genetic testing.

Thank-you and please let me know if there is anything else our team can provide to you in advance of publication.

Sincerely,
Dr. Fred Ashbury