

RESEARCH ARTICLE

Quantitative Review of Oral Cancer Research Output from Pakistan

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Abstract

Background: Oral cancer is the most common cancer among men and second only to breast cancer among women in Pakistan. For the effective control and prevention of oral cancer, Pakistan needs to recognize the importance of research and generation of the evidence-base which can inform policy making and planning and implementation of intervention programs. The objective of this review was to quantify oral cancer research output in Pakistan. **Materials and Methods:** A systematic electronic search in “Medline”, “ISI-Web of Science” and “Pakmedinet”, supplemented by a Google search, was carried out in January and February, 2014, to identify literature from Pakistan relevant to oral cancer. The selection of publications for the review was carried out according to preset criteria. Data were recorded and analyzed using Microsoft Excel. **Results:** A total of 166 publications comprising 62 case series, 36 cross sectional, 31 case control, 10 basic laboratory research, eleven reviews and two trials, were included in this review. Some 35 % of the publications focused on risk factors for oral cancer. COMSATS Institute of Information Technology was the institution with the highest contribution. **Conclusions:** There is a lack of research in the field of oral cancer research in Pakistan. Focused efforts should be put in place to improve both quality and quantity of oral cancer research in the country.

Keywords: Oral cancer - research - Pakistan

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Introduction

Oral cancer affects around 14.1 million people, making it one of the most prevalent cancers in the world (Warnakulasuriya, 2009). Developing countries, especially those from the South Asian region, have a higher burden of oral cancer compared to developed countries (Cancela et al., 2010; Krishna Rao et al., 2013; Mishra and Meherotra, 2014). With an estimated increase of 13,000 new cases each year, oral cancer is the most common cancer among men and second only to breast cancer among women in Pakistan. It also has the second highest cancer related mortality rates in the country (IARC, 2012). Oral cancer thus warrants immediate public health attention and evidence based concerted efforts for its control and prevention in Pakistan.

Research into non-communicable oral disease such as oral cancer is high on the agenda of the World Health Organization’s (WHO) “Oral health program” (Petersen, 2005). Research is considered to be a central component of any cancer control strategy (Sullivan et al., 2014) and efforts made to reduce cancer burden involve plans and actions based on sound intervention and surveillance research, which are important for knowledge synthesis (Best et al., 2003). The application of such knowledge

and current results of research can help in tackling cancer mortality and morbidity in low and middle income countries (Sankaranarayanan and Boffetta, 2010). Global cancer research priorities exist (National Cancer Institute, 2012) and new trends are emerging in oral cancer research in developed countries. However, for developing countries it is imperative that they set their own cancer research priorities, based on their needs rather than following an agenda set up by high income countries (Sullivan et al., 2014). The setting up of research priorities and agenda is a process that should be founded on available evidence and information. However, often it is a problem for policy makers to identify and collect such information (Nuyens, 2007).

The aim of this paper is to provide an overview, including a quantitative analysis of published literature from Pakistan in the field of oral cancer. The specific objectives are: *i*) to analyze the growth pattern of oral cancer literature from Pakistan, *ii*) to examine the types of research studies, *iii*) to assess the focus of oral cancer publications in Pakistan, and *iv*) to identify institutions contributing literature on oral cancer and the core journals publishing this literature. This information can be useful for policy makers, future researchers and other stake holders.

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Materials and Methods

Literature search

A systematic search was conducted in the following electronic databases: “PubMed”, “ISI-Web of Science” and “Pak Medinet”, using various combinations of the words “oral cancer”, “oral carcinoma”, “head and neck cancer”, “oral neoplasia”, “squamous cell carcinoma of the oral cavity” and “Pakistan”, from January 7, 2014 till February 29, 2014. No filters were used for the search process. A supplementary search in the web search engine www.google.com.pk and choosing the option “Pages from Pakistan” was also carried out to minimize the possibility of missing potential literature. Bibliographies of the selected publications were additionally searched to identify any further relevant studies.

For the purpose of this literature search, oral cancer was defined as “cancer that forms in tissues of the oral cavity (the mouth) or the oropharynx (the part of the throat at the back of the mouth)” (National Institute of Health, 2014)

Inclusion criteria

Publications were included in the review if they fulfilled the following criteria: *i*) With the exemption of review articles, the research described in the publication was carried out in Pakistan or was in the context of Pakistan. *ii*) Oral cancer was the main focus or one of the foci of the publication. *iii*) Manuscript published in an indexed or non-indexed journal up to 29.02.2014

Exclusion criteria

iv) Publications focusing solely on salivary glands or laryngeal or oesophageal cancers. *v*) Publications (except review articles) by authors affiliated to an institution in Pakistan but not carried out in Pakistan or in the context of Pakistan.

Selection of publications

The selection of the publications for this review was carried out in three stages: *i*) Screening of titles of publications identified through the electronic search, *ii*) scrutiny of abstracts of the publications selected after the first step and acquisition of the full texts of the selected abstracts and *i*) selection of publications to be included in this review based on the scrutiny of full texts (Figure 1).

Data abstraction

Two authors (Z.K and J.T) separately abstracted the following data from the selected publications on a spreadsheet in Microsoft Excel: first author, journal name, year of publication, study type, sample size, main focus of the study and the first authors’ institutional affiliation. The data were later compared and any discrepancies or differences were assessed and dealt with by mutual agreement.

The assessment of institutional research output was done using the first author’s institutional affiliation as stated in the publication. Research output on the basis of geographical location (District or Division taken as an administrative unit) was ascertained by the district or

division where the institution to which the first author is affiliated, is located.

Publications were also divided into two groups: those which were published in indexed journals and those in non-indexed journals. Journals indexed in “Medline” or “Embase” were classified as “indexed journals”. In addition, the WHO database “Index Medicus for the Eastern Mediterranean region” was searched to identify journals that are indexed with it. However, these were only classified as “Indexed” if they were also indexed in Medline or Embase.

Data analysis

Analyses involving the calculation of frequencies and percentages were carried out using Microsoft Excel. The institutions and geographical administrative units in Pakistan with the most number of publications, as well as the journals in which the identified publications were published, were identified. Foreign collaboration was also assessed on the basis of the presence of an author belonging to an institute/body outside Pakistan. A quantitative summation of the different research foci and study designs of the included publications was carried out. The cumulative number of research publications was plotted against the corresponding year to analyze research productivity over time. To identify the core journals, Bradford-Zipf plotting (Tsay and Yang, 2005) was carried out.

Results

The search in the three electronic databases returned a total of 1692 publications, including duplications. 1196 publications were left after the exclusion of duplications. After application of the selection criteria, a total of 151 publications were eligible to be included in the final review. A further 12 full text publications were identified through the google search and three more were identified through a search of the bibliographies of the selected papers. In total 166 publications were included in the final review (Figure 1). Important characteristics of the included studies, such as author and publication year, along with their references are given in the supplemental Table 1. Full texts/abstracts of a further six papers selected after the first step of publication selection could not be retrieved. The titles of these papers were however suggestive of oral cancer being the main focus and thus have been included in the supplemental table for reference. These publications were also incorporated in the “Journal, geographical and author affiliation” analysis as the data pertaining to these could be extracted.

Oral cancer literature growth in Pakistan

The first oral cancer publication from Pakistan was published in 1972, while the latest publication at the time of writing this review was from April 2014 (“Article in press” version was available at the time of our electronic search). The cumulative growth of oral cancer research over time is shown in fig 2. 13% (n=22) of the publications were published before the year 2000, 38% (n=64) were published between 2000 and 2009, while 48% (n=80)

Table 1. Top Ranked Journals According to the Number of Oral Cancer Publications from Pakistan

Rank	Journal Name	Number of publications	Cumulative number of publications (%)	Impact factor of Journal	Indexed with Medline	Indexed with Embase	Subject area
1	J Pak Med Assoc	18	18 (11)	0.4	✓	✓	Medicine and Dentistry
2	Asian Pac J Cancer Prev	15	33 (19)	1.5	✓	✓	Cancer
3	J College of Physic and Surg, Pakistan	12	45 (26)	0.3	✓	✓	Medicine and Dentistry
4	J Pakistan Dental Assoc	9	54 (31)	N/A	X	X	Dentistry
5	Pakistan J Otolaryngol, Head and Neck Surg	8	62 (36)	N/A	X	X	Otolaryngology and head and neck surgery
5	J Ayub Med College	8	70 (41)	0.1	✓	✓	Medicine and Dentistry
5	Pakistan Oral and Dent J	8	78 (46)	N/A	X	X	Dentistry
5	Ann King Edward Med University	8	86 (51)	N/A	X	X	Medicine and Dentistry

were published from 2010 till February, 2014. There were no publications in the years 1973 to 1975, 1978 to 1985, 1988 to 1991 and 1993. The most productive year, in terms of publications, was 2013. The average number of publications per year after the first publication from 1972 up to 2000 was less than one. The average number of publications increased to 7.5 per year between 2001 and 2010, and to 20 per year between 2011 and 2013.

Type of research

36% (n=60) were case series studies, 21% (n=36) were cross sectional surveys of which five studies were of a comparative type and one was a national pathfinder survey. 18% (n=31) were case control studies, of which only 6 were about modifiable lifestyle risk factors while the rest were molecular, chemical, viral and genetic epidemiology studies. 11% (n=19) were reviews while five (Six)% (n=10) were basic laboratory research studies. Four% (n=7) were case reports. There were two clinical trials among the included studies.

Foci of research

57 (34%) of the studies focused on different risk factors for oral cancer, among which 31 studies were of case control and two of cross sectional comparative design. Among these studies 12 focused on genetic risk factors, 13 on viral, chemical or molecular risk factors and six on lifestyle risk factors. Most of the publications focusing on genetic epidemiology were published from 2010 onwards. There was only one epidemiological case control study focusing on lifestyle risk factors post year 2000.

34 (20%) of the selected publications focused on the distribution and hospital/clinic based frequencies of oral cancer. 24 (15%) studies focused on treatment modalities for oral cancer. 16 (9%) were based on diagnostic procedures while 10 (5%) studies focused on histopathological characteristics of oral cancer cases. Seven studies assessed knowledge and/or attitudes of different population groups regarding oral cancer. Four studies reported on follow up outcomes of oral cancer. Three studies were about quality of life in oral cancer patients and two studies focused on cancer care.

Core journals

The included publications were published in a total of 65 journals, 39 of which were indexed with "Medline" and/or "Embase". 66% (n=111) of the articles included

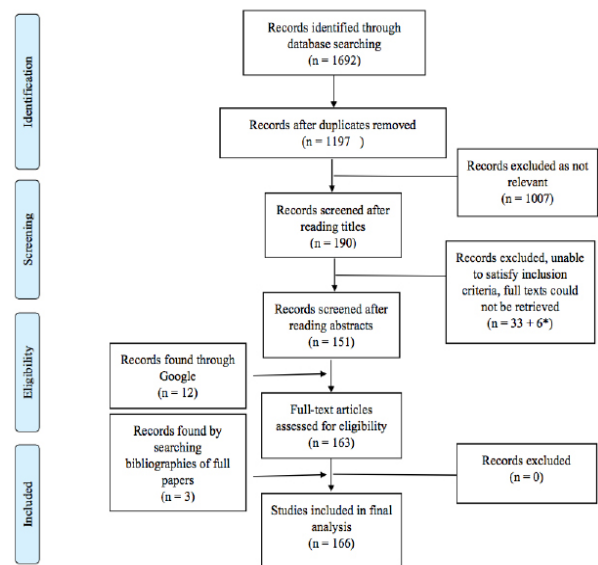
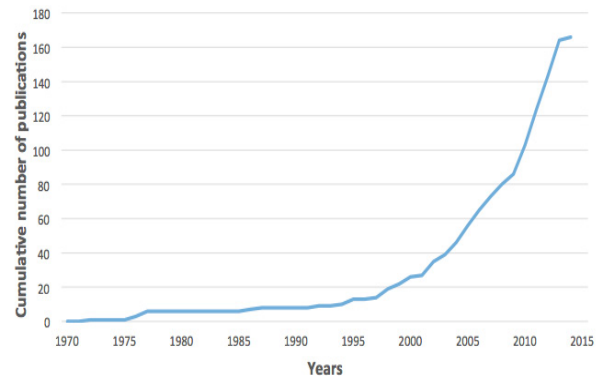
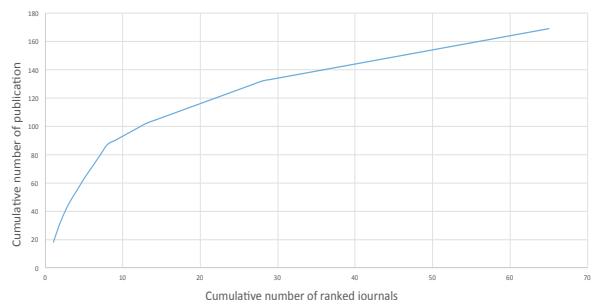
**Figure 1. Flow Chart of Publication Selection Process****Figure 2. Cumulative Growth of Oral Cancer Literature in Pakistan from 1972 till February 2014****Figure 3. Distribution of Oral Cancer Publications from Pakistan Over Research Journals**

Table 2. Major Oral Cancer Research Producing Institutions in Pakistan

Institution	City	No. of publications
Comsats institute for information technology	Islamabad	16
Jinnah post graduate medical centre	Karachi	12
Karachi cancer registry	Karachi	11
Aga Khan university	Karachi	11
King Edward medical university	Lahore	10
Dow university of health sciences	Karachi	10
Khyber college of dentistry	Peshawar	8

in this review were published in journals indexed with these two databases, while 33% (n=54) were published in journals that are currently not indexed with them. However, 44 of the latter were published in journals that are currently indexed with the WHO Index Medicus for the Eastern Mediterranean region. Three journals were indexed with all three databases, while 18 of the “non-indexed” journals were indexed in the WHO database.

More than half of the included articles were published in eight of the 65 journals (Figure 3), with three journals publishing more than a third of the articles: the Journal of Pakistan Medical Association (n=18), the Asian Pacific Journal of Cancer Prevention (n=15), and the Journal of College of Physicians and Surgeons, Pakistan (n=12) (table 1). These select few journals can be termed as “Core journals” for oral cancer publications from Pakistan.

Geographical distribution of included publications

Karachi has the highest number of publications with 65 (38%), followed by Lahore with 27 (15%), Islamabad with 24 (14%), Rawalpindi with 16 (9%), and Peshawar with 11 (6%). Other notable contributors include Jamshoro and Abbottabad with 5 publications each. Only two publications were from Quetta. Provincially, Sindh has contributed 42% of the total publications. Punjab has 30%, Khyber Pakhtunkhwa 10% and Baluchistan 1%. The federal capital Islamabad contributed 15% of the total included studies. There were no publications from Gilgit/Baltistan or the federally administered tribal areas.

Institutional output

A total of 63 institutions contributed to oral cancer research output in Pakistan. Table 2 includes the major institutional oral cancer research producers in Pakistan. Other notable contributors include Liaquat University of Medical and Health Sciences and Armed Forces Institute of Pathology (five publications each), Shaikat Khanum Memorial Cancer Hospital, Ayub Medical College and University of Karachi (four publications each).

Discussion

Historically, in Pakistan, Government policies including those in the field of health, have neither emphasized on, nor clearly defined its research priorities (Government of Pakistan, 2001; Government of Pakistan, 2011), thus underscoring the importance of research. This, among many factors, has contributed to a lack of research culture in the country, evidenced by Pakistan's poor performance in the field of research, where it has

contributed less than 0.1% of the world's research output, including health research (Mushtaq et al., 2012). Our study shows that the scarcity of research output in Pakistan (Akhtar, 2004) also holds true in the field of oral cancer, one of the most prevalent non-communicable diseases in the country.

At first glance, oral cancer research output in Pakistan appears to have grown exponentially over time. This growth is however relative rather than absolute, since publication numbers were very small at the beginning. The growth trend in oral cancer research is in contrast to the field of clinical radiology in Pakistan, the only medical field in which research output analysis has been carried out. No differences in clinical radiology research output were seen before or after the year 2000 (Akhtar et al., 2009). The general pattern of oral cancer literature growth in Pakistan however is comparable to the Indian cancer research output (Sullivan et al., 2014; Lewison and Roe, 2012), where oral cancer is one of the most researched cancers due to its huge burden of disease. Oral cancer research output in both countries has seen a rapid growth post year 2000 (Ghaffar et al., 2013).

The numerical increase in research output in Pakistan post year 2000 can be attributed to the emergence of the Higher Education Commission (HEC) in the early 2000s (Qureshi et al., 2013). The commission issued a directive that educational institutions be more research oriented and also introduced schemes for students to pursue research degrees such as Master and Doctoral programs, where publications are a requirement. Additionally, a minimum number of research publications are now required for promotion to a higher post in academia. The latter was implemented in the medical/dental colleges and universities by the Pakistan Medical and Dental Council (PMDC) and the HEC (Ghaffar et al., 2013). Although these steps have contributed to the total number of publications, there is a lack of good quality output with meaningful impact.

An essential aim of cancer research in low and middle income countries should be to understand the social, environmental, behavioral and biological determinants of the disease in a local context, so as to be able to assess efficacy of treatment protocols and interventional research (Sankaranarayanan and Boffetta, 2010). Epidemiological case control and cohort studies are effective research approaches to understand various risk factors or determinants of disease (Song and Chung, 2010). Our study data, however, shows a significant lack of such epidemiological studies in Pakistan. Although an increase in genetic epidemiological studies was observed, we did not find any studies on lifestyle and environmental risk factors published after the year 2000. More importantly, all the case control studies on lifestyle risk factors were carried out in one single city and are therefore most likely not generalizable to the whole of Pakistan. Further, the majority of the included case control studies were laboratory based and investigated molecular and genetic risk factors. The practical implementation of such studies into public health policy is however difficult, considering Pakistan's restricted resources. Overall, case series studies were the primary study form, reporting simple

descriptions of oral cancer cases or histo-pathological findings from some tumor samples. These studies hardly added new knowledge to, nor aided the prevention and control of oral cancer in Pakistan. There is also a distinct lack of clinical trials on oral cancer in Pakistan, with just two trials being conducted, both of which were not randomized (Shaharyar et al., 2006; Masud et al., 2007). Trials are an important tool for establishing cost effective treatment and prevention measures, and should be the priority of cancer research in low and middle income countries (Sankaranarayanan and Boffetta, 2010; Magrath, 2010). In contrast, in India cancer research, including oral cancer, comprises of a number of case control studies. Although these studies might not be up to the standards of those in developed countries, this is the right approach to assess risk factors (Sullivan et al., 2014). In addition to these, focusing on established lifestyle factors (Gupta and Johnson, 2014), a few cohort and interventional studies have also been well documented (Gupta et al., 1986; Muwonge et al., 2008; Jayalekshmi et al., 2009; Jayalekshmi et al., 2011).

Our finding that almost 50% of the total publications included in this review were published in just eight of the 65 journals which published oral cancer research from Pakistan, is comparable to similar studies in cancer research and other fields of health research around the world (Tsay and Yang, 2005; Patra and Bhattachariya, 2005). These journals can therefore be regarded as core journals which form the literature basis for oral cancer research in Pakistan (Garfield, 2006). The previously mentioned directive by the governing bodies of medicine and education on having a certain number of publications for promotion purposes resulted in authors publishing in certain journals, which are recognized by the HEC and PMDC, but are often non-indexed with the globally recognized Indices (Ghaffar et al., 2013; Mushtaq et al., 2012). These journals have limited circulation and often very little web presence, making it difficult to reach potential stakeholders and policy makers. In conducting this review, we were faced with difficulties in finding articles from some of these non-indexed journals. This highlights the fact that the research findings published in these journals may have little impact if they fail to reach the intended audience.

Karachi is the biggest metropolis in Pakistan (World Population Statistics, 2013) and has the highest concentration of medical universities in Pakistan. Hence it is not surprising that it has the highest research output among all the Pakistani cities. The point of concern however is the lack of oral cancer research output from the bigger cities such as Quetta and Peshawar, which, despite having a heavy burden of oral cancer, have contributed very little to its research (Begum et al., 2009; Roohullah et al., 2012). Also of concern is the lack of research from the FATA and Gilgit Baltistan provinces. There are no epidemiological data whatsoever available on the prevalence or incidence of oral cancer in these areas. There appears to be a gradient of inequality in oral cancer research carried out in Pakistan, with less research being done in areas with poorer access to healthcare. This scenario as a whole is comparable to oral health

improvement and disease prevention on a global level, where marked inequalities exist both inter and intra regionally (Sgan-Cohen et al., 2013). Oral cancer research output appears to be associated with the regional human development index of Pakistan (Jamal and Khan, 2007), with, as observed in our study, districts which score high on the human development scale having more research output and vice versa.

With regards to institutions, the trend is similar to that of the geographical distribution, with institutions based in larger cities producing more research publications than those in smaller, less developed cities. The Comsats institute of information technology is a relatively new academic institution which is principally non-medical. Despite this, it has produced the most number of publications, and along with Karachi cancer registry and King Edward medical university, has collaborative publications with authors from other countries. A finding of this review which is of great concern is the lack of recent publications from the Karachi cancer registry. A possible explanation could be the death of its founder who was the principal author in most studies produced from the registry. This is a possible indication that research in Pakistan is generally not institutionalised, but rather depends on personal motivation, and in some cases, is an activity imposed by the respective authorities (15).

A further finding of concern is the lack of research output from the cancer specialty hospitals of the Pakistan atomic energy commission (PAEC) and the biggest cancer hospital in the country, Shaukat Khanum memorial cancer hospital (SKMCH). There are just three publications by first authors affiliated to the PAEC hospitals, and four publications from the SKMCH.

In conclusions, oral cancer is a big public health problem in Pakistan and as such needs a serious commitment and a holistic approach to tackle it. The lack of timely and quality research informing policy and practice can be a hindrance to such an approach. This study highlights the fact that oral cancer research output from Pakistan is lacking in both relative and absolute terms, and also that the type of research studies carried out may not be in line with the cancer research needs of Pakistan.

Cancer is a heterogeneous disease. Hence, the strategies needed for its prevention as well as the research needed to devise such strategies should be heterogeneous. Although the publications on oral cancer from Pakistan reviewed in this paper do tackle various topics regarding oral cancer, much of the research done is of a very basic level. Most publications are based on institutional records and there is a lack of population based studies.

To our knowledge, this research work is the first effort which has been made to collect and summarize all the oral cancer research done in Pakistan for future use by researchers and other relevant stakeholders. This review was based entirely on electronic search, and though we tried to include all relevant studies, it cannot be ruled out that we missed some of the literature. Citation analysis, which is sometimes used in such publications could not be carried out due to the incompleteness of suitable data required for such an exercise. This was due to the presence of a considerable number of studies that are unfortunately

not included in ISI-Web of Science or Scopus databases, where data is available for more complex bibliometric analysis.

The government needs to look into setting up a national oral cancer research agenda based on local needs. This should be done in collaboration with the various stake holders such as the Pakistan Medical Research Council, PAEC, academia, SKMCH, the Karachi and Punjab cancer registries, the pharmaceutical industry and provincial health departments. Once an agenda and research priorities are set, research projects in the area of need, should be commissioned to the educational and research institutes. These in turn should carry out these projects in collaboration with clinicians and hospital staff, who otherwise are unable to conduct research on their own, due to a heavy patient load.

Although communicable diseases are often on the priority list of policy makers in Pakistan, the importance of non-communicable diseases such as oral cancer need to be realized and more concerted efforts should be made for their prevention and control. Strategies should be devised to combat the high incidence of oral cancer in the country and such strategies should be based on sound scientific research. A holistic approach to cancer research, bringing together both medical and non-medical institutions with relevant expertise, should be implemented, so that researchers with different skills complement each other. Research linkages between institutes working on oral cancer research should be established. The Pakistan medical research council (PMRC), with offices in all major cities of Pakistan, can act as a liaison among these institutions. The Offices of research, innovation and commercialization (ORIC) at the medical and general universities, which are responsible for research related activities in these universities and also coordinate with the HEC on research related funding, can help PMRC in bringing together these institutions.

At an institutional level, efforts should be made to forge links with international cancer research institutes, which can provide technical assistance in carrying out novel research projects. Collaborative research with these partners and the resultant publications can help increase the research understanding of local researchers, resulting in well executed research projects and high quality publications having an impact on oral cancer prevention, treatment and control.

At the individual level, authors should strive to publish research which has a direct impact on disease prevention and outcomes, and to come up with efficient and effective methods for the control of oral cancer, keeping the local context in mind. In choosing journals for publication, authors should try and publish their research work in journals which have a good scientific standing among the cancer research community and are easily accessible to potential stake holders, so that their research reaches its intended audience.

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