

## Undertaking Cancer Research in International Settings: Report from the American Society for Preventive Oncology Special Interest Group on International Issues in Cancer

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### Abstract

The mission of the American Society for Preventive Oncology Special Interest Group in International Issues in Cancer is to serve as a worldwide cancer prevention resource. At the 2013 annual meeting, we presented three early career investigators who conducted research with international collaborators as part of postdoctoral studies. We present a synopsis of each of the scientific presentations. The investigators also highlight useful strategies to encourage a more successful international collaboration, including seeking out existing collaborations between colleagues and international researchers, maintaining awareness and sensitivity of cultural norms, establishing clear communication about investigator roles and expectations, and persevering in the face of potential challenges due to the nature of these collaborations. Incorporation of these key elements could prove useful for researchers interested in pursuing cross-country projects. *Cancer Epidemiol Biomarkers Prev*; 22(9); 1638–41. ©2013 AACR.

### Introduction

For all investigators, the development of an international research proposal can be daunting and challenging. The goal of our report is to provide perspective from early career public health scientists on the potential for international collaborations and present lessons learned from their international research experience. We provide an overview of the research conducted and presented at the 2013 American Society for Preventive Oncology (ASPO) annual meeting in Memphis, TN, in the Special Interest Group for International Issues in Cancer. Furthermore, we propose steps to establish and maintain more successful international collaborations.

### Case Study 1—Dr. Kitahara: Danish Study of Early Growth and Thyroid Cancers

#### Synopsis of presentation

Thyroid cancer incidence has rapidly increased over the past few decades in several countries, including Denmark

(1). The relatively young age at onset of thyroid cancer compared with most other malignancies suggests a possible role of early-life exposures in thyroid cancer development (2). Body size and growth during childhood are influenced by numerous factors including genetics, early-life nutrition, and levels of certain hormones (e.g., insulin-like growth factor), all of which may be involved in the etiology of thyroid cancer (3, 4). Results from several epidemiologic studies (1–7), including those conducted by Dr. Kitahara and her colleagues, have shown that greater body mass index and taller height in middle-to-older adulthood is associated with an increased risk of thyroid cancer in both men and women. However, only a few studies have examined the influence of childhood or adolescent body size on this risk (1, 4, 5). These studies were based on height and weight values recalled by the participants many years later, which introduces the potential for bias. Studies evaluating direct measurements of body size during childhood in relation to cancer incidence in adulthood have been rare due to the large sample sizes and long follow-up periods required, particularly for less common outcomes such as thyroid cancer.

Dr. Kitahara collaborated with Drs. Jennifer Baker, Michael Gamborg, and Thorkild Sorensen at the Institute of Preventive Medicine (Copenhagen, Denmark) to prospectively investigate the association between measured height and weight at each age between 7 and 13 years and thyroid cancer risk using data from the Copenhagen School Health Records Register (CSHRR; 5, 6). The CSHRR is a unique and valuable resource to evaluate these questions as it includes height and weight measurements on a very large number of individuals (nearly all schoolchildren born on or after 1930 in Copenhagen) and has been linked to other national registers, including the

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Danish Cancer Registry, using personal identifying numbers (7). During the period of the follow-up from 1968 to 2010, there were 235 incident cases of thyroid cancer diagnosed among 321,085 individuals included in the CSHRR. Preliminary results suggest that taller height and greater body mass index during childhood may be associated with an increased risk of thyroid cancer later in life.

### Case Study 2—Dr. Tamers: Tobacco Smoking and Stressful Life Events in France

#### Synopsis of presentation

Stressful life events (SLE) requiring substantial adjustments can have implications for health and health behaviors (8, 9). SLEs may play a role in disease (10), directly through stress responses (11) or indirectly through health behaviors (12, 13). Tobacco intake is one such behavior used as a coping mechanism for dealing with stress and SLEs (13–16). Alternatively, evidence suggests that certain events may also be linked to healthy changes in tobacco use (17). Methodologic approaches used in previous studies have curbed our understanding of the relationship between these factors.

In collaboration with Dr. Cassandra Okechukwu from the Harvard School of Public Health (Boston, MA) and Dr. Miguel Marino from Oregon Health and Science University (Portland, OR), Dr. Tamers examined the impact of interpersonal- (i.e., marriage, divorce, children leaving home, widowhood, death of loved ones) and financial-related (employment promotion, important purchase, retirement) SLEs on tobacco prevalence among middle-aged and older French adults. She used data from the GAZEL cohort provided by collaborators Drs. Marie Zins, Marcel Goldberg, and Alice Guéguen from L' Institut National de la Santé et de la Recherche Médicale (Marseille Cedex, France). GAZEL consists of 20,625 employees [15,010 men (73%)] of the French National Gas and Electricity Company, followed annually since 1989 (18). Preliminary results showed a decrease in tobacco prevalence in relation to a number of SLEs for both women and men, before, during, and after experienced events. Research is ongoing and continued studies are needed to understand the means by which important life changes may influence tobacco behavior across time.

### Case Study 3—Dr. Al-Temimi: Head and Neck Cancer Survival in Central and Eastern Europe

#### Synopsis of presentation

Cancers of the oral cavity, pharynx, and larynx are collectively known as head and neck cancer (19), which is the fifth most common cancer by incidence worldwide (20). The Central and Eastern European region is among the world regions with highest burden of head and neck cancer incidence and mortality, particularly for males. The age-adjusted incidence of head and neck cancer among men in Central and Eastern Europe is 22.7 per 100,000 male population compared with 15.7 per 100,000 male population in the United States and 12.7 per 100,000

male population worldwide. This region also has higher mortality rate (14.1 per 100,000 males) of head and neck cancer than the United States (3.4 per 100,000 males) and the world (7.4 per 100,000 males; 20). Despite the high incidence and mortality of head and neck cancer in Central and Eastern Europe, limited number of studies have been conducted to identify the determinants of survival among patients with head and neck cancer in this region.

Under the supervision of Drs. Mia Hashibe and Yuan-Chin Amy Lee from the University of Utah (Salt Lake City, UT), Division of Public Health, Dr. Al-Temimi analyzed data of 469 patients with head and neck cancer who were recruited by the International Agency for Research on Cancer [IARC] case-control study in Central and Eastern Europe (2000–2004; 21). The follow-up of the cases and the use of the questionnaire data from the case-control study was carried out in collaboration with the principal investigators of the case-control study, including Dr. Paolo Boffetta from Mount Sinai School of Medicine (New York, NY); Dr. Paul Brennan from IARC; Dr. Eleonora Fabianova from the Regional Authority of Public Health in Slovakia; Dr. Jola Lissowska from the Maria Skasodowska-Curie Memorial Cancer Center and Institute of Oncology (Warsaw, Poland); and Dr. Neonila Szeszenia-Dabrowska from the Institute of Occupational Medicine (Lodz, Poland).

Dr. Al-Temimi and colleagues successfully followed more than 95% of the cases from the date of cancer diagnosis to the end of the study until participant death or 2011. They estimated the survival rates of the patients and analyzed the patient-, treatment-, and cancer-related factors as determinants of survival. The preliminary result of the study suggests that patient age, treatment modality, and tumor stage are independent predictors of survival among patients with head and neck cancer within this cohort.

#### Discussion

##### What were some of the steps that helped carry out these international studies more successfully?

*A passion for international research.* All three presenters expressed a strong personal interest in working on international studies. As such, they each sought out opportunities through mentors at their host institutions to develop collaborative working relationships within their postdoctoral training. The presenters acknowledge that international work should rarely be the sole, or even primary, focus of postdoctoral trainees, as these projects generally span a longer time frame and may have a lower probability of success than studies conducted more locally. This is especially true with international studies involving primary data collection. Nonetheless, the three case studies presented here were analyses of data that had been already collected, thus alleviating some of the challenges associated with international collaborations.

*Successful prior and concurrent collaborations between mentors and the data-coordinating institute.* Drs. Kitahara, Tamers, and al-Temimi highlighted that existing collaborations between colleagues at their current host

institution and international researchers with available data were helpful to conduct their studies.

**Visiting the data-coordinating institute.** Both Drs. Kitahara and Tamers were able to visit their data-coordinating institutes. Dr. Kitahara made a two-week visit to Denmark, funded by the National Cancer Institute (Rockville, Maryland), which allowed her to meet some of the individuals involved in the development of the CSHRR, learn more about the history of the cohort, and work directly with her collaborators on the analysis. A subsequent visit by her Danish collaborators to the National Cancer Institute a few months later gave them the chance to present findings from the cohort to a large group of cancer experts, and gave the research team another opportunity to meet to discuss the project and plans moving forward. Similarly, Dr. Tamers was funded through the host site to work onsite in France to develop a research proposal and obtain required data to conduct her analysis. Upon returning to the United States, she continued to work closely with colleagues on both continents to analyze data, present results at conferences, and submit articles for publication.

**Planning and maintaining open/ongoing communication within research team.** In international collaborations, it is important to be adaptable to changes in expectations and plans and to persevere through the complexity of bi- or multicultural and bi- or multinational projects. As such, all presenters spoke to the importance of establishing investigator roles, including plans for article development and authorship, before the initiation of a project. Although these steps are important in all collaborations, be they international or not, they are even more crucial when faced with less frequent in-person interactions, different time zones, language barriers, and distinct norms. Given these additional challenges, regular/ongoing email communication of roles, expectations, and updates can facilitate the ease of collaboration, as well as help address any issues if or when they arise.

### **What is the role of culture in conducting international projects?**

**Awareness and sensitivity.** All presenters acknowledged the need to be aware of cultural differences and to be sensitive to the cultural norms within the data-coordinating institute and country. Displaying a lack of consideration can hinder the collaboration, the research process, and potentially damage future or ongoing collaborations. In contrast, showing cultural knowledge and consciousness can help foster more effective communication and build trust with collaborators. For example, as a bilingual dual citizen (U.S./France), Dr. Tamers had an added grasp of French culture that undoubtedly helped her undertake her research. However, she contends that any researcher interested in collaborating on international projects can do so more successfully by gaining more understanding and appreciation for these important distinctions. For instance, it is important to respectfully navigate differences in work-life balance norms that

might impact project scheduling, turnaround times, and deadlines, especially poignant at certain times of the year.

**A shared language.** Being able to communicate in a shared language is essential. All presenters spoke to the need to communicate effectively in a shared language, either in English or fluency in their international collaborators native tongue. Regardless, efforts to communicate with collaborators in their native language are always appreciated.

### **What are the key lessons learned?**

**Setting clear expectations and goals is essential.** Dr. Kitahara learned that the expectations and goals for the project often differ for individuals both within and across institutions, and these may be especially divergent across different cultural settings. Both effective communication of these expectations and trust are essential for a successful and mutually beneficial international collaboration. Before initiating the project, Dr. Kitahara and her colleagues agreed upon a plan for the study objectives, statistical analysis, timeline, and authorship on the resulting article. This agreement has been invaluable for clarifying the responsibilities of each member of the research project and has aided in focusing the scope and tracking the progress of the study. Similarly, Dr. al-Temimi learned that the most important factors for success and sustainability of international collaborations include excellent leadership from the different participating institutions and clearly defined collaboration goals, a committed team, and mutual trust. Successful earlier studies within Dr. Al-Temimi's collaboration created trust among the investigators and raised their confidence in their collaboration. Other factors that helped establish such trust were aligning the incentives of the collaborators, developing clear roles, and responsibilities and giving fair credits to the collaborators based on their contributions to the study.

**Maintain patience and flexibility despite complexities or setbacks.** During the process of establishing and maintaining the international alliance, Dr. Tamers learned that geographic distance, distinct cultural norms, and potential language barriers can sometimes engender additional impediments. Nonetheless, Dr. Tamers affirms what can be gleaned from further international collaborative research is invaluable in the ongoing quest to understand the underlying mechanisms that impact cancer prevention and control.

**International research provides unique scientific perspective to our understanding of cancer prevention and control.** Findings from international work in one context may be applicable or beneficial to other geographic regions. This is true of all three aforementioned projects. Given the need to mitigate increasing health care costs in countries such as the United States, there may be lessons in cancer prevention and control to be learned from other geographic regions. Findings from the Danish study would be valuable to understand the potential implications of the childhood obesity epidemic in the United

States and other developed countries. Exploring the relationships between SLEs and tobacco in non-U.S. contexts is vital to further the field, in view of the great social and cultural distinctions in both the aging process and tobacco intake in European contexts. Identifying unique determinants of head and neck cancer survival in Central and Eastern Europe might be important when assessing the prognosis of newly diagnosed patients with cancer in middle resource countries. Despite the challenges of international collaborations, ultimately, all members of the collaboration have a shared goal: advancement of cancer prevention and control.

## Conclusions

We present three ongoing international collaborations executed by early career investigators. They highlighted practical steps to help enable a more successful international collaboration, including developing a personal interest in international research, identifying existing collaborations between colleagues and international researchers, maintaining sensitivity to cultural differences, and establishing open communication and guide-

lines for investigator roles and expectations. It is important to note that these three case studies and shared experiences are undoubtedly not applicable or generalizable to all international collaborations. There are likely other considerations when conducting primary data collection and if collaborations involve lower-income countries, for instance. Nevertheless, lessons learned in these case studies may still be useful for researchers undertaking future international collaborations.

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