

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Lynette Denny

eRA COMMONS USER NAME: LYNETTE DENNY

POSITION TITLE: Chair and Head, Department of Obstetrics & Gynaecology, University of Cape Town

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
University of Cape Town, Cape Town, South Africa	MChB	1983	Medicine
University of Cape Town, Cape Town, South Africa	MMed	1994	Obs & Gynae
South African Colleges of Medicine	FCOG (SA)	1993	Obs & Gynae
University of Cape Town, Cape Town, South Africa	PhD	2000	Obs & Gynae

A. Personal Statement

I am a gynaecologic oncologist and have been working in the field of cervical cancer prevention in collaboration with colleagues from Columbia University, New York since 1995. We began our collaboration with the intention of evaluating alternative strategies for the prevention of cervical cancer in low resource settings. Cervical cancer was and remains the commonest cancer diagnosed among women living in poor countries due to the failure to either initiate or sustain cytology based screening programs. Our group pioneered the search for alternative protocols for the prevention of cervical cancer in community-based research sites in townships just outside of Cape Town. Since that time I have had extensive research experience in cervical cancer prevention, including three cross-sectional studies comparing different screening tests (such as HPV testing and VIA to cytology) and a randomized controlled trial of over 6500 women using HPV testing, VIA and delayed treatment in the three armed trial. Women with positive tests were treated with cryotherapy, In addition, we performed a prophylactic HPV vaccine trial (with bivalent vaccine) in HIV positive women and a therapeutic vaccine trial in HPV negative women. We participated in a three country trial of HPV genotyping in women with invasive cervical cancer (other centres were in South Africa, Ghana and Nigeria). We are currently engaged in a NCI funded trial evaluating screen and treat with the HPV Xpert Cepheid HPV test. I am still fully functional as a clinician in all aspects of gynaecology oncology and have was appointed the director of the SA Medical Research Council Gynaecological Cancer Research Centre, with 5 years of guaranteed funding.

- Denny L, Kuhn L, De Souza M, Pollack AE, Dupree W, Wright TC jr. Screen-and-treat approaches for cervical cancer prevention in low-resource settings: a randomized controlled Trial. JAMA 2005;294(17);2173 - 81
- Lynette Denny, Isaac Adewole, Rose Anorlu, Greta Dreyer, Manivasan Moodley, Trudy Smith, et al. Human papillomavirus prevalence and type distribution in invasive cervical cancer in sub-Saharan Africa. Int J Cancer 2014; 134: 1389-98
- Denny L, Hendricks B, Gordon C, Thomas F, Hexareh M, Dobbelaere C et al. Safety and Immunogenicity of the HPV-16/18 ASO4-adjuvanted vaccine in HIV-positive women in South Africa: a partially -blind randomized placebo- controlled study. Vaccine 201337(48):5745 - 53
- CL Trimble, MP Marrow, KA Kraynyak, X Shen, M Dallas, J Van, L Edwards, R Lamar Parker, L Denny et al. Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic DNA vaccine targeting human papillomavirus 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised. Double-blind, placebo=controlled phase 2b trial. Lancet September 17, 2015;1-11

B. Positions and Honors

Positions and Employment

1984	Internship, Groote Schuur Hospital/University of Cape Town
1985	Senior House Officer, Red Cross Children's Hospital, Cape Town
1986-1987	Senior House Officer, Dept of Obstetrics & Gynaecology, Groote Schuur Hospital
1987	Senior House Officer, Dept of Medicine, Groote Schuur Hospital, Cape Town
1988-1989	General practitioner, Cape Town
1989-1993	Registrar, Dept of Obstetrics & Gynaecology, Groote Schuur Hospital, Cape Town (including Fellowship in Gynecologic Oncology)
1994-1997	Specialist, Dept of Obstetrics & Gynaecology, Groote Schuur Hospital, Cape Town
1997-2005	Associate Professor & Senior Specialist, Dept of Obstetrics & Gynaecology, UCT
2005-Jul 2007	Professor & Principal Specialist, Dept of Obstetrics & Gynaecology, UCT
Aug 2007-2010	Professor & Principal Specialist, Dept of Obstetrics & Gynaecology, UCT
Jan 2010-	Head of Department, Obstetrics & Gynaecology, University of Cape Town/Groote Schuur Hospital
July 2005	Director, South African Medical Research Council Gynaecological Cancer Research Centre

Other Experience and Professional Memberships

2003 –2018	Secretary-Treasurer, African Organisation for Research and Training in Cancer (AORTIC)
2004 – 2015	Appointed to FIGO (International Federation of Gynecology and Obstetrics) Gynaecological Cancer Committee
2006 – 2011	Co-chair of FIGO Gynecology Cancer Committee
2012	Chair FIGO Gynecology Cancer Committee
2015	Expert Panel member of American Society of Clinical Oncology Immediate Past President of International Gynecologic Cancer Society (IGCS) and Immediate Past Chair of FIGO Gynaecologic Cancer Committee
2016 – 2019	Member of FIGO committee for Gynaecological cancer and committee for revision staging of cervical cancer

Honors

NRF B2 Rated Scientist by National Department Science and Technology, South Africa, 2011.

2006	Distinguished Scientist for Improvement of Quality of Life of Women awarded by the Dept of Science and Technology, SA
2006	JC Coetzee Prize for best original research in Obstetrics & Gynaecology, University of Cape Town
2008	Nominated for German Africa Award
2008	Honorary Member German Society of Obstetrics & Gynaecology (Sept 2008)
2009/10	Yvonne Parfitt Prize for best publication, Dept Obstetrics & Gynaecology, UCT
2012	Fellowship ad eundem of Royal College of Obstetricians & Gynaecologists, London, UK
2012	South African Medical Association Award for Extra-Ordinary Service to Medicine
2014	British Society of Colposcopy & Cervical Pathology Founders' Medal, London, UK
2015	CANSA AG Oettle Memorial Award
2015	International Federation of Gynaecology and Obstetrics Award in Recognition of Women Obstetricians and Gynaecologists, Vancouver, Canada
2016	International Agency for Research on Cancer Medal of Honour Award, Lyon, France
2016	Global Humanitarian Award, International Gynaecologic Cancer Society

C. Contribution to Science

1. Our first project involved recruiting just under 3000 women, aged 35 – 65 years of age from the community of Khayelitsha, which was then a largely informal settlement outside Cape Town, an area characterized by high rates of poverty, ill health, HIV and crime. All women were screened using HPV DNA testing, Visual inspection with acetic acid (VIA), cytology and cervicography. At the time we worked out of a second hand adapted caravan parked alongside a primary care clinic. We later upgraded to second hand shipping containers, out of which we still work. All women who were positive on any one of the tests were referred to me for colposcopy. This first study formed the basis of my PhD. The second 3000 women were recruited over the next two years – all women underwent colposcopy, and all women underwent HIV testing, which at the time was a bold step as the disease was highly stigmatized and its existence denied by the government of the time. Having demonstrated good sensitivity, albeit lower specificity of both VIA and HPV DNA testing in these two cross-sectional studies we progressed to a randomized controlled trial to evaluate the safety, acceptability and efficacy of 'screening and treating' women with positive VIA and HPV DNA tests compared to a control group. These three very large clinical trials required a holistic approach as we also performed in-depth analyses of appropriate educational materials, logistics of motivating and retaining women in screening programs, community acceptability of research projects, HIV testing and many other complexities. We achieved a high level of science and have subsequently been honoured on many occasions for this work. In addition to the three large clinical trials described above, we recruited 3000 women aged 18 – 34 years which enabled us to perform HPV DNA typing by HIV status in women from this cohort and our previous trials, giving us a unique dataset of HPV typing in women aged 18- 65 years. Our work has been imitated in many other settings and countries and informed the deliberations of the World Health Organisation on its policy regarding cervical cancer prevention. In summary, our group have a very in-depth and extensive experience of running cervical cancer prevention studies and are ideally suited to perform the current trial.
 - Lynette Denny, Louise Kuhn, Amy Pollack Thomas Wright Jr. Direct Visual Inspection for cervical cancer screening: an analysis of factors influencing test performance. *Cancer* 2003;94:1699- 707
 - Denny L, Kuhn L, De Souza M, Pollack AE, Dupree W, Wright TC jr. Screen-and-treat approaches for cervical cancer prevention in low-resource settings: a randomized controlled Trial. *JAMA* 2005;294(17);2173 - 81
 - Alicia C McDonald, Ana I Tergas, Louise Kuhn, Lynette Denny, Thomas C Wright. Distribution of human papillomavirus genotypes among HIV-positive and HIV-negative women in Cape Town, South Africa. *Front Oncol* 2014;doi:10.3389
2. In the midst of this trial we participated in a three-country study of HPV genotyping of women with invasive cervical cancer (South Africa, Ghana and Nigeria). The work has been published and is particularly helpful in planning HPV vaccination strategies.
 - Lynette Denny, Isaac Adewole, Rose Anorlu, Greta Dreyer, Manivasan Moodley, Trudy Smith, et al. Human papillomavirus prevalence and type distribution in invasive cervical cancer in sub-Saharan Africa. *Int J Cancer* 2014; 134: 1389-98
3. When the South African Medical Council decided to create Comprehensive Cancer Centres for the first time in South Africa, our group were selected for a full award of R2.5 million per year for 5 years. We have a team of 16 basic scientists, public health specialists and clinicians working collaboratively on a number of key projects and our members consist of A and B rated South African researchers (awarded by the National Research Foundation). In our work we have collaborated extensively with previously disadvantaged Universities and have established a registry of gynaecological cancer cases diagnosed and treated in the Eastern Cape of South Africa, which is one of the most under-resourced provinces in the country (so far over 9000 cases have been recorded, the first ever attempt at quantifying the quantum of gynaecological

cancer in the area). Similarly, over the same period, over 9000 patients have been registered at our hospital in Cape Town, Groote Schuur Hospital.

- Publications from this work are pending
4. We are currently completing a phase 2 clinical trial of point of care testing using HPV Expert – initially between 2015/16 we recruited just over 1000 HIV positive and HIV negative women to undergo screen and treat using this test and thermocoagulation for treatment of suitable cases. We have now recruited a further over 3000 women to undergo screen and treat in an implementation phase. We are busy following up recruited women.
 - R Saidu, J Moodley, A Tergas, M Momberg, R Boa, T Wright, S Campbell, C Svanholm-Barrie, D Persing, L Kuhn, L Denny. South African women's perspectives on self-sampling for cervical cancer screening: A mixed-methods study. *S Afr Med J* 2019; 109(1): 47-52. DOI:10.7196/SAMJ.2019.v109i1.13278
 5. Simultaneously we are conducting a second randomized placebo controlled therapeutic vaccine trial against HPV 16-18 CIN 2/3 for Inovio and are one of the lead teams with successful recruitment.
 - CL Trimble, MP Marrow, KA Kraynyak, X Shen, M Dallas, J Van, L Edwards, R Lamar Parker, L Denny et al. Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic DNA vaccine targeting human papillomavirus 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised. Double-blind, placebo-controlled phase 2b trial. *Lancet* September 17, 2015;1-11
 - (First paper published)
 6. I was instrumental in resuscitating African Organisation for Research and Training in Cancer (AORTIC) and built the organization from a baseline of \$80 000 to \$2 million. I have subsequently trained a senior radiation oncologist to take over from me but remain involved in the background. This organization grew from 60 members in 2005 to over 500 in 2018.
 7. We have two major clinical sites, the Colposcopy Clinic at Groote Schuur Hospital which accepts referrals from women with abnormal cervical smears and a site at a primary care clinic in a peri-urban area that serves a population characterized by poverty, high burden of disease, violence/crime and HIV. The latter site is created by shipping containers and contains all equipment needed for diagnosis and management of lower genital tract disease, including cervical cancer prevention which is our primary research focus. It requires no capital injection and can proceed immediately with implementing new studies, has the support of the local community and the local and provincial departments of Health in the public sector

List of Published Work (2014-2019) out of 126

- Lynette Denny, Isaac Adewole, Rose Anorlu, Greta Dreyer, Manivasan Moodley, Trudy Smith, et al. Human papillomavirus prevalence and type distribution in invasive cervical cancer in sub-Saharan Africa. *Int J Cancer* 2014; 134: 1389-98
- Alfred Bere, Shahila Tayib, Jean-Mari Kriek, Lindi Masson, Shameem Z Jaumdally, Shaun L Barnabas, William H Carr, Bruce Allan, Anna-Lise Williamson, Lynette Denny, Jo-Ann S Passmore. Altered phenotype and function of NK cells infiltrating Human Papillomavirus (HPV)-associated genital warts during HIV infection. *Clin Immunol* 2014;150: 210-219
- David Mutch, Lynette Denny, Michael Quinn. Hereditary gynecologic cancers. *Int J Gynecol Obstet* 2014;124: 189-92
- Alicia C McDonald, Ana I Tergas, Louise Kuhn, Lynette Denny, Thomas C Wright. Distribution of human papillomavirus genotypes among HIV-positive and HIV-negative women in Cape Town, South Africa. *Front Oncol* 2014;doi:10.3389

- Denny L. Control of Cancer of the Cervix in Low – and Middle-Income Countries. *Ann Surg Oncol* a. 2015;22(3):728-33
- LA Denny. Questions We Should be Asking about Bevacizumab for Cervical Cancer. Editorial: Liu FE, Cripe J, Tewari KS. *Anti-Angiogenesis Therapy in Gynecologic Malignancies.Oncology* 2015; 282-294
- L Denny. HIV and HPV as Fatal Partners. *Curr Obstet Gynecol Rep* 2015;4:143-8.
- L Denny, N Bhatla. Preface for Best Practice and Research Clinical Obstetrics and Gynaecology: Staging in Gynaecologic Oncology. *Clin Obstet Gynecol* 2015;29.6:765-6.
- CL Trimble, MP Marrow, KA Kraynyak, X Shen, M Dallas, J Van, L Edwards, R Lamar Parker, L Denny et al. Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic DNA vaccine targeting human papillomavirus 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised. Double-blind, placebo=controlled phase 2b trial. *Lancet* September 17, 2015;1-11
- Denny L, Prendiville W. Cancer of the cervix: Early detection and cost-effective solutions. *Int J Gynecol Obstet* 2015; 131:S28-S32.
- H Gelband, R Sankaranarayanan, CL Gauvreau, S Horton, BO Anderson, F Bray, J Cleary, AJ Dare, L Denny et al. The costs, affordability, and feasibility of an essential package of cancer control interventions in low-income and middle-income countries: key messages from Disease Control Priorities, 3rd edition. *Lancet* 2016; 387:2133-2144.
- N Mbatani, T Adams, L van Wijk, C Behrens, T Tam, T Wright, M Stoler, L Denny. Performance of a Human Papillomavirus Test in Samples from Women with Histopathologically confirmed Invasive Cervical Cancer. *J Lower Gen Tract Dis* 2016;20:151-153
- Nancy Santesso, Reem A Mustafa, Holger J Schunemann, Marc Arbyn, Paul Blumenthal, Joanna Cain, Michael Chirenje, Lynette Denny et al. World Health Organization Guidelines for treatment of cervical intraepithelial neoplasia 2-3 and screen-and-treat strategies to prevent cervical cancer. *Int J Gynecol Obstet* 2016;132:252-258.
- J-M Kriek, SZ Jaumdally, L Masson, F Little, Z Mbulwa, Pamela P Gumbi, Shaun L Barnabas, J Moodley, L Denny et al. Female genital tract inflammation, HIV co-infection and persistent mucosal Human Papillomavirus (HPV) infections. *Virology* 2016;493: 247-254.
- Kuhn L, Denny L. The time is now to implement HPV testing for primary screening in low resource settings. *Prev Med* 2017 ;98:4 2- 44
- R Saidu, J Moodley, A Tergas, M Momberg, R Boa, T Wright, S Campbell, C Svanholm-Barrie, D Persing, L Kuhn, L Denny. South African women’s perspectives on self-sampling for cervical cancer screening: A mixed-methods study. *S Afr Med J* 2019; 109(1): 47-52. DOI:10.7196/ SAMJ.2019.v109i1.13278
- Denny L, de Sanjose S, Mutebi M, Anderson BO, Kim J, Jeronimo J et al. Interventions to close the divide for women with breast and cervical cancer between low income and middle income countries and high income countries. *Lancet* 2017;389(10071):861- 870
- Paul A Cohen, Anjua Jhingran, Ana Oaknin, Lynette Denny; Cervical Cancer. www.thelancet.com Vol 393 January 12, 2019
- Neerja Bhatla, Jonathan S Berek, Mauricio Cuello Fredes, Lynette A Denny, Seoka Grenman, Kanishka Karunaratne, Sean T Kehoe, Ikuo Konishi, Alexander B. Olawaiye, Jaime Prat, Rengaswamy Sankaranarayanan.
- Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynecol Obstet* 2019; 1-7

D. Additional information: Research Support and/or Scholastic Performance

Research Support

Parthenon Trust and Trust Fund of Bristol-Myers Squibb. Denny (PI) Study closed.
Long term follow up of cervical disease in HIV infected women.
Role: PI

Inovio Denny (PI) 2018
Randomised double-blinded trial of a therapeutic vaccine against types 16/18 in women with proven CIN2/3.
Role: PI

UH2/3.CA 189908 Kuhn/Denny (PI) 19/9/2014-31/8/2019
Improving specificity of HPV Screen-and-Treat in South Africa.
Role: PI

SA MRC Gynaecological Cancer Research Centre: R2.5 per year for 5 years
Study to address the cancer-related burden of disease in South Africa. (Director, L Denny)

Completed Research Support

Gates Foundation/Engender Health Denny (PI) 1996 – 2006
Cervical Cancer Prevention in Lesser Developed Regions: A Demonstration Project for Evaluating Alternative Strategies in Khayelitsha, South Africa. To investigate alternative methods of screening for cervical cancer in low resource settings: including HPV DNA testing direct visual inspection, and screen and treat algorithms from.
Role: PI

Graham Beck Endowment Denny (PI) 2006 – 2007
Graham Beck personal endowment for ongoing research into cervical cancer prevention
Role: PI

Merck Investigator Study Program Denny (PI) 2012
Prospective study of 150 women with genital warts who presented to Colposcopy Clinic at Groote Schuur Hospital – all women underwent HPV DNA typing, HIV testing and testing for lower genital tract intra-epithelial neoplasia.
Role: PI

GlaxoSmithKline Denny (PI) 2012
African Women with Cervical Cancer (AWACC) Study. Study recruited 567 women with invasive cervical cancer from Nigeria, Ghana and South Africa. All biopsy specimens were typed for HPV at a central laboratory.
Role: PI

GlaxoSmithKline Denny (PI) 2013
Evaluation of the safety and immunogenicity of GlaxoSmithKline Biologicals' HPV Vaccine 580299 in adult Human immunodeficiency virus infected female subjects. This was the first study of the safety and immunogenicity of the HPV vaccine against types 16 and 18 performed in HIV positive women.
Role: PI