

## INSIDE THIS ISSUE:

The Platinum Study Conference 1

Featured Clinician: Dr. M. Eileen Dolan 1-2

Summary of Publications: 2-3

Impact of Pain and Adverse Health Outcomes on Long-term U.S. Testicular Cancer Survivors

Comprehensive Audiologic Analyses After Cisplatin-based Chemotherapy: Progression of Hearing Loss, Influence of Dose, and Functional Impairment in Adult-onset Cancer Survivors

Clinicians' Corner: Welcome Dr. Sean Kern! 3

Principle Investigator's Corner: Dr. Lois Travis 4

We Would Love to Hear From You

Stay connected with The Platinum Study Team! If you have moved, changed your email address, or have a new phone number, please notify your clinic or study team or you may share your contact information with the current study headquarters at Indiana University by:

- Calling us toll-free at 833-770-8700
- Emailing us at [ptstudy@iu.edu](mailto:ptstudy@iu.edu)

# Platinum Study Newsletter

SUMMER 2024

## The Platinum Study Conference: Need More Surveys

In November of 2023, The Platinum Study team and its leaders held a conference with interested parties, including an external board of advisors. Our purpose was to evaluate the progress of the study and decide on research directions for the future. Our board was impressed with the many major clinical and scientific findings made by the study over the last 10+ years. The Platinum Study has indeed made critical and important contributions to the clinical literature and to the practice of oncology in terms of information that helps not only you, the study participant, but the almost 6,000,000 patients each year who are eligible to receive the platinum drugs.

A challenge identified by the board, is that despite all our contributions, the rate of survey completion in The Platinum Study II is relatively low against national

benchmarks. The standard is that around 80% of all patients enrolled in the initial phase of any cohort study should also complete subsequent questionnaires so that longitudinal data can be obtained. Thus, if you have not yet either consented to Part II of the study, or if you have consented and not completed your questionnaire, we would like you to know that your responses are extremely important.

Please let us know how we can help you in this regard by contacting us by phone at 833-770-8700 or by e-mail at [ptstudy@iu.edu](mailto:ptstudy@iu.edu). Thank you again to all the study participants who have answered the questionnaire and continued to provide important data.

## Featured Clinician: Dr. M. Eileen Dolan

Dr. M. Eileen Dolan, Professor of Medicine at the University of Chicago, received her PhD in Medicinal Chemistry from Purdue University and pursued her post-doctoral fellowship at Penn State College of Medicine



in Hershey, PA. Dr. Dolan's expertise is in the pharmacogenomics of anticancer agent toxicity. To this end, she identifies how genetic variation plays a role in identifying patients at greatest risk for severe toxicity following chemotherapy or radiation. For the Platinum Study, her laboratory identifies genetic variants, clinical factors and modifiable risk factors associated with cisplatin-related hearing loss, tinnitus and peripheral neuropathy. Her laboratory has developed cell-based mod-

els to study mechanisms of chemotherapy-related toxicities using neuronal cells derived from stem cells. She has been a part of the Platinum Study group for more than 12 years.

Dr. Dolan is currently the Deputy Director of the University of Chicago Comprehensive Cancer Center (UCCCC), having previously served as Associate Director for Education for 12 years as well as co-leader of the Clinical and Experimental Therapeutic program for 20 years. She also serves on External Advisory Committees of several NCI-designated cancer centers. She is highly regarded as a mentor and educator for aspiring scientists with over 70 trainees from high school through post-doctoral fellows having worked in her laboratory. During her tenure as the UCCCC's Associate Director for Education, she initiated five unique training pro- (Continued on next page)

**(Cont'd)** -grams committed to increasing diversity within the biomedical research workforce by providing laboratory research experiences as well as career and skill building lectures. As a testament to Dr. Dolan's decades of mentorship and dedication to diversity, she received both the 2016 Distinguished Educator/Mentor Award and the 2021 Distinguished Leader for Diversity and Inclusion Award from the Biological Sciences Division at the University of Chicago.

Dr. Dolan has also received numerous external awards including Purdue University Distinguished Women Scholars Award, Purdue University School of Pharmacy Distinguished Alumni Award; University of Dayton Distinguished Alumni Award; and the American Cancer Society, IL Presidential Award for Volunteer Contributions to Research. On a personal note, she enjoys running and spending time with her husband and 2 children.

## Summary of Publications

### Impact of Pain and Adverse Health Outcomes on Long-term U.S. Testicular Cancer Survivors

Dinh Jr. P. C.; Monahan P.O.; Fosså S.D.; Sesso; H.D.; Feldman D.R.; Dolan M.E.; Nevel K.; Kincaid J.; Vaughn D.J.; Martin N.E.; Sanchez V.A.; Einhorn L.H.; Frisina R.; Fung C.; Kroenke K.; Travis L.B.

**Background:** Long-term survivors of testicular cancer are known to experience adverse health outcomes. Until now, no studies have examined the extent to which neuropathic pain and adverse health outcomes may affect the physical and mental health of survivors, and none have measured their impact on day-to-day "functioning," as reported by survivors themselves. New measurements and patient feedback are critical to understanding these complexities and improving care for survivors.

**What we did:** Three hundred fifty-eight testicular cancer survivors treated with cisplatin-based chemotherapy and already enrolled in the Platinum Study completed surveys about their physical health, mental health, pain, and more. Their answers to these surveys were examined alongside their health history for 25 adverse health outcomes, to see which have the greatest measurable impact on the physical and mental health scores.

**What we found:** Having more adverse health outcomes was associated with poorer physical and mental health scores. Poorer physical health scores were associated with diabetes, obesity, peripheral neuropathy, depression, balance/dizziness problems, and with difficulty thinking. Poorer mental health scores were associated with chemotherapy-induced neuropathic pain, diabetes, obesity, and fatigue. Being married or living-as-married benefited mental health. Reduced functioning was associated with peripheral artery disease and with neuropathic pain in the lower extremities.

**What does the study mean:** In this study, we provided the first measured assessment of the impact of pain and adverse health outcomes on the physical and mental health and self-reported functioning of testicular cancer survivors. This information enabled us to identify risk factors that require monitoring, counseling, and intervention. Chemotherapy-induced neuropathic pain was very detrimental to the health and functioning of survivors and must be addressed in follow-up evaluations.

Citation: *Journal of the National Cancer Institute* 2023, djad236. Advance online publication. <https://doi.org/10.1093/jnci/djad236>.

### Comprehensive Audiologic Analyses After Cisplatin-based Chemotherapy: Progression of Hearing Loss, Influence of Dose, and Functional Impairment in Adult-onset Cancer Survivors

Sanchez V.A.; Dinh Jr. P.C.; Monahan P.O.; Althouse S.; Rooker J.; Sesso H.D.; Dolan M.E.; Weinzerl M.; Feldman D.R.; Fung, C.; Einhorn L.H.; Frisina R.D.; Travis L.B.

**Background:** Cancer patients treated with cisplatin-based chemotherapy are at increased risk of hearing loss. Complete and thorough hearing measures and identifiable risk factors are needed to define individual risk, assess functional hearing ability and loss, and develop care plans for those with cisplatin-related hearing loss. No prior studies have used comprehensive measures of hearing or examined progression of hearing loss in relation to possible risk factors, such as other health concerns or how much **(Background cont'd)** total cisplatin a patient has received.

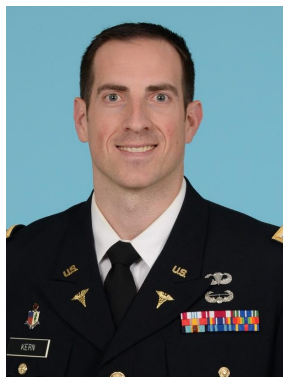
**What we did:** One hundred testicular cancer survivors in the Platinum Study agreed to undergo extensive hearing tests and evaluations over the course of several years to determine their functional hearing ability, loss, and progression over time. Hearing tests of particular interest were the words-in-noise test and the combined-ears high frequency pure-tone average. We also examined several factors that could possibly contribute to each participant's risk of hearing loss, including cisplatin dose, high blood pressure, high cholesterol, diabetes, tobacco use, physical inactivity, body mass index, family history of hearing loss, cognitive dysfunction, psychosocial symptoms, and tinnitus.

**What we found:** Participants had no hearing loss at the beginning of the study. Over time, poorer performance on the words-in-noise test was strongly associated with severity of hearing loss, with high cholesterol, and with a lower level of education. Hearing loss progression was strongly associated with high cholesterol, with increasing age, and with a higher cumulative cisplatin dose. Patients treated with <300 mg/m<sup>2</sup> of cisplatin experienced less hearing loss progression than those treated with >300 mg/m<sup>2</sup>.

**What does the study mean:** Our study was the first to demonstrate that regular, comprehensive hearing assessments and treatment of high cholesterol are essential for the care of adult-onset cancer survivors with cisplatin-related hearing loss. Importantly, this study demonstrates that patients who receive higher total amounts of cisplatin have increased risk of hearing loss progression. Thanks to the help of our participants, this study will help to improve evaluation and follow-up of patients and survivors in the hopes of improving treatment plans and reducing cisplatin-related hearing loss.

The full published version of these articles can be accessed on our website at:  
<https://cancer.iu.edu/patients/surviving/platinum-study/index.html>

## Clinician's Corner: Welcome Dr. Sean Kern!



Our Platinum Study Team welcomes Dr. Sean Kern, a testicular cancer survivor, as the newest member of our External Advisory Board. Dr. Kern is a Urologic Oncologist at the Walter Reed National Military Medical Center in Bethesda, Maryland, and a Lieutenant Colonel in the United States Army. After completing his urology residency training at Tripler Army Medical Center in Honolulu in 2015, he was stationed at Fort Belvoir, Virginia, where he became Chief of Urology. Due to his oncology interests, he later completed a two-year Urologic Oncology Fellowship at Indiana University in 2021. He is grateful for his mentors there: Drs. Lawrence Einhorn, Nabil Adra, Tim Masterson, Clint Cary, and Richard Foster. Upon completing his fellowship and returning to Washington DC, Dr. Kern had an interest and passion in improving testicular cancer treatment and survivorship in the military and veteran population. He, thus, established and became the founding Director of the U.S. military's Testicular Cancer Enterprise for Survivorship, Treatment, and Investigational Sciences ("TESTIS") Program. Dr.

Kern is also the Program Director of the Walter Reed Urology Residency and enjoys teaching residents and medical students. Ironically, Dr. Kern was himself diagnosed with testicular cancer in 2023, requiring 3 cycles of BEP (bleomycin, etoposide, cisplatin) chemotherapy treatment by Dr. Einhorn. Dr. Kern draws on his clinical expertise and personal experience with the disease to advocate for better treatment, survivorship, and improved understanding of the late effects of platinum-based chemotherapy.

## Principle Investigator's Corner: Dr. Lois Travis

The Mediterranean diet has received increasing attention in the last few years because of its documented health benefits. Thus, our team thought it might be helpful to pass along some information about it excerpted from the Mayo Clinic website ([www.mayoclinic.org](http://www.mayoclinic.org)) where the entire article is housed. It is entitled: "Mediterranean Diet for Heart Health," and was written by Mayo Clinic staff.

The Mediterranean diet is a healthy-eating plan focused on plants and includes the traditional flavors and cooking methods of that region. Diet is known to influence long-term diseases, including cardiovascular disease (CVD). Observations from a study in the 1960s found that CVD was linked to fewer deaths in some Mediterranean countries, such as Greece and Italy, than in the U.S. and northern Europe. More-recent studies have linked the Mediterranean diet with lower risk factors for heart disease, such as high cholesterol and high blood pressure.

Today, the Mediterranean diet is one of the healthy eating plans that American nutrition experts recommend. It's also as such recognized by the World Health Organization. Many cultures have eating patterns like the Mediterranean diet, including Japan, for example. And other diets have some of the same recommendations as the Mediterranean diet. Two examples are the Dietary Approaches to Stop Hypertension (DASH) diet, and the Dietary Guidelines for Americans. Research suggests that it's key to follow the Mediterranean diet over the long term for your heart to benefit. The diet is high in vegetables, fruits, whole grains, beans, nuts/seeds, and olive oil. The main steps for this diet include: each day eat vegetables, fruits, whole grains and plant-based fats. Each week, have fish, poultry, beans, legumes and eggs. Enjoy moderate portions of dairy products. Limit how much red meat you eat and foods with added sugar.

Unsaturated fats are a strength of the Mediterranean diet. They're eaten instead of saturated and trans fats, which play roles in heart disease, with olive oil and nuts the main fat sources providing unsaturated fat. When unsaturated fat comes from plant sources, it seems to lower levels of total cholesterol as well as low-density lipoprotein, also called LDL or "bad" cholesterol. Replacing saturated fat with polyunsaturated fat lowers risk of CVD events and death related to CVD, according to the Dietary Guidelines for Americans. Fish also are a key part of the Mediterranean diet. Some healthy choices are mackerel, herring, sardines, albacore tuna, salmon, anchovies. These are known as fatty fish and they contain omega-3 fatty acids, which are unsaturated fats that may lower immune system action in the body known as inflammation. They also may help reduce blood fats called triglycerides. Omega 3s may also lower the risk of stroke and heart failure too. Lean fish (e.g., cod, haddock, hake, whitefish) and shellfish also are included in the Mediterranean diet.

## We Would Love to Hear from You

Is there anything in your survivorship journey that you would like for others to know? Something that might be helpful for them? We would be happy to put it in one of our future newsletters. Please just e-mail us at [PtStudy@IU.edu](mailto:PtStudy@IU.edu) Also, in past newsletters, we have had the Clinician's Corner discuss ototoxicity, fertility concerns, neuropathy, and others. Is there any other survivorship issue that you would like for one of our expert clinicians to cover? Just let us know, and we would be happy to cover it, too. Shown below is Dr. Lawrence Einhorn with some of his patients in 2003.

**Tour of Hope, Indianapolis, Indiana, October 16, 2003: Dr. Einhorn with His Patients**

