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Jacques Rossouw, MBChB, FCP (SA), MD

WHI Researcher Profile

INCE 1991, Dr. Jacques Rossouw has been at the helm of the WHI program at the National Heart, Lung, and Blood Institute— the sponsoring institute that has provided research funding and support to the WHI. He has been a champion of the WHI since the study's beginning. He retired

from his role as WHI Branch Chief in 2014 but still remains active with WHI. His research interests included postmenopausal hormone therapy, cardiovascular disease, and nutrition. We connected with Dr. Rossouw to learn more about his experience with the WHI program.



How did you first come to be involved with the WHI and ultimately become its Project officer and Branch Chief?

A Prior to emigrating from South Africa to the US in 1989, my research had already been focused on nutrition and the prevention of cardiovascular disease. After my arrival to the US, the potential for menopausal hormone therapy to prevent cardiovascular disease became an intriguing prospect. So I jumped at the opportunity to participate in the planning for the WHI program, announced by NIH Director Dr. Bernadine Healy in early 1991. After all, the research agenda included prevention of disease, nutrition, and menopausal hormone therapy! Later in 1991, I was asked to be the first Project Officer of WHI at the National Institutes of Health, and while my title changed over time to Branch Chief, my involvement and interest remained constant until my retirement in 2014. Now retired, I remain involved and interested in an advisory capacity.

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WHI RESEARCHER PROFILE

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What did you like most and least about working with the WHI program?

A I will always treasure the privilege of being able to work with an outstanding and collegial group of investigators and hearing their accounts of the enthusiasm that women have had as participants of the WHI. Those experiences, and the fact that the WHI findings have made a lasting contribution to the health of women, far outweighed any burden of having to deal with the administrative tasks needed to keep the program moving forward.

(Q) What WHI achievements are you most proud of? A There are so many achievements, but the one that changed the world were the findings from the hormone therapy trial. Though complex and sometimes controversial—since hormone therapy has so many effects, some good, some bad—the basic message that hormone therapy is not a good prevention strategy for chronic diseases in aging women has stood the test of time and has been incorporated into the treatment guidelines of all the major professional societies. The drop in hormone prescriptions since these WHI findings were revealed has been calculated to save many women from disease and save health care dollars at the same time. In other words, the investment in WHI by the NIH, the investigators, and the participants has paid off!

What have been the biggest challenges of the WHI?

At the outset some were skeptical that such an ambitious program, enrolling more than 160,000 women in clinical trials and an observational study, could even be accomplished. At times there were challenges, but ultimately teamwork and problem solving overcame these. After the announcement of the hormone trial findings, the uproar was considerable and commensurate with the mountain of previous beliefs that was overturned. The WHI team stood together, continued to work and publish, and eventually prevailed.

Where do you see the WHI going in the next 5 years? 10 years?

A Some 25 years after the first participant was enrolled in 1993, the WHI program has moved on from the original trials and transformed itself into a program studying the resilience of aging women to disability and disease. Conversely, all the women remaining in WHI are now decades older yet are survivors. Many remain in excellent health. What determines healthy aging is a fascinating question engaging the investigators now and into the future.

Although a study of women, is there anything you have learned from the WHI and applied to your personal life (or recommended to the women in your life)?

A The hormone findings color my recommendations to women in my life, though of course the ultimate decision is between them and their own physician. For myself, the findings from the dietary trial have been reassuring, since a dietary pattern which increases carbohydrates versus fats did not lead to any adverse consequences in terms of weight gain, diabetes, or cardiovascular disease. Despite the media hype that carbohydrates need to be cut and fats increased (as in Atkins, Paleo, Low Carbohydrate High Fat diets), WHI has conclusively shown that carbohydrates are not necessarily bad for you. Of course, the quality of carbohydrates matter, as also indicated by WHI analyses showing that a focus on whole grains, cereals, fruits and vegetables as sources rather than sugar or other refined carbohydrates is the way to go.

Is there anything else you wish to share, either about yourself or about the WHI, to the wonderful women who have been WHI study participants?

Without the wonderful participants, there is no WHI. Amazingly, after all these years they still come back to volunteer more of themselves. This short column touches on some of the contributions they have made to their health, and the health of others. They have made a difference!



Focus on Findings

OU HAVE SHARED how much you appreciate reading how your participation in the WHI continues to contribute to the research on women's health. We also enjoy reviewing the ever-growing list of publications and looking for the topics that would be most interesting to highlight. Here again we summarize just a handful of the WHI research papers published in the last year. (If you ever wish to read the full version of any of the papers described in this section, contact us! We'd be happy to send you a copy.)

■ Diet Quality and Type 2 Diabetes

(Journal of the Academy of Nutrition and Dietetics, May 2017)

Dietary energy density is defined as the ratio of a food's energy (its calories) to its weight (grams) and describes one aspect of diet quality. Healthier foods, such as vegetables and whole grains, have low energy density, while not-so-healthy foods, like sugary drinks and fried food, have high energy density. A study led by Dr. Melanie Hingle investigated the association between dietary energy density and the risk of developing Type-2 diabetes in over 143,000 WHI women. Dietary energy density was calculated using a woman's overall diet as reported in the food frequency questionnaire collected at WHI baseline. Over the next nearly 13 years, women with higher dietary energy densities at baseline had an 8-24% higher risk of developing diabetes compared to women who had the lowest dietary energy densities at baseline, even after accounting for a number of other factors like age, race/ethnicity, smoking status, physical activity, and family history of diabetes. Recognizing the strong influence of obesity on diabetes risk, the researchers also showed that women with higher dietary energy densities plus a waist circumference of 35 inches or more had a 9-12% greater risk of developing diabetes than women with waist circumference of less than 35 inches. More research is needed—for example, it is not known whether improving one's diet quality, by lowering dietary energy densities, can lower the risk of developing Type-2 diabetes.

Periodontal Disease and Cancer Risk

(Cancer Epidemiology Biomarkers and Prevention, August 2017)

Gingivitis is the earliest form of periodontal or gum disease. If gingivitis goes untreated, it can progress to periodontitis, in which plaque has developed below the gum line. The bacteria in the plaque can cause an inflammatory response and lead to tooth loss. Statistics indicate that over 70% of Americans over age 65 years have periodontal disease. Research has shown that periodontal disease is associated with an increased risk of cancer, but few studies have been done in older women. To address this gap, the research team led by Dr. Ngozi Nwizu examined nearly 66,000 women from the WHI Observational Study. They found that women with a history of periodontal disease had a higher risk of developing cancer, including specific cancer types like breast, lung, esophagus, gallbladder, and melanoma skin cancer. The results were similar when the analysis only included never-smokers, indicating that smoking status does not influence the associations.

Long-Term Bisphosphonate Use and Fracture Risk

(Journal of the American Geriatrics Society, September 2017)

Osteoporosis is a condition characterized by low bone mineral density and deteriorating bone structure. It increases the risk of a fracture and it affects about 30% of postmenopausal women.



Bisphosphonates (e.g., Actonel, Fosamax) are commonly prescribed medications that increase bone mineral density and are the first line of defense to combat osteoporosis. Yet, it is unclear whether bisphosphonates continue to prevent fractures when taken for many years. Dr. Rebecca Drieling and colleagues examined 5,120 WHI women who reported taking bisphosphonates for at least 2 years to see if fracture risk depended on how long these medicines were taken. They did not find a higher (or lower) fracture risk among women who took bisphosphonates for 3 to 9 years continuously compared to women who took the medication for only 2 continuous years. However, women who took bisphosphonates continuously for 10 to 13 years had a 29% higher risk of fracture, even after accounting for other risk factors for fracture.

Statins and Risk of Endometrial and Ovarian Cancers

(Gynecologic Oncology, February 2018)

Statins are commonly prescribed cholesterol lowering medications that reduce inflammation and might also limit cancer cell growth. Dr. Pinkal Desai and colleagues were interested in finding out if statin use was related to endometrial and ovarian cancer risk. They found that longer term use of statins (i.e., from WHI baseline and into the follow-up period) was not associated with a higher risk of endometrial cancer. However, they discovered that longer term use of a statin called Pravastatin was related to a higher risk of ovarian cancer. The authors were not sure why higher risks of ovarian cancer were seen in long-term Pravastatin users and recognized that these results should be confirmed in other research studies.

Genes for Depression and Risk of Stroke (Stroke, March 2018)

Genetic data provided by a select sample of WHI participants have allowed researchers to examine the role genes might play in health and disease.

For example, large cohort studies, like the WHI study, have consistently shown that having a history of depression increases one's risk for stroke, but it is not clear why. The team led by Dr. Sylvia Wassertheil-Smoller decided to explore if the connection between depression and stroke might be due to shared genes. Using a database that pooled genetic data from several different research studies, including the WHI study, they found that higher genetic risk scores for major depressive disorder were associated with increased risk of ischemic stroke in people with European or African ancestry. This finding suggests that depression and ischemic stroke might share some of the same genes.

Sleep Duration and Sleep Quality with Mortality

(Sleep Medicine, June 2018)

A study led by Dr. Geoffrey Kabat examined how the amount of sleep, the use of medication or alcohol as a sleeping aid, and having insomnia are related to dying. Using sleep information and deaths among 157,554 WHI women, they found that either too little or too much sleep was associated with higher death rates. Specifically, they found that, compared to women who slept 7 hours per night, women who slept 5 or less hours per night had a 10% higher risk of all-cause mortality and a 16% higher risk of cardiovascular disease mortality and women who slept 9 or more hours per night had a 67% higher risk of all-cause mortality, 66% higher risk of cardiovascular disease mortality, and a 84% higher risk of cancer mortality. In addition, they reported that women taking a sleeping aid had a 10-13% higher risk of all-cause, cardiovascular disease, and cancer mortality. However, they did not find any relationship between having insomnia and the risk of dying. Since sleep information was self-reported, the authors suggested that these associations be validated in other studies that collected sleep data objectively, such as through sleep monitors.



Maintaining Your Oral Health

S YOU READ in the Focus on Findings section, taking care of your mouth, teeth, and gums is very important for your overall health. Yet, older adults have the highest prevalence of gum (periodontal) disease, tooth loss, and oral cancer of any age group. The reasons why are likely complex but contributing factors include:

- Changes in dexterity or grip strength or health conditions, such as arthritis, make it challenging to hold a toothbrush or dental floss.
- Use of certain medicines that cause dry mouth, a condition that decreases your saliva, which hastens tooth decay and other infections.
- Inability to visit a dentist. Many lose dental insurance after retirement and Medicare does not provide routine dental coverage.

Here are some tips to helping you maintain your oral health:

- Continue to brush your teeth at least twice a day and floss once a day. If gripping a standard toothbrush handle is hard, consider switching to a child-sized or electric toothbrush, which have bigger handles. Or, modify your toothbrush handle with a tennis ball or foam tube to make it easier to hold. If holding dental floss is a challenge, consider using disposable floss picks or a water flossing device.
- Use a smaller amount of toothpaste if it is difficult for you to spit, since the foam created by toothpaste can cause choking. Consider

- including a nonalcoholic, fluoride rinse in your brushing routine.
- Prevent dry mouth! If the medicines you take cause dry mouth, talk to your doctor about alternative medication options. If you experience dry mouth, consider chewing sugar-free gum or mints, which can increase saliva production, drink plenty of water, don't smoke, and limit your alcohol use.
- If you have dentures, keep them clean by brushing them daily with a denture-care product and soaking them at night. Tell your doctor or dentist if they change how they fit in your mouth, which might be an indication that they need to be adjusted.
- See a dentist regularly, even if you wear dentures.
 Only a dentist can diagnose certain conditions, such as periodontitis and oral cancer. If dental care seems too costly, visit the website listed below for strategies on finding low-cost dental care.

For more ideas and information, visit the National Institute of Aging page on oral health at https://www.nia.nih.gov/health/taking-care-your-teeth-and-mouth and www.toothwisdom.org, a project by Oral Health America whose aim is to improve oral health outcomes for adults age 65 years and older.

Find low-cost dental care in your location on the Tooth Wisdom website at https://www.toothwisdom.org/care/.





Pedestrian Safety

By WHI Participant Janey M. Rifkin



but three states ban text messaging while driving, but what about pedestrians, which applies to everyone? Last October, Honolulu, Hawaii became the first major city where pedestrians could be fined for crossing the street while looking at their mobile device. Time will tell whether this new law will help keep pedestrians safer, but evidence suggests these are dangerous times! The GHSA reported that nearly six thousand pedestrians were killed in 2016 and in 2017—a 27% increase from 2007 and an indication that the problem is not improving.

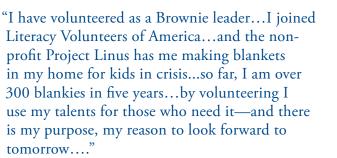
Therefore, take precautions while you are on the street walking, jogging, or even biking. Instead of looking at your phone, be aware of your surroundings! This includes not only looking out for cars and buses that may be driving by, but also curbs, signposts, stairways, and other hazards. As a pedestrian, follow basic safety rules, such as following the crosswalk signals, walking within the marked area, and using the sidewalks instead of the street. If you are out at night, wear light colored or reflective clothes and put on a headlamp or flashing light. If you are walking or jogging with music, keep your phone or headphone volume low enough that you can hear approaching vehicles, bicyclists, and other pedestrians.

Additional precautions should be taken if you are on a bicycle. This includes biking with the flow of traffic, using the bike lanes if they are available in your area, wearing a helmet, and avoiding alcohol, which can impair judgment and make you less alert. It is also a good idea to regularly check your bike for damage and ensure all the parts are working properly.

And, if you are behind the wheel, remember that pedestrians and cyclists may be distracted too. Walkers, joggers, and bicyclists who use earbuds or are on their phone may not hear or notice your car as it approaches. Whether driving, biking, or walking after dark, extra vigilance is required. Staying safe and out of harm's way on the road means not allowing yourself to become distracted. Being alert may save your life! And, remember, the consequences are far too dire to be thinking you have the right of way! It is not worth risking your life to win that argument!

Letters to the Editor— WHI Participants Definitely Volunteer!

We asked you to share with us your volunteer efforts and we received numerous responses! We were amazed to read about all the work and support you provide in your communities and to people all over the world. While we cannot share every letter we received, here are a few excerpts:



—Participant in Scottsdale, AZ

"I am a volunteer for the Orange County Fire Authority...I love going to work and I know how much I am appreciated because they never stop thanking me for coming in....It warms my heart to know that even at 83 I can still be useful and respected for what I know."

—Participant in Orange, CA

"When I was ready to retire from a school office position, a person that volunteered faithfully for me for 9 years said, 'Find something you will enjoy. Something to look forward to each day.' Wise advice...I volunteered for the presidential election...to get new voter registrations....I volunteered on a Habitat for Humanity build site... led me to 9 years involvement with Habitat...I even got to meet President Carter and his wife Roslyn....My life is full and never boring. It also keeps me active and I do look forward to getting up each day."

—Participant in Orange City, FL

Dear WHI...

"Would it be of any interest that I am 95 and I volunteer at our local Senior Center? I tutor once a week in our English as a second language class, and once a month as a facilitator in a 'Writing Our Memoirs' class."

—Participant in Baltimore, MD

CORRESPONDENCE

We enjoy receiving feedback on the newsletter and we have E-mail!

Email us at: whimatters@whi.org

Or, send letters to:

Fred Hutchinson Cancer Research Center 1100 Fairview Ave. N

M3-A410 P.O. Box 19024 Seattle, WA 98109 Due to the volume of correspondence we receive, we will not be able to respond to everyone individually. We also regret that we cannot answer questions about individual medical conditions.

Staff Information:

WHI Matters is produced by the WHI Coordinating Center at the Fred Hutchinson Cancer Research Center.







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