

Destination: South Africa

South Africa has always delivered substantial contributions to medical innovation. An example of this radical pioneering work is most aptly illustrated by Dr Christiaan Barnard, who was the first surgeon to perform a human heart transplant on 3rd December, 1967.

A lesser-known fact, but just as important, is that Barnard also developed a system of post-operative intensive care that greatly influenced the survival rates of all critically ill patients. Barnard is also credited with developing a new design for artificial heart valves, performing heart transplants on animals, and correcting the problem of the blood supply to the foetus during pregnancy. (1, 2)

Career-long dedication in the field of clinical research is not unknown in South Africa, with numerous internationally renowned professionals devoting a substantial part of their careers towards promoting the South African industry through their efforts.

South Africa certainly has a wealth of clinical trials experience. There is an ever-increasing number of dedicated, focused individuals who on an ongoing and daily basis are contributing to the development of medicine and the improvement of patient care in the country.

This is well illustrated by another team from Groote Schuur, who, 40 years later, pioneered a technique to transplant kidneys between HIV-positive donors and recipients. Dr Elmi Muller, a surgeon at the University of Cape Town's (UCT) Department of Surgery in the Faculty of Health Sciences, performed the first such kidney transplant in September 2008. (20)

South Africa is the leading economy in Africa and a major gateway into the rest of the continent. What makes this even more impressive is that its geographic area is 1,219,090km², slightly less than twice the size of Texas or twice the size of France.

It has a stable political environment, allowing it to be an influential member of major political and economic African associations, e.g. OAU and SADC.

Almost 50% of the members of the American Chamber of Commerce in South Africa are Fortune 500 companies; over 90% operate beyond South Africa's borders in southern Africa and across the continent.

Its GDP of \$489.7 billion (2008 estimate), supports its ranking of 32nd out of 181 countries on the World Bank Ease of Doing Business index, and 2nd of 46 countries in sub-Saharan Africa. It is also ranked joint 9th (with the UK) of 181 in Investor Protection. (7, 22)

Something that makes South Africa attractive to international drug development companies is the fact that the regulatory environment is very conducive to clinical trials. The regulatory

authority, the Medicines Control Council, was established in 1965. It reviews over 400 clinical trial applications per annum and has approved over 20,000 medicines.

The National Health Research Ethics Committee oversees and accredits all ethics committees, whether they are academic (affiliated to medical schools) or private (for private sector physicians).

South Africa has an estimated population of 49 million, of which nearly 11% (5.2 million) is living with HIV. The age-standardised death rate indicator shows that HIV/AIDS, and TB among HIV-positive as well as -negative people, are the leading causes of death. However, non-communicable diseases, cardiovascular diseases, cancer and injuries are also contributing heavily to the mortality rate. Shockingly, though not surprisingly, the causes of death among children under five years of age are neonatal causes, HIV/AIDS, diarrhoeal diseases, measles, pneumonia and injuries. This substantiates the concept that South Africa has a distribution of First and Third World diseases. Also, the rich cultural diversity of the population makes it the ideal destination for inter-ethnic studies. An added advantage is the reverse seasons from the Northern Hemisphere, essentially allowing more time for recruitment on global studies. (6, 7, 8)

There are five major cities where clinical trials are focused, although they are certainly not limited to these cities alone. These cities are Johannesburg (population circa 3 million), Pretoria (1.6 million), Cape Town (2.4 million), Durban (2.1 million), Bloemfontein (0.35 million), with Port Elizabeth (0.75 million) and George (0.094 million) also contributing to a slightly lesser extent due to the smaller population, although they have a bigger catchment area per site. (6, 9)

Clinical trial sites are located in the public and private sector. There are academic sites associated with government hospitals, in addition to clinics, which are the first entry point into the health system. The private healthcare network consists of major groups such as Netcare and Life, as well as other smaller, independent institutions and individuals. The Netcare Group comprises 57 hospitals, 8713 registered beds, 319 operating theatres and 87 retail and hospital pharmacies countrywide. Their Primary Care Division operates medical and dental provider services through Medicross, as well as a managed care organisation, Prime Cure Medicentre, which focuses on the low-income market. This includes a national network of 108 Medicross and Prime Cure Medicentres, with 41 retail pharmacies and 12 day-theatres. Furthermore, a group of 590 independent doctors and dentists provide comprehensive primary health services

to about 3.5 million patients. Prime Cure manages a designated provider network of more than 10,000 health service providers, which includes 3877 contracted doctors and dentists. (10)

Life Healthcare's extensive hospital network includes 63 hospitals, 7776 registered beds - including 664 ICU and 316 high care beds, 308 theatres, 12 cardiac units, four renal dialysis facilities, and 41 accident and emergency units providing a range of healthcare services throughout South Africa. The group has hospitals in seven of the country's nine provinces, and in the country's most populous metropolitan areas, including Johannesburg, Pretoria, Cape Town, Durban, Port Elizabeth, East London and Bloemfontein. Life Healthcare operates a range of facilities adapted to meet the local demand in the various regions of the country, including high technology, multi-disciplinary hospitals, community hospitals and specialised stand-alone facilities to provide the appropriate scope of healthcare services. (11)

The main differences between the public and private hospitals are that the public hospitals normally have academic affiliations and fall within the remit of a specific university and its corresponding research ethics committee. Private hospitals fall within the remit of central research ethics committees and individual hospital review boards. Also, the public hospitals are mainly used by government-subsidised, mostly lower income patients, while the private hospitals are mostly frequented by patients with privately (self) paid medical insurance. That said, there is an increasing implementation of hybrid models, as demonstrated by the Netcare Group and Charlotte Maxeke Johannesburg Hospital, servicing both private and public sector patients.

A prime example of a public hospital is the Chris Hani Baragwanath Hospital, in Soweto, Johannesburg. With its 2964 beds, it is the largest acute hospital in the world. The hospital grounds cover an area of 173 acres, consisting of 429 buildings with a total floor area of 233,785.19m². It is the only public hospital serving approximately 3.5 million people, and it provides half of all the hospital services in Southern Gauteng. Being a specialist hospital, referrals for specialist treatment are received from all over the country, as well as surrounding African states.

Chris Hani is one of 40 provincial hospitals in the Gauteng Province, financed and run by the Gauteng provincial health authorities.

The hospital has a staff establishment of nearly 5000, of which 600 are doctors and 2000 are nurses. The greater part of the teaching and clinical research for the Faculty of Health Sciences of the University of the Witwatersrand takes place at this hospital. (12)

Of course, we cannot fail to mention the site of the first heart transplant - Groote Schuur Hospital. It is a central hospital which forms part of the Western Cape Provincial Department of Health. In addition to specialised and super-specialised care for patients, it serves as a world-class academic training site for interns and residents. This is supplemented by the fact that it is still, as it was in 1967, a world-renowned research hospital. The hospital has 3663 staff, who accommodate 560,000 referrals and inpatient admissions per year. (12)

South Africa has many internationally recognised research units actively contributing to the advancement in the fight against HIV/AIDS and tuberculosis. As a point of interest, South Africa participated in the Starting Antiretroviral Therapy at Three Points in Tuberculosis (SAPiT) study, designed to determine the optimal time to initiate antiretroviral therapy in patients with HIV and tuberculosis co-infection, who were receiving tuberculosis therapy. Based on the results of this study, the World Health Organization guidelines for treatment of TB and HIV co-infection were revised in late 2009, and on World AIDS Day in 2009, President Zuma of South Africa announced the new policy, to provide ART to all TB patients with HIV infection and CD4 counts below 350 cells per cubic millimetre. (14)

The results from the microbicide study conducted in 889 South African women and completed in 2010, showed that Tenofovir Vaginal Gel reduces the HIV transmission risk by 39%. This was commented on by the CDC at the XVIIIth International AIDS Conference, and published by AVAC. What makes it extraordinary is that the gel was designed in South Africa. (16, 17, 18, 19)

Throughout the public hospital and private hospital groups there are experienced clinical trial sites, as well as independent, private sites successfully executing clinical trials from Phase I – III in infectious diseases and chronic lifestyle diseases, in fields such as cardiovascular, respiratory, gastroenterology, endocrinology, oncology, central nervous system, gynaecology and obstetrics, haematology, nephrology, orthopaedics, pain and urology.

South Africa boasts five major units specialising in early phase development, located in Pretoria, Bloemfontein, George and Port Elizabeth. These units have experience in conducting difficult Phase I first-in-man studies, and have the global support and expertise to support them.

Indicating that all this translates into an environment optimum for the conduct of clinical trials, a large number of international CROs and pharmaceutical companies have a presence in South Africa, including PPD, Quintiles, Parexel, ICON, AstraZeneca, Pfizer, Novartis, and Sanofi-Aventis, to name but a few. There are also a number of local CROs, as well as generic companies such as Adcock Ingram and Aspen, occupying most of the market share.

In summary, bringing Destination South Africa to bear on clinical trials from a truly South African perspective:

South Africa ranks 10th in terms of contribution to clinical trials in the world, while maintaining high standards of clinical practice, as demonstrated by the fact that the pass rate of site audits by multinational companies and FDA in South Africa is high.

Guidelines for clinical trials in South Africa are stringent, and comply with both ICH and local health regulatory and ethical review policies.

All investigators are trained in good clinical practices (GCP) as it is a requirement by the regulatory authority before participating in clinical trials.

In the sciences, English is the preferred language in South Africa.

The value of clinical research in South Africa was estimated at US \$265 million (approx. ZAR2.2 billion) in 2008. (15, 21)

In conclusion, carrying forward the good work of Professor Barnard and others, South Africa and its clinical trials industry remains focused on maintaining exceptional standards, innovation and patient care, not only in the southernmost part of Africa, but also around the globe.

This is Destination, South Africa.

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