Article details: 2017-0005	
Title	Follow-up imaging after nephrectomy for cancer in Canada: urologists' compliance with guidelines using observational data
Authors	Alice Dragomir PhD, Armen Aprikian MD, Anil Kapoor MD, Antonio Finelli MD, Frédéric Pouliot MD, Ricardo Rendon MD, Peter C. Black MD, Ronald Moore MD, Rodney H. Breau MD, Jun Kawakami MD, Darrell Drachenberg MD, Jean Baptiste Lattouf MD, Simon Tanguay MD
Reviewer 1	Dr. Christopher John Longo
Institution	McMaster University, Business, Hamilton, Ont.
General comments (author response in bold)	This manuscript investigates the use of chest and abdominal imaging for nephrectomy patients in Canada over a 72 month period. It highlights the overuse and underuse of imaging in relation to Canadian guidelines and their financial implications for the Canadian health care system. General comments This is a clear and concise description of the research undertaken, however I find that the interpretations do not explore the discrepancies sufficiently 1. In the discussion/interpretation although some consideration has been given to both the under and over utilization of imaging a more fulsome discussion would have been helpful. As just one illustration in the case of overutilization of abdominal imaging no possible explanation was put forward. It strikes me that one possible reason is related to communication between facilities, often requiring that repeat procedures are needed to confirm a patient's current status. Although I am unclear what level of detail is available in the dataset it might be possible to see if repeat tests in a short time period (less than 1 month) at different centres might suggest that this is the primary cause of overuse. If this example were true, and I have no data at present to support this, then the conclusions would be quite different. Rather than suggesting an issue with adherence to guidelines the conclusion would be to determine a better method to ensure sharing of data between facilities to reduce duplication of tests. **Authors' response: We completely agree with reviewer's comment. When calculating the number of imaging tests, repeat tests performed in within a 30-day interval, have been excluded from the calculation. In the page 4, 2nd paragraph it was mentioned : ''Any imaging tests performed during the first 28 postoperative days, as well as repeated tests were excluded from this calculation. A test was considered to be a repetition if the same test was identified at the same location within the previous 30 days.''** 2. Similarly it is less clear why underuse for chest imaging occurs. Were any regressions considered? Although these appear to be teaching hospitals and hence more urban than rural is there any literature that looks different when rural centres are considered. Is there any information on whether patients traveled significant distances to receive treatment and if so might there be a difference in these patients versus those who were more local. **Authors' response: As specified in the interpretation section ''The results revealed under-compliance of chest imaging of 29.3%'', which are very similar with the results of 2 other studies mentioned in the 3rd paragraph of the interpretation section. In addition, the CKCis database does not include information of patients' distance traveled to receive treatment. However, if this were a factor explaining the underuse for chest imaging, this would also affect the use of abdominal tests. The overuse of abdominal test does not sustain this hypothesis.** Specific comments 1. Pg. 3 of 20 line 13 "is prospectively populated database" should be " is A prospectively populated database" Authors' response: This was done. 2. Pg. 5 of 20 line 56 "…chest and abdominal imaging tests was in agreement…" should be "…chest and addominal tests WERE in agreement…" **Authors' response: This was done.** 3. Pg. 6 of 20 line 27 "…four provinces.." should be "…five provinces…" Authors' response: The sentence was deleted as it was relating with the cost evaluation. 4. Pg. 9 of 20 line 34 State "difference in cost of chest CT and chest XR is considerable". It may be helpful to state which is more expensive (noted this shows up in table 6, but without knowing where this might be placed in the final proofs, best to state it here). **Authors' response: The sentence was deleted as it was relating with the cost evaluation.** 5. Pg. 11 of 20 Figure 1 It appears that the column on the right are the excluded cases. I would consider either putting a box around the three categories of exclusions and labeling it as such or make it clear that the right column is a list of exclusions. **Authors' response: This was done.**
Reviewer 2	Ms. Shelly-Anne Li MSc
Institution	University of Toronto, Toronto, Ont.
General comments (author response in bold)	1. Abstract: Please include a sentence describing how the evaluation of compliance was done. **Authors' response: The following sentence was added to the Methods section: ''The level of compliance was measured by weighted Kappa and Pearson correlation statistics. Multivariate logistic regression was used to evaluate factors associated with noncompliance of chest and abdominal imaging tests in the post-nephrectomy surveillance period.''** Introduction: 2. Please insert references for phrases "Despite the overall underutilization of post-nephrectomy imaging, concerns regarding possible overuse in patients at low risk for recurrence and underuse in those at greater risk have been suggested" and "new surveillance imaging guidelines may reduce unwarranted variability and promote risk-based, cost-effective post-nephrectomy management." If the latter is a proposal from this study's authors, I suggest removing it, because it is not backed up by published empirical research (unless

	there is - which should be referenced). **Authors' response: Both phrases have been removed.** 3. You introduced two guidelines in the introduction. Please specify which guidelines you are referring to when you conducted this study. If you intended to refer to both of them, please make this explicit. And, which section(s) of the guidelines form the basis of your research? It would be highly unlikely that urologists are noncompliant for all of the recommendations listed out on the guidelines. **Authors' response: The phrases were modified to reflect this comment as follows: '' In 2009, the Canadian Urological Association (CUA) approved guidelines for the follow-up of patients with localized and locally advanced RCC after partial or radical nephrectomy, with a reprint in 2012 (9, 10).'' While the 1st publication refers entirely to the follow-up after radical and partial nephrectomy, the 2nd publication refers to this 1st publication in the section entitled : Surveillance schedules after radical or partial nephrectomy.** 4. Also, please elaborate on the rationale of studying both the compliance with guidelines for and cost for surveillance together. Why is it so important to study both together? What are the potential implications for this? Authors' response: We excluded the cost of surveillance from the current study. 5. The paragraph about cost of surveillance seem to come out of nowhere (starting on Line 43). Please tie this paragraph with a connecting statement from previous paragraph. **Authors' response: We excluded the cost of surveillance from the current study.** 6. For phrase "CKCis is a multicentre collaboration of 15 academic hospitals in six Canadian provinces." - which six Canadian provinces? This may help readers understand the demographics of the participants a bit better. **Authors' response: The phrase was completed as follow: ''CKCis is a multicentre collaboration of 15 academic hospitals in six Canadian provinces: Alberta, British Colombia, Quebec, Ontario, Manitoba and Nova Scotia''. page 3** Methods: 7. Please provide justification on using the prospective cohort design. **Authors' response: We added the following phrase: ''To evaluate compliance with the 2009 published guidelines, only prospectively collected patients were included.'' Additionally, excluding retrospective patients decreased the risk of survival and selection biases.** 8. Line 51: Please specify what you mean by 'Canadian level' - isn't the cohort study conducted in Canada? Authors' response: This was related to the cost evaluation section, which was deleted. Discussion: 9. Please include the limitations of the methods you used for extrapolation to arrive at the expected costs for your cohort under investigation. Also, I suggest including a line about the limitation of not contacting urologists for further information about this cohort. It is likely that these urologists have legitimate reasons for over or under screening. Authors' response: This was related to the cost evaluation section, which was deleted. In addition, the urologists treating the patients included in this study, are all co-authors in this study. As such they agreed with the results and the manuscript of this study. 10. Please elaborate on the generalizability and implications of the study findings. **Authors' response: The limitation section was modified as follow: ''First, all the patients included in the cohort were followed in academic institutions, therefore results may have limited generalizability in non-academic institutions or in countries with very different surveillance patterns.''** General: 11. Please ensure that the manuscript follows STROBE guidelines. 12. For example, how did you eliminate any sources of bias? Authors' response: As suggested the STROBE checklist was used. This is available upon request.
Reviewer 3	Dr. Susan Baxter
Institution	Vancouver, BC
General comments (author response in bold)	You have written an excellent, detailed and readable economic analysis for which you are to be commended. Your data is extremely well presented and thorough and on first glance there is little wrong with this piece. However, given that the guidelines on which you base your cost analysis are - by your own admission as well as by the guideline writers' - flawed, the amounts you cite need to be presented with less certitude. **Authors' response: We thank the reviewer for the appreciation of our study.** 1. Your study, nevertheless, has the potential to further the guidelines and begin that open "discussion and create awareness" you mention at the end of your piece, provided you shift your focus somewhat, acknowledge that the costs you cite are, at best, estimates (based on poor quality evidence) and expand on the possible reasons for the postsurgical surveillance discrepancies between actual and observed tests. You suggest at the very end that "there might be "a discrepancy in recurrence patterns between the guideline recommendations (i.e. the available evidence) and what urologists actually encounter in their clinical practice" and this bears further discussion. Given that you have rather a lot of MD's on your author roster and are at the Department of Urology, you would seem to have access to the necessary expertise to do this, even anecdotally. **Authors' response: The cost component was removed from the manuscript and so, no further acknowledgement of the estimates quality was needed. Yes indeed, all urologists treated the patients included in the study are co-authors in this study.** 2. Somewhat concerning is the fact that you never mention patients - preferences, fears, concerns, etc. - and patients are more than a collection of objective factors like age and sex. Cancer is an emotive term. Patients with more minor disease can often be more fearful (and symptomatic) than those with more obvious signs, which could explain some of the discrepancy between T2 and 3 in terms of abdominal imaging; patients could report more problems. People are often not that precise in describing the site of their pain or

	discomfort (scar tissue? postsurgical pain?) and I am unclear as to precisely how one would differentiate, as a patient, between chest and abdominal regions or know exactly how a physician would differentiate between those regions if a patient describes problems. **Authors' response: We completely agree with the reviewer. As the available data didn't allow to account for patient reported symptoms or outcomes, we add this as a limitation of this study.** **(I appreciate that your disciplinary aim is health economics, but the basis for your cost analysis is medical evidence/guidelines. And EBM is three pronged: evidence, clinician expertise and individual patient issues.)** In terms of imaging technologies, there's no question that culturally we tend to value what is perceived as "objective" information far more than other types of information; this could play a part in both doctors' and patients' affinity for overuse of the "newer" CT's versus old fashioned X-rays. A journal you might consult for articles around this topic is Social Science and Medicine. **Authors' response: We thank the reviewer for the suggestion.** 3. Finally, on a somewhat pedantic note, your first reference to the guidelines (5) contains a non-functional link. The subsequent one does (17) but I am not sure I skimmed the correct guidelines. And any reference that contains a link needs to specify the date you accessed it. **Authors' response: We fixed this problem.** Overall you make some excellent, thought provoking points about guidelines and clinical practice (e.g., how guidelines and imaging technologies may be resulting in incidental findings of tumours that don't necessarily want to be found) and your brief comments regarding the disconnect between the clinical picture and guidelines, notably in your Interpretation section, are most interesting. Your economic analysis is valid and detailed but in my view it loses legitimacy when you cite too-precise amounts when the guidelines do not seem that reliable. Here your language needs to reflect that uncertainty: you need more of the subjunctive, more terms such as "might" or "could"; qualifiers along the lines of "if the guideline recommendations are correct then approximately X amount could be saved over such and such period of time". The broader points, framed within your economic analysis, could transform this piece from a slightly questionable cost analysis to another step forward towards the next version of those guidelines. **Authors' response: We thank the reviewer for the appreciation of our study. Although, the cost analysis was removed from the present study, we will try to detail it and further publish it as a separate paper.**