An international partnership was instrumental in building blood transfusion research capacity in South Africa

U Jentsch,¹ MB ChB, DTM&H, MMed (Microbiology); K van den Berg,¹ MB ChB, MMed Sci; M Vermeulen,¹ MTech; R Reddy,¹ MBA; E L Murphy,² MD, PHD; R Swanevelder,¹ MSc, for the REDS-III South Africa Program

¹ Medical Department, South African National Blood Service, Johannesburg, South Africa

² Departments of Laboratory Medicine and Epidemiology/Biostatistics, School of Medicine, University of California, San Francisco, and Vitalant Research Institute, San Francisco, USA

Corresponding author: U Jentsch (Ute.Jentsch@sanbs.org.za)

Background. The South African National Blood Service participated in the Recipient Epidemiology and Donor Evaluation Study (REDS-III) multicentre study between 2011 and 2019. The goal of this partnership was to perform cutting-edge research in transfusion medicine while at the same time building a broad base of local research capacity. This is a challenge in low- and middle-income countries such as South Africa (SA) for multifactorial reasons.

Objectives. To evaluate the outcome of the research capacity-building initiative.

Methods. The REDS III study provided multiple opportunities for local research participation in projects designed to reduce the impact of HIV on the SA blood supply. Research capacity building initiatives included research training courses in SA and internationally for promising junior SA investigators under the separate Fogarty International HIV training grant. In addition, junior researchers were provided with ongoing mentorship and collaborative interactions with experienced researchers. Research outputs directly and indirectly linked to REDS III are described.

Results. Over a 9-year period, the following research capacity building was accomplished: the core study team of 12 staff were trained in the responsible conduct of research, 34 staff attended local research training and 6 young investigators were trained internationally in manuscript writing. Three staff developed a study database. Five staff expanded the existing biorepository. Sophisticated laboratory and clinical skills were taught to 9 staff to enable large leukapheresis collections and performance of specialised laboratory tests locally. A functional research office was established by 4 study members. A total of 91 abstracts were presented at international and national conferences. Twenty-three transfusion-related manuscripts have been published in reputable journals. Six staff attained further qualifications, of which an additional three are PhDs in progress. A long-term plan to establish a research academy at the SA National Blood Service (SANBS) has been initiated.

Conclusion. Significant research capacity and output was established at SANBS through a successful North-South collaboration effecting blood transfusion safety in SA. Achieving sustainability was an early commitment, and has resulted in the establishment of a research academy and multiple local and international collaborations.

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In 1990, the Commission on Health Research for Development stated that strengthening research capacity in low- and middleincome countries (LMICs) is 'one of the most powerful, costeffective and sustainable means of advancing health and development'.⁽¹⁾This was echoed by the World Health Organization (WHO)'s landmark report on 'closing the gap in a generation', recommending a focus on the central importance of monitoring research development and training in order to address the social determinants of health and health inequities.^[2]

According to Ezeh *et al.*,^[3] Africa contributes less than 1% of scientific publications globally. This is in stark contrast to the fact that LMICs account for 85% of the world's population and 92% of

the global disease burden. They attract only 10% of global funding for health research to address these persistent health challenges, highlighting the need for development in this area.

A meta-narrative review of health research capacity in LMICs by Franzen *et al.*^[4] has highlighted the fact that the barriers and the lack of research output are multifactorial. Research efforts are often not sustainable without ongoing foreign support, research agendas are set and led by high-income country researchers, and LMICs leadership and authorship on publications and presentations are often underplayed. Potential researchers struggle to find the time for research and development of research leadership skills in their environment, owing to pressing commitments in clinical medicine or service delivery. Knowledge transfer and translation into policy remain challenging in sub-Saharan Africa. They are often 'patchy', and do not integrate social and institutional components adequately, and may lack an interactive, comprehensive framework that takes into account the local context.^[5,6]

Furthermore, while LMICs as a whole may show evidence of research integration, certain communities lag behind, such as those in rural, disadvantaged areas, and women. There is a dire need to rapidly upskill health capacity and training in in these settings. INTREC [INDEPTH Training and Research Centres of Excellence] is an example of an intervention that was established in three African countries, including SA, to provide training for those researchers most in need in this network regarding the social determinants of health, formulating findings in a way that can inform health policy.^[7]

The 1990s saw a surge in investment in conducting health research and building research capacity specifically aimed at addressing the health needs of LMICs. This included various models of grant-funded research collaborations, and development of centres of excellence, North-South partnerships and networks. Several highly successful research collaborations have been established within certain SA healthcare settings, either locally or with other African and international partners. These have mainly focused on addressing pressing healthcare issues such as TB, HIV/AIDA and cancer.^[8-11] In particular, despite some SA publications in the field of transfusion medicine (TM), the focus and scope of these publications are very narrow, and the challenge remained to develop sustainable, equitable research capacitation in the field of TM.

Today, 30 years later, discourse continues as we re-think capacity-building approaches. Gautier *et al.*^[12] suggest that health issues should be regarded as a global academic discipline, and that transformative partnerships are vital to overcome the one-sided nature of earlier collaborations. Initiatives must be cross-cultural and cross-disciplinary and include training in global health ethics. Young researchers must be capacitated with structured learning programmes using suitable toolkits, have opportunities for mentoring and fellowships, so that they can translate knowledge into practice and take on research leadership locally.^[13,14]

We therefore thought it valuable to analyse specific research outputs and capacity development from a long-term research collaboration in the field of blood transfusion. This article aims to describe the research capacity built at the South African National Blood Service (SANBS,) while participating in the US National Heart, Lung and Blood Institute (NHLBI) Recipient Epidemiology and Donor Evaluation Study - III (REDS-III) multicentre study between 2011 and 2019. The SA component was part of a larger NHLBI REDS-III programme, which included domestic (US) collaborative research to improve blood transfusion safety as well as HIVfocused programmes in SA, Brazil and China.^[15] SANBS was funded via a subcontract relationship from the University of California San Francisco (UCSF) and its affiliated Vitalant Research Institute. RTI International provided study management and data analysis services via a separate REDS-III contract. The goal over 9 years was to perform cutting-edge research in TM while at the same time making a concerted effort to build local research capacity and

better understand aspects of TM in the local context of SA. Ethical oversight was provided by SANBS and UCSF institutional review boards (IRBs) and the REDS-III observational study monitoring board. SANBS IRB approved this study on 3 March 2011 (ref. no. 2011/07).

Methods

The REDS-III collaboration included both clinical and epidemiological studies, providing opportunities for building capacity throughout the full research cycle. These consisted of four HIV-related clinical/ epidemiological REDS-III projects that provided opportunities for research output and capacity building. The studies were: (*i*) the Transfusion in Pregnancy (TIP) study that analysed the role of HIV in obstetric haemorrhage and blood transfusion; (*ii*) the donor recruitment study that examined motivators and deterrents to blood transfusion among potential donors at low risk of HIV; (*iii*) the HIV/HBV case-control study that analysed risk factors for incident HIV and HBV infection among prospective blood donors; and (*iv*) the Monitoring and Acute Treatment of HIV Study (MATHS) that studied the impact of very early antiretroviral therapy on the latent HIV reservoir.

In parallel, a donor and donation database was developed to provide statistics on viral prevalence, HIV incidence and blood donation patterns. Finally, there was ongoing skills development in protocol development, data analysis and manuscript writing. Ethical clearance for all studies was obtained locally and internationally.

In 2017, an HIV training grant was obtained from the US National Institutes of Health Fogarty International Centre to build upon the HIV research opportunities within REDS-III, and focused specifically on research training for young investigators. The Fogarty programme includes: (*i*) short courses on protocol writing and manuscript preparation; (*ii*) medium-term training in epidemiology, biostatistics, research ethics and manuscript preparation; (*iii*) a mini grant competition to fund trainee research; and (*iv*) long-term Master's and PhD degree enrolment at the University of Cape Town. The Fogarty programme also collaborated with the UCSF International Training in AIDS Prevention Studies (ITAPS) programme, which offers in-depth training in manuscript preparation, scientific mentorship and grant writing.

A retrospective review of research capacity-building initiatives and outputs attained directly or indirectly during the REDS-III study between 2011 and 2019 was conducted. These included enumeration of the extent of human resources capacitation that resulted in additional academic achievements, training received locally or internationally in research methods, attendance and/ or abstract presentation at international and national conferences and acquisition of specialised laboratory and other skills required for study. In addition, internally maintained registers and PubMed searches were reviewed to document the number and topics of publications to date. The outcome of a future vision for a dedicated research office was also assessed.

Results

Table 1 highlights the human resources capacity-building activities in clinical research over the 9-year period of the REDS-III study.

Table 1. Research capacity-building activities							
Research capacity	Staff capacitated, n	Activity					
Training in the responsible conduct of	12	Ethics training					
research	8	GCP training					
	3	Grant writing training					
Local research training	34	Training in research methods including protocol and abstract writing					
Research administration	4	Project management					
		Financial grant management					
		Stakeholder management					
Database development	3	Database set-up and management for more than 5 million donation events					
		from 1.2 million donors, available for ongoing analysis of research topics					
REDS investigator status	7	Study investigator training and application					
Specialised technical laboratory skills	4	Specialised laboratory skills in PBMC processing and HIV diagnostics					
Specialised clinical skills	5	Large-volume leukapheresis					
Biorepository expertise	5	Expansion of biorepository and training on shipping medical specimens					
UCSF ITAPS training	6	Manuscript writing and mentorship					
Abstract presentations at conferences	18	47 international					
		43 national					
Publications	15	11 published, 4 submitted or in preparation					
Additional qualifications achieved	6	4 Master's completed					
		2 Master's in progress					
		3 PhDs in progress					

GCP = good clinical practice; REDS = Recipient Epidemiology and Donor Evaluation Study; PBMC = peripheral blood mononuclear cells; UCSF ITAPS = University of California San Francisco International Training in AIDS Prevention Studies programme

A total of 55 staff members attended a combination of didactic research training programmes, including online, classroomtype and blended learning programmes, covering responsible conduct of research, biomedical research ethics, good clinical practice training and abstract, protocol and manuscript-writing programmes. This enabled the development of a REDS research team to actively manage the clinical studies in accordance with the various regulatory and ethical requirements, and with strict adherence to the study protocols.

As no mature research administration and management system was available at the start of this collaboration, local REDS investigators and team members developed processes that were refined and expanded over time. SANBS provided the necessary facilities and resources to make this possible. The SANBS Human Research Ethics Committee was a key partner, and instrumental to ensuring strong local regulatory oversight.

To ensure accurate data management and analysis of the results, it was critical to develop a study database independent of the existing SANBS operational data systems. Three staff members from the SANBS Information Technology (IT) Business Intelligence Department were co-opted and trained on study data requirements. IT resources were utilised to develop a large REDS database consisting of more than 5 million donation transactions between 2012 and 2016. It also included all related viral test results, donor adverse events as well as donor deferral details. Study-specific electronic management systems were developed and set up for each study protocol.

Seven local young investigators were mentored to perform an active role as local REDS investigators. This required the development and application of special skills, such as data management, project management, development of manuals of procedures and study training material, as well as protocol, abstract and manuscript writing. All REDS-III team members had exposure to international research collaboration, working group meetings, networking and practical grant management, as well as opportunities to attend or present at international conferences.

Four technical staff acquired and implemented specialised laboratory procedures in processing of peripheral blood mononuclear cells and performance of HIV recency assays. This internal capacitation allowed performance of these assays locally at SANBS rather than outsourcing to either local or international laboratories.

In addition, SANBS collaborated with two SA academic institutes: the National Institute of Communicable Diseases and Division of Clinical Pharmacology laboratory, University of Cape Town, to perform other required specialised testing. Furthermore, SANBS biorepository's service was expanded to also perform cryostorage.

The MATHS protocol for investigation of the latent HIV reservoir required the collection of large volume leukapheresis samples from selected donors. Standardised leukapheresis procedures were developed and validated using routine apheresis collection machines. After validation, five nurses competent in apheresis platelet procedures were trained in this specialised technique. Through this programme, the geographic spread from which these procedures could be performed was dramatically increased, while the use of routine SANBS equipment and staff resulted in reduced collection costs compared with what is seen in similar programmes. This capability has subsequently been made available to other SA HIV research teams on a fee-for-service basis. Six staff attended training and were mentored in scientific manuscript writing internationally in San Francisco, with the objective of developing a TM-related publication in a reputable journal. Three manuscripts have been published: the first evaluated whether there was an association of water administration and the risk of syncope and pre-syncope during blood donation; the second assessed the implementation of a script for personation interviews on the impact on HIV risk in SA blood donors; and the third described the discovery of 'false HIV elite controllers'. Two other manuscripts are in progress.

Eighteen staff members, mostly from the laboratories and the medical department, presented 91 abstracts at conferences (Table 2): 44 at local and 47 at international conferences. The authors of the abstracts had the following levels of tertiary education: Bachelor in Medical Technology (41%); medical clinical degrees (27%); Master's in Medical Technology (21%); nursing degrees (8%); and IT qualifications (3%).

To date, 23 publications related to the REDS-III study have been accepted by reputable journals on HIV- and transfusion-related topics of direct relevance to the SA transfusion setting (Table 3). The publications address specific blood transfusion challenges and safety in our environment, and all primary authors are South African. Three publications address SA's challenge to maintain a stable and adequate black African blood donor base in the setting of high HIV prevalence.[17-19] Four additional publications looked at the interplay of HIV and obstetric haemorrhage and transfusion practices in this setting.^[20,22-24] Additional publications include articles on laboratory screening to monitor prevalences of transfusion-transmitted infections,[25-34] an article on HIV incidence in blood donors^[35] and a publication on the phenomenon of 'false HIV elites'.^[36] Lastly, two recent publications address convalescent plasma as a potential therapy for Covid-19.[37,38] Four additional publications are pending.

Six staff attained additional qualifications including Master's in Medical Technology (n=2), Public Health (n=1), MMedSci in Transfusion Medicine (n=1) and Business Administration (n=2). Two PhD theses supported by the Fogarty HIV training programme are in progress, and one additional PhD is in development as a product of research collaborations. The topics focus on 'The intersection of the HIV epidemic and blood donation in South Africa' and 'The impact of individual donation nucleic acid testing for HIV and HBV on blood safety in South Africa'. The third PhD topic evaluates 'The need for education of HIV physicians for good clinical transfusion practices' in the era of patient blood management.

Discussion

This is the first article describing research capacity-building initiatives in the field of blood transfusion in SA through a 9-year North-South collaboration with researchers in the USA. The research capacity built was integrated into strong local and international regulatory oversight provided by SANBS and UCSF IRBs and the REDS-III observational study monitoring board.

Local research output has effected improvements in donor management, laboratory testing and understanding the HIV epidemic in the blood service.

Key to the capacity-building outputs were enthusiastic local staff with scientific, medical, IT or laboratory technical skills who were self-driven and keen to venture into unknown territory. Over a short time, project management skills and processes were built to take care of the project's operational, financial management and trouble-shooting needs.

The appointment of local investigators with high potential to have a local research impact has been shown to be a key facilitator in achieving research capacitation.^[13,39] SANBS was able to identify such individuals across various departments of the blood transfusion value chain who were eager to participate and to develop research skills ranging from operational research skills to attaining higher qualifications, such as PhDs.

Another key ingredient has been a productive collaborative North-South relationship that engrained a research culture locally with a long-term vision of sustainability. The collaborating external researchers were highly committed and engaged in order to facilitate knowledge transfer, which went beyond the achievement of the study objectives. They shared their knowledge and expertise, and provided direct mentorship and training over an extended period and beyond the study duration.

In addition, a deliberate decision was made to appoint SA investigators as lead authors on all publications, providing them with the necessary support to develop publications acceptable to international journals.

While the official REDS-III programme ended in March 2019, collaborative data analysis and manuscript writing continues to date. This contributes to ongoing research output, and is facilitated by the maintenance of archival databases and biospecimen collections in SA for future secondary analyses.

Research capacity building was cultivated from the beginning of the programme, with the goal of creating a sustainable research environment. A SANBS research academy was established in 2019 to conduct research locally and independently, aiming to

Table 2. Abstracts presented at conferences, <i>n</i>									
	Staff qualifications								
Presentation types	BTech	Clinician	IT	MTech	Nursing	Total			
International conferences	12	19	3	9	4	47			
Oral presentation	3	6	1	5	1	16/47			
Poster presentation	9	13	2	4	3	31/47			
Local conferences	25	6	0	10	3	44			
Total, <i>n</i> (%)	37 (41)	25 (27)	3 (3)	19 (21)	7 (8)	91 (100)			

BTech = Bachelor of medical technology; IT = information technology; MTech = Master of medical technology.

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Table 3. Published research from the programme by SA first authors		
Торіс	Publication	SA first author
Water administration and the risk of syncope and pre-syncope during blood donation:	Transfusion 2012	Van den Berg K, et al. ^[16]
Window period transmission of henatitis B virus by blood screened by individual	Transfusion 2012	Vermeulen M et al [24]*
donation nucleic acid tecting		vermeulen wi, et al.
Sensitivity of individual donation- and minipool-nucleic acid amplification test options	Transfusion 2013	Vermeulen M et al [25]*
in detecting window period and occult benatitis B virus infections. Implications for		vermeulen wi, et al.
removing transmission risk		
Comparison of HIV assays in window phase and elite controller samples: Viral load	Transfusion 2013	Vermeulen M et al [26]*
distribution and implications for transmission risk		vermedien wi, et al.
A mathematical approach to estimate the efficacy of individual donation- and	Transfusion 2014	Vermeulen M et al [27]*
minipool-nucleic acid amplification test options in preventing transmission risk by		vermeulen m, et al.
window period and occult hepatitis R virus infections		
Focus groups of motivators and deterrents to donation in black donors	Transfusion Medicine, 2015	Muthivhi TN, et al. ^[17]
The impact of HIV infection on obstetric baemorrhage and blood transfusion in	Transfusion 2015	Bloch FM et al [20]
South Africa		DIOCH EIW, et al.
The current status of nucleic acid amplification technology in transfusion-transmitted	ISBT Science Series 2016	Vermeulen M et al [28]*
infectious disease testing	ISBT Science Series, 2010	vermeulen m, et al.
Obstetric transfusion practices in the Eastern Cape Province of South Africa	SAMI 2016	Van den Berg K <i>et al</i> [21]
Use of blood donor screeping to monitor for HIV and benatitis B and C. South Africa	Emerg Infect Dis 2017	Vermeulen M <i>et al</i> ^[29]
Rick factors for peripartum blood transfusion in South Africa: A case control study	Transfusion 2018	Bloch FM et al [22]
Ractorial surveillance of apheresis platelets in South Africa (January 2011 -	ISBT Science Series 2018*	loptsch II <i>et al</i> ^[30]
December 2016)	ISBT Science Series, 2016	Jentsch O, et al.
Using a motivator and deterrent questionnaire to predict actual donation return	Transfusion, 2019	Swanevelder R, et al.[18]
behaviours among first-time African-origin blood donors		
Assessment of HIV transfusion transmission risk in South Africa: A 10-year analysis	Transfusion, 2019	Vermeulen M, et al. ^[31] *
following implementation of individual donation nucleic acid amplification technology		
testing and donor demographics eligibility changes		
Health economic implications of testing blood donors in South Africa for HTLV 1 & 2	Vox Sanguinis, 2019	Vermeulen M, et al. ^{[32]*}
infection		
The prevalence of human T-lymphotropic virus type 1 & 2 in South African	Vox Sanguinis, 2019	Vermeulen M, et al. ^{[33]*}
blood donors		
Reassessment of hepatitis B virus window periods for two transcription-mediated	Transfusion, 2019	Vermeulen M, et al. ^{[34]*}
amplification assays using screening data of South African blood donors		
Implementation of a script for personation interviews: Impact on HIV risk in South	Transfusion, 2019	Mitchell J, et al. [19]†
African blood donors		
Discovery of 'false elite controllers': HIV antibody-positive RNA-negative blood donors	J Infect Dis, 2019	Sykes W, et al. [36]T
found to be on antiretroviral treatment		
HIV incidence in South African blood donors from 2012 to 2016: A comparison of	Vox Sanguinis, 2021	Vermeulen M, et al. ^[35]
statistical models		
Antenatal blood transfusion in South Africa: Indications and practice in a high-HIV-	Transfusion, 2020	Bloch EM, et al. ^[23]
prevalence setting		
COVID-19: Convalescent plasma as a potential therapy	SAMJ, 2020	Van den Berg K, et al. ^[37] *
Guidance for the procurement of COVID-19 convalescent plasma: Differences between	Vox Sanguinis, 2020	Bloch EM, et al.[38]*
nigh- and low-middle-income countries		
SA = South Africa: ISBT = International Society of Blood Transfusion: SAMI = SA Medical Journal		

 SA = South Affragates, ISB = international society of blood fransitistion, SAW = SA Medical South REDS/Fogarty alumnus or principle investigator.
Mentored in manuscript preparation by other SA National Blood Service junior scientists.

direct the future of blood transfusion research in SA. The current research programme focuses on donor care, traditional transfusion practice, emerging infections and cellular therapies, convalescent plasma for therapeutic uses (of particular importance in the COVID-19 era) and molecular and genetic diagnostics.

Our strategy remains to ensure ongoing knowledge transfer and identification of new young staff with a passion for research. Being an attractive partner for research grants, publishing articles and striving to become financially sustainable are critical to remain a recognised blood transfusion research institution in Africa and beyond our borders.

True success in capacity building is measured in the sustainability of research output once the founding programme ends. To this end, our team successfully collaborated in applying for a Fogarty

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grant and more recently, in obtaining grant funding from the SA Medical Research Council (SAMRC) for COVID-19-related clinical trials. Sustainability is the key goal of the Fogarty International HIV training programme, which continues to support the development of human capacity at SANBS in partnership with the University of Cape Town. This programme supports Master's and PhD training in clinical research, with the goal of enhancing in-country research mentorship capability. The grant funding from the SAMRC enables SANBS to demonstrate our ability to develop large research networks and collaborations across a wide spectrum of stakeholders, a key component of developing a sustainable programme that can competitively compete for external research funding.

In conclusion, this 9-year North-South collaboration was effective in producing tangible research capacity building at SANBS. All research output is relevant to critical health questions in relation to TM in SA and internationally. SANBS staff have become respected researchers who continue to mentor and grow the next generation of young investigators within the SANBS research academy.

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