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Overall cancer risk not increased with use of popular diabetes medication, IU study finds

Sept. 21, 2017

People taking a new oral medication for Type 2 diabetes can breathe a sigh of relief concerning suspicions they might be at an increased risk for many types of cancer, according to Indiana University researchers.

A review of 46 clinical trials involving more than 34,000 patients and [published in the July online issue of the journal *Diabetologia*](#) showed no increased risk of developing most forms of cancer for individuals taking sodium-glucose cotransporter 2 (SGLT2) inhibitors. The article is the first meta-analysis looking at the risk associated with SGLT2 and cancer using multiple resources including all available randomized clinical trials, multiple subgroup analyses, as well as meta-regression and sensitivity analyses.

Researchers from the Indiana University Melvin and Bren Simon Cancer Center and the Richard M. Fairbanks School of Public Health at IU conducted the analysis.

"It is important to note that the evidence from our meta-analysis of available randomized clinical trial data is suggestive of, but not conclusive for, the potential impact by SGLT2 inhibitor use on cancer risk," said co-author Yiqing Song, MD, ScD, professor of epidemiology at the Fairbanks School of Public Health and a researcher at the IU Simon Cancer Center. "Given rapidly increasing use of SGLT2 inhibitors, it is our hope that long-term safety of its use be carefully monitored in future clinical trials and real-world settings."

SGLT2 inhibitors are a class of prescription oral medications approved by the FDA in 2013 to be used in combination with diet and exercise to lower blood sugar in adults with type 2 diabetes. SGLT2 is a protein found in the kidney that helps the body reabsorb glucose. SGLT2 inhibitors specifically block that process, resulting in increased renal glucose excretion and decreased levels of blood glucose.

A growing body of evidence suggests that people with Type 2 diabetes are at elevated risk for cancer. Obesity is a known risk factor for developing both cancer and diabetes. Although all the mechanisms at play for this elevated risk are unknown, physicians do know that several glucose-lowering drugs have the potential to affect cancer risk, according to the study's co-author Jiali Han, PhD, professor and chair of the Department of Epidemiology at the Fairbanks School of Public Health and the Rachel Cecile Efrogmson Professor of Cancer Research at the IU Simon Cancer Center.

"Metformin therapy has been shown to decrease the risk of cancer while other drugs may increase the risk of specific cancers," Dr. Han said. "For instance, in 2011 a federal report raised concerns about the risk of bladder and breast cancer associated with dapagliflozin, but a later analysis of 21 clinical trials suggested it was more likely the increased incidence was due to under-diagnosis prior to patients being randomized to the trial."

Dapagliflozin (Forxiga) is one of three SGLT2 inhibitors recently approved for use by the FDA and reviewed in the literature for this study. The others are canagliflozin (Invokana) and empagliflozin (Jardiance).

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Jiali Han, PhD

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Yiqing Song, MD, ScD

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“In addition to lower glucose levels, SGLT2 inhibitors may offer other benefits, such as weight loss and lowering blood pressure,” Dr. Han said. “More and more patients will use SGLT2 inhibitors, with more than 12 million U.S. prescriptions to date just for canagliflozin.”

The researchers screened for the risk of all forms of cancer and then looked at the risk of specific cancers such as skin, breast, respiratory, gastrointestinal, bladder, prostate and renal.

Diabetes and obesity are known risk factors for bladder cancer but the exact mechanisms involving SGLT2 inhibitors and the increased risk for that cancer, as well as urinary tract infections, are unknown. The meta-analysis did not detect an increased risk associated with use of SGLT2 inhibitors for breast cancer or other cancers, but the authors caution that an increased risk cannot be ruled out without more randomized clinical trials.

“Our study provides the latest evidence about the association between use of SGLT2 inhibitors and risk of cancer and will help physicians and patients to better understand the risk when choosing these drugs. However, due to the relatively short term of randomized trials, our study also requires further long-term studies,” Dr. Han said.

The IU Health - IU School of Medicine Strategic Research Initiative and the IU Simon Cancer Center supported this research. Also contributing to the paper was Huilin Tang, MSc, research associate in the Fairbanks School of Public Health's Department of Epidemiology.

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With an eye on best practices, Dr. Einhorn began ASCO Review at IU 22 years ago

By Mary Hardin

Bigger isn't always better.

That was the thinking of [Lawrence Einhorn](#), M.D., when he envisioned a slimmed down version of the world's largest annual oncology meeting. His thought was to take days of presentations, hundreds of posters, and countless abstracts and exhibits, and boil them down to a one-day review that would feature the highlights of the annual American Society of Clinical Oncology Annual Meeting. Thus was born ASCO Review at IU.

This year marked the 22nd annual ASCO Review at the IU Simon Cancer Center. On July 21, 240 professionals dedicated to all aspects of the treatment of cancer gathered at Hine Hall Auditorium on the IUPUI campus to hear the most significant findings from the ASCO Annual Meeting this past June in Chicago. That meeting brings together more than 35,000 oncology professionals from 100 countries who come to hear the latest practice-changing research and network with internationally recognized experts in a broad range of specialties.

In 1995, Dr. Einhorn started what has become an annual tradition at IU and its success prompted similar programs to be hosted elsewhere in the United States and around the globe. His idea to summarize the most relevant ideas from the huge international meeting and present them to other oncologists in the area started with about 250 medical professionals in attendance. Junior IU oncology faculty and fellows were invited.

Never one to impede the flow of knowledge, Dr. Einhorn, who is a Distinguished Professor of Medicine at IU, thought fellows from other major cancer centers might benefit from the one-day review. He arranged for pharmaceutical companies to provide grants to pay all expenses for fellows, a practice that lasted for about 10 years until rule changes in the pharmaceutical industry prohibited that type of support.

The scope of the [ASCO Annual Meeting](#) is mind boggling even for veteran attendees. For new oncologists, the experience can be daunting.

The 2017 ASCO Annual Meeting was attended by more than 39,000 physicians, nurses, researchers, pharmacists, biostatisticians, epidemiologists, students and other professionals focused on oncology. Of those, 17,168 were from the United States with the remainder representing Japan, Germany, France, United Kingdom, China, Canada, Brazil, Switzerland and Italy. Add to that more than 500 exhibitors and it is easy to see why the ASCO Annual Meeting is the largest oncology gathering on the planet.

“Trying to synthesize what you learned at this meeting can be overwhelmingly complicated for junior faculty and fellows,” said Dr. Einhorn, who served as ASCO president from 2000 to 2001. His idea to pare down the five-day meeting to a digestible one-day synopsis was well accepted

from the start. Today, it's an IU Simon Cancer Center tradition that brings fellows, oncologists, hematologists, pharmacologists, nurses and other specialists together from across the state.

““Trying to synthesize what you learned at this meeting can be overwhelmingly complicated for junior faculty and fellows.”Lawrence Einhorn, M.D.

Word of the success of the review spread and other university cancer centers began holding similar synopses. In addition to those reviews, the Best of ASCO meeting was endorsed in 2002 by the ASCO board of directors. The first Best of ASCO meeting was held in 2003 in Boston; now the board hosts three regional [Best of ASCO meetings](#) domestically each year with attendance ranging between 400 and 600 people, according to ASCO.

ASCO also offers a licensed Best of ASCO program, which allows organizations in more than 25 countries to hold their own regional meetings using ASCO-approved content. This year, 28 [regional meetings](#) took place in 26 countries across the globe.

Nabil Adra, M.D., assistant professor of clinical medicine, said attending the ASCO Review at IU is “a very high priority” for him, so much so that he’s attended five since he was an internal medicine resident at IU. This summer, he completed his three-year fellowship in hematology/oncology and joined the IU faculty.

“It is very difficult to keep up with all the advances,” Dr. Adra said. “Even if you attend the ASCO Meeting, it is difficult to process all the data and discussions by thought leaders and other leaders in cancer treatment.”

Dr. Adra, whose focus in the clinic and in research is prostate, kidney, bladder and testicular cancers, said he welcomes the opportunity to learn from senior faculty at IU.

“A very important part of the review is the interpretation. First the presenter will present the data and then the interpretation of the data,” he said. “Lots of times, I think that’s the most valuable part. It gives you an idea of how to evaluate research and clinical trials; how to determine the value of the clinical trial, and if the population included is large enough to generalize to our patients we are seeing in clinic.”

[Nasser Hanna](#), M.D., professor of medicine, has been attending the ASCO Annual Meeting for more than 20 years. “The meeting, which has grown exponentially over the years, has become this magnificent, yet overwhelming, experience,” he said.

Dr. Hanna, a specialist in thoracic oncology and germ cell tumors, is one of the faculty who presents at the ASCO Review at IU. This year, he and [Shadia Jalal](#), M.D., assistant professor of clinical medicine, tackled a two-part session on thoracic tumors. He also has presented at Best of ASCO multiple times.

Dr. Hanna’s participation in the review course goes back to 1998 when he was an oncology fellow at IU. “I remember those days when fellows from across the country packed the auditorium, balcony and overflow room at the campus conference center,” he said.

The event sees fewer fellows these days but oncologists from across the state attend to gain the insights and perspective of the IU Simon Cancer Center physicians and to network, he said.

We discuss supportive care, new standards of care, clinical studies that come up short, as well as practice altering research, with our statewide colleagues,” Dr. Hanna said.

The following IU faculty provided a review and interpretation of the 2017 ASCO Meeting:

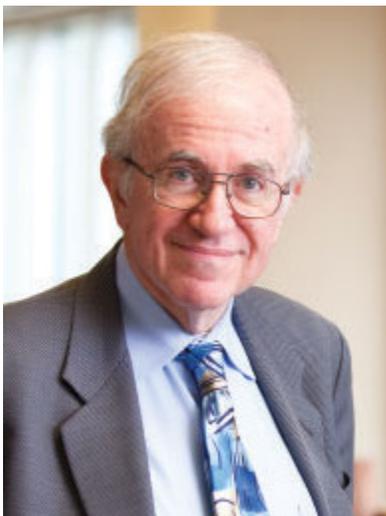
- [Costantine Albany](#), M.D.
- [Paul Helft](#), M.D.
- [Theodore Logan](#), M.D.
- [Kathy Miller](#), M.D.
- [Bert O’Neil](#), M.D.
- [Michael Robertson](#), M.D.
- [Bryan Schneider](#), M.D.
- [Safi Shahda](#), M.D.

Jarushka Naidoo, MBBCh, assistant professor of oncology at Johns Hopkins University, led the noon discussion panel “Managing Toxicities of Immunotherapy.”

Dr. Einhorn still plays a major role in the review, and presents the introduction and conclusion, and moderates the meeting

Some say the best way to learn is to teach and the annual review is no exception. The ASCO Review energizes IU faculty to fine-tune their knowledge of the latest and most promising oncology innovations so they can present to junior faculty and fellows.

“We have fun doing it and it promotes camaraderie within our faculty,” said Dr. Einhorn, whose foresight and dedication to knowledge fostered a learning opportunity for oncologists worldwide.





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News briefs

Dr. Haggstrom leads new IUPUI Signature Center



Haggstrom

Following three successful years of formative work, the [Center for Cancer Population Analytics and Patient-Centered Informatics](#) has been named an IUPUI Signature Center. Led by [David Haggstrom](#), MD, MAS, the center's scientific core – representing productive collaborations with the IU Schools of medicine, informatics and computing, nursing, public health, and more – have conducted critical work in assembling and validating cancer population data, developing and testing an electronic, multi-dimensional patient-reported outcome platform, and developmental evaluation and feasibility testing of a personal health record for colon cancer survivors.

Komen Central Indiana announces research grants to IU

Susan G. Komen Central Indiana has announced that IU Simon Cancer Center researchers will receive \$1,550,000 in funding. The 2017 recipients are:

Komen Scholar [Sunil Badve](#), MD, will receive \$250,000 to understand how RNA controls genes in breast cancer and how this leads to therapy resistance and metastasis.

Komen Scholar [Harikrishna Nakshatri](#), PhD, will receive \$700,000 to better understand the molecular mechanisms involved in ER+ breast cancer growth and recurrence.

Komen Scholar [Bryan Schneider](#), MD, will receive \$600,000 to continue his research to understand why some patients suffer chemotherapy-related side effects, such as peripheral neuropathy and therapy-induced heart failure, while others do not.

Additionally, the [Susan G. Komen Tissue Bank at the IU Simon Cancer Center](#), the world's only biorepository of normal breast tissue, will receive \$550,000. This grant supports the collection and storage of whole blood, DNA, serum, plasma, and healthy breast tissue from women not known to have breast cancer, as well as the distribution of the samples to researchers worldwide.

NCI releases "Annual Plan"

The National Cancer Institute has released its "NCI Annual Plan and Budget Proposal." It highlights the impact of the nation's continuing investment in cancer research and directs attention to several areas for which additional support will enable greater and faster progress.

[More.](#)

Vera Bradley Scholar wins postdoc award



Schneider, Wu

Vera Bradley Foundation Scholar Xi Wu, PhD, is the recipient of the third annual Outstanding Postdoc award, presented by IU School of Medicine's Office of Postdoctoral Affairs. The award is designed to recognize and honor the achievements of postdocs, not only as exceptional researchers, but also as mentors, role models, and advocates for fellow postdocs and students at IU School of Medicine. Dr. Wu works in the laboratory of [Bryan Schneider](#), MD.

Case-Eads presents at Onsemble conference

Somer Case-Eads, administrator for protocol operations at the IU Simon Cancer Center's Clinical Trials Office, recently presented "Site and Customer Experience Nimblify Participant Payments" at the Onsemble conference in Madison, Wisc. The conference brings together users of OnCore, which is largely composed of users from cancer centers, children's hospitals, and academic medical centers. OnCore is the comprehensive clinical research management

system, which supports the IU Simon Cancer Center's clinical trials. Case-Eads is also a leader of the Forte Midwest Empowerment Group, where she leads sessions about knowledge sharing and experiences with OnCore.



[Rafat Abonour](#), MD, crosses the finish line Sept. 16 in Indianapolis after riding nearly 200 miles for the 13th running of Miles for Myeloma. The two-day cycling event took Dr. Abonour and other riders from Indy to Muncie and then back to Indy, all while raising awareness of multiple myeloma, an incurable blood cancer, as well as funds for myeloma research at the IU Simon Cancer Center and myeloma patient care at IU Health. To date, nearly \$5 million has been raised. [Take a look at this year's ride.](#)

Upcoming Events

Oct. 9-10: 14th annual Indiana Life Sciences Summit

The 14th annual Indiana Life Sciences Summit conference is Oct. 9 and 10 at the JW Marriott. The two-day summit features a business track and scientific track with TED-like talks by thought leaders on global health and evidence-based medicine. Presentations on curing Ebola, HIV, Hepatitis E, and more are scheduled. An expanded scientific track will feature speakers talking about immunology and oncology. [Learn more and register.](#)

Big Ten Cancer Research Consortium Summit is Oct. 21

Hosted by the University of Illinois Cancer Center and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, the Big Ten Cancer Research Consortium Summit brings together members from Big Ten Cancer Research Consortium member institutions to explore the role of precision oncology and using cancer genomic data tailored to individual patients. Held Oct. 21, this year's theme is "Precision Oncology." Visit the [summit Website](#) for all of the details.

ACS CAN hosts "Achieving Health Equity in Indiana" Oct. 25

The American Cancer Society Cancer Action Network Indiana Policy Forum is 8:30 a.m. to 11:15 a.m. Oct. 25. All are welcome. The forum's focus is achieving health equity in Indiana. [Learn more and register.](#)

Cancer center members in the news



- [David Roodman](#), MD, was named the 2017 recipient of the Lawrence G. Raisz Award for his outstanding achievements in preclinical translational research (cellular or in animals) in the bone and mineral field by the American Society for Bone and Mineral Research. The society is the leading professional, scientific, and medical society established to bring together clinical and experimental scientists involved in the study of bone and mineral metabolism.
- [Melissa Kacena](#), PhD, was awarded a Fuller Albright Award by the American Society for Bone and Mineral Research. This award is given in recognition of exemplary achievements in the bone and mineral field to researchers under the age of 45.
- [Theresa Guise](#), MD, was recently named a recipient of the Philip S. Hench Distinguished Alumni Award from the University of Pittsburgh School of Medicine.
- [Lawrence Einhorn](#), MD, has been named to Medscape's "[25 Most Influential Physicians in the Past Century](#)."
- Outrun the Sun Inc. has made a \$50,000 endowed gift to the Richard M. Fairbanks School of Public Health at Indiana University-Purdue University Indianapolis to create the Outrun the Sun scholarship. The scholarship, which will exist in perpetuity, will support public health students who are studying epidemiology and are interested in working on melanoma- and skin cancer-related projects. The scholarship will provide students the opportunity to work alongside [Jiali Han](#), PhD, on melanoma- or other skin cancer-related projects.
- [Heather O'Hagan](#), PhD, is among the authors of "Chronic Cigarette Smoke-Induced Epigenomic Changes Precede Sensitization of Bronchial Epithelial Cells to Single-Step Transformation by KRAS Mutations." It was published in the Sept. 11 issue of [Cancer Cell](#).

- A new video series about IU research includes the work of [Thomas Gardner](#), MD. He and his colleagues are working to create a new, non-invasive method to screen men for prostate cancer by replicating the cancer-sniffing power of the canine nose. [Take a look](#).
- [Thomas Hurley](#), PhD, has been named [associate dean for research and graduate studies](#) at IU School of Medicine.

New members

[Sarath Chandra Janga](#), PhD
IU School of Informatics
Unaligned member

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