



AllerGen International Research Visit to Karolinska Institutet: Final Report

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Research setting

With the support of AllerGen NCE's International Research Visit Award, I participated in a research visit to Karolinska Institutet (KI) from May 4, 2015 to August 21, 2015.

KI is a prestigious medical university located in Stockholm, Sweden. According to the 2015 Academic Ranking of World Universities (ARWU), KI is ranked 48th among all universities assessed by ARWU worldwide—12th in the category of Clinical Medicine and Pharmacy and 1st among all universities in Sweden. Medical research activities at KI include basic science, nursing, patient-level and population-level research¹.

I completed my research visit at KI's Institute for Environmental Medicine, in the Environmental Epidemiology Unit. I was supervised by Dr. Anna Bergström and Dr. Jennifer Protudjer, who is a post-doctoral fellow under the supervision of Dr. Anna Bergström and Dr. Magnus Wickman.

The project

My research visit to KI involved the use of data from BAMSE—a population-based Swedish birth cohort of 4,089 Swedish children recruited from 1994 to 1996, and followed from the age of 2 months to adolescence².

The objective of the research project that I worked on was to examine the effects of early-life exposure to secondhand smoke (SHS) on the development of food reported symptoms (FRS) from childhood to adolescence among children in the BAMSE birth cohort. While the research group at KI had previously looked into the relationship between SHS and sensitization to food allergens, they had not investigated the link between SHS and clinical symptoms experienced by children.

What was accomplished

Over the course of the 4-month research visit, I had the opportunity to follow this project along from preliminary literature review and descriptive statistics to analytic statistics, the drafting of a scientific manuscript and dissemination of research results in oral and poster presentations.

My review of the scientific literature allowed me to get a better understanding of the relationship between environmental pollutants and allergic diseases. I was able to identify the research gap that our research project was filling; namely, that very few studies had previously investigated the link between early-life SHS exposure and symptoms to foods. Furthermore, I learned that these few studies generally examined sensitization to food allergens as an indirect measure of disease burden, rather than reported symptoms to foods themselves. I was able to put our study in context and highlight the contribution that it offered to the scientific literature.

The descriptive statistics that I performed for this study allowed me to quantify and characterize environmental exposures and allergic disease health outcomes in a large birth cohort. I was able to describe the prevalence of the exposure (SHS exposure at age 2 months) and outcomes (FRS, including sensitization to food allergens, particular symptoms and reported symptoms to particular foods) over time. I was also able to contrast demographic characteristics of children who were exposed to secondhand smoke versus those who were not.

I statistically analyzed relationships between SHS exposure at age 2 months and FRS in the BAMSE cohort using generalized estimating equations (GEE). In doing so, I was able to characterize the strength and direction of the association between the exposure and outcome using odds ratios and 95% confidence intervals. The GEE analysis allowed me to assess the nature of this relationship over time; I looked at outcomes at ages 1, 2, 4, 8, 12 and 16 years. Not only did I examine FRS as a whole, but I also characterized FRS as occurring in combination with sensitization to food allergens or in the absence of sensitization to food allergens. Finally, I also performed logistic regression analyses to examine the association between SHS exposure at age 2 months and particular symptoms, as well as reported symptoms to particular foods.

With the support of co-authors, I drafted a first-authored scientific manuscript detailing the rationale, methods, results and interpretation of the research. We are currently in the process of formatting this manuscript for submission to *The BMJ*.

Finally, I had the chance to disseminate research findings in the form of oral and poster presentations. During my last week at KI, I gave a 20-minute oral presentation to the Environmental Epidemiology Unit at KI, summarizing the work that I had done during my research visit. This presentation was followed by a 10-minute question period during which I received valuable feedback from PhD students and senior scientists. I also had the opportunity to present my research findings as a 2-minute oral presentation and poster presentation at the AllerGen Poster Competition, held during the 2015 Canadian Society for Allergy and Clinical Immunology meeting. I was awarded 2nd place in the Masters category for the poster presentation that I gave at the AllerGen Poster Competition.

Barriers encountered

Originally, we planned to look at data on epinephrine auto-injector usage among children in the birth cohort. When we reviewed the planned analyses, we realized that it would be unrealistic to pursue this aspect of the research, as it would have been very time-consuming, and may not have added valuable information to the study. Therefore, I did not get the experience of seeing how national health administrative data would be linked to the birth cohort study data. However, I was able to perform some linkage between laboratory data (blood testing for Immunoglobulin E reactivity to peanut components) and the main birth cohort data. Therefore, although I did not get to familiarize myself with the planned data linkages, I was still able to see how datasets were merged together; I even had the opportunity to perform this merging myself.

What is left to be completed

We are in the process of formatting a scientific manuscript based on this research visit for submission to *The BMJ*. I have virtual access to the data housed at KI, which enables me to complete this work from Toronto.

Value added

Over the course of this research visit, I had the opportunity to acquire and enhanced several core competencies that have been identified as being important for public health epidemiologists³. In this way, the AllerGen International Research Visit has been instrumental in enhancing my career development. Some of these competencies included:

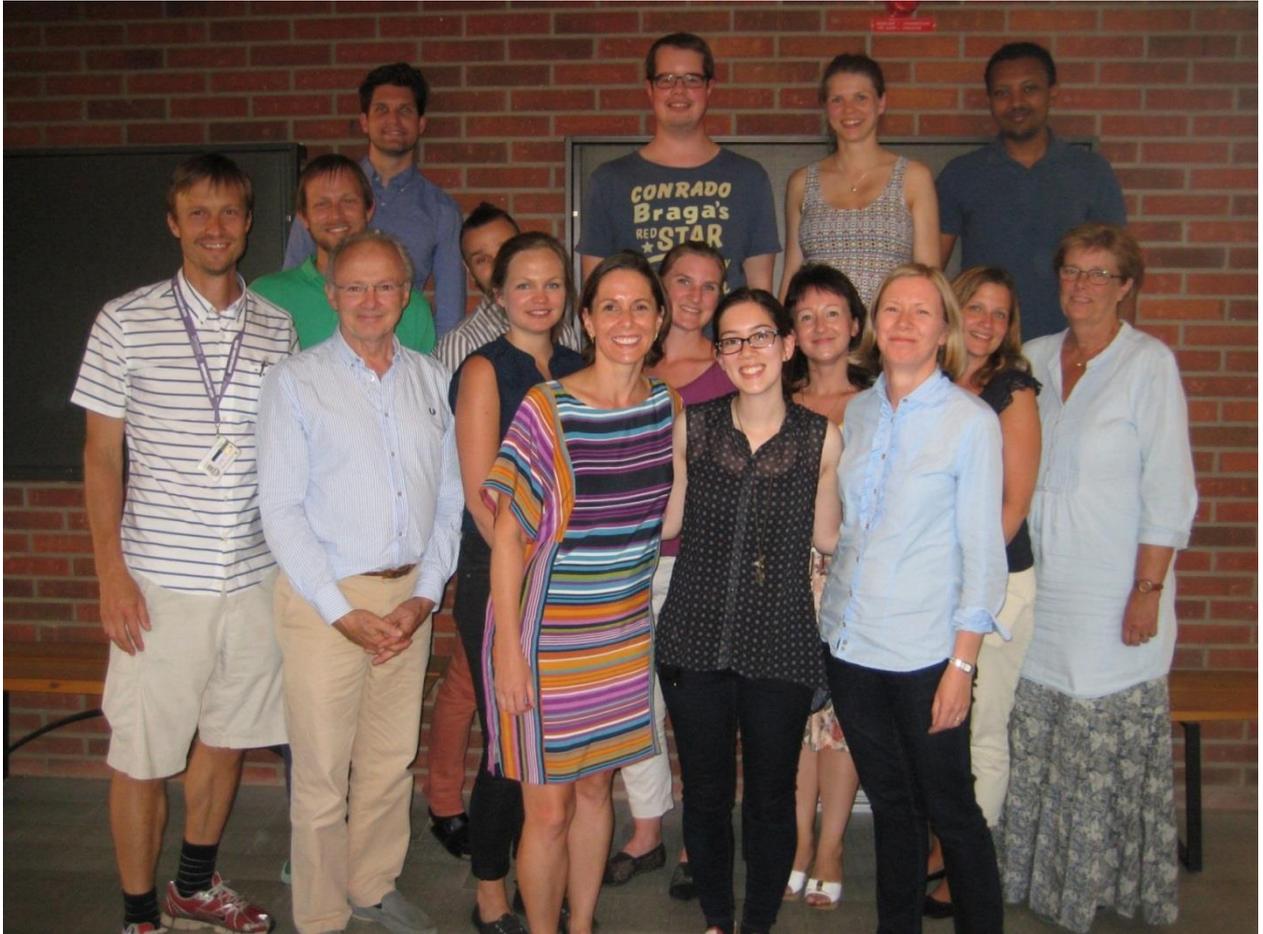
- Critical thinking and analysis/appraisal skills:
 - The analysis done during this research visit was not straightforward, and required critical thinking—particularly in choosing confounders to adjust for and in

interpreting findings. My supervisors, with their expertise in the area of SHS and allergic disease, were able to help me understand and handle the subtleties we encountered.

- In writing the discussion section of the study manuscript, I was able to thoughtfully discuss why our study results were meaningful, particularly in light of differences between our study and previous findings.
- Time and project management:
 - I only had 16 weeks to perform the necessary analysis and draft a scientific manuscript. This time pressure enabled me to enhance my time management skills, in order to complete everything that needed to be done in just a few months.
 - I also learned how to prioritize certain projects over others, in order to make sure that the most important and urgent tasks were completed first.
- Collaboration and interpersonal skills:
 - Completion of this project required input from a range of team members, including PhD students, senior researchers, a statistician and a post-doctoral epidemiologist. This challenged me to learn how to collaborate with many people with diverse experiences, interests and skills. Ultimately, I was able to manage even conflicting advice, by acknowledging the merit of all suggestions and being very open about why a particular course of action was taken.
 - This research visit additionally challenged me to enhance my interpersonal skills in a cultural setting that differed from Canadian research environments. I learned to build positive and productive relationships with my Swedish colleagues.

Closing remarks

This once-in-a-lifetime opportunity to participate in a 4-month research visit to Sweden's Karolinska Institutet would not have been possible without the generous support of AllerGen NCE. As a result of this research visit, I have been able to meaningfully contribute to the scientific literature surrounding the impact of environmental exposures on allergic disease outcomes. I have also experienced immense growth as an epidemiologist-in-training and have been able to build valued personal and professional relationships—a process that was facilitated by pre-existing networks developed through previous AllerGen-funded collaborations. Following this research visit, I am more capable and more confident in my ability to participate in international research collaborations throughout the rest of my career.



Back row (from left): Jesse Thacher, Niklas Andersson, Anna Gref, Simon Kebede Merid

Middle row (from left): Dr. Erik Melén, Petter Ljungman, Michal Korek, Erica Schultz, Dr. Olena Gruzieva, Sara Nilsson, Eva Hallner

Front row (from left): Dr. Magnus Wickman, Sandra Ekström, Dr. Jennifer Protudjer (supervisor), Laura Feldman (AllerGen trainee), Dr. Anna Bergström (supervisor)

References

1. Shanghai Ranking Consultancy. Academic Ranking of World Universities 2015 [cited 2015 August 30]. Available from: www.shanghairanking.com.
2. Wickman M, Kull I, Pershagen G, Nordvall SL. The BAMSE project: presentation of a prospective longitudinal birth cohort study. *Pediatr Allergy Immunol*. 2002;13(s15):11-3.
3. Bondy SJ, Johnson I, Cole DC, Bercovitz K. Identifying core competencies for public health epidemiologists. *Canadian Journal of Public Health/Revue Canadienne de Santé Publique*. 2008:246-51.

Appendix

Abstract

Background

Secondhand smoke (SHS) exposure in early life may be associated with sensitisation to food allergens, but the association with symptoms following food consumption is less clear.

Objective

To assess the association between SHS exposure at age 2 months and the development of food reported symptoms (FRS), including phenotypes based IgE reactivity to food allergens.

Methods

We used data from a Swedish birth cohort with 4,089 children followed to adolescence. We used generalised estimating equations and logistic regression to assess the association between parent-reported smoking at age 2 months and parent-reported symptoms following consumption of specific foods. We considered phenotypes of IgE reactivity based on sensitisation to 6 common food allergens (cow's milk, hen's egg, codfish, wheat, soybean and peanut—including peanut components Ara h 1, 2 or 3 and Ara h 8 or 9) at ages 4, 8 or 16 years.

Results

SHS exposure at age 2 months was significantly associated with FRS with IgE reactivity (OR 1.37; 95%CI 1.01–1.84) and increased odds of dermatological symptoms with IgE reactivity (OR 1.99; 95%CI 1.10–3.61). SHS was associated with increased odds of symptoms to peanut with IgE reactivity (OR 1.73; 95%CI 1.03–2.89), particularly symptoms to peanut with IgE reactivity to the peanut components Ara h 1, 2 or 3 (OR 2.51; 95%CI 1.05–5.99).

Conclusion

SHS exposure in the first 2 months of life may increase the odds of FRS with IgE reactivity to age 16 years – particularly reported symptoms to peanut with IgE reactivity to the peanut components associated with true peanut allergy – and may also increase the odds of dermatological symptoms with IgE reactivity.