Signature Center Initiative: Final Report

Name of Center: Center for HPV Research (http://pediatrics.iu.edu/center-hpv-research/about-us/)

Directors of Center: Gregory D. Zimet & J. Dennis Fortenberry
Section of Adolescent Medicine, Department of Pediatrics
Indiana University School of Medicine

Year SCI funds were awarded: 2012

1. Mission of the Center for HPV Research:

The overall mission of the Center for HPV Research is to improve understanding of HPV transmission and infection, and prevention of HPV infection and its consequences. Under the leadership of Professors Gregory Zimet and Dennis Fortenberry of the Department of Pediatrics, the Center for Human Papillomavirus (HPV) Research at IUPUI fosters cohesion and collaboration among investigators pursuing HPV-related research. This group of scholars represents a growing synergy between the disciplines of medicine, health marketing, psychology, and public health and will capitalize on IUPUI’s remarkable culture of collaborative and interdisciplinary research, establishing a world-class center for HPV research, research training, and research translation.

2. Unique and Distinctive Features

Our center includes faculty and fellows from four Indiana campuses (IUPUI, IUB, Purdue, and Notre Dame) and eight schools within those four campuses. Research ranges from basic laboratory science to public health policy, enabling unique opportunities for cross-disciplinary team science. The collaborative environment nurtured by the Center for HPV Research is reflected in the publication in 2015 of a book, “Human Papillomavirus (HPV)-Associated Oropharyngeal Cancer”, which was co-edited by Sharon Stack, who is a member of our center and is Professor of Chemistry & Biochemistry and Director of the Harper Cancer Research Institute at University of Notre Dame. Through contacts made via our Center, Dr. Stack recruited other Center member from the IU School of Medicine to contribute chapters to this book, including Teresa Anderson (Infectious Diseases), Elliot Androphy (Dermatology), Aaron Ermel (Infectious Diseases), and Michael Moore (Otolaryngology-Head & Neck Surgery).

3. Research & Scholarly Activities

Center for HPV Research Goals:

a. To create recognition around IUPUI’s outstanding strengths and accomplishments in the area of HPV research [Achieved – We have received recognition in several campus publications].

b. To foster world-class, collaborative research that leads to coauthored publications and multi-investigator research grants that support the submission of an NIH-sponsored, HPV-focused program project/center grant application within 3 years’ time. [Achieved in part. We have funded several pilot research projects that have led to NIH applications and funding. An HPV-related center grant (U19) was submitted (Loehrer, PI; Brown, project PI, Ermel, Co-I) and funded by NIH and built, in part, on a pilot project funded by the Center].

d. To disseminate relevant research findings related to prevention of HPV infection and HPV-
related cancers to the community through outreach and health policy advocacy. [Achieved. Members of the Center have worked together to advocate for more effective policy around HPV vaccination. Many of us have met with community organizations and given talks/served on panels to address issues related to cervical cancer prevention, including screening and vaccination. As a group, we have also published numerous research articles in scientific journals related to our research on HPV and presented our research via presentations at national and international professional and scientific meetings.]

e. To fund interdisciplinary biological, clinical, and behavioral/social science pilot research projects that lead to independent extramural funding. [Achieved. As noted above, we funded several pilot projects that led to NIH applications and funding].

f. To support the professional development of junior faculty who engage in trans-disciplinary HPV research through association with the Center, pilot project funding, and community engagement. [Achieved. Junior faculty and research fellows have benefited from Center activities and meetings through pilot research projects and mentorship].

4. Collaborations & Partnerships Facilitated by the Center for HPV Research

Internal Partnerships:

Collaboration between Elliot Androphy (IUSM) and V. Jo Davisson (Purdue)

Collaboration between Darron Brown (IUSM) and Peter Ortoleva (IUB)

Collaboration between Gregory Zimet (IUSM) and Beth Meyerson (IUB)

Collaboration between Gregory Zimet (IUSM), Dennis Fortenberry (IUSM), Katherine Head (IUPUI) and Stewart Chang Alexander (Purdue)

Collaboration between Gregory Zimet (IUSM) and Wanzhu Tu (IUSM)

Collaboration between Sharon Stack (Notre Dame), Elliot Androphy (IUSM), Aaron Ermel (IUSM), Teresa Anderson Batteiger (IUSM), and Michael Moore (IUSM).

External Partnerships:

Linda Fu, MD. Clinical Research Institute and Goldberg Center for Community Pediatric Health, Children’s National Health System. Washington, DC. [with G. Zimet]

Spring Chenoa Cooper, PhD. The University of Sydney, Sydney, Australia. [with G. Zimet]

Vanessa Schick, PhD. University of Texas, Houston. [with J.D. Fortenberry]

Holly Fontenot, PhD, RN. Boston College. [with G. Zimet & N. Stupiansky]

Suellen Hopfer, PhD. Pennsylvania State University & UC Irvine. [with G. Zimet]

Noel Brewer, PhD. University of North Carolina. [with G. Zimet & L. Sturm]

Susan Vadaparampil, Moffitt Cancer Center. [with G. Zimet]
5. Grants and Contracts in Support of Signature Center (Center members' names bolded)

5A. Grants from center activities with more than one center member

Investigators: **Zimet & Downs (Co-PIs), Wanzhu Tu (Co-I), Darron Brown (Co-I),** and pre-doctoral fellow **Monica Kasting (RA).**

Title: “HPV Vaccination: An Investigation of Physician Reminders and Recommendation Scripts”.

Funded by: The Merck-Regenstrief Program in Personalized Health Care Research and Innovation (Project 14).


Total Direct Costs: $316,000.

Description: The goal of this project is to evaluate the effects of physician-targeted automated HPV vaccination reminders alone and reminders plus a recommended script on HPV vaccination rates among 9-12 year old male and female patients.

Investigators: **Loehrer (PI), Brown, Project PI; Ermel, Co-I.**

Title: “AMPATH-Oncology Institute: HPV and Cervical Cancer in Kenyan Women with HIV/AIDS”.

Funded by: NIH/NCI: U54CA190151.


Investigators: **Zimet (PI), Sturm (Co-I), Brewer (Co-I),** Center fellows **Kelly Donahue (Co-I) and Monica Kasting (Co-I).**

Title: "Physician-Patient Discourse about HPV Vaccination".

Funded by: Merck Investigator-initiated proposal


Total Direct Costs: $30,000

Description: The major goal of this project is to evaluate pediatrician-caregiver/patient communication about HPV vaccination and to assess caregiver/patient responses to pediatricians.

Investigators: **Zimet G & Downs S (Co-PIs), Wanzhu Tu (Co-I)** and pre-doctoral fellow **Monica Kasting (RA).**

Title: “Use of a Patient Education/Messaging Platform to Increase Uptake and Series Completion of HPV Vaccine”.

Funded by: The Merck-Regenstrief Program in Personalized Health Care Research and Innovation (Project 20).


Total Direct Costs: $286,674.

Description: The major goal of this project is to evaluate the effect of a tablet-based, parent-directed information messaging system on acceptance and follow-through with HPV vaccination.
Investigators: **Zimet G & Downs S (Co-PIs), Wanzhu Tu (Co-I) and pre-doctoral fellow Monica Kasting (RA).**

**Title:** “HPV Vaccination: Evaluation of Reminder Prompts for Doses 2 & 3”.

**Funded by:** The Merck-Regenstrief Program in Personalized Health Care Research and Innovation (Project 21).

**Dates:** February, 2015 – May, 2016.

**Total Direct Costs:** $196,287

**Description:** The major goal of this project is to evaluate the effect of physician reminder prompts on delivery of the 2nd and 3rd doses of HPV vaccine.

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Investigators: **Meyerson (PI), Comer (Co-I), Zimet (Co-I).**

**Title:** “Cervical Cancer Policy Communication Dashboard”.

**Funded by:** Roche Diagnostics Corporation.

**Dates:** May, 2015 – December, 2015.

**Total Direct Costs:** $40,000

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Investigators: **Meyerson (PI), Comer (Co-I), Zimet (Co-I).**

**Title:** “Cervical Cancer Policy Communication Dashboard”.

**Funded by:** The Anita Aldrich Foundation.

**Dates:** May, 2015 – April, 2016.

**Total Direct Costs:** $30,000

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**Androphy E & Davisson VJ.** “Drug-like inhibitors of HPV-16 E6”. Indiana CTSI Collaboration in Translational Research grant award.

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**Brown, Ermel, Ortolova.** HPV grant funded by IU Simon Cancer Center.

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**5B. Grants with one Center member as the PI**

**Androphy (PI).** Control of papillomavirus expression and transformation”. Funded by NIH/NCI: R01 CA58376-20. 9/24/1993-6/30/2020.


**Shew (Site PI).** V503-003: A Phase III Clinical Trial to Study the Tolerability and Immunogenicity of V503, a Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine, in 16- to 26-Year-Old Men and 16- to 26- Year-Old Women. Merck & Co. July 1, 2012 - March 31, 2014.

**Antony (PI).** VA Merit Review Award grant. “Nutritional folate deficiency, HPV16 DNA integration into genomic DNA, & carcinogenesis”. 2013-2016.

**Zimet.** International Research Collaboration Award, University of Sydney, Australia. July 1, 2013 – August 1, 2013.


**Meyerson (PI).** “Cervical Cancer and HPV standing in state comprehensive plans”. 
Funded by Cervical Cancer Free Coalition. September 2013 – August 2014.

5D. Unfunded grant proposals


6. Publications (Center members’ names bolded; Center fellow’s names underlined):

For each of the listed publications, the center and its resources contributed in one or more of the following ways: 1. Through direct funding of pilot research; 2. Through support of pre- and post-doctoral fellows; 3. Through creation, enhancement, and support of collaborative relationships among Center members.

6A. Publications with two or more Center members as authors


6b. Publications with one Center member as 1st, corresponding, and/or senior author


6C. Conferences, Workshops, Seminars, Invited Presentations

*Meetings/Speakers Sponsored by the IUPUI Center for HPV Research:*

1. May, 2013. Visiting Faculty Hosted by the IUPUI Center for HPV Research: John Schiller, PhD. Dr. Schiller is the Head, Neoplastic Disease Section, Laboratory of Cellular Oncology, Center for Cancer Research, National Cancer Institute. He played a central role in research that led to the development of current HPV vaccines and is continuing work on developing second-generation HPV vaccines. We arranged for him to come to IUPUI for two days, during which he gave two lectures and spent time meeting with Center members regarding their research.  
Lecture 1: "**HPV Vaccines: Past, Present & Future**"  
Lecture 2: "**Understanding how HPVs Infect Cells, and Why it Matters**"

2. May, 2014. The Center co-sponsored the Midwest AIDS Training & Education Center (MATEC) Meeting: “**HIV/AIDS Update**”. May 15, 2015. We invited Jessica Kahn, MD, MPH as a Keynote Speaker. Dr. Kahn is professor of pediatrics in the Division of Adolescent and Transition Medicine at Cincinnati Children’s Hospital Medical Center and the University of Cincinnati College of
Medicine. She is also Assistant Chair of Pediatrics for Academic Affairs and Faculty Development. Dr. Kahn is one of the world’s foremost researchers and experts on HPV vaccination. She has received multiple grants from NIH for her research and has worked with the World Health Organization on HPV vaccine policy. In addition, Dr. Kahn has led research studies on HPV vaccination immunogenicity among HIV-infected young men and women through the Adolescent Trials Network for HIV/AIDS interventions.

Keynote Talk: “HPV and HPV Vaccines in HIV-Infected Individuals”

3. May, 2015. The Center co-sponsored the Midwest AIDS Training & Education Center (MATEC) Meeting: “HIV/AIDS Update”. We invited Joel Palefsky, MD as a Keynote Speaker. Dr. Palefsky is professor of medicine at UCSF and an internationally recognized expert on molecular biology, treatment, pathogenesis and natural history of HPV infection. He founded the International Anal Neoplasia Society and, at the time of this conference, was president of the International Papillomavirus Society.

Keynote Talk: “HPV-Related Cancers in HIV-Infected Men and Women: Incidence and Prevention”

Invited Workshops/Seminars Conducted by IUPUI Center for HPV Research Faculty at National and International Meetings:


6D. Patents & Disclosures


6E. Other Activities, Including Service Activities/Community Outreach


Zimet GD. "Cervical Cancer Prevention & Control in Indiana". Presented at the Rally at the Rotunda for Cervical Cancer Awareness Month. Sponsored by the Indiana Cancer Consortium.
Indianapolis, IN, January 22, 2014.

Cervical Cancer-Free Indiana (CCFIN) is an organization committed to development of education and intervention programs directed at cervical cancer prevention. Dr. Zimet is PI of the CCFIN initiative and Rivienne Shedd-Steele is the CCFIN Director. We have been able to join the Center for HPV Research with CCFIN initiatives to reach at-risk populations with education programming and research. Venues have included the Black & Minority Expo Health Fair, where we had a CCFIN booth in 2011, 2012, 2013, and 2015. HPV Center research studies were integrated into the booth activities, resulting in several publications and presentations.

Center members have been involved in community outreach education by participating as speakers and panel members at numerous programs. For example, Dr. Shew spoke at a recent “Cervivor School” meeting, a national organization for cervical cancer patients and survivors. Drs. Shew, Zimet, and Robbins have frequently served as panelist after public screenings of the movie, “Someone You Love”, a documentary about several women who were diagnosed with cervical cancer. In 2014 Drs. Brown, Shew, and Zimet each gave presentations for a webcast organized by the Indiana State Department of Health.

7. Self-Sufficiency

Dr. Dennis Fortenberry, Co-Director of the Center for HPV Research, is also the Adolescent Medicine Section Chief. He is committed to ongoing in-kind support from the Section of Adolescent Medicine, including provision of meeting space, administrative support, and provision of research expertise. Several faculty in the Section of Adolescent Medicine are also faculty in the Center for HPV Research, including Dr. Fortenberry, Dr. Zimet, Dr. Shew, Dr. Stupiansky, Dr. Kester, and Dr. Robbins.

There are limited funds available to cover salaries/fellowships going forward. However, as we have done in the past, we will have pre- and post-doctoral fellows funded through other mechanisms that will benefit from involvement in the Center. Other such mechanisms have included:

1. Leadership Education in Adolescent Health (LEAH), an MCHB-funded interdisciplinary training program located in the Section of Adolescent Medicine, Department of Pediatrics.

2. Behavioral Oncology Training Program funded by an R25 grant to Dr. Victoria Champion in the School of Nursing.

3. T32 research training grants from the Division of Infectious Diseases in the Department of Medicine and from the IU School of Nursing.

Faculty with the Center for HPV Research have indicated a commitment to continue involvement in the Center and fully support our application for Signature Center Status.

8. Conclusion

The IUPUI Center for HPV Research has met many, but not all of its goals. Challenges include identifying mechanisms for sustainable funding through research grants. There remains no avenue for directing indirect funds from IUSM grants to support Center activities. Another challenge has been to develop ways to enhance collaboration across all types of research represented within the Center. This particularly applies to bridging gaps between basic laboratory HPV research, clinical HPV research, and behavioral/population science HPV research. Recent
Center meetings have been very well attended and there is great enthusiasm for ongoing efforts to enhance collaborations among Center members and to develop research proposals. This no-cost extension year has been a year of consolidation. Findings from several pilot research projects are in the process of being fully analyzed and will support several planned NIH submissions over the next year. We plan to make full use of our newly constituted (and growing) external advisory board to provide us with guidance on how to most effectively develop HPV research programs that will result in externally-funded proposals.
Appendix 1 - Center Personnel

Gregory Zimet, PhD (Co-Director), IUSM (Pediatrics)
Joined in 2012 - Faculty. Also faculty for the Indiana Center for AIDS Research.

J. Dennis Fortenberry, MD, MS (Co-Director), IUSM (Pediatrics)
Joined in 2012 - Faculty. Also faculty for the Indiana Center for AIDS Research.

Andreia Alexander, PhD, IUSM (Pediatrics)
2012-2014 Postdoctoral Fellow (MD/PhD Program)

Stewart Chang Alexander, PhD, Purdue University, College of Health & Human Sciences (Consumer Science)
Joined in 2014 - Faculty.

Elliot Androphy, MD, IUSM (Dermatology)
Joined in 2012 - Faculty.

Asok C. Antony, MBBS, IUSM (Medicine)
Joined in 2012 - Faculty.

Matthew Barlowits, PhD, Purdue University College of Pharmacy (Medicinal Chemistry & Molecular Pharmacology)
Joined in 2013 – Postdoctoral Fellow.

Teresa Batteiger, MD, IUSM (Medicine)
Joined as Post-Doctoral Fellow (funded by the Center) in 2012 and as faculty in 2015.

Darron Brown, MD, MPH, IUSM (Medicine & Microbiology/Immunology)
Joined in 2012 - Faculty.

Anthony Cox, PhD, IU Kelly School of Business (Marketing)
Joined in 2012 - Faculty. Also faculty for the Center for Civic Literacy.

Dena Cox, PhD, IU Kelly School of Business (Marketing)
Joined in 2012 - Faculty.

William Crabtree, PhD, IUSM (Pathology & Laboratory Medicine)
Joined in 2013 - Faculty.

Teresa Cummings, IUSM (Pediatrics)
Joined in 2012 – MPH student.

V. Jo Davisson, PhD, Purdue University College of Pharmacy (Medicinal Chemistry & Molecular Pharmacology)
Joined in 2012 - Faculty.

Kelly Donahue, PhD, IUSM (Pediatrics)
2013-2015 – Postdoctoral Fellow funded by the Center for HPV Research
Aaron Ermel, MD, IUSM (Medicine)  
Joined in 2012 - Faculty.

Kenneth Fife, MD, PhD, IUSM (Medicine)  
Joined in 2012 - Faculty.

Barbara Frain, MS, IUSM (Pathology & Laboratory Medicine)  
Joined in 2013 - Faculty.

Katherine Head, PhD, IU School of Liberal Arts (Health Communication)  
Joined in 2014 - Faculty.

Hiremagalur Jayaram, PhD, IUSM (Biochemistry)  
2012-2015 – Faculty.

Monica Kasting, IU Fairbanks School of Public Health (Epidemiology)  
Joined in 2013 – Pre-doctoral Fellow

Laura Kester, MD, IUSM (Pediatrics)  
Joined in 2012 - Faculty.

Nolan Kline, PhD, MPH, Purdue University, College of Health & Human Sciences (Consumer Science)  
Joined in 2015 - Faculty.

Patrick Loehrer, MD, IUSM (Medicine & Director IUSCC)  
Joined in 2012 - Faculty.

Avinash Mantravadi, MD, IUSM (Otolaryngology-Head & Neck Surgery)  
Joined in 2014 – Faculty.

Beth Meyerson, MDiv, PhD, IU Bloomington School of Public Health (Applied Health Science)  
Joined in 2012 - Faculty.

Patrick Monahan, PhD, IUSM (Biostatistics)  
Joined in 2012 - Faculty.

Michael Moore, MD, IUSM (Otolaryngology—Head & Neck Surgery)  
Joined in 2012 - Faculty.

Vaughn Rickert, PsyD, IUSM (Pediatrics)  
2012-2015 – Faculty

Anne Rietz, PhD, IUSM (Dermatology)  
Joined in 2013 – Postdoctoral Fellow funded by the Center for HPV Research.

Cynthia Robbins, MD, MS, IUSM (Pediatrics)  
Joined in 2015 - Faculty.

Rivienne Shedd-Steele, IUSCC (Office of Health Disparities & Outreach)  
Joined in 2012 - Faculty.

Marcia Shew, MD, MPH, IUSM (Pediatrics)
Joined in 2012 - Faculty.

Ross Silverman, JD, MPH, IU Fairbanks School of Public Health (Health Policy & Management)
Joined in 2014 - Faculty.

Sharon Stack, PhD, University of Notre Dame (Chemistry & Biochemistry and Director, Harper Cancer Research Institute)
Joined in 2012 - Faculty.

Nathan Stupiansky, PhD, IUSM (Pediatrics)
Joined in 2012 - Faculty.

Lynne Sturm, PhD, IUSM (Pediatrics)
Joined in 2012 - Faculty.

Jaime Taylor, DO, IUSM (Pediatrics)
Joined in 2013 – Postdoctoral Fellow.

Wanzhu Tu, PhD, IUSM (Biostatistics)
Joined in 2012 - Faculty. Also faculty for the Center for Pediatric Obesity & Diabetes Prevention Research.

Barbara Van Der Pol, PhD, IU Bloomington School of Public Health (Applied Health Science)
2012-2014 – Faculty.

Bree Weaver, MD, IUSM (Medicine)
Joined in 2012 - Faculty.

Shannon Wilson, IUSM (Pediatrics)
Joined in 2015 - Staff

Joseph Winger, IUPUI School of Science (Psychology)
Joined in 2013

Kara Wools-Kaloustian, MD, IUSM (Medicine)
Joined in 2012 - Faculty.
Appendix 2 – External Advisory Board

Ideally, we should have put an EAB in place early in the first year of funding. We are committed to correcting this oversight and have taken steps to develop an EAB. To date, we have recruited three internationally-known HPV experts to serve on our external advisory board (EAB). These three researchers, Joel Palefsky, John Schiller, and Jessica Kahn, were our invited Center speakers for 2013, 2014, and 2015. All three have agreed to serve on our EAB. They are all familiar with our Center and are enthusiastic about providing guidance to us over the coming years. Our plan is to recruit two more members to serve on the EAB, which will meet two times a year via conference call. Prior to each call we will provide EAB members with a summary of progress.

1. Joel Palefsky, MD. Professor of Medicine and Laboratory Medicine, University of California San Francisco.

   Dr. Joel Palefsky is the Chair of the HPV Working Group of the AMC and is the head of the AMC HPV Virology Core Lab. He has extensive experience in studying the biology of HPV infection, HPV infection in HIV-positive men and women, HPV vaccines and in the design and implementation of clinical research trials of HPV-related disease. He has published over 250 papers and is the PI on several laboratory-based and clinical research studies of HPV-associated neoplasia, particularly in the setting of HIV infection. Anal dysplasia occurs in men and women and is especially common among patients infected with the human immunodeficiency virus (HIV). He also specializes in the biology and development of new treatments for HPV and Epstein-Barr virus. He is the founder and president of the International Anal Neoplasia Society and Past-President of the International Human Papillomavirus Society. He is actively involved in training students in clinical and translational research and has led the Doris Duke Charitable Foundation (DDCF) program at UCSF since its inception in 2001.

2. John T. Schiller, PhD. Deputy Chief, Laboratory of Cellular Oncology, Head, Neoplastic Disease Section, National Cancer Institute Center for Cancer Research.

   Dr. Schiller and his co-PI Dr. Douglas Lowy led the initial development and characterization of the HPV prophylactic vaccines that ultimately became the commercial vaccines Cervarix and Gardasil. They currently study basic aspects of the papillomavirus life cycle, second-generation HPV vaccines, and HPV capsid-based vaccines against other infection agents and cancers. The lab is also developing cancer therapies based on the preferential binding of HPV capsids to tumor cells.

3. Jessica Khan, MD, MPH. Associate Chair, Academic Affairs and Career Development, Professor, University of Cincinnati Department of Pediatrics, Division of Adolescent and Transition Medicine at Cincinnati Children’s Hospital Medical Center.

   Dr. Kahn is one of the world’s foremost researchers and experts on HPV vaccination. She has received multiple grants from NIH for her research and has worked with the World Health Organization on HPV vaccine policy. Dr. Kahn has led research studies on HPV vaccination immunogenicity among HIV-infected young men and women through the Adolescent Medicine Trials Network for HIV/AIDS Interventions.