## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Cohort Profile: The Upper Gastrointestinal Cancer Registry (UGICR) - a clinical quality registry to monitor and improve care in upper gastrointestinal cancers |
| **AUTHORS** | Maharaj, Ashika; Holland, Jennifer; Scarborough, Ri; Evans, Sue; Ioannou, Liane; Brown, Wendy; Croagh, Daniel; Pilgrim, Charles; Kench, James; Lipton, Lara; Leong, Trevor; McNeil, John; Nikfarjam, Mehrdad; Aly, Ahmad; Burton, Paul; Cashin, Paul; Chu, Julie; Duong, Cuong; Evans, Peter; Goldstein, David; Haydon, Andrew; Hii, Michael; Knowles, Brett; Merrett, N; Michael, Michael; Neale, Rachel E.; Philip, Jennifer; Porter, Ian; Smith, Marty; Spillane, John; Tagkalidis, Peter; Zalcberg, John |

## VERSION 1 – REVIEW

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| **REVIEWER** | Joonas H. Kauppila<br>University of Oulu, Finland and Karolinska Institutet, Sweden |
| **REVIEW RETURNED** | 07-Jun-2019 |

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| **GENERAL COMMENTS** | The authors Maharaj et al present a cohort profile on a prospective upper GI cancer clinical quality registry. I want to congratulate the authors on their efforts to build this kind of registry, which will surely improve the clinical management and registry research of upper gi cancers in the Australia. The manuscript is mainly well-written and flows nicely. The methods of data collection and the responsibilities of each group have been clearly described. The strengths and limitations are frankly described and seem adequate. I have some specific comments on the manuscript that require authors' attention.<br><br>1. The study is submitted as a cohort profile. In the author instructions of the BMJ Open, it is recommended to present the characteristics of the patients in the cohort, as well as drop-out rates, which has been done in the cohort profiles published earlier in the Journal. However, no data from the currently collected material has been presented. I feel that the authors should present some basic data from the cohort on a certain time period (i.e. characteristics, survival), as well as the completeness of the data and variables. In its present form the manuscript would be more suitable to be submitted as a study protocol, not a cohort profile.<br><br>2. For me as a non-Australian reviewer/reader, it is unclear what is the nationwide coverage of the cohort. If the cohort is nationwide, it should be clearly identified as such in the title, abstract and the text. If not, the approximate coverage of the population and the states/areas should be indicated in the methods section. A map of the current situation, or an additional table, might help. |

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| | 3. What is the involvement of the private sector in relation to the treatment of these cancers in Australia? To what extent the private sector is involved in the collection of the data (if applicable)? Please elaborate in the protocol.<br><br>4. Which PROs have the authors considered? EORTC or other validated measurements? How have they planned the collection and follow-up of the PROs? |

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| **REVIEWER** | Dr Sam Merriel<br>University of Exeter, UK |
| **REVIEW RETURNED** | 28-Jun-2019 |

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| **GENERAL COMMENTS** | This manuscript outlines the establishment, governance and structure of a national upper gastrointestinal (UGI) cancer registry in Australia. The registry will recruit patients with a new diagnosis of UGI cancers from participating institutions, and collect detailed clinical data about their tumour, and their treatment outcomes. The registry steering committee intends to integrate patient reported outcomes into the minimum dataset, and act as a platform for future research on UGI cancers. The manuscript is well-written, flows well for the reader, and uses tables and figures appropriately to support the text.<br><br>There are a few points the authors need to consider for this manuscript prior to publication:<br><br>1. The article is described as a cohort profile, and it mentions that the registry opened in 2015, but no data is presented about any members of the cohort to date. It would be of interest to readers and potential future research collaborators to know at least something about initial recruitment figures, patient demographics, missing data and early trends in the data. If there is no data available yet, reference to a cohort profile should perhaps be removed.<br>2. The authors very rightly point out the poor outcomes for UGI cancers that persist today in Australia and globally, particularly for pancreatic cancer, and this provides a strong justification for the establishment of a national clinical quality registry for these cancer types. A major driver for these poor outcomes is stage at diagnosis, which is often late for UGI cancers, and thus improving early diagnosis needs to be a major focus to achieve better outcomes for UGI cancer patients. Improving early diagnosis is not addressed at all in this manuscript, neither is the possibility of linking with primary care or emergency department datasets to gather more information about presentation and routes to diagnosis for patients included in the registry. If there are any plans to gather and/or analyse data about routes to diagnosis this would be relevant to UGI cancer care and should be included in the manuscript.<br>3. The 'Patient and Public Involvement' section needs re-writing. Opt-out approaches, consent procedures and ethical approval are not PPI. The NHMRC has guidance on consumer involvement (https://www.nhmrc.gov.au/guidelinesforguidelines/plan/consumer-involvement), which the authors may find informative for their revision. |

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| **REVIEWER** | Valentina Bianchi Galdi, MD<br>Ente Ospedaliero Cantonale<br>General Direction - Supportive Area<br>Via Lugano 4D<br>6500 Bellinzona<br>Switzerland |
| **REVIEW RETURNED** | 07-Jul-2019 |

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| **GENERAL COMMENTS** | Dear Dr. Maharaj and Colleagues,<br>congratulations for the great work performed until now. I've found your methodology accurate and comprehensive of all the main items useful to build a new quality cancer registry. The multicentricity of the registry's data increases its strength. Considering all the items requested for the evaluatio of the paper, I give my total approval with no needs for revision.<br><br>Valentina Bianchi Galdi, MD |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer One: Joonas H. Kauppila
Reviewer Comment: The study is submitted as a cohort profile. In the author instructions of the BMJ Open, it is recommended to present the characteristics of the patients in the cohort, as well as drop-out rates, which has been done in the cohort profiles published earlier in the Journal. However, no data from the currently collected material has been presented. I feel that the authors should present some basic data from the cohort on a certain time period (i.e. characteristics, survival), as well as the completeness of the data and variables. In its present form the manuscript would be more suitable to be submitted as a study protocol, not a cohort profile.
Author Response: Thank you for your feedback. We have undertaken the necessary work to produce Table 4 that displays data from the pilot phases of developing the pancreatic cancer (PC) and oesophagogastric cancer (OGC) modules. We have include a new section in the manuscript titled 'Results from the pilot studies from the PC and OGC modules'. We will be publishing data from an expanded data set in the near future, which will include survival. The pilot data sets for pancreatic and OG modules provide an insight into the development phases of the modules. Please see tracked changes within the manuscript as follows:
LINE 275 … The results of the pilot phase for both PC and OGC modules are displayed in Table 4. Of the 123 participants eligible for the PC module and 189 for the OGC module, 8 (6.5%) and 9 (4.8%) opted out of the registry, respectively. Clinical stage at diagnosis was not well documented in both the PC module (n = 80, 70%) and OGC cancer module (n = 82, 46%) and is an area for future quality improvement. Around 20% of the pancreatic cohort received surgery as first treatment which is broadly representative of surgical treatment in patients with PC.43 Further, 73 participants in the PC and 94 participants in the OGC module had documented reasons for no surgery. The pilot results for both modules identified areas for improving data completeness, definitions, items and structure of data collection forms. Following the pilot phase, the registry focused on improving these areas before expanding to other participating hospitals.
Reviewer Comment: For me as a non-Australian reviewer/reader, it is unclear what is the nationwide coverage of the cohort. If the cohort is nationwide, it should be clearly identified as such in the title, abstract and the text. If not, the approximate coverage of the population and the states/areas should be indicated in the methods section. A map of the current situation, or an additional table, might help.
Author Response: Currently, the UGICR is aiming for nationwide coverage. It was established in 2015 in Victoria and has since expanded to the state of New South Wales, Australia. This has been updated in the manuscript. We have also included a separate section that includes data on population coverage. Please see the following sections in the manuscript that address your comment:

LINE 187 … The UGICR is a multi-centre, population-based, non-interventional prospective cohort study. It was established in 2015 in Victoria and has since expanded to the state of New South Wales, Australia.
LINE 290: Population coverage in Victoria is based on data from the Victorian Cancer Registry. The population coverage in the pilot phase was 19% for the PC module and 11% for the OGC module. Current coverage is 73% for PC and 55% for the OGC module. In New South Wales, data is currently only being collected on the PC module with an estimated population coverage of 55%.
LINE 339 … Funding is another challenge faced by CQRs. As with many healthcare initiatives, the financial burden can be a major impediment.25 Data from CQRs are held in positive regard by clinicians, health managers and government. However, further funding will be required to progress national rollout of the registry.
Reviewer Comment: What is the involvement of the private sector in relation to the treatment of these cancers in Australia? To what extent the private sector is involved in the collection of the data (if applicable)? Please elaborate in the protocol
Author Response: This has been updated in Table 1, Eligibility Criteria, discussion point (ii). Patients are eligible for inclusion if they have been assessed or received care at either a private or public hospital.
Table 1… Patient has been assessed or received care at a participating public or private hospital or private clinician rooms
Reviewer Comment: Which PROs have the authors considered? EORTC or other validated measurements? How have they planned the collection and follow-up of the PROs?
Author Response: Apart from our original discussion points, we have not elaborated on the above comment. The systematic review mentioned in the original submission is currently under review and we are unable to share the results of this review due to journal restrictions. However, the necessary work was undertaken to identify the most appropriate PROMs for the registry which our statement captures below:
Line 262… The registry has future plans to begin the collection of Patient Reported Outcomes (PROs) and Patient Reported Experiences (PREs) to provide valuable patient perspectives. As an initial step, a systematic review evaluating Patient Reported Outcome Measures (PROMs) in pancreatic cancer has been undertaken by the UGICR team to define which PROMs are most appropriate for this group of patients.

Reviewer Two: Dr Sam Merriel
Reviewer Comment: The article is described as a cohort profile, and it mentions that the registry opened in 2015, but no data is presented about any members of the cohort to date. It would be of interest to readers and potential future research collaborators to know at least something about initial recruitment figures, patient demographics, missing data and early trends in the data. If there is no data available yet, reference to a cohort profile should perhaps be removed.
Author Response: Thank you for your feedback. We have undertaken the necessary work to produce Table 4 that displays data from the pilot phases of developing the pancreatic cancer (PC) and oesophagogastric cancer (OGC) modules. We have include a new section in the manuscript titled ‘Results from the pilot studies from the PC and OGC modules’. We will be publishing data from an expanded data set in the near future, which will include survival. The pilot data sets for PC and OGC modules provide an insight into the development phases of the modules. Please see tracked changes within the manuscript as follows:
LINE 275 … The results of the pilot phase for both PC and OGC modules are displayed in Table 4. Of the 123 participants eligible for the PC module and 189 for the OGC module, 8 (6.5%) and 9 (4.8%) opted out of the registry, respectively. Clinical stage at diagnosis was not well documented in both the PC module (n = 80, 70%) and OGC cancer module (n = 82, 46%) and is an area for future quality improvement. Around 20% of the pancreatic cohort received surgery as first treatment which is broadly representative of surgical treatment in patients with PC.43 Further, 73 participants in the PC

and 94 participants in the OGC module had documented reasons for no surgery. The pilot results for both modules identified areas for improving data completeness, definitions, items and structure of data collection forms. Following the pilot phase, the registry focused on improving these areas before expanding to other participating hospitals.

Reviewer Comment: The authors very rightly point out the poor outcomes for UGI cancers that persist today in Australia and globally, particularly for pancreatic cancer, and this provides a strong justification for the establishment of a national clinical quality registry for these cancer types. A major driver for these poor outcomes is stage at diagnosis, which is often late for UGI cancers, and thus improving early diagnosis needs to be a major focus to achieve better outcomes for UGI cancer patients. Improving early diagnosis is not addressed at all in this manuscript, neither is the possibility of linking with primary care or emergency department datasets to gather more information about presentation and routes to diagnosis for patients included in the registry. If there are any plans to gather and/or analyse data about routes to diagnosis this would be relevant to UGI cancer care and should be included in the manuscript.
Author Response: We have addressed the above and referenced accordingly in the manuscript as follows:
LINES 245… There are currently no clinical quality indicators that measure care for the prevention and early detection of pancreatic cancer. However, the UGICR is participating in a collaborative project, Symptom-UGI: Upper Gastrointestinal Cancer Symptom Study, to map the patient pathways from onset of symptoms to cancer diagnosis. Details of this study can be found within the UGICR website (https://ugicr.org.au/associated-studies/).

Reviewer Comment: The 'Patient and Public Involvement' section needs re-writing. Opt-out approaches, consent procedures and ethical approval are not PPI. The NHMRC has guidance on consumer involvement (https://www.nhmrc.gov.au/guidelinesforguidelines/plan/consumer-involvement), which the authors may find informative for their revision.
Author Response: Thank you. This section has been re-written as follows:

Line 373… Consumer representatives are involved at the level of the steering committee and provide oversight on the relevant modules as they are developed by the UGICR. Consumers representatives will also be involved in future studies which include the selection of a core-set of PROMs.

Reviewer Three: Valentina Bianchi Galdi, MD
Reviewer Comment: I give my total approval with no needs for revision.
Author Response: Amazing, Thank you!

## VERSION 2 – REVIEW

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| **REVIEWER** | Joonas Kauppila<br>University of Oulu, Finland, and Karolinska Institutet, Sweden |
| **REVIEW RETURNED** | 28-Aug-2019 |

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| **GENERAL COMMENTS** | My previous comments on the manuscript have been satisfactorily addressed. |

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| **REVIEWER** | Samuel Merriel<br>University of Exeter<br>United Kingdom |
| **REVIEW RETURNED** | 30-Aug-2019 |

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| **GENERAL COMMENTS** | Thank you to the authors for addressing the reviewers' comments. I have no further suggestions for improvement. |