


# International train the trainer neonatal antibiotic stewardship program for South African pharmacists

Debra A. Goff Pharm.D., FCCP<sup>1,2</sup>  | Pavel Prusakov Pharm.D.<sup>3</sup> |  
 Julie E. Mangino M.D.<sup>4</sup> | Pablo J. Sanchez M.D.<sup>5</sup> | Benedict Nwomeh M.D.<sup>6</sup> |  
 Angeliki P. Messina MPharm.<sup>7</sup> | Natalie Schellack Ph.D.<sup>8</sup> |  
 Ama S. Annor MScPharm<sup>8,9</sup> | Azraa Cassim MSPharm<sup>10</sup> |  
 Sonya Kolman MSPharm<sup>11,12</sup> | Lindie Van Tonder MSPharm<sup>13</sup> |  
 Dini Mawela MBChBMMedPaed<sup>14</sup> | Sithembiso C. Velaphi MBChB<sup>15</sup> |  
 Pinky Lea Chirwa MBChB<sup>16</sup> | Dena van den Bergh EngD<sup>17</sup>

<sup>1</sup>Department of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, Ohio, USA

<sup>2</sup>Division of Pharmacy Practice, The Ohio State University College of Pharmacy, Columbus, Ohio, USA

<sup>3</sup>Department of Pharmacy, Nationwide Children's Hospital, Columbus, Ohio, USA

<sup>4</sup>Department of Internal Medicine and Division of Infectious Diseases, The Ohio State University and the Ohio State University Wexner Medical Center, Columbus, Ohio, USA

<sup>5</sup>Department of Pediatrics, Divisions of Neonatology and Pediatric Infectious Diseases, Nationwide Children's Hospital, Center for Perinatal Research, Abigail Wexner Research Institute at Nationwide Children's Hospital, Columbus, Ohio, USA

<sup>6</sup>Department of Pediatric Surgery, Nationwide Children's Hospital, Columbus, Ohio, USA

<sup>7</sup>Division of Pharmacy, Netcare Hospitals Ltd, Johannesburg, South Africa

<sup>8</sup>Department of Pharmacology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

<sup>9</sup>Department of Pharmacy, Dr. George Mukhari Academic Hospital, Ga-Rankuwa, South Africa

<sup>10</sup>Department of Pharmacy, Chris Hani Baragwanath Academic Hospital, Soweto, South Africa

<sup>11</sup>Department of Pharmacy, Nelson Mandela Children's Hospital, Johannesburg, South Africa

<sup>12</sup>Department of Pharmacy and Pharmacology, School of Therapeutic Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

<sup>13</sup>Department of Pharmacy, Netcare Femina Hospitals Ltd., Pretoria, South Africa

<sup>14</sup>Department of Paediatrics and Child Health, Dr George Mukhari Academic Hospital, Ga-Rankuwa, South Africa

<sup>15</sup>Department of Pediatrics and Child Health, Chris Hani Baragwanath Academic Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

<sup>16</sup>Department of Neonatology, Nelson Mandela Children's Hospital, Johannesburg, South Africa

<sup>17</sup>Division of Infectious Diseases & HIV Medicine, Department of Medicine, Groote Schuur Hospital University of Cape Town, Cape Town, South Africa

## Correspondence

Debra A. Goff, Department of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, OH, USA.  
 Email: debbie.goff@osumc.edu

## Abstract

Hospital-acquired antimicrobial-resistant infections are a leading cause of neonatal mortality in South African (SA) neonatal intensive care units (NICU). There is an urgent need for NICU Antibiotic Stewardship Programs (ASP). We describe the development of an international Train-the-Trainer (TTT) NICU-ASP mentoring program for SA pharmacists. A partnership between the South Africa Antimicrobial Stewardship

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2021 The Authors. JACCP: Journal of the American College of Clinical Pharmacy published by Wiley Periodicals LLC on behalf of Pharmacotherapy Publications, Inc.

**Funding information**

Pfizer; International Scholars Program at Nationwide Children's Hospital, The Ohio State University

Program (SAASP) and ASP experts from two United States (US) hospitals was formed in 2019. A baseline assessment of four SA NICUs was done to guide the development of a TTT NICU-ASP mentoring of SA pharmacists utilizing the existing workforce. The program included bilateral site visits. Pre-post surveys were used to assess SA mentee's NICU experiences, barriers to clinical pharmacy services and confidence to train additional pharmacists in NICU ASP. Four mentees from private ( $n = 1$ ) and public hospitals ( $n = 3$ ) completed a 2-week TTT NICU-ASP in the US that included; education, patient care rounds, role-playing, peer-to-peer sessions and behavioral interventions followed by ongoing support and mentoring by SAASP mentors. None of the hospitals had pharmacists participating in daily patient care rounds or had multidisciplinary NICU-ASPs due to lack of NICU trained pharmacists and dedicated time for ASP. Post surveys showed improved confidence to train additional pharmacists in NICU-ASP. Subsequently, these SA mentees provided NICU-ASP education to over 700 health care professionals and trained six additional pharmacists in NICU-ASP. Mentors and mentees developed a comprehensive NICU ASP toolkit for ongoing training of additional pharmacists. A new research collaboration between TTT NICU-ASP mentors, mentees and physician members of the South Africa National Neonatal Sepsis Task Force has formed and the first national NICU-ASP study is underway in 12 hospitals. Shared leadership between U.S. and SA mentors led to developing a TTT NICU-ASP for pharmacists tailored to existing resources and local needs.

**KEYWORDS**

antimicrobial stewardship, global health, mentoring, neonatal intensive care unit, neonates, pharmacists

## 1 | INTRODUCTION

More than 214 000 infants die each year from multidrug-resistant (MDR) infections.<sup>1</sup> Most of these deaths occur in low-middle income countries (LMIC). In South Africa, neonatal deaths account for approximately 40% of all deaths in children <5 years of age.<sup>1</sup> Data obtained in 2020 from the largest ( $n = 142$  bed) neonatal intensive care unit (NICU) in South Africa found hospital-acquired antimicrobial-resistant infections are the leading cause of late neonatal mortality.<sup>2</sup> The authors recommend implementation of NICU antimicrobial stewardship programs (ASP).

While progress has been made with adult ASPs in South Africa<sup>3,4</sup> NICU-ASPs are largely not present in South African hospitals due to few physicians and pharmacists trained in infectious diseases (ID) and neonatal ASP. The benefit to implementing NICU-ASPs in resource constrained South African hospitals could result in mortality reduction from MDR infections. Large outbreaks of bacterial infections in South Africa NICUs have resulted in the death of many neonates. One hospital reported a 3-fold increase in neonatal deaths from 48 to 140 in 1 year, due to multidrug-resistant *Klebsiella pneumoniae*.<sup>5</sup> Another hospital reported 10 infants died over a 2-month period following an outbreak due to Carbapenem-resistant Enterobacteriaceae (CRE).<sup>6</sup> Factors associated with this outbreak were identified to be overcrowding, understaffing and inadequate infection control practices (ICP).

In 2019, South African physicians launched a new National Neonatal Sepsis Task Force to tackle neonatal sepsis with uniform guidelines and protocols.<sup>7</sup> However the task force did not include a role for pharmacists. In South Africa, the pharmacists' role in NICUs is primarily for the provision of medications.<sup>8</sup> The need for clinical NICU pharmacy services was identified in a 2017 study. The authors report<sup>9</sup> neonates are three times more likely to experience a medication error than adults, 78% of patients had one or more medication error(s) and anti-infectives (43%) had the most errors. Inadequate knowledge and insufficient training were identified as major causes of medication errors. Implementing NICU-ASPs with pharmacists requires redistributing and retraining the existing pharmacist workforce. The purpose of this paper is to describe the development and impact of an international Train the Trainer (TTT) NICU-ASP for South African pharmacists.

## 2 | METHODS

### 2.1 | ASP in South Africa

The South African Antibiotic Stewardship Programme (SAASP) was founded in 2012. A partnership was formed in 2012 between The Ohio State University (OSU) ID pharmacist and SAASP to develop a

TTT ASP for South African pharmacists. The program implementation, outcomes and nine-year sustainability were previously described.<sup>10</sup> South African pharmacy schools do not offer ID or neonatal postgraduate training programs. Pharmacists providing NICU clinical pharmacy services are often self-taught or learn on the job.

## 2.2 | NICU-ASP call to action

In response to a 2018 CRE outbreak that resulted in the death of neonates at Chris Hani Baragwanath Academic Hospital (CHBAH) in Soweto, South Africa, the US Centers for Disease Control and Prevention (CDC) was asked to conduct an infection control practices (ICP) assessment and identify opportunities for improvement. The hospital did not have a NICU-ASP and the pharmacist role was limited to providing ward stock from the pharmacy located three blocks away. Nurses were responsible for calculating, preparing, and administering all NICU intravenous (IV) medications prepared without a laminar flow hood or consistent proper sterile technique. The CDC identified the urgent need for safe preparation and administration of IV medications and recommended that a pharmacist dedicated solely to the NICU oversee all medication prescriptions, preparation, stock control, and training of healthcare workers on medication safety. In addition, the CDC recommended developing a NICU-ASP to promote the judicious use of antimicrobials. The CDC requested the OSU ID pharmacist TTT-ASP program director to assist in developing NICU-ASP clinical pharmacy services at CHBAH. After discussions with SAASP pharmacist leaders to determine the feasibility and willingness to expand existing ASP efforts by pharmacists to NICU's a collaborative decision was made to provide assistance to CHBAH's NICU using the TTT-ASP model.

## 2.3 | Train the trainer program for NICU-ASP

A partnership was formed in September 2018 between faculty from OSU and Nationwide Children's Hospital (NCH) in Columbus Ohio. The OSU ID pharmacist TTT program director for adult ASP and an OSU ID physician collaborated with a pediatric ID neonatology physician, NICU ASP pharmacist, and pediatric surgeon to develop the NCH on-site training program for South African pharmacists using similar methodology to the adult TTT-ASP for South African pharmacists. The OSU-NCH faculty partnered with three SAASP pharmacists to co-develop TTT NICU-ASP. The OSU TTT program director received a grant to fund the program.

## 2.4 | Baseline assessment of NICU pharmacy services and NICU ASP

The OSU-NCH mentors worked with SAASP pharmacist mentors in four South African NICUs, one based on the CDC's request and three based on the OSU-SAASP mentor's 9-year involvement with TTT ASP for adult patients. The goal of the visit was to conduct an assessment

of NICU pharmacy services, engage with key stakeholders for NICU-ASP and interview pharmacists for TTT NICU-ASP at NCH in Columbus Ohio. Table 1 provides a comparison of the four hospitals. The OSU-NCH and SAASP mentors had no prior experience working with the physicians or pharmacists at CHBAH. The physician Head of Paediatrics received a 2018 Bill and Melinda Gates Foundation grant to reduce NICU healthcare-associated bloodstream infections and improve neonatal survival by addressing gaps identified during a CDC assessment of a CRE outbreak in the NICU. The grant provided one-year funding for a pharmacist to prepare IV medications in a designated area in the NICU. The OSU-NCH and SAASP mentors met with the neonatologists, pharmacy managers and the new NICU pharmacist to review the pharmacy gaps identified by the CDC. Prior to the outbreak, the neonatologist's interactions with the pharmacy department were limited to medication delivery and ward stock issues. The OSU-NCH mentors and SAASP pharmacist mentor participated in NICU patient care rounds with the neonatologists. The new pharmacist had no prior NICU training nor clinical pharmacy experience but was motivated to learn how to provide clinical pharmacy services in addition to preparing IV medications. The OSU-NCH mentors selected an experienced pharmacist with a permanent position at CHBAH for the TTT NICU ASP. Three additional pharmacists selected for TTT NICU ASP were from public and private hospitals, which included Dr George Mukhari Academic Hospital (DGMH), Nelson Mandela Children's Hospital (NMCH), and Netcare Femina Hospital (NFH).

## 2.5 | The TTT NICU ASP at Nationwide Children's Hospital (NCH) Columbus OH

The US component of the bilateral TTT NICU-ASP provides 2-weeks of training in a Level IV NICU with an established multidisciplinary NICU-ASP at NCH.<sup>11,12</sup> Our goal was to teach South African pharmacists the role of a NICU pharmacist to promote the judicious use of antimicrobials and enhance the quality of care of neonates. The aim of the program was to ultimately facilitate a sustainable South African NICU pharmacist's network using existing workforces in public and private sector hospitals. The US and SAASP mentors conducted six conference calls over 2 months to design a program that also addressed cultural context in South Africa. The physician faculty included a NCH neonatologist, ID physician, pediatric surgeon and an OSU ID physician. Pharmacy faculty included NCH NICU and pediatric pharmacists, pharmacy managers and the OSU ID TTT program director. The four mentees were interviewed January 2019 in South Africa and completed the TTT NICU-ASP in the US with two in May and two in August 2019. Prior to their arrival at NCH, the US mentors conducted three webinars with patient cases on early and late onset sepsis, appropriate antimicrobial therapy and therapeutic drug monitoring. These sessions included copies of the required readings. In contrast to US hospitals, none of the four South African hospitals provide free access to medical journals; mentees fund this personally to acquire access. They completed a survey to determine individual goals, NICU knowledge, clinical pharmacy experience, and









**TABLE 1** Comparison of South African hospitals and Neonatal Intensive Care Unit Pharmacy Services<sup>a</sup>

	Chris Hani Baragwanath Academic Hospital	Doctor George Mukhari Academic Hospital	Nelson Mandela Children's Hospital	Netcare Femina Hospitals Ltd
Number of beds	3400	1650	200	120
Number of neonatal beds	185	55	24	24
Number of clinical pharmacists	0	1	1	1
Number of NICU trained pharmacists	0	0	0	0
NICU ASP <sup>b</sup>	No	No	No	No
NICU antibiogram	No	No	No	No
NICU MDR outbreaks <sup>c</sup>	Yes	Yes	No	No
Therapeutic drug monitoring service	No	Yes	Yes	Yes
Pharmacists daily participation in patient care rounds	No	No	No	No
Pharmacists responsible for dispensing and ward stock	Yes	Yes	Yes	Yes
Pharmacy provides unit-dose medication	No	No	No	No

<sup>a</sup>NICU neonatal intensive care unit.

<sup>b</sup>ASP Antimicrobial Stewardship Program.

<sup>c</sup>MDR multidrug resistant.

	<b>Education<sup>a</sup></b> Provide required readings with patient cases, webinars, and one on one learning sessions. The NICU-ASP toolkit is used by the mentees to train additional pharmacists		<b>Behavior Change<sup>a</sup></b> Sessions on how to apply the social determinants of antimicrobial prescribing including relationships, fears, perceptions, and contextual factors
	<b>Patient Care Rounds<sup>a</sup></b> Participate in multidisciplinary NICU rounds to learn the role of the pharmacist		<b>Peer-to-Peer<sup>a</sup></b> Mentees interact with NICU <sup>d</sup> pharmacists, pharmacy managers, residents, students, and TTT <sup>e</sup> Program Director
	<b>Role playing<sup>a</sup></b> One on one sessions with physician and pharmacist mentors to practice how to make NICU ASP recommendations		<b>Mentoring and Sponsorship<sup>b</sup></b> Mentors address barriers, skills development, management support, and change leadership
	<b>Toolkit Development<sup>b</sup></b> Mentors and mentees develop a toolkit based on local context to support the training of additional pharmacists		<b>System and Culture change<sup>c</sup></b> One on one and team based sessions to address challenges and ensure strategies are in place for implementation

**FIGURE 1** Components of an International Train the Trainer Neonatal Antimicrobial Stewardship Program. <sup>a</sup>United States components. <sup>b</sup>United States and South Africa components. <sup>c</sup>South Africa components. <sup>d</sup>NICU neonatal intensive care unit. <sup>e</sup>TTT Train the Trainer

behavior change concepts for ASP. Figure 1 shows the eight US and South Africa components of the program including education, patient care rounds, role-playing sessions, peer-to-peer sessions, behavioral

change interventions to support judicious use of antibiotics, mentoring and sponsorship, toolkit development and system and cultural change to support implementation.

During their time at NCH, the pharmacist and physician mentors worked in individualized sessions with mentees to increase their NICU knowledge and confidence to make recommendations and interventions to physicians. Mentees learned how to build support for NICU clinical pharmacy services. To build confidence, the mentees participated in daily multidisciplinary NICU patient care rounds to learn the role of the NICU pharmacist including how to assess the patient, make interventions and verbalize recommendations with documentation. The NICU team at NCH consisted of a neonatologist, medical resident, fellow, advanced medical nurse practitioner, NICU pharmacist, dietitian, patient discharge coordinator and parents. The mentors met with the mentees to review drug therapy recommendations, therapeutic drug level monitoring, cultures and antimicrobial therapy. To increase the mentees confidence to engage with physicians in NICU-ASP, physicians (ID, neonatologist, pediatric surgeon) and pharmacists (ID and NICU) conducted one on one role-playing sessions with each mentee. Patient scenarios were presented to mentees to practice how to verbalize recommendations on antimicrobial optimization to the physician. The mentors addressed the mentees challenges with physician hierarchy, age and gender issues that the mentees described as barriers to making drug therapy recommendations.

To address how to start NICU clinical pharmacy services, the mentees met with a retired NICU pharmacist who started NICU clinical pharmacy services at OSU in 1987.<sup>13</sup> The pharmacist described the “baby steps” she took to introduce clinical pharmacy services to neonatologists and nurses, whose only prior experiences were interactions on providing medications. Initially, physicians and nurses had not seen a role for a NICU pharmacist; but she started by documenting medication errors. Her contributions to medication safety broke ground for her to participate in NICU patient care rounds. Notably, this method of implementing NICU clinical pharmacy services in 1987 was successful and sustained over 40 years.

Mentees recorded a podcast about their experience to share on WhatsApp with colleagues. After the mentees returned to South Africa, the US mentors conducted four monthly webinars to continue to advance their NICU knowledge.

## 2.6 | The TTT NICU ASP in South Africa

Upon returning to South Africa, the SAASP mentors continued to support, mentor, and sponsor the mentees. These mentors conducted one-on-one sessions to address challenges and barriers to implementing NICU-ASP. In addition, OSU-NCH and SAASP mentors had monthly calls to discuss each mentees progress and maintain momentum for NICU-ASP.

## 3 | RESULTS

Four South African pharmacists came to the US and completed the US component of TTT NICU-ASP. Table 2 lists post survey verbatims comments and outreach from this program. Mentees conducted

NICU-ASP educational programs reaching over 700 healthcare providers and contributed to six multimedia interviews to raise NICU-ASP awareness. The three public sector pharmacists each trained one additional pharmacist at their hospital and the private sector pharmacist trained three pharmacists.

### 3.1 | Survey—changes in skills and confidence

The pre-survey identified the mentees' greatest fear was approaching a physician to make NICU-ASP recommendations and interventions. All mentees listed their confidence level to make these interventions as “low,” due to lack of NICU-ASP experience or limited knowledge. Lack of access to publications was identified as a problem by all mentees. Three mentees stated they had a relationship with the neonatologist, but did not have daily patient care interactions due to dispensing responsibilities. All mentees stated they had no experience observing a pharmacist participating in patient care rounds while making recommendations or interventions as part of a multidisciplinary NICU-ASP team.

In the *post survey*, mentees showed improvement in applying NICU knowledge based on their ability to make appropriate antibiotic recommendations in six patient case scenarios presented by the OSU-NCH mentors. Mentees described improvement in their confidence level to recommend and monitor empiric antimicrobials, assess appropriate antimicrobial durations and make NICU-ASP interventions. Mentees highly valued the one-on-one role-playing and peer-to-peer sessions with physicians and pharmacist mentors to foster confidence to make NICU-ASP recommendations to physicians. The one-on-one sessions with physician and pharmacist mentors addressed the mentees' fears. Mentors stressed the importance of building a relationship, leveraging the power of face-to-face interactions, and using “handshake stewardship.” Physicians shared how trust in the pharmacist accumulates over time based on repeated positive interactions. All mentees stated this was their first experience to role-play in one-on-one learning sessions with physicians or pharmacist. During the sessions, mentors discussed the social determinants of prescribing antimicrobials including relationships between pharmacists and physicians, their expanding knowledge, risks, perceptions of antimicrobial resistance, NICU-ASP and contextual factors. These behavior change concepts addressed real-world situations that required new behaviors by the mentees. The TTT program provided daily opportunities for the mentees to learn how to review antimicrobial therapy, cultures, and laboratory values and then observe how NICU pharmacists made recommendations on rounds. Mentees applied these new behaviors during the peer-to-peer sessions. The mentees highly valued the sessions on patient cases, therapeutic drug level monitoring, and learning what information to document for clinical pharmacy services. Mentees appreciated meeting with pharmacy managers to learn how to support and justify new pharmacy services as well as participating in round table discussions with OSU's Dean of the College of Pharmacy, faculty, residents and students. On the last day, the mentees presented a lecture to OSU-NCH faculty to share their TTT

**TABLE 2** Train the Trainer Neonatal Stewardship Program survey results, educational programs and outreach

Survey verbatim feedback from mentees			
Mentee 1	Mentee 2	Mentee 3	Mentee 4
<p>“My greatest fear was talking to a surgeon about their antibiotics. The one on one session with the surgeon mentor was my NICU ASP ‘aha moment.’ He taught me why I do not need to be afraid to make antibiotic recommendations to a surgeon.”</p>	<p>“The 2 week TTT program gave me the confidence to believe I can make NICU ASP interventions that will improve the care of neonates. I want to make a meaningful difference.”</p>	<p>“I have never experienced one on one training sessions with physicians and clinical pharmacists who were dedicated to helping me succeed. I feel empowered and confident that I will be able to train additional pharmacists.”</p>	<p>“I learned so many valuable lessons during patient care rounds. I could not believe that the parents were invited by the neonatologist to join rounds. He answered all of their questions. The neonatologist said the parents are the voice for the baby. The pharmacist made recommendations on every patient. They asked for his opinion. The rounds were multidisciplinary and everyone contributed equally without hierarchy. I have read about multidisciplinary rounds but being a part of them and seeing first hand the role of the NICU pharmacist was motivational. I will work to have this in my hospital.”</p>
Translating learning into actions in South Africa			
Mentee 1	Mentee 2	Mentee 3	Mentee 4
<ul style="list-style-type: none"> <li>• Provided input into quality improvement project on medication safety with antibiotics, injection techniques, compounding accuracy.</li> <li>• Pharmacy representative on outbreak response team for neonatal and pediatric wards.</li> <li>• Review of treatment protocols to include learning from US mentors.</li> <li>• Improved relationships with doctors. Felt more confident to engage and was able to provide structured feedback so actions were more clear.</li> <li>• New mentoring to postgraduate student research. These students are often reluctant to do research in neonatal units.</li> <li>• Mentored new pharmacist and pharmacy interns during neonatal rotation.</li> </ul>	<ul style="list-style-type: none"> <li>• New level of participation in NICU multidisciplinary ward rounds due to improved confidence and better interprofessional communication skills.</li> <li>• Provided more thorough evidence based research by using resources such as “up-to-date” taught by US mentors.</li> <li>• Introduced new infection control protocol with chlorhexidine in appropriate dilution for neonates undergoing surgery based on practice at NCH.</li> </ul>	<ul style="list-style-type: none"> <li>• Implemented stewardship intervention on antibiotic duration of therapy in sepsis.</li> <li>• Increased engagement with neonatologists, more confident with asking questions and making antibiotic recommendations.</li> <li>• Improved credibility with neonatologists and nurses—greater adoption of ideas for improvement in stewardship.</li> <li>• Started a project on reducing “just in case” antibiotic prescriptions at discharge.</li> <li>• Mentored a new pharmacist.</li> <li>• Completed of Master’s thesis on Amikacin peak and trough levels in neonates and submitted the manuscript in collaboration with one of the mentors.</li> </ul>	<ul style="list-style-type: none"> <li>• My increased confidence to contribute in antibiotic stewardship committee meetings resulted in becoming an active member of the stewardship committee and pharmacy and therapeutic committee.</li> <li>• Reviewed empiric antibiotic guidelines for neonates using local antibiograms.</li> <li>• Improved the compliance to our antibiotic guidelines and use of restricted antibiotics.</li> <li>• Reviewed colistin use in the NICU to improve compliance to guidelines and ensure regulatory compliance.</li> <li>• Wrote a new standard of practice for colistin regulatory compliance.</li> <li>• The improved communication with the multidisciplinary NICU team has enabled more pharmacist involvement.</li> <li>• Mentored other pharmacists to improve their role in antibiotic stewardship.</li> <li>• Appointed to oversee the NICU and pediatric unit pharmacy service.</li> </ul>
NICU Educational Programs Conducted by Mentees			
South Africa	Audience	Number	Format and Topic
Netcare Femina Hospital (NFH)	Pharmacists, MD’s, Microbiologist, Hospital Managers	17	Feedback session to antibiotic stewardship committee on lessons learned and ideas for consideration at NFH.
Netcare Healthcare System (56 hospitals across South Africa)	Pharmacists and Pharmacy Managers	±95	Skype training session on neonatal medication safety and stewardship best practices.
Netcare Femina Hospital	NICU nurses	5	Workshop on the importance of antibiotic stewardship in neonates
Netcare Femina Hospital	NICU nurses	8	Workshop on antibiotic intravenous safety in neonates
Netcare Femina Hospital	NICU nurses	6	Workshop on common antibiotic dosage errors and challenges for neonates

(Continues)



TABLE 2 (Continued)

NICU Educational Programs Conducted by Mentees			
South Africa	Audience	Number	Format and Topic
Netcare Femina Hospital	NICU nurses	7	Workshop on essential information on antibiotic use in neonates.
Doctor George Mukhari Academic Hospital	Pharmacists SMU and DGMAH	15	Lecture—shared experience and learning from time at OSU and NCH. Explored ideas for implementation at DGMAH and ways to support students at SMU to practice neonatal stewardship
Doctor George Mukhari Academic Hospital	Fourth year pharmacy students	±50	Delivered lecture on neonatal stewardship to pharmacy students at SMU. Applied information from NCH experience to enhance the knowledge of students during their NICU rotation.
ODI District Hospital	Pharmacists, MD's, nurses	16	Lecture with feedback session on importance of antibiotic stewardship and medication safety for antibiotics.
Doctor George Mukhari Academic Hospital	NICU PICU nurses, pharmacists	35	One-day workshop with fellow trainee and mentor. Workshop topics included why antibiotic stewardship is important, medication safety for antibiotics and roles and responsibilities of different health professionals in antibiotic stewardship
Doctor George Mukhari Academic Hospital	Pharmacists, nurses	10	Workshop on antibiotic intravenous guidelines
Nelson Mandela Children's Hospital (NMCH)	Pharmacists, nurses, MDs, ICP	12	Feedback session on learning from NCH hospital experience, including ideas for improvement of neonatal stewardship at NMCH.
Nelson Mandela Children's Hospital	Wits University Pharmacy students	±40 students	Mentored the University of Wits pharmacy students on NICU rotation
South African Society of Clinical Pharmacy (SASOCP) annual conference	Pharmacist delegates	±200	Joint presentation with fellow TTT NICU ASP trainees on pharmacist's role in neonatal sepsis and antimicrobial stewardship.
Chris Hani Baragwaneth Academic Hospital (CHBAH)	Pharmacists, Neonatologists, nurses	5	Round table discussion with South Africa mentors
Chris Hani Baragwaneth Academic Hospital	Pharmacists, pharmacy managers	12	Lecture to share the experience at NCH and OSU and discuss ideas on how to take stewardship forward.
Chris Hani Baragwaneth Academic Hospital	MD's, pharmacists, nurses	110	Invited lecturer at the first Antimicrobial Stewardship Training Course for staff at CHBAH. Now completed 3 rounds of this course and will extend to primary care clinics in the future.
United States	Audience	Number	Format and topic
Decennial 2020 sixth International Conference Atlanta GA. USA	CDC, physicians, pharmacists, nurses, ICP	Cancelled due to COVID-19	Platform presentation titled <i>Improving neonatal survival through preventing infections in a resource constrained environment (INSPIRE) A quality project in a South African hospital</i>
The Ohio State University College of Pharmacy	The College of Pharmacy Dean, faculty, PharmD and Masters students, PGY1, PGY2 residents, College of Medicine faculty, Office of Outreach and Engagement, Office of International Affairs	60	Lecture followed by group discussion with the Dean, selected faculty and students
The Ohio State University Wexner Medical Center	PGY1, PGY2, Master first and second year students, PharmD students	12	Meet and greet with a round table discussion

TABLE 2 (Continued)

United States	Audience	Number	Format and topic
Nationwide Children's Hospital	Pharmacy director, NICU pharmacists, neonatologists, nurses, and surgeon	25	Lecture followed by round table discussion
Multimedia contributions to increase awareness for NICU ASP			
	Description		Link
YouTube video by the Centers for Disease Control and Prevention	"Fighting a Global Threat: CDC and Partners Combat Antibiotic Resistance" featuring the neonatologist and NICU pharmacist at CHBAH viewed 3756		<a href="https://www.youtube.com/watch?v=q8f1gYlcf4">https://www.youtube.com/watch?v=q8f1gYlcf4</a>
The Columbus Dispatch Newspaper	An interview with US mentors and South African pharmacists describing the international collaboration and Train the Trainer Program at Nationwide Children's Hospital in Columbus OH.		<a href="https://www.dispatch.com/news/20190817/columbus-hospitals-train-south-african-pharmacists-to-stem-antibiotic-resistant-diseases-in-newborns">https://www.dispatch.com/news/20190817/columbus-hospitals-train-south-african-pharmacists-to-stem-antibiotic-resistant-diseases-in-newborns</a>
The Ohio State University "The Lantern" campus online newspaper	An interview with US mentors describing the TTT NICU ASP program and how the international collaboration contributes to the global mission of OSU.		<a href="https://www.thelantern.com/2019/08/ohio-state-helps-fight-south-african-superbugs/">https://www.thelantern.com/2019/08/ohio-state-helps-fight-south-african-superbugs/</a>
ContagionLive infectious diseases news organization video	Live interview from IDWeek featuring the US mentors describing the TTT NICU ASP viewed 1300 times		<a href="https://www.contagionlive.com/view/implementing-the-train-the-trainer-program-in-south-africa">https://www.contagionlive.com/view/implementing-the-train-the-trainer-program-in-south-africa</a>
Nationwide Children's Hospital (NCH) monthly magazine	An interview with US mentors and South African pharmacists describing the global collaboration and their experience at NCH		
Beckers Healthcare online newsletter	Why these Columbus hospitals are training South African pharmacists on antibiotic resistance		<a href="https://www.beckershospitalreview.com/quality/why-these-columbus-hospitals-are-training-south-african-pharmacists-on-antibiotic-resistance.html">https://www.beckershospitalreview.com/quality/why-these-columbus-hospitals-are-training-south-african-pharmacists-on-antibiotic-resistance.html</a>
Podcasts	Four narrated stories by mentees describing the impact of the Train the Trainer NICU ASP and how they will apply their new knowledge		

experiences, describe how they would apply the lessons learned, exchanged ideas to sustain the program, and discussed the mutually beneficial value to collaborative global engagement.

### 3.2 | Applying new knowledge in four South Africa NICUs

At CHBAH, the mentee applied her new knowledge and skills to train the NICU pharmacist on how to provide clinical pharmacy services in addition to compounding IV medication. The TTT mentee worked with three SAASP mentors and the NICU pharmacist and assisted in co-developing standard operating procedures for medication preparation using sterile technique, administration, how to document NICU ASP activities including medication errors, review of cultures, antimicrobial use, dose, and duration recommendations. The NICU pharmacist was taught to obtain the neonate's weight prior to dispensing medications to assure the appropriate dose was prescribed. The OSU mentor provided the NICU pharmacist with hard copies of the Pediatric & Neonatal Dosage Handbook.<sup>14</sup> The neonatologist and nurses' perspective of the pharmacist changed over the following months. Initially nurses told the pharmacist that they were very hesitant to follow

the CDC's recommendation to give up medication compounding to the new pharmacist; however, with on-going support from the TTT NICU-ASP mentee the NICU pharmacist's role changed from "provider of ward stock" to an essential NICU team member. The neonatologist co-authored an abstract with the TTT NICU-ASP mentee, NICU pharmacist, OSU mentor and CDC physician that was accepted to the 2020 US Decennial Infectious Diseases Conference. The mentee pharmacist decreased the medication error rate from 17% to 3% over 7 months. When the grant funding expired, the NICU pharmacist position was approved as a permanent post, due to the documented impact of pharmacists on patient care. Based on the high performance of the TTT NICU-ASP mentee, she was promoted to manager of the NICU pharmacist, NICU and pediatric pharmacy services, and ASP. Additional accomplishments from the TTT NICU-ASP are listed in Table 2.

At DGMAH, the pharmacist mentee applied her new skills to train one pharmacist in NICU-ASP, and mentor pharmacy interns and students during their NICU rotation. Her leadership skills led to an appointment on the outbreak response team for the neonatal and pediatric wards, and input into a quality improvement project for medication safety. Another pharmacist was assigned to assist in dispensing and the mentee had 2 hours daily to provide clinical pharmacy



services and participate in patient care rounds. The neonatologist continued to mentor the pharmacist to enhance her NICU knowledge and to implement multidisciplinary NICU ASP. Additional examples of the mentee translating learning into actions are listed in Table 2.

The NMCH pharmacist mentee trained one pharmacist in NICU-ASP and applied her improved confidence and communication skills to make drug therapy recommendations on patient care rounds. She observed the transfer of neonates from CHBAH to NMCH resulted in the importation of the first MDR infection to their new NICU. The use of paper charts at CHBAH precluded efficient ways for NMCH to rapidly obtain antibiotic information and cultures at time of transfer. The TTT NICU-ASP mentees at CHBAH and NMCH agreed to call each other to communicate the current antibiotics and cultures. This allowed the NMCH pharmacist to share critical results and discuss appropriate antibiotics during patient care rounds with NMCH's neonatologists. The OSU-NCH mentors assisted in developing the NICU antibiogram to help guide appropriate empiric antibiotic therapy. In September 2019, the NICU ASP mentee learned the South African physicians launched a new National Neonatal Sepsis Task Force to tackle neonatal sepsis with uniform guidelines and protocols. The task force did not include pharmacists; the NICU-ASP mentee confidently contacted the physician to discuss her joining the task force. The neonatologists not only welcomed the NICU-ASP mentee to the task force, but also asked to collaborate with the SAASP mentor. Table 2 lists additional ways this mentee applied new clinical pharmacy skills she observed while at NCH.

The pharmacist mentee from NFH observed improved credibility with the neonatologists and nurses due to her increased confidence to make NICU-ASP recommendations with acceptance by the physicians. The mentee trained three Netcare pharmacist in NICU-ASP.

The small NICU at NFH had a low incidence of MDR pathogens and low antibiotic use; however, the mentee successfully worked with the neonatologists and implemented the first NICU-ASP intervention to shorten the duration of antibiotic therapy in early-onset sepsis. Additional NICU initiatives by the mentee are listed in Table 2.

### 3.3 | Collaboration to develop the NICU ASP toolkit

Lastly, the OSU-NCH SAASP mentors and mentees developed a comprehensive 110-page TTT NICU-ASP toolkit for South African pharmacists. Mentees worked to develop content during the TTT NICU-ASP; the mentors completed the toolkit over the next several months. Mentees and mentors are using the toolkit to train additional South African pharmacists in NICU-ASP. Figure 2 shows the hard copy table of contents and topics tailored to the local needs of South African pharmacists.

### 3.4 | Outcome

The TTT NICU-ASP catalyzed a new research collaboration between the mentors, mentees and physician members of the South Africa National Neonatal Sepsis Task Force to conduct the first national NICU ASP study using interventions by trained NICU pharmacists in 12 hospitals to shorten the duration of antimicrobial therapy in culture negative sepsis in public and private hospitals across South Africa. The mentees and the additional trained pharmacists will make interventions and document the acceptance rate by physicians.

Table of Contents	
<b>5</b>	<b>Introduction</b>
<b>9</b>	<b>Meet the Mentors</b>
<b>19</b>	<b>South Africa NICU Facts and Information</b>
21	NICU Collaborative Care
22	In the News
27	SASOCP Position Statement on ASP
<b>37</b>	<b>Understanding Antimicrobial Resistance (AMR)</b>
<b>39</b>	<b>NICU Terminology</b>
<b>41</b>	<b>Getting Started</b>
43	The NICU ASP Team
45	Prepare Your NICU Toolkit
46	A Systems Prospective
48	NICU-ASP Checklist
49	4 Moments of Antibiotic Decision-making
50	Microbiology Antibiogram (Bug-Drug Matching)
52	Sterile IV Preparation Checklist
<b>53</b>	<b>How To Make NICU ASP Interventions</b>
54	Hangtime
59	Medication Errors
<b>61</b>	<b>Sepsis</b>
62	General Information (Early and Late Onset Sepsis, Culture Negative Sepsis)
66	Duration of Antibiotic Therapy
67	Risk of Giving Extra Days of Antibiotics
68	Checklist to Rule Out Sepsis
70	Call to Action for South Africa NICU Study
<b>74</b>	<b>Infection Control for the Pharmacist</b>
<b>79</b>	<b>Twitter for ASP</b>
<b>83</b>	<b>Check Your NICU Knowledge</b>
<b>91</b>	<b>References to Read</b>

NICU-ASP Mentors			
			
Natalie Schellack	Dena van den Bergh	Anjelki Messias	
			
Lindie Van Tonder	Ama Annor	Sonya Kolman	Azraa Paruk
			
			
Julie Mangino	Debbie Goff		
			
			
Pablo Sanchez	Pavel Prusakov	Ben Nwometh	

FIGURE 2 Examples from the Neonatal Antibiotic Stewardship toolkit

The COVID-19 pandemic delayed our ability to complete additional NICU-ASP pharmacists training and conduct the study in 2020, therefore the impact and outcome of TTT NICU-ASP on patient care is forthcoming.

## 4 | DISCUSSION

In response to an urgent request by CDC physicians responding to a CRE outbreak in a South African NICU an international TTT NICU-ASP was developed. The request catalyzed SAASP leaders to also identify the broader need for NICU-ASP. The partnership between OSU-NCH and SAASP was formed around the pillars of global engagement: shared leadership, mutually beneficial partnership, local needs based care, host-driven education, and sustainability.<sup>15</sup> Four South African pharmacists completed the bi-directional program and have since provided NICU education to over 700 healthcare providers (ie, pharmacists, nurses, and physicians) and trained six additional pharmacists in NICU-ASP. Selecting enthusiastic dedicated pharmacists willing to become NICU-ASP champions to learn new skills was the key component for this program's success. The implementation of NICU clinical pharmacy services at the hospital experiencing the CRE outbreak, contributed to the improved quality of care by decreasing the medication error rate.

The high antimicrobial resistance and the burden of neonatal sepsis will continue to increase in South Africa NICUs unless measures are taken to implement NICU-ASP. The four pharmacists who completed the TTT NICU-ASP are prepared to continue to train additional pharmacists in NICU-ASP together with SAASP leaders and mentors. The implementation of NICU-ASPs in South African hospitals is in its infancy, primarily due to limited resources of skilled healthcare professionals to lead the initiative. In addition, there are many unique challenges to NICU-ASP in comparison to adult ASPs. One US study showed significant gaps in the adherence of newborn-specific ASPs to CDC recommendations.<sup>16</sup> The authors suggested the low adherence is because the CDC recommendations for ASPs were initially described at the hospital-level, not a NICU unit-level. The study found wide variation in antibiotic use and a high rate of ongoing antibiotic treatment without positive cultures. Similarly, during their time working in four South Africa NICUs, the OSU-NCH mentors observed a high rate of ongoing antibiotic use and variability without positive cultures. Prolonged antibiotic durations for culture-negative sepsis were observed despite studies that show 5 days is sufficient.<sup>12</sup> A recent global survey of antimicrobial use in 84 NICUs found antibiotic use was frequent and prolonged regardless of culture results.<sup>11</sup> NICU-ASPs were associated with lower antibiotic utilization rates, suggesting the need for their implementation worldwide.

We designed the TTT NICU ASP program assuming pharmacists may only have one-hour daily of dedicated NICU-ASP time. Understanding the social context of the health system is critical to the implementation of NICU-ASP. The TTT NICU-ASP follows a similar model to our TTT-ASP for adult patients that proved successful and sustainable.<sup>10</sup> We added elements of behavior change science and social determinants of antimicrobial prescribing, since antibiotic

stewardship is a highly social interaction influenced by human behaviors.<sup>17,18</sup> The addition of behavior change science to the TTT NICU-ASP was highly valued by each mentee. The comprehensive NICU-ASP toolkit and ongoing support from mentors provide mentees with the necessary tools to train and motivate pharmacists for NICU-ASP. The need for NICU-ASP across South African hospitals is providing pharmacists with new opportunities to build relationships and collaborations with physician members of the South Africa National Neonatal Sepsis Task Force to improve both the quality of care and outcomes of neonates. In addition, the OSU-NCH-SAASP partnership and the bidirectional components of TTT NICU-ASP have led to lasting relationships and collaborations that are mutually beneficial to mentors and mentees.

The first limitation to the TTT NICU-ASP was funding for only four pharmacists; however, their impact was pronounced based on their subsequent education provided to over 700 healthcare providers and training of six additional pharmacists in NICU-ASP. The US component was limited to two-weeks, due to funding and the pharmacists approved time away from their full-time hospital positions. We believe it was important to have the pharmacists work in a US hospital with robust clinical pharmacy services so they could observe the role of a NICU pharmacist on a multidisciplinary ASP. The TTT NICU-ASP was designed for South African pharmacists and may not be applicable in other LMICs. The OSU-NCH and SAASP mentors assessments of four South African NICUs were limited to a one-two day observational visits and did not allow for an in-depth analysis of each NICU. However, the SAASP mentors did conduct an in-depth analysis of the medication process and antibiotic use at CHBAH in addition to the CDC analysis. In the other three hospitals, the OSU mentors had a nine-year established relationship with physicians and pharmacists and were familiar with their pharmacy services and ASPs for adult patients. A prospective multicenter NICU-ASP study with OSU-NCH, SAASP mentors, mentees and physician members of the South Africa National Neonatal Sepsis Task Force is currently underway.

## 5 | CONCLUSION

An international collaboration between OSU-NCH and SAASP pharmacists and physicians achieved its goal to develop a robust TTT NICU-ASP for South African pharmacists. While the COVID-19 pandemic delayed the implementation of planned NICU-ASP studies, the TTT program has provided a foundation for expanding NICU-ASP to additional hospitals in South Africa.

## ACKNOWLEDGMENTS

We acknowledge the contributions of the pharmacists, physicians and staff with the International Scholars Program at Nationwide Children's Hospital, The Ohio State University faculty and students, and Donna Kraus PharmD for donating copies of the Pediatric & Neonatal Dosage Handbook: A Comprehensive Resource for all Clinicians Treating Pediatric and Neonatal Patients. This program was made possible through a grant from Pfizer.

## CONFLICT OF INTEREST

D. G., P. P., J. M. have received grants from Merck and Pfizer. P. S. has received a grant from Merck. A. M., N. S. are consultants on a Bill and Melinda Gates grant. S. V. received a Bill and Melinda Gates Foundation grant.

## ORCID

Debra A. Goff  <https://orcid.org/0000-0001-7686-0670>

## REFERENCES

- Partnership GARPD. Children's Antibiotics 2019. Available from: <https://gardp.org/programme/childrens-antibiotics/>.
- Madhi SA, Pathirana J, Baillie V, et al. Unraveling specific causes of neonatal mortality using minimally invasive tissue sampling: An observational study. *Clin Infect Dis*. 2019;69(Suppl 4):S351–S360.
- van den Bergh D, Messina AP, Goff DA, et al. A pharmacist-led prospective antibiotic stewardship intervention improves compliance to community-acquired pneumonia guidelines in 39 public and private hospitals across South Africa. *Int J Antimicrob Agents*. 2020;56(6):106189.
- Brink AJ, Messina AP, Feldman C, et al. Antimicrobial stewardship across 47 South African hospitals: An implementation study. *Lancet Infect Dis*. 2016;16(9):1017–1025.
- Moatshe R. Alarming rate of baby deaths at Dr George Mukhari Academic Hospital 2019. Available from: <https://www.iol.co.za/pretoria-news/alarming-rate-of-baby-deaths-at-dr-george-mukhari-academic-hospital-37993267.3>.
- T. H. Tembisa Hospital: 10 babies confirmed dead after CRE outbreak 2020. Available from: <https://www.thesouthafrican.com/news/tembisa-hospital-babies-dead-death-toll-what-is-cre-how/>.
- Dramowski A, Velaphi S, Reubenson G, et al. National Neonatal Sepsis Task Force launch: Supporting infection prevention and surveillance, outbreak investigation and antimicrobial stewardship in neonatal units in South Africa. *S Afr Med J*. 2020;110(5):360–363.
- De Jager Z, Schellack N, Gous A. What role does the clinical pharmacist play in the neonatal intensive care unit? *S Afr Pharm J*. 2014;81:7–10.
- Truter ASN, Meyer JC. Identifying medication errors in the neonatal intensive care unit and paediatric wards using a medication error checklist at a tertiary academic hospital in Gauteng, South Africa. *S Afr J Child Health*. 2017;11:5–10.
- Goff DA, Bauer KA, Brink A, et al. International train the trainer antibiotic stewardship program for pharmacists: Implementation, sustainability, and outcomes. *J Am Coll Clin Pharm*. 2020;3(5):869–876.
- Prusakov P, Goff DA, Wozniak PS, et al. A global point prevalence survey of antimicrobial use in neonatal intensive care units: The no-more-antibiotics and resistance (NO-MAS-R) study. *EClinicalMedicine*. 2021;32:100727.
- Cantey JB, Wozniak PS, Pruszynski JE, Sanchez PJ. Reducing unnecessary antibiotic use in the neonatal intensive care unit (SCOUT): A prospective interrupted time-series study. *Lancet Infect Dis*. 2016;16(10):1178–1184.
- Gardner DK, Siegel J, Pathak DS. Adaptive approaches to the implementation of new clinical services: A case study of neonatal ICU pharmacy services. *Top Hosp Pharm Manage*. 1990;9(4):58–72.
- Taketome CK, Kraus DM, Hurlburt H. *Pediatric & Neonatal Dosage Handbook*. Riverwoods, IL: Lexicomp, 2019.
- Crowe SJ, Karwa R, Schellhase EM, et al. Pillars for global health engagement and key engagement strategies for pharmacists. *J Am Coll Clin Pharm*. 2020;3:1097–1112.
- Ho T, Buus-Frank ME, Edwards EM, et al. Adherence of newborn-specific antibiotic stewardship programs to CDC recommendations. *Pediatrics*. 2018;142(6):e20174322.
- Charani E, Castro-Sanchez E, Sevdalis N, et al. Understanding the determinants of antimicrobial prescribing within hospitals: The role of "prescribing etiquette". *Clin Infect Dis*. 2013;57(2):188–196.
- Szymczak JE, Feemster KA, Zaoutis TE, Gerber JS. Pediatrician perceptions of an outpatient antimicrobial stewardship intervention. *Infect Control Hosp Epidemiol*. 2014;35(Suppl 3):S69–S78.

**How to cite this article:** Goff DA, Prusakov P, Mangino JE, et al. International train the trainer neonatal antibiotic stewardship program for South African pharmacists. *J Am Coll Clin Pharm*. 2021;4(12):1572–1582. doi:10.1002/jac5.1517