



CAPRISA IS A UNAIDS COLLABORATING CENTRE FOR HIV PREVENTION RESEARCH

A history of HIV research in South Africa: What's next?

SA HIV Clinicians Society Conference 2012

Salim S. Abdool Karim

President, Medical Research Council of South Africa Director: CAPRISA & Pro Vice-Chancellor (Research): University of KwaZulu-Natal Professor in Clinical Epidemiology, Columbia University Associate Member, Ragon Institute of MGH, MIT and Harvard Adjunct Professor of Medicine, Cornell University





Overview

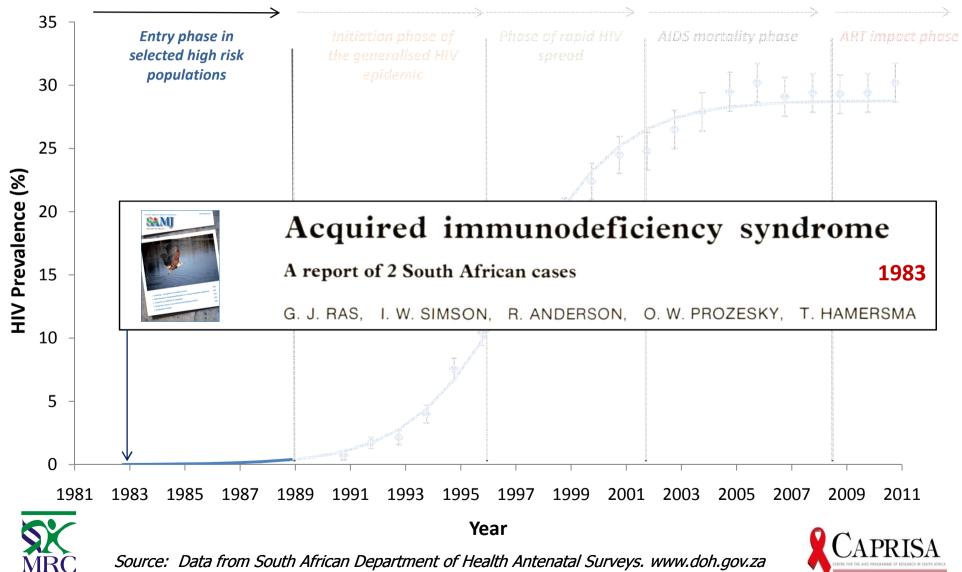
Historical phases of the HIV epidemic in South Africa

- 1. Entry phase in selected high risk populations
- 2. Initiation phase of the generalised HIV epidemic
- 3. Phase of rapid HIV spread
- 4. AIDS mortality phase
- 5. ART impact phase
- Milestone events in 20 years of the HIV epidemic in SA
- Major South African scientific contributions in HIV
- What's next in HIV research in South Africa?
- Conclusion





Historical phases of the HIV epidemic in SA: HIV infection among pregnant women



Phase 1: Entry phase in selected high risk populations in South Africa



 Absence of HIV infection in prostitutes and women attending sexually-transmitted disease clinics in South Africa
BARRY D. SCHOUB, SUSAN F. LYONS, GILLIAN M.
MCGILLIVRAY, ALAN N. SMITH, SYLVIA JOHNSON AND EPHRAIM L. FISHER

1987



AIDS and South Africa — towards a comprehensive strategy

Part I. The world-wide experience

C. B. IJSSELMUIDEN, M. H. STEINBERG, G. N. PADAYACHEE, B. D. SCHOUB, S. A. STRAUSS, E. BUCH, J. C. A. DAVIES, C. DE BEER, J. S. S. GEAR, H. S. HURWITZ

An and a state of the state of

Screening antenatal blood samples for anti-human immunodeficiency virus antibodies by a large-pool enzyme-linked immunosorbent assay system

1989

1988

Results of an 18-month investigation M. SHAPIRO, R. L. CROOKES, E. O'SULLIVAN

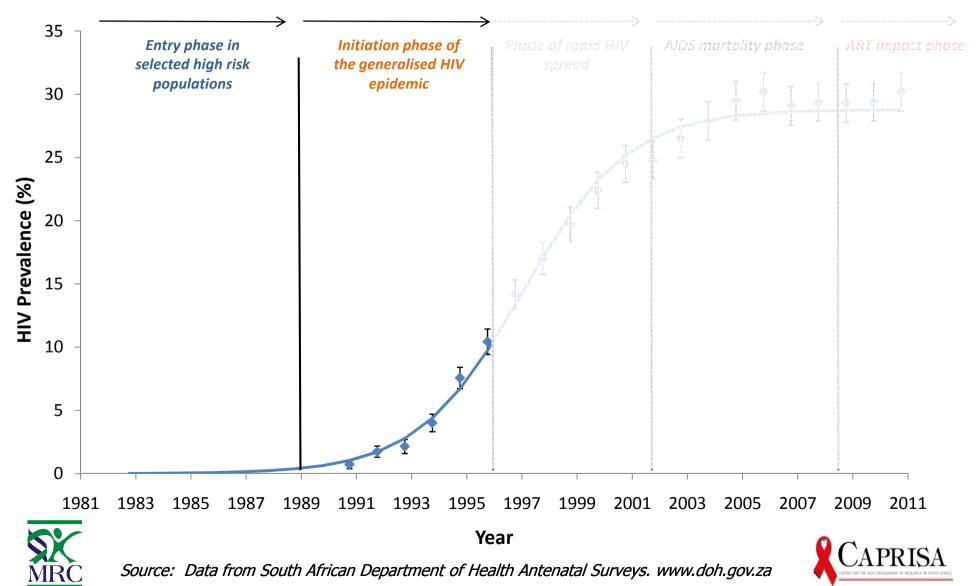


Transfusion-related human immunodeficiency virus in patients with haemophilia in Johannesburg

1990

R. J. COHN, A. P. MACPHAIL, E. HARTMAN, R. SCHWYZER, R. SHER

Historical phases of the HIV epidemic in SA: HIV infection among pregnant women



From phase 1 to phase 2: Two independent HIV epidemics

THE LANCET

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HIV-1 subtypes in different risk groups in South Africa

*Carolyn Williamson, Susan Engelbrecht, Maureen Lambrick, Estrelita J van Rensburg, Robin Wood, Wilhelmina Bredell, Anna-Lise Williamson

HIV prevalence in the general population 1985-1987

Year	Province	Group	Ν	%
1985	KwaZulu Natal	Rural community	441	0.00
1986	Transvaal	Miners	17 021	0.01
	Transvaal	Sex workers	1 200	0.00
1987	KwaZulu Natal	Antenatal women	500	0.00
		Outpatient	268	0.00



Source: Abdool Karim SS. S Afr Med J, 1999; 89: 609-611 Dusheiko GM. Am J Epidemiol. 1989; 129(1):138-45.



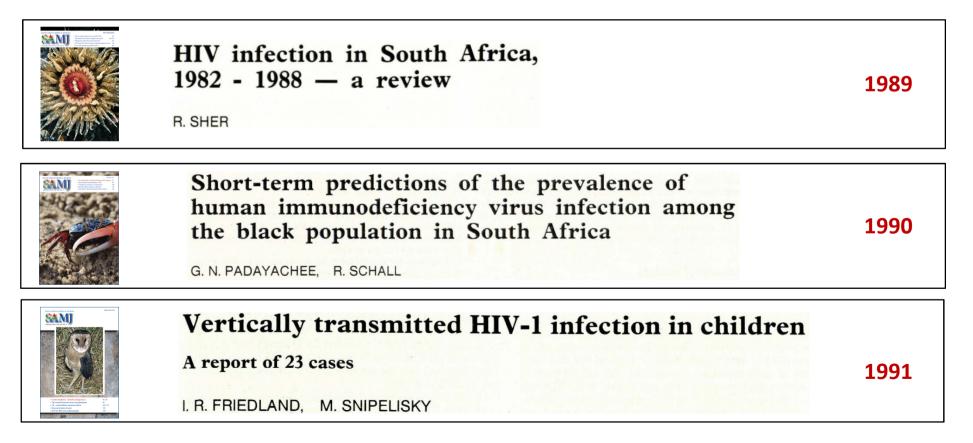
Phase 2: Initiation phase of the generalised HIV epidemic



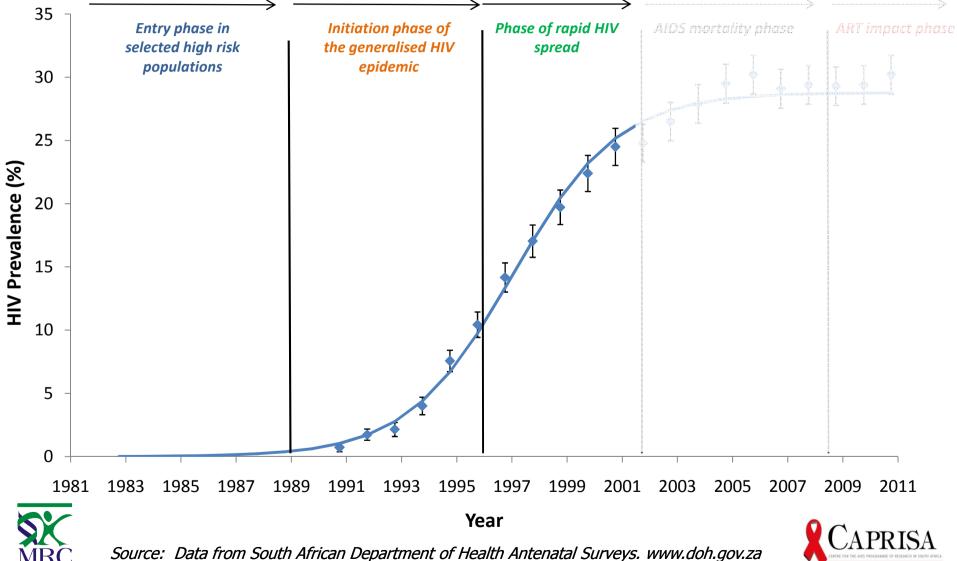
AIDS clinic — a year on

1989

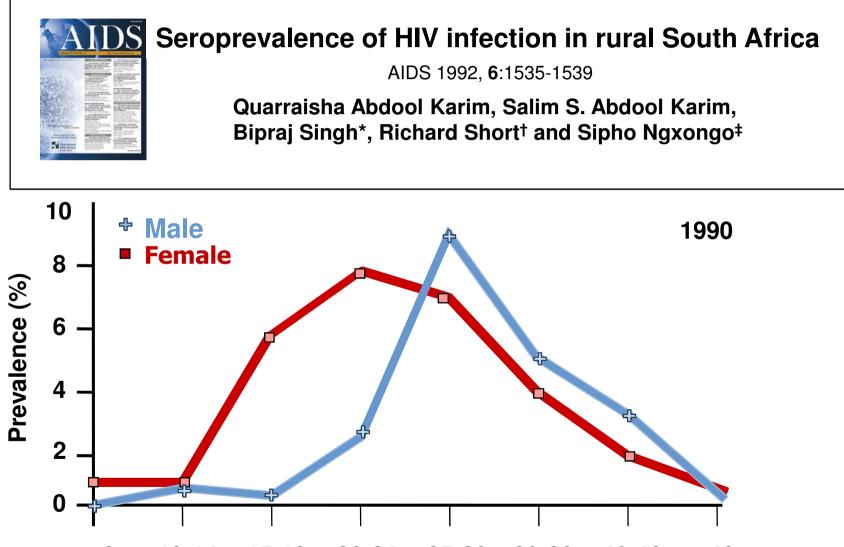
D. J. MARTIN, J. F. G. TILLEY, A. N. SMITH, B. D. SCHOUB



Historical phases of the HIV epidemic in SA: HIV infection among pregnant women



Why is HIV so severe in South Africa?



<9 10-14 15-19 20-24 25-29 30-39 40-49 >49

Phase 3: Phase of rapid HIV spread Temporal trends in HIV prevalence in a rural district in South Africa

Age Group	1992	1995	1998	2001
20-24	6.9%	21.1%	39.3%	50.8%
25-29				
30-34				
35-39				



Source: Wilkinson D, Abdool Karim SS, Williams B, Gouws E. High HIV incidence and prevalence among young women in rural South Africa: developing a cohort for Intervention Trials. J Acquir Immune Defic Syndr 2000; 23: 405-409



Phase 3: Phase of rapid HIV spread Temporal trends in HIV prevalence in a rural district in South Africa

Age Group	1992	1995	1998	2001
20-24	6.9%			50.8%
25-29	2.7%			47.2%
30-34	1.4%			38.4%
35-39	0.0%			36.4%



Source: Wilkinson D, Abdool Karim SS, Williams B, Gouws E. High HIV incidence and prevalence among young women in rural South Africa: developing a cohort for Intervention Trials. J Acquir Immune Defic Syndr 2000; 23: 405-409



Phase 3: Phase of rapid HIV spread Temporal trends in HIV prevalence in a rural district in South Africa

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20-24	6.9%	21.1%	39.3%	50.8%
25-29	2.7%	18.8%	36.4%	47.2%
30-34	1.4%	15.0%	23.4%	38.4%
35-39	0.0%	3.4%	23.0%	36.4%



Source: Wilkinson D, Abdool Karim SS, Williams B, Gouws E. High HIV incidence and prevalence among young women in rural South Africa: developing a cohort for Intervention Trials. J Acquir Immune Defic Syndr 2000; 23: 405-409



Phase 3: Phase of rapid HIV spread



High HIV Incidence and Prevalence Among Young Women in Rural South Africa: Developing a Cohort for Intervention Trials

2000

*†David Wilkinson, *S. S. Abdool Karim, ‡Brian Williams, and *Eleanor Gouws



Prevalence of HIV and HIV-related diseases in the adult medical wards of a tertiary hospital in Durban, South Africa

2001

2002

M Colvin MS MBChB¹, **S Dawood** MBChB FCP², **I Kleinschmidt** MSc¹, **S Mullick** MSc MBChB³ and **U Lallo** MBChB MD²



Prevalence of HIV Among Truck Drivers Visiting Sex Workers in KwaZulu-Natal, South Africa

GITA RAMJEE, MSc, PHD, AND ELEANOR GOUWS, MSc, MPH

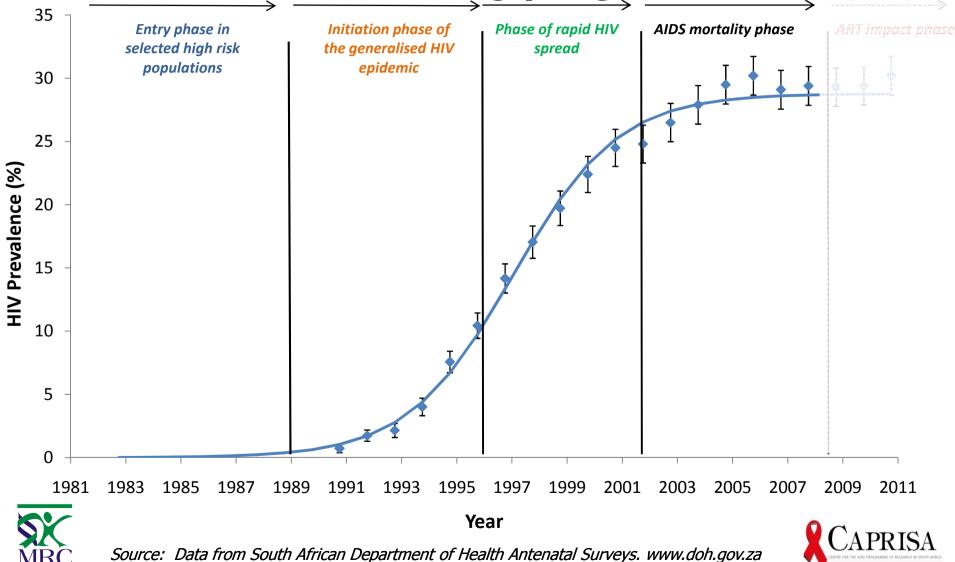


High Incidence of HIV-1 in South Africa Using a Standardized Algorithm for Recent HIV Seroconversion

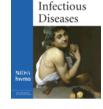
2002

*Eleanor Gouws, †Brian G. Williams, ‡Haynes W. Sheppard, ‡Barryett Enge, and *Salim Abdool Karim

Historical phases of the HIV epidemic in SA: HIV infection among pregnant women



Phase 4: AIDS mortality phase



Clinical

Morbidity and Mortality in South African Gold Miners: Impact of Untreated Disease Due to Human Immunodeficiency Virus

Elizabeth L. Corbett,¹ Gavin J. Churchyard,³ Salome Charalambos,³ Badara Samb,² Vicky Moloi,³ Tim C. Clayton,¹ Alison D. Grant,¹ Jill Murray,⁴ Richard J. Hayes,¹ and Kevin M. De Cock¹



SOUTH AFRICAN CAUSE-OF-DEATH PROFILE IN TRANSITION — 1996 AND FUTURE TRENDS

Debbie Bradshaw, Michelle Schneider, Rob Dorrington, David E Bourne, Ria Laubscher



High AIDS-related mortality among young women in rural KwaZulu-Natal 2007

M Mashego, D Johnson, J Frohlich, H Carrara, Q Abdool Karim



Effect of Human Immunodeficiency Virus Treatment on Maternal Mortality at a Tertiary Center in South Africa

A 5-Year Audit

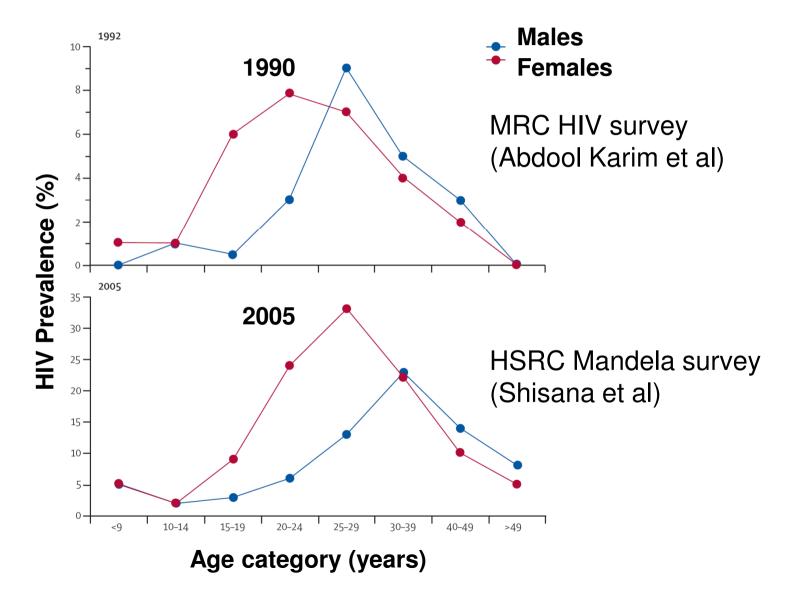
Vivian Black, MD, Sebastian Brooke, BS, and Matthew F. Chersich, MD, PhD

2002

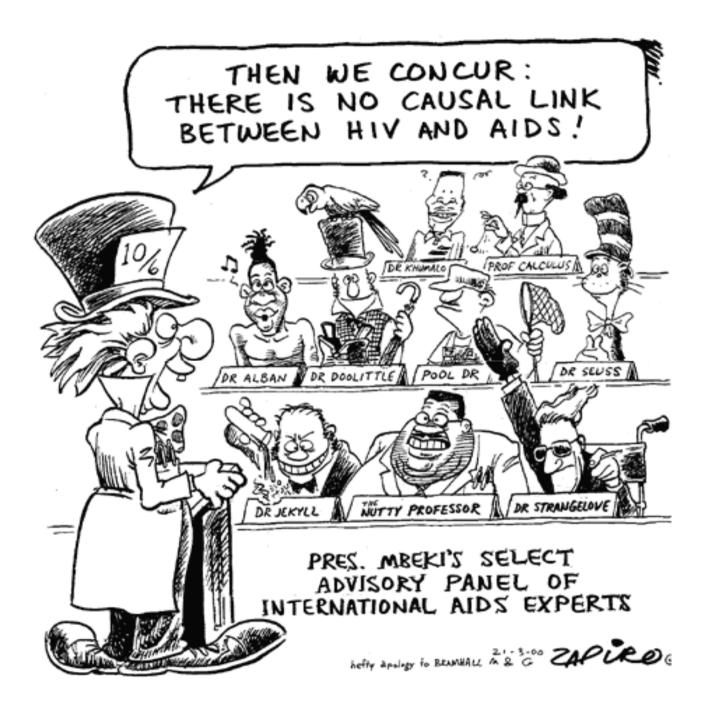
2002

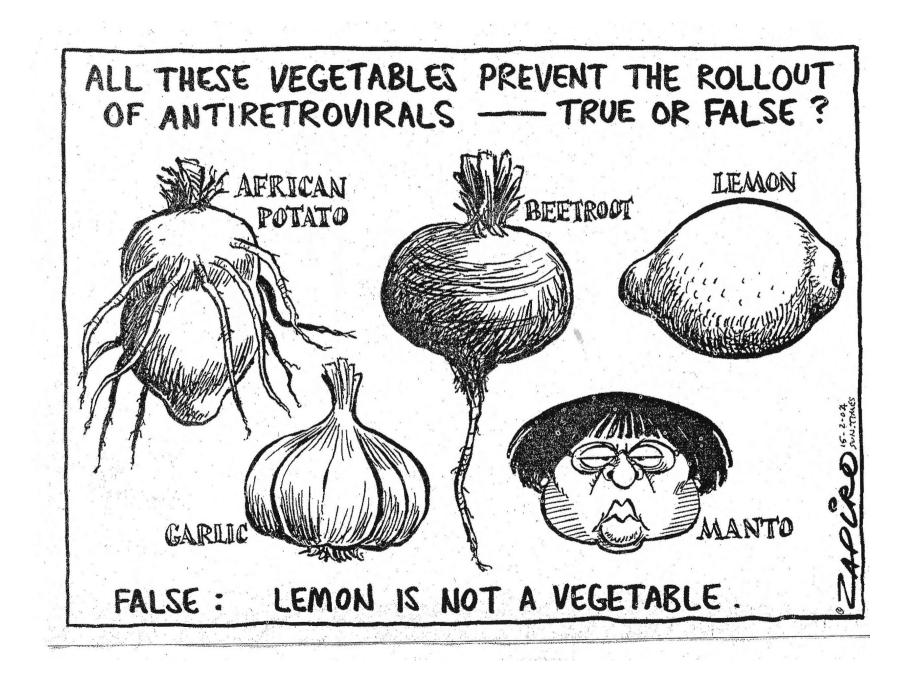
2009

Phase 4: AIDS mortality phase Has HIV incidence changed from 1990 to 2005?

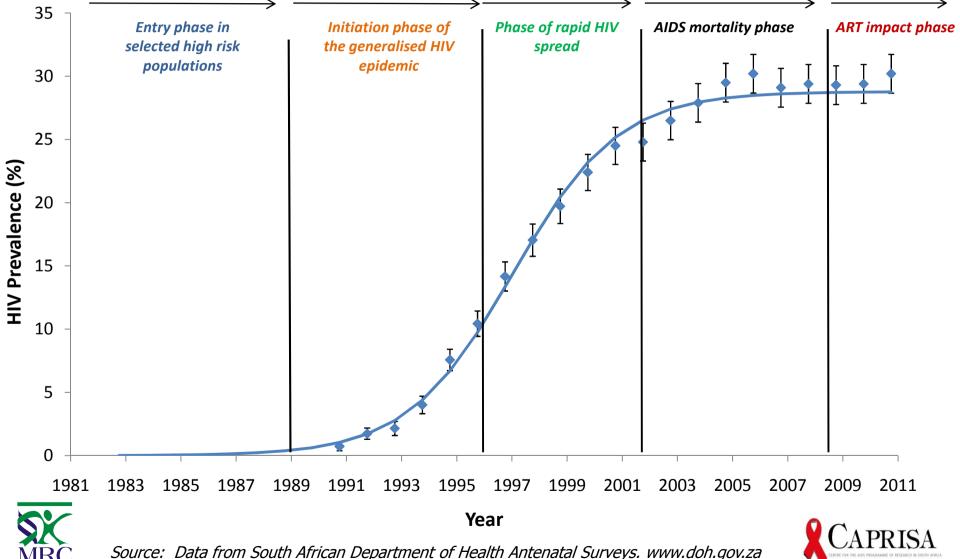








Historical phases of the HIV epidemic in SA: HIV infection among pregnant women



Phase 5: ART impact phase



Daniel R. Kuritzkes, MD, I Vincent C. Marconi, MD,# and Jean B. Nachega, MD, MPH, PhD**





Major South African scientific contributions in HIV

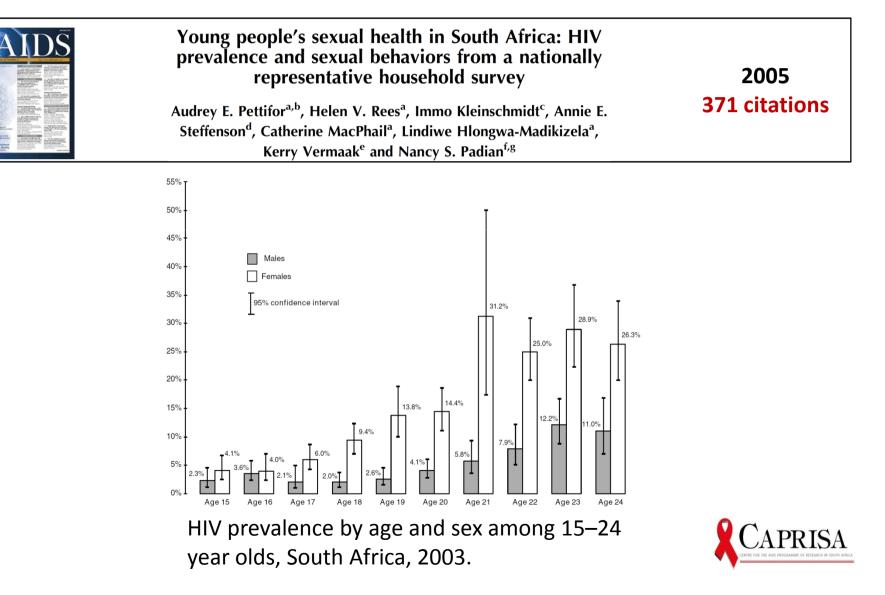
Major contribution = Article with a South African as first or last author AND >100 citations in Scopus

- HIV epidemiology
- Preventing mother to child transmission
- Preventing sexual transmission of HIV in men and women
- HIV pathogenesis and vaccines
- Tuberculosis and HIV co-infection
- HIV Treatment

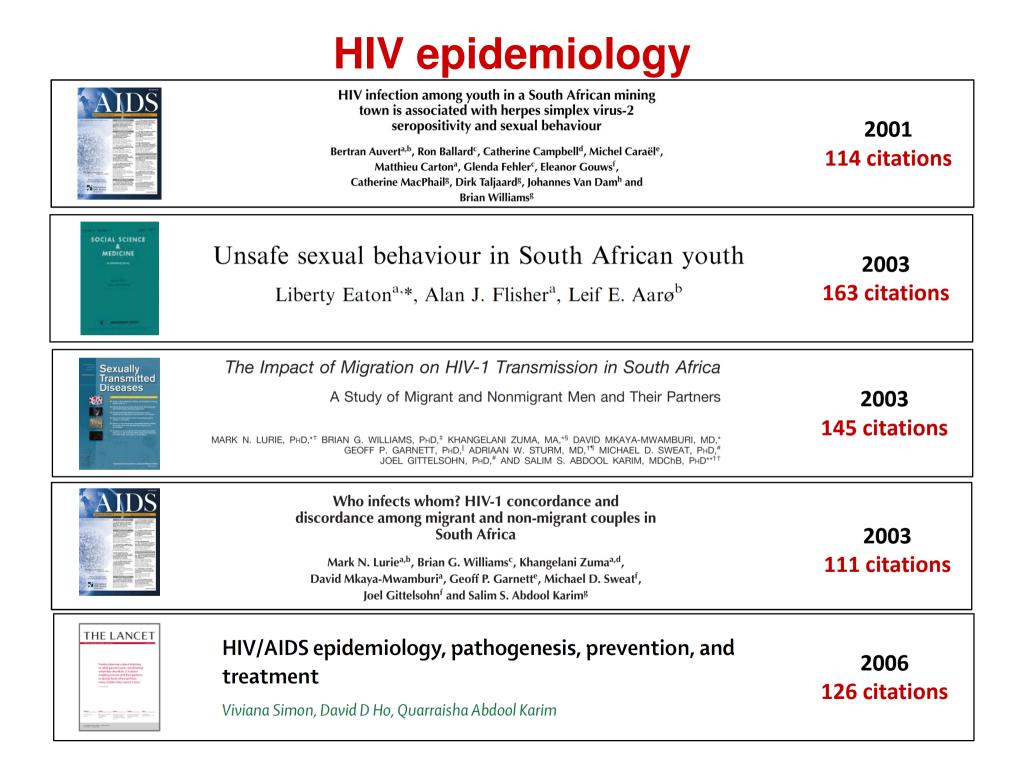




Major contributions to understanding HIV epidemiology







Major contributions to the prevention of mother to child transmission



Influence of infant-feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa: a prospective cohort study **371** citations

Anna Coutsoudis, Kubendran Pillay, Elizabeth Spooner, Louise Kuhn, Hoosen M Coovadia, for the South African Vitamin A Study Group*

Method of feeding and transmission of HIV-1 from mothers to children by 15 months of age: prospective cohort study from Durban, South Africa	2001
Anna Coutsoudis ^a , Kubendran Pillay ^a , Louise Kuhn ^b ,	232 citations
Elizabeth Spooner ^a , Wei-Yann Tsai ^c and Hoosen M. Coovadia ^a , for the South African Vitamin A Study Group [*]	
for the south African Vitamin A Study Group	



Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study

2007 248 citations

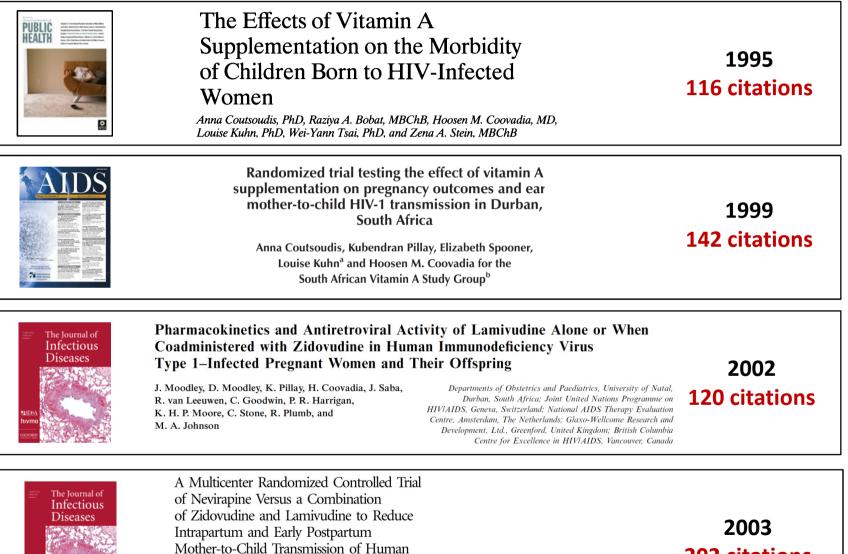
1999

Hoosen M Coovadia, Nigel C Rollins, Ruth M Bland, Kirsty Little, Anna Coutsoudis, Michael L Bennish, Marie-Louise Newell





Preventing mother to child transmission



Dhayendre Moodley,¹ Jagidesa Moodley,¹ Hoosen Coovadia,¹ Glenda Gray,² James McIntyre,² Justus Hofmyer,³ Cheryl Nikodem,³ David Hall,⁵ Maria Gigliotti,⁵ Patrick Robinson,⁵ Lynette Boshoff,⁴ and John L. Sullivan,⁶ for the

Immunodeficiency Virus Type 1

South African Intrapartum Nevirapine Trial (SAINT) Investigators

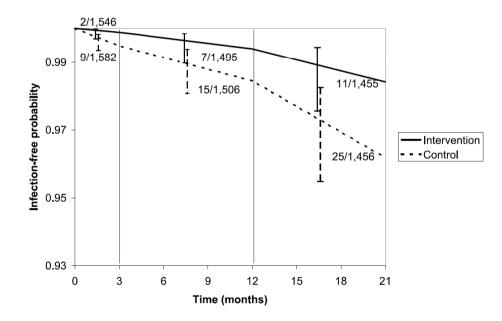
202 citations

Major contributions to the prevention of sexual transmission in men

Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial

2005 728 citations

Bertran Auvert^{1,2,3,4*}, Dirk Taljaard⁵, Emmanuel Lagarde^{2,4}, Joëlle Sobngwi-Tambekou², Rémi Sitta^{2,4}, Adrian Puren⁶



Infection-Free Probability As a Function of Time and of Randomization





PLOS MEDICINE

Major contributions to the prevention of sexual transmission in women



Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,^{1,2,*}† Salim S. Abdool Karim,^{1,2,3}* Janet A. Frohlich,¹ Anneke C. Grobler,¹ Cheryl Baxter,¹ Leila E. Mansoor,¹ Ayesha B. M. Kharsany,¹ Sengeziwe Sibeko,¹ Koleka P. Mlisana,¹ Zaheen Omar,¹ Tanuja N. Gengiah,¹ Silvia Maarschalk,¹ Natasha Arulappan,¹ Mukelisiwe Mlotshwa,¹ Lynn Morris,⁴ Douglas Taylor,⁵ on behalf of the CAPRISA 004 Trial Group‡

0.20 0.18 Probability of Infection Placebo 0.16 0.14 P=0.017 0.12 Tenofovir 0.10 0.08 0.06 0.04 0.02 0.00 Months of follow-up 6 12 18 24 30 37 Cumulative HIV endpoints 65 88 97 98 Cumulative women-years 432 833 1143 1305 1341 HIV incidence rates 6.0 vs 11.2 5.2 vs 10.5 5.3 vs 10.2 5.6 vs 10.2 5.6 vs 9.1 (Tenofovirvs Placebo) Effectiveness 47% 50% 47% 40% 39% (P-value) (0.064)(0.007)(0.004)(0.013)(0.017)





2010

569 citations

Prevention of sexual transmission



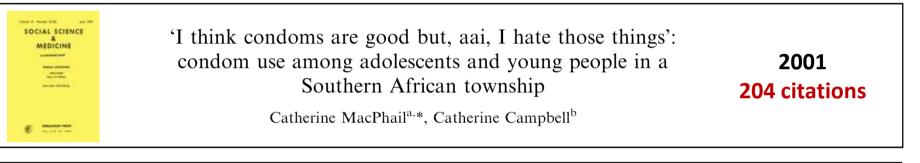
Reducing the Risk of HIV Infection among South African Sex Workers: Socioeconomic and Gender Barriers

1995 101 citations

2002

121 citations

Quarraisha Abdool Karim, MS, HED, Salim S. Abdool Karim, FFCH(SA), MMed(CH), MS, DipData, Kate Soldan, MS, and Martin Zondi







Peer education, gender and the development of critical consciousness: participatory HIV prevention by South African youth Catherine Campbell^{a,*}, Catherine MacPhail^b

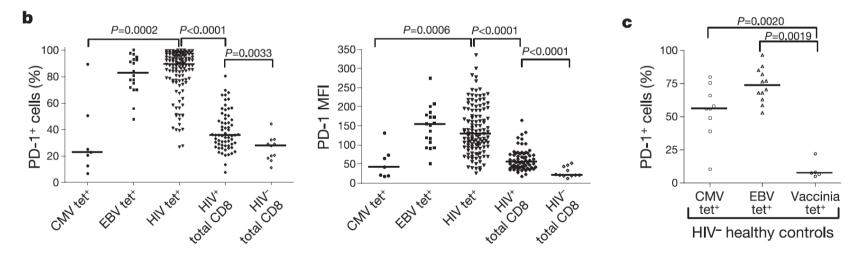
Major contributions to HIV pathogenesis and vaccine research



& Bruce D. Walker^{1,2,7}

PD-1 expression on HIV-specific T cells is associated with T-cell exhaustion and disease progression

Cheryl L. Day^{1,2,3}*, Daniel E. Kaufmann²*, Photini Kiepiela¹, Julia A. Brown⁴, Eshia S. Moodley¹, Sharon Reddy¹, Elizabeth W. Mackey², Joseph D. Miller⁵, Alasdair J. Leslie³, Chantal DePierres¹, Zenele Mncube¹, Jaikumar Duraiswamy⁵, Baogong Zhu⁴, Quentin Eichbaum², Marcus Altfeld², E. John Wherry⁶, Hoosen M. Coovadia¹, Philip J. R. Goulder^{1,2,3}, Paul Klenerman³, Rafi Ahmed⁵, Gordon J. Freeman⁴



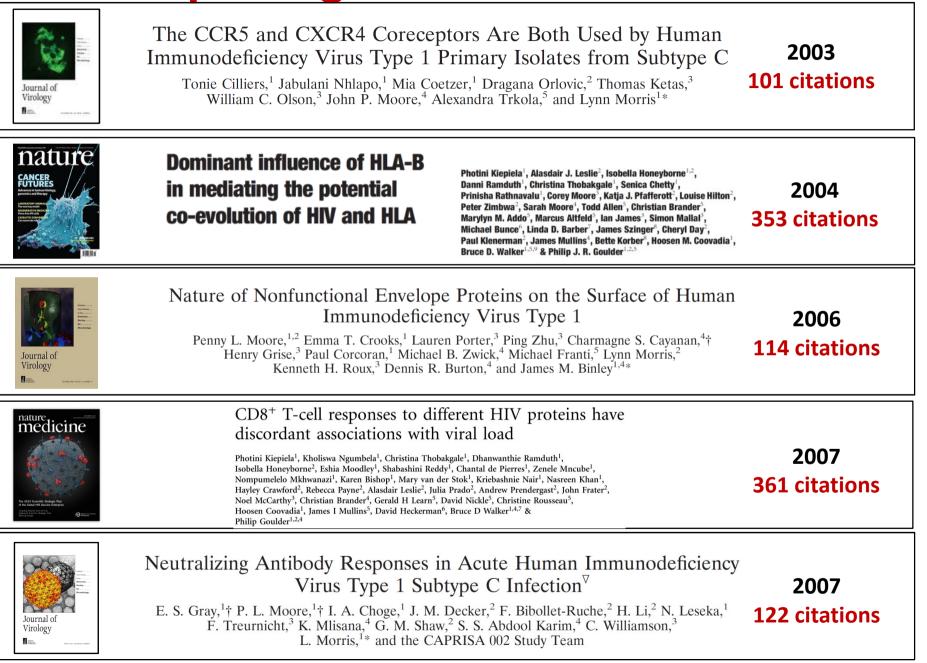
PD-1 is upregulated on HIV specific CD8 T cells





2006

HIV pathogenesis and vaccines



Major contributions to HIV and TB co-infection

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G Effect of highly active antiretroviral therapy on incidence of tuberculosis in South Africa: a cohort study

Motasim Badri, Douglas Wilson, Robin Wood

2002 332 citations

	HAART			Non-HAART		
	Number of cases of tuberculosis	Patient- years	Incidence*	Number of cases of tuberculosis	Patient- years	Incidence*
Overall	9	375.1	2.4	82	848.2	9.7
CD4 count (d	cells/μL)					
<200 200–350 >350	5 2 2	148 121·2 100·1	3·4 1·7 2·0	41 27 14	235 225 388·3	17·5 12·0 3·6
WHO stage 1 or 2 3 or 4	1 8	219 172·75	0·5 4·6	36 46	657·4 190·8	5.5 24.1
Socioeconon	nic status					
Low High	6 3	166·21 208·89	3·6 1·44	65 17	514·34 333·86	10∙9 5∙09

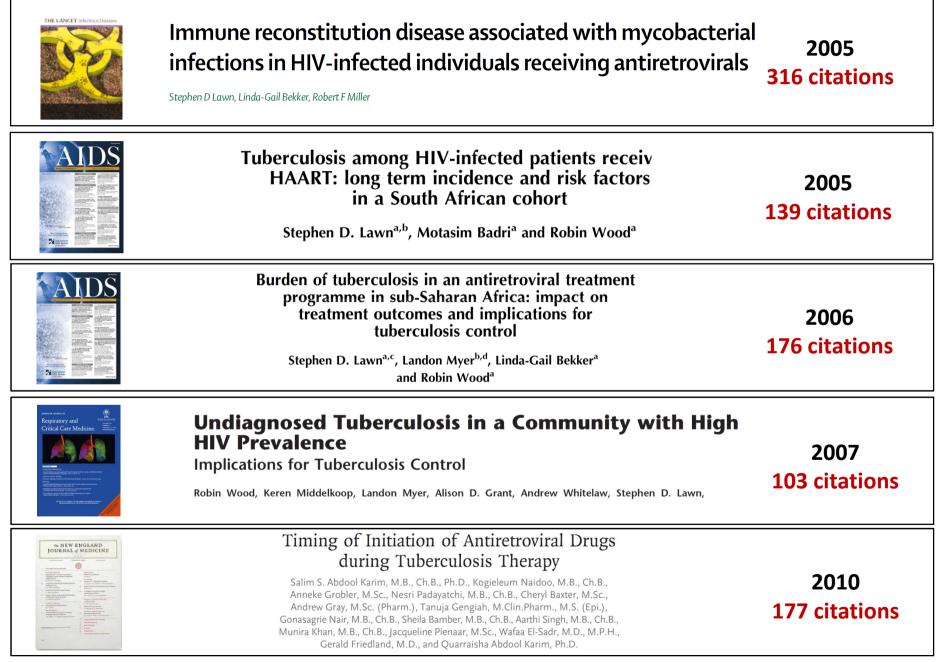
HAART=highly active antiretroviral therapy. *Per 100 patient-years.



Tuberculosis incidence and cases averted, stratified by baseline CD4 count, WHO stage, and socioeconomic status



HIV and TB co-infection

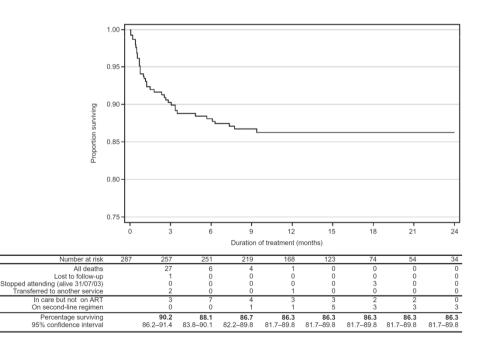


Major contributions to HIV treatment



Outcomes after two years of providing antiretroviral treatment in Khayelitsha, South Africa

David Coetzee^a, Katherine Hildebrand^a, Andrew Boulle^a, Gary Maartens^b, Francoise Louis^c, Veliswa Labatala^c, Hermann Reuter^c, Nonthutuzelo Ntwana^c and Eric Goemaere^c







2004

351 citations

Survival of adults on antiretroviral treatment

HIV treatment



Early mortality among adults accessing a communitybased antiretroviral service in South Africa: implications for programme design

Stephen D. Lawn^{a,c}, Landon Myer^{a,b,d}, Catherine Orrell^a, Linda-Gail Bekker^a and Robin Wood^a 2005 201 citations

Patient Retention in Antiretroviral Therapy Programs $PLOS_{MEDICINE}$ in Sub-Saharan Africa: A Systematic Review

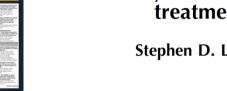
2007 271 citations

2008

222 citations

Sydney Rosen^{1,2*}, Matthew P. Fox¹, Christopher J. Gill^{1,3}





arly mortality among adults accessing antiretrovira treatment programmes in sub-Saharan Africa

Stephen D. Lawn^{a,b}, Anthony D. Harries^{b,c,d}, Xavier Anglaret^{e,f}, Landon Myer^{g,h} and Robin Wood^a

What's next in HIV research in South Africa?



Evolution of an HIV glycan-dependent broadly neutralizing antibody

epitope through immune escape

Penny L. Moore^{1,2}, Elin S. Gray¹, Constantinos Kurt Wibmer^{1,2}, Jinal N. Bhiman^{1,2}, Molati Nonyane¹, Daniel J. Sheward³, Tandile Hermanus¹, Shringkhala Bajimaya⁴, Nancy L.
Tumba¹, Melissa-Rose Abrahams², Bronwen E. Lambson¹, Nthabeleng Ranchobe¹, Lihua
Ping⁵, Nobubelo Ngandu³, Quarraisha Abdool Karim⁶, Salim S. Abdool Karim⁶, Ronald I. Swanstrom⁵, Michael S. Seaman⁴, Carolyn Williamson² and Lynn Morris^{1,2}*

mature



Evaluation of the Effectiveness of the National Prevention of Mother-to-Child Transmission (PMTCT) Programme on Infant HIV measured at Six Weeks Postpartum in South Africa

Ameena Goga, Thu-Ha Dinh, Debra Jackson et al



FACTS 001: A Phase III, Multi-Centre, Randomised Controlled Trial to Assess the Safety and Effectiveness of the Vaginal Microbicide 1% Tenofovir Gel in the Prevention of Human Immunodeficiency Virus Type 1 Infection in Young Women, and to Examine Effects of the Microbicide on the Incidence of Herpes Simplex Virus Type 2 Infection *Helen Rees, Glenda Gray et al.*



Effect of ART coverage on rate of new HIV infections in a hyper-endemic, rural population: South Africa



Frank Tanser, Till Bärnighausen, Erofili Grapsa and Marie-Louise Newell

Converting Science into Policy HIV prevention successes: 2010 - 2012

- HIV testing campaign: 13million HIV tests in 2010/1
- Condoms: 492m male condoms in 2010 (↑ by 30% in 5yrs)
- Preventing mother-to-child transmission:
 - 98% of women receive HIV test during pregnancy
 - 92% of HIV+ mothers receive ART prophylaxis
 - Vertical transmission rate in 2011 = 2.7%





Source: Mayosi BM, Lawn JE, van Niekerk A, Bradshaw D, Abdool Karim SS, Coovadia H. Health in South Africa. Lancet 2012 (in press)



South Africa's laudable achievements: Deaths are lower & people are living longer than 5 years ago - due to AIDS treatment

- **1. Deaths in children <5yrs:** \downarrow **43%** (42 per 1000 live births in 2011)
- **2.** Adults deaths: \downarrow **20%** (40% premature deaths in 2011)
- **3. Life expectancy:** \uparrow **by 6 years** (60 years in 2011)





Source: Bradshaw D, Dorrington R, Laubscher R. Rapid Mortality Surveillance Report 2011. Medical Research Council, August 2012



Acknowledgements

Thanks to the HIV Clinician's Society for their untiring efforts over many years to improve the quality of care we, as clinician's, can offer our patients.

Thank you to the many great scientists whose work I have cited - for their seminal contributions over the last 30 years of the HIV epidemic.

Thanks to all those patients, participants, advocates and research teams that have made South Africa a powerhouse of AIDS research globally



