

Richard Doll Prize Lecturer George Davey Smith Focuses On The Role Of Epidemiology In The Age Of Big Data

Is there a role for epidemiology in the age of big data? That is the question posed and answered in the affirmative by the University of Bristol's George Davey Smith, the recipient of this year's Richard Doll prize, in his lecture delivered by video to the International Epidemiological Association (IEA) at its triennial meeting in Japan last month.

Davey Smith did not hold his audience in suspense for very long as he confessed early in the lecture that there is an exciting future for epidemiologists in the era of big data and it is important for epidemiologists to enthusiastically embrace the opportunities afforded.

He outlined his talk to cover five

- Doll continues on page 2

Former CDC Director Frieden To Head New Global Initiative To Prevent Heart Disease, Stroke, And Epidemics

Focus Is On "Low Hanging Fruit" In Global Health

In contemplating his next career move, former CDC Director Tom Frieden asked himself where and how he could make the most difference, and global public health was his answer. Now, in what appears to be a global public health initiative customized to his experience, skills, and interests, Frieden has been selected to head Resolve To Save Lives, a five year initiative launched this month with 225 million dollars from the Bloomberg Philanthropies,

the Chan Zuckerberg Initiative, and the Bill & Melinda Gates Foundation .

Two Efforts Under One Initiative

The initiative brings together under one leader efforts to combat both communicable and non-communicable diseases, two very different "families" of public health challenges. Working on such dissimilar threats is something rarely

- Frieden cont'd on page 7

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topics, namely

- Epidemiology and causation--
role of genetics and
biomarkers
- Exposure and outcome
assessment
- Levels of causation
- Limits of prediction
- A role for epidemiology

Early Career

Davey Smith began by recounting his experiences in studying cardiovascular disease in the 1980's when observational studies suggested that elevated levels of HDL cholesterol could be protective against cardiovascular heart disease (CVD). He described a study demonstrating the challenges in disentangling HDL and triglyceride measurements in studying CVD. He called these and other CVD measurement issues "intractable problems" which influenced him to study other more epidemiologically tractable questions, for example ones around HIV/AIDS and diarrhoeal disease in childhood. These appeared less susceptible to measurement issues and the results had more direct implications for public health.

New Approaches

Davey Smith recounted how during the 2,000's the incorporation of data on molecular genetic variation into observational epidemiological studies - and in particular Mendelian randomization (MR) - could be used to overcome some biases in studies and help strengthen causal inference.

He highlighted the benefits of triangulation or comparing different study approaches to obtain more reliable or accurate answers to research questions, including those around the role of elevated levels of HDL. Large scale randomized controlled trials and MR studies converged on providing strong evidence that modifying circulating HDL levels did not improve cardiovascular outcomes. It is difficult to think of how any other developments in epidemiological methodology had made a serious contribution to understanding this crucial issue.

In discussing other transformational changes that have taken place around exposure and outcome assessment, Davey Smith used DNA methylation and how it indexes exposure to smoking more accurately than self-reported smoking data. It can even assess in utero exposures that took place decades earlier. Other innovations he described include the use of cameras which can be worn by infants to collect digital data on parent-child interactions, something Davey Smith described as "a complete transformation" and one small indicator of the opportunities that can be afforded by digital and big data.

Levels of Causation

In discussing levels of causation, he reminded the audience that much of the big data collected is at the individual level and of itself may not be of particular relevance to interpreting the effects of broader, underlying social and economic influences on levels and trends in populations. He warned

- Doll continues on page 4

Mystery Still Surrounds Occurrence Of Zika In Northeast Brazil

More than two years after Zika virus was linked to microcephaly cases in northeast Brazil, there is still plenty of mystery surrounding why the outbreak was so severe and did not spread in the same way to other countries of the region. Also, cases did not materialize in a second wave in 2016 in northeast Brazil as anticipated.

Recent articles in the Globe and Mail entitled “Zika virus: still no clear answers” and at Vocativ.com entitled “Two Years Later, Zika Virus Is Still A Big Mystery” highlight the unanswered questions and describe some of the hypotheses epidemiologists and other have advanced to explain the Zika observations.

Why?

The first key question is whether or not the apparent increase in microcephaly cases in northeast Brazil was a real increase or an artifact of reporting.

While the number of reported cases of microcephaly was in the low thousands, there are no reliable data on the number of affected persons in the population and no reliable data on the number of Zika infected pregnant women. If the number of infected pregnant women was in fact very large because the virus was newly introduced to the population, then the rate of microcephaly cases may not have been higher than what was seen in other populations. Also, it is possible there was overreporting of cases once the alarm about the risk of microcephaly was recognized.

Gut Feeling

Laura Rodrigues, a Brazilian epidemiologist at the London School of Hygiene and Tropical Medicine, told the Globe and Mail “My personal gut feeling is that we had large Zika epidemics with lots of mosquitoes and most people getting infected, in northeast Brazil, and in Cape Verde and French Polynesia...and in other places transmission was much slower, with fewer mosquitoes, more air conditioning, and so on, so it will take years for the same proportion of people to get infected, and microcephalic babies will not peak but are spread over years...[but] a gut feeling is not science.”

Another opinion expressed in the articles is that the lower attack rate in less affected areas may have been reduced because of effective mosquito control efforts, or more widespread use of abortions in populations which had more advance warning than in northeast Brazil.

Data from a registry of pregnant women with Zika infection in the US has shown a rate of approximately 5%.

Co-Factors

Fatima Marinho, Brazil’s coordinator of epidemiological analysis and information in the Ministry of Health, told the Globe and Mail “It is becoming increasingly clear that something beyond Zika virus occurred in a part of the northeast region and was one of the causative factors of microcephaly...We have always been

“... a gut feeling is not science.”

“It is becoming increasingly clear that something beyond Zika virus occurred in a part of the northeast region ...”

“Whether [any particular] exposed subject does or does not develop a cancer is largely a matter of luck...”

epidemiologists that it is important not to become distracted by the excitement around big data from the main objective of epidemiology to impact population health by creating population level interventions. While MR is a powerful tool, it does not in itself help us develop interventions at the population level, said Davey Smith.

Doll on Luck

He quoted from Richard Doll to highlight the role of luck or chance in determining which individuals actually come down with disease, and to point out that the influence of stochastic factors limits the accuracy of predictions that will be possible about individual health outcomes.

According to Doll, “Whether [any particular] exposed subject does or does not develop a cancer is largely a matter of luck; bad luck if the several necessary changes all occur in the same stem cell when there are several thousand such cells at risk, good luck if they don’t. Personally, I find that makes good sense, but many people apparently do not.” Davey Smith called this fact “good news” for epidemiologists because it means that population level interventions – which is what epidemiologists study – are crucial to improving public health.

Guiding Lights for Epi

In enthusiastically embracing big data, Davey Smith exhorted his audience not to forget that it is the factors at the population level that should be the focus for epidemiologists and that attention to basic principles will pay off. He encouraged epidemiologists to

embrace the important and exciting role of grasping the opportunities provided by big data, whilst not being distracted from the major task of the discipline.

The lecture is available at:
<https://tinyurl.com/y7c6shoh>
with a 2 minute animation outlining Mendelian randomization that it contains also available at:
<https://tinyurl.com/yba55mag>

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-Zika cont'd from page 3

been betting on an environmental co-factor, like water, which could carry various contaminants, even biological ones.”

Assuming there was a real increase in the rate of birth defects, why was the rate higher than reported in other areas? Was there some other environmental co-factor that could explain the unusual number of microcephaly cases?

Hypotheses

Multiple hypotheses have been advanced or are being investigated including lower than average pre-existing immunity to other arboviruses acquired naturally or from vaccination which could have provided cross-protection against Zika.

Another hypothesis is derived from the observation that there is a high seroprevalence of dengue antibodies in the north of Brazil. Did possible previous exposure to a related arbovirus cause the Zika virus to be more virulent?

- Zika continues on page 8

Incoming IEA President Barros Presents Plan For 2017-2020

Calls For Multiple Actions, Including Deeper Engagement With Populations Studied

[Ed. Following is the statement released by Henrique Barros in taking over as President of the International Epidemiological Association at the Incoming Council meeting held in Japan last month. According to IEA, as of August, 2017, there were about 1800 IEA members from over 100 countries, including:

Africa 135	North America 261
Europe 278	South East Asia 419
Latin American and Caribbean 129	Western Pacific 457]

"...IEA has been shaping the field of epidemiology around the world."

Barros Statement

Building on Previous Work

This plan is intended to build upon the work done during the previous years, following Cesar Victora intense efforts to increase IEA membership and to support the development of epidemiology and the affirmation of low and middle income countries epidemiologists, and Valerie Beral leadership through difficult financial times and the process of changes in one of the IEA most respected symbols, the IJE. It is thus essential to guarantee during the upcoming triennium that we continue to increase and diversify the membership, more visibility is given to emerging societies, the IEA press remains the most respected journal in its scientific field and we manage to do it keeping a healthy financial context.

Expanding IEA Influence

In 2019 we will celebrate six decades on the adoption of the present Association title, and during this period IEA has been shaping the field of epidemiology around the world. The IEA Members, and in particular those that served as Councilors, comprise some of the most influential epidemiologists in different countries and helped to make epidemiology a respected scientific discipline, evolving into different inspiring directions. One way to keep on track while further exploring new venues is to broaden the influence of IEA to a larger geographical area and to make it the leading association of those involved in the everyday epidemiological labor.

Work with Regions

We will work with the Regions to take advantage of different traditions in terms of education, training and practice of epidemiology, sharing best practices, standards, ways of overcoming difficulties and organizational solutions, lobbying towards agreed targets. The IEA needs to be more visible, approximating international Agencies and Organizations involved in decision making in health, at the Regional and Worldwide levels.

Field Epidemiologists

Epidemiology has been a scientific discipline and an area of applied work be it in relation with public health operations or in the clinical arena. It is important to the IEA to become also the voice of field epidemiologists as it has been so clearly for those more academically oriented. The IEA needs to put more effort in exploring the labor market for epidemiologists, thus going beyond the more traditional Academic perimeter, towards the public and private health and allied services

"...the leading association of those involved in the everyday epidemiological labor."

and seeking the needs and interests of non-governmental organizations. A structure will be developed, made of voluntary members available to help NGOs to incorporate epidemiological methods in the design of their interventions or in the process of evaluation. It would enlarge the past activity of mentoring early career epidemiologists, a service provided by some IEA senior members that was highly valued and that needs now a formal evaluation and a new frame of offers.

Founding Spirit Continued

Working groups on such topics as genetics, data protection, big data or globalization, with an interregional dimension, based on different solutions to communicate (internet, two-day workshops) will be strongly encouraged and with it we deeply believe to continue the founding spirit of IEA. The issued documents will promote the presence of IEA in different fora and will expectedly increase our influence as evidence providers near policy makers.

Cooperative activities with other societies will be seek to increase the IEA presence and avoid losing those that due to their more specialized field of interests tend to join preferentially other societies or professional organizations. It will help to keep present the specificities of our methodological approaches in broader contexts, and gain inspiration from other areas.

Younger Epidemiologists

We will promote links between young and early career Epidemiologists in order to facilitate collaboration in scientific research, promote funding, international exchange of researchers and mentoring. The high-quality educational programs for graduate students or epidemiologists in training need to be offered to a wider audience reaching more geographical areas. A scale-up of IEA presence in well established courses, such as Florence, its expansion to other regions or the active promotion of partnerships with national societies can be a winning strategy.

Open Access Publishing

The International Journal of Epidemiology is an excellent ambassador for IEA but engaging in a new open-access medium might be a successful way to increase IEA relevance while offering an additional source of financing.

Participatory Vision

Finally, as epidemiology is a population science, a deeper engagement of the representatives of those populations - be it by means of patient organizations, community leaders or other - would increase the chance for a more participatory vision of research and a larger resonance of our work once we would be more able to put the population and their interests at the center of our concerns.

Governing Documents

To make some of these proposals reality and to proceed in a sustainable track there are aspects of our constitution and by-laws that need to be revisited, and the Handbook updated, completing the work initiated during Valerie Beral Presidency. A urgent major change involves the development of a formal framework considering the election procedures and the institutional role of Early Career Epidemiologists representatives.

I look forward to work with you in Saitama and Tokyo and for the next three years

August 10, 2017

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"...important to the IEA to become also the voice of field epidemiologists..."

"...we would be more able to put the population and their interests at the center of our concerns."

seen before in launches of new public health initiatives, for example those targeted against tobacco, drug abuse, road accidents, or obesity.

Resolve To Save Lives will tackle heart disease and stroke and infectious disease epidemic prevention. While the approaches to combatting each of these will require very different actions, what they have in common is that proven effective interventions exist to combat both sets of problems, and these interventions are underutilized, especially in low to middle income countries. This is the opportunity Frieden is trying to capitalize on to save 100 million lives over the next thirty years.

According to Resolve, "Both of these issues are at a tipping point. Without significant investment and attention now---millions of preventable deaths will continue to occur and the world will not be safe from the next disease threat." In short, they represent "low-hanging fruit" in global public health.

Interventions

What are these interventions? For heart disease and stroke, Resolve will work to increase blood pressure control, reduce dietary sodium intake, and eliminate artificial trans fats. To prevent epidemics, Resolve will develop surveillance systems, train more epidemiologists or disease detectives, support public health labs, and develop rapid response teams when outbreaks occur.

As Frieden told the New York Times in an interview about the new initiative, "why are we only focusing on sodium reduction, trans fats, and

blood pressure control? There are other things [such as a Mediterranean diet or increase physical activity] that either work but haven't been scaled up, or that we don't know how to do. The Resolve interventions are all actions where evidence exists to demonstrate effectiveness.

Benchmarks

For example, Resolve cites the success in Canada in achieving nearly 70% blood pressure control, the success in Denmark and New York City in eliminating trans fats from foods, and the success in the United Kingdom in decreasing sodium consumption and associated heart disease and stroke. In short, there are public health interventions that have been successfully scaled up and produced measurable impacts in different populations and these have created and these have created benchmark goals that are attractive and achievable for other countries. In short, there is "proof of concept" for the interventions envisaged by Resolve and the entire initiative could be framed as a major push to better translate proven data into action. According to Frieden, "There are proven strategies every country can use to prevent deaths from heart disease, stroke, and epidemics - but progress has been painfully slow..."

Goals for the Initiative

In setting goals for these interventions, Resolve has targeted increasing global control of blood pressure from 12 to 50%, reducing global dietary sodium intake by 30%, and eliminating trans fats completely. In preventing outbreaks, Resolve has

" Without significant investment and attention now--- millions of preventable deaths will continue to occur..."

"...there are public health interventions that have been successfully scaled up and produced measurable impacts..."

"... others have considered the role of the public health system itself in intensifying the outbreak..."

understandably not provided the number of epidemics it will seek to prevent or lives it will seek to save, however, the proven valuable activities they will undertake include

- Implement and strengthen disease tracking systems - so that unusual events are noticed and investigated.
- Support laboratory networks - so that new and emerging threats are identified promptly.
- Develop and support "disease detectives" - epidemiologists to track and investigate diseases and outbreaks.
- Develop rapid response teams - to investigate and stop outbreaks, working out of functional emergency operations centers which operate under structured, effective incident management systems.

Resolve will be implemented by a team of global health experts at Vital Strategies, a New York-based global health organization that works in more than 60 countries.

"...we need to get a handle on what the risk is."

To learn more about the new initiative, visit :

<https://www.resolvetosavelives.org/>



From the observation that more cases occurred in less populated small cities and rural areas, some investigators speculate that prior exposure to livestock viruses could have enhanced the response to Zika infection.

Still others have considered the role of the public health system itself in intensifying the outbreak since many of the cases occurred in poor, younger mothers who access these services.

No Answers Soon

The difficulties of conducting the research needed to answer these questions are being compounded in Brazil by budget cuts, competing priorities because of other outbreaks, political turmoil in Brazil, and the difficulty of finding new cases to study. Yale university epidemiologist Albert Ko told the Globe and Mail, "The virus is obviously circulating in Africa and Asia causing outbreaks. It may be a large proportion of women of child bearing age who are susceptible and we need to get a handle on what the risk is."



Notes on People



Died: Louisa Chapman, aged 64, medical epidemiologist and an associate director for science at CDC. Since 1988 she served in many roles at the agency and was an expert in viral epidemiology and served as a reviewer/consultant for multiple organizations. As stated in her obituary, "Louisa was full of generosity, grace and grit. Once she was diagnosed with late stage cancer, she never indulged in self-pity, or wallowed in complaints, but fought back with humor and strength and continued to live life fully for another 8 years."



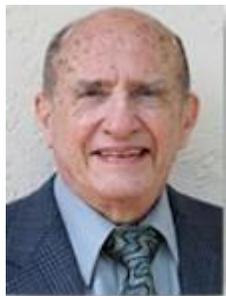
Taking Office: Henrique Barros, as President of the International Epidemiological Association at its recent meeting in Japan. In his President's plan for 2017-2020, Dr Barros called for multiple actions, including deeper engagement with the representatives of the populations studied (See related article in this issue). Dr Barros is President of the Institute of Public Health, University of Porto in Portugal and will serve a three year term until the next IEA meeting in Australia in 2020.



Invited Speaker: Danielle Buttke, DVM, PHD National Park Service epidemiologist will speak about her work responding to urgent and emergent public health issues in over 400 National Park units at College of the Atlantic's next Human Ecology Forum on September 19, 2017 in Bar Harbor Maine. Dr. Buttke conducts both human and veterinary disease surveillance activities, consults parks on zoonotic disease issues such as tularemia, plague, West Nile Virus, Lyme, and tick-borne relapsing fever, coordinates public education and messaging, and has led public health investigations into a hantavirus outbreak and two human plague cases.



Winner: Lorena Pacheco, in the Student Research Paper Contest sponsored by the journal Preventing Chronic Diseases. Pacheco, one of the top five winners, is an epidemiology doctoral student at the University of California San Diego – San Diego State University Joint Doctoral Program.



Honored: Bruce Kaplan, with the Meritorious Service Award from the American Veterinary Association. The award is conferred for bringing distinction to the veterinary profession through personal, professional, or community service activities outside organized veterinary medicine and research. He held positions as an epidemiologist at the CDC and with the USDA. He has promoted the ONE HEALTH concept that human, animal, and environmental health are inextricably interconnected.

- Notes on People continues on page 8

Notes on People



Awarded: To Kristina Rodriguez, the David Rosenstein Award for Best Student Abstract for her APHA abstract entitled "*Comparing MSM on PrEP to those who meet CDC guidance for PrEP use, but are not taking it: Results from a U.S. National Sample.*" Rodriguez is an epidemiology doctoral student at the City University of New York Graduate School of Public Health and Health Policy. The award will be presented at the APHA annual meeting in Atlanta, GA in November.



Died: Kathryn Marie Rose, age 59, on September 5th, 2017 after a long battle with cancer. Dr Rose was a member of the Cardiovascular Disease Epidemiology Department at UNC and during the final years of her career at Social & Scientific Systems. "Kathy made many contributions to our department's research on cardiovascular disease, including risk factors for and outcome from migraine headaches," according to Andrew Olshan chair of the Gillings School epidemiology department. "She also was very interested in neighborhood socio-economic status and contextual aspects of community and their role in determining cardiovascular health. She is fondly remembered as a student mentor and engaged faculty member."

Information For "Notes on People"

The Epidemiology Monitor is always interested in information about fellow epidemiologists at all stages of their careers and lives.

Please forward any information for future issues to:

epimon@aol.com / 678.361.5170

Toronto Epidemiologist Clarifies Stance On Glyphosate And Themes Relevant For Epidemiology

[Ed. Last month we published an article about the categorization of glyphosate as probably carcinogenic by the International Agency for Research on Cancer and the related controversy swirling around this issue. In the article, we reported a quote attributed to the University of Toronto's [John McLaughlin](#) saying that despite unpublished negative data he was aware of, this information had not changed his views about the overall categorization of glyphosate as probably carcinogenic. McLaughlin wrote the commentary below to expand on his views.]

Dear Sir,

Thank you EM for the thoughtful update on glyphosate and various media responses, which highlights several themes relevant to the field of epidemiology.

On the basis of a reporter's online article (by C. Gillam), EM commented that it was "not clear" how I had made a particular decision. I would have gladly spoken with EM, which would have shown close agreement with your main messages and with Dr. Blair's well-reasoned conclusions.

To clarify where EM was not clear, I stated that: (1) there are merits in making decisions based on all published evidence; (2) I continued to stand by the IARC decision, due to the rigour, comprehensiveness and transparency of the IARC decision-making process; and (3) it is standard practice to re-evaluate past decisions as new evidence emerges.

This leads to a further point that the reporter did not convey, which fits with the 'big picture perspective' noted in EM's conclusion. The essential role for epidemiological evidence in weighing risks and benefits is well appreciated, and EM readers know that to deliver evidence that reliably informs decision-making, studies must meet high quality standards (e.g., requiring strong designs, large sample sizes, detailed exposure information, covariate adjustment, replication, etc.). What is not widely recognized is that even with global interest and many decades of use, there are very few human studies that can contribute substantially to cancer hazard assessments for many environmental exposures. Accordingly, this 'big picture perspective' could also consider the forces that influence research investments, and with broad stakeholder engagement and partnerships would better support the epidemiological community in addressing society's needs, while also delivering sustainable systems that can answer important questions of the future.

John McLaughlin
Chief Science Officer
Ontario Public Health
And
Professor
University of Toronto

■

"...I continued to stand by the IARC decision..."

"...there are very few human studies that can contribute substantially to cancer hazard assessments for many environmental exposures."



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The deadline for applications to be submitted is October 15, 2017 but the search remains open until the positions are filled. The anticipated start date is July 1, 2018. Informal inquiries may be submitted to episearch@ph.ucla.edu.

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More Info: <http://www.epimonitor.net/2017-2383.htm>

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MEDICAL CENTER

Epidemiology: Tenure-track or Tenured Faculty

The Vanderbilt Epidemiology Center at Vanderbilt University Medical Center (VUMC) invites candidates to apply for tenured or tenure-track faculty positions. More than 50 epidemiologists at Vanderbilt conduct clinical and population-based studies, including three large cohort studies in the U.S. and abroad with survey data and biological samples from approximately 225,000 study participants. Areas of ongoing research include diet and nutrition, health behaviors, environmental exposures, reproductive epidemiology, genetic and other biomarkers for disease risk and progression, and racial disparities in health outcomes. The Center is particularly interested in expanding its research and training programs in epidemiology of cancer and other chronic diseases.

Successful candidates will have a doctorate in epidemiology or a related field with additional training or experience in epidemiologic research, and a demonstrated ability to develop and sustain an independent research program. Vanderbilt fosters a rich environment of cross-disciplinary collaboration, providing exciting opportunities to work on cohort consortium projects and collaborate on ongoing research projects in epidemiology.

Vanderbilt University School of Medicine is ranked #14 on the recent US News and World Report list of top medical schools for research in the US and is in the Top 10 for NIH-funded research. VUMC is home to the Vanderbilt-Ingram Cancer Center, an NCI-designated Cancer Center. VUMC is an Equal Opportunity/Affirmative Action employer.

Nashville, the state capital, is the largest metropolitan area in Tennessee, with temperate climate, low cost of living, affordable residential areas, vibrant cultural activities and abundant recreational opportunities.

To apply, email a cover letter, briefly describing research experience and interests, and curriculum vitae to kim.kreth@vanderbilt.edu. Address the cover letter to: Dr. Wei Zheng, c/o Kim Kreth, Vanderbilt University Medical Center, 2525 West End Ave., 8th floor, Nashville TN 37203-1738. Vanderbilt Epidemiology Center online: <https://www.vumc.org/vec/>.

K12 Career Development Opportunity

The **UCSF-Kaiser Permanente Urological Epidemiology Research Career Development Program (UCSF-KPNC UroEpi)** is seeking a highly qualified, motivated MD, PhD, or comparable doctoral degree in early faculty or final year post-doctoral positions.

The UroEpi Program seeks to :

- Recruit individuals committed to becoming an independent clinical researcher in the epidemiology of benign urological conditions at Kaiser.
- Develop Scholars' proficiency in epidemiology, research field methods, research ethics, leadership, manuscript preparation, and grantsmanship.
- Individualize each scholar's career development plan according to his or her background and future career goals.

Salary support of up to \$100,000 per year is provided. The awardee must devote 75% of full-time professional effort (50-75% for surgical specialties) to conducting research and research career development

For more information, please contact:

Stephen K. Van Den Eeden, PhD at Stephen.Vandeneeden@kp.org

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