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A GLOBAL PERSPECTIVE OF THE ROLES OF THE PHARMACIST IN THE NICU

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ABSTRACT:

Objectives: To describe pharmacist practice and roles performed in the neonatal intensive care unit (NICU) worldwide and to map these findings along the medicines management pathway (MMP).

Method: Quasi-systematic review

Search Strategy: Google Scholar, Medline/PubMed and Embase were searched utilising the selected MeSH terms.

Results: Thirty sources of information were reviewed. Overall, pharmacist practice in the NICU involves a wide-range of roles, with the most commonly reported involving patient medication chart review, therapeutic drug monitoring and the provision of medication information. Studies highlight that pharmacist contribution to total parenteral nutrition (TPN) regimens and patient medication chart review is beneficial for patient outcomes. Roles beyond the regular scope of practice included involvement in immunisation programs and research. Most of the data were collected from the USA (13 of 30), followed by the UK (6 of 30) and reports from other countries. The American, British, South African and Australian articles have reported very similar roles, with a pharmacist firmly integrated into the overall structure of the NICU team.

Conclusion: The literature identifies that there is insufficient evidence to describe what roles are currently performed in NICUs worldwide. This is due to the lack of recently published articles leading to a large gap in knowledge in understanding what contemporary pharmaceutical services in the NICU comprise. Further research is required to address these gaps in knowledge, and identify the impact of the pharmacist's role on neonatal patient outcomes as well as to determine how to better resource NICUs to access pharmacy services.

Key Words: Pharmacist roles, Pharmacy services, Neonatal Care, Neonatal Intensive Care Unit

1. INTRODUCTION

The World Health Organisation (WHO) recognises pharmacists as essential resources for the safe and effective use of medicines.^[1] With the outcomes of pharmacist interventions including improved patient quality of life, as well as reduced medication errors and adverse drug events, there are clear benefits to providing clinical pharmacy services to hospitalised patients.^[2-6] Current studies describe pharmacist roles within a range of adult settings, including participation in ward rounds, medication reconciliation upon admission and therapeutic drug monitoring (TDM).^[4-6, 3] However, there is minimal corresponding literature reporting on pharmacist roles within the neonatal intensive care unit (NICU).

As the NICU population possesses characteristics of vulnerability, which predispose them to a high-risk of medication misadventure, the use of medication in these patients poses significant challenges for the treating team. Current studies showcase pharmacist interventions as having a significant impact on decreasing medication errors in the NICU, however they fail to describe roles beyond those performed as experimental interventions.^[7, 8] The roles and practices of pharmacists vary from country to country, and as such it is prudent to explore these differences to determine whether there are any inequalities in medication management in the NICU and where pharmacists focus their practice. Therefore, the purpose of this review is to provide an overview of pharmacist practice in the NICU and identify, describe and compare pharmacist roles as reported globally in published and grey literature. A specific objective of the review is to map the findings along the medicines management pathway (MMP).^[9]

2. METHOD

A quasi-systematic review (a review that possesses some elements of a systematic review, including pre-defined selection criteria, however includes grey literature and does not present a critical evaluation of the quality of studies) extracted relevant publications relating to roles, interventions, activities and functions performed by pharmacists in the NICU.^[10-12] A robust systematic review could not be performed due to the nature of the literature collected, with the majority consisting of grey literature, review articles and reports and a distinct lack of published studies. The amount and type of literature collected influenced the

format of the review, precluding the full application of PRISMA guidelines, and leading to the adoption of a quasi-systematic review.

Literature was retrieved by searching the following electronic databases: Embase, PubMed and Google Scholar. All sources of information including relevant studies, review papers and other publications were canvassed. It is acknowledged that particularly where practice is well established, it is not necessarily based on well-designed clinical trials. Therefore, a broader perspective was obtained by performing a supplemental Google search using the same search terms to identify relevant grey literature.

2.1 SEARCH STRATEGY

A two-tiered search strategy was used. (Figure 1) In Tier 1, a search was performed utilising the following MeSH headings/keywords: *pharmacist interventions, clinical pharmacist, neonatal intensive care, neonate/infant/newborn, pre-term, protocols, pharmacist role/activities, pharmacist responsibilities, and pharmacist impact*. The Boolean operator 'AND' was employed to combine the search terms. Manual bibliographic searches of all relevant articles were also performed in order to identify any articles that were not identified in the electronic searches. In Tier 2 of the search, relevant grey literature was identified through a Google search using the same MeSH terms. This tier was dedicated to finding service standards, position descriptions as well as descriptive reports.

2.2 STUDY SELECTION

The selection criteria for the searches restricted the content to the following: (i) review articles (including literature reviews and opinion pieces), research articles, or grey literature (ii) with results containing information on pharmacist led activities relating to neonatal patients in the NICU setting and (iii) written in the English language. All full text articles meeting this criteria were retrieved and all evaluations pertaining to the types of pharmacist roles in the NICU were included in the review. Due to the minimal amount of literature available reporting on pharmacist roles in the NICU, no date limits were applied, enabling the collection of data from a broader range of resources.

2.3 THE MEDICINES MANAGEMENT PATHWAY

The pharmacist roles identified in the review were mapped out against the medicines management pathway (MMP). The MMP is a process map that describes the full range of cognitive and physical steps involved in the utilisation of pharmacotherapy in any patient group with the aim of improving the quality use of medicines and identifying any potential safety system improvements.^[9] Published by the Society of Hospital Pharmacists Australia (SHPA) the MMP is cyclical in nature and highlights that each element relates to another. (Figure 2)^[9]

2.4 DATA EXTRACTION AND ANALYSIS

The data extraction and mapping of the roles against the MMP was performed by Author 1 and verified by Author 2. A standard data extraction form was used to describe the studies and the pharmacist roles performed in NICU's worldwide. The articles retrieved from each tier of searching were pooled for analysis, in-line with the study objectives. The extracted information consisted of a description of the roles performed by pharmacists, the frequency at which they were performed, and the country from which the study originated.

3. RESULTS

A total of thirty sources of information were included in the review.^[13-42] This literature was collected from a range of countries, predominantly from the USA (13 of 30) and UK (6 of 30) with reports from Australia, South Africa and Ireland. The types of articles collected consisted of qualitative (5) and quantitative studies (4) (total 9 of 30), review articles (6 of 30) and reports (4 of 30) as well as grey literature including a descriptive article (1 of 30) position descriptions (8 of 30) and neonatal service standards (2 of 30). It was noted that there were no articles that utilised randomised control trials or cohort study designs. Table 1 provides an overview of the articles used in the review.

Overall, there is limited published literature comprehensively exploring the current roles of pharmacists in NICUs. Most of the published literature collected was approximately 10 years old or older, with seven articles published before the year 2000, and three published prior to 2006.^[14, 16, 19-22, 24, 30, 32, 33] As such, grey literature including service standards, guidelines and position statements were used to describe a more contemporary practice where other

literature was dated or absent. Due to the lack of available literature, several articles were utilised that were primarily paediatric based, but included a sub-section of neonatal patients within their evaluation.^[16, 21, 23, 28, 30] Overall, out of the total proportion of articles included in the review, 24 were specifically related to pharmacists working within NICUs and neonatal care, with the remaining 6 referring to pharmacists working in paediatric settings, including PICUs, children's hospitals and a women's hospital that involved elements that also addressed neonatal patients.

Each of the roles identified were matched to the steps of the MMP; no specific pharmacist roles were identified that could be mapped against the following steps: record of medication order, administration of medication and transfer of verified information.

THE ROLES OF THE NICU PHARMACIST MAPPED AGAINST THE STEPS OF THE MEDICINES MANAGEMENT PATHWAY (MMP)

1.1 DECISION TO TREAT AND PRESCRIBE

The NICU pharmacist has been recognised as an important contributor to the prescribing process. Within relatively older literature, it was reported that pharmacists routinely assisted in the appropriate selection of medications, suggested dose changes, routes of administration, and advised on potential side-effects.^[18, 20, 24, 33] Pharmacists most commonly contributed to the prescribing process by participating in medical ward rounds.^[18, 20, 24, 33] Ward rounds in the NICU provided an opportunity for pharmacists to engage in bedside pharmacotherapeutic consultations and improve inter-professional communication.^[18, 24, 33] These findings are also reflected in the British Association of Perinatal Medicine (BAPM) service standards and in the position descriptions, which detail that NICU pharmacists are required to attend multidisciplinary ward rounds on a daily or weekly basis, as well as provide input at relevant clinical meetings.^[34, 37, 38, 40, 42, 13] The Australian position description states that NICU pharmacists are expected to be active members of the multidisciplinary NICU team to optimise patient care, and it has been reported that during ward rounds medical staff rely on the pharmacist to provide accurate medication information and to transmit new research relating to pharmacotherapy in the neonate.^[33, 35]

NICU pharmacist involvement was acknowledged in the prescribing of nutritional supplements for neonates.^[18, 20, 22, 29, 33, 19, 26] In particular, Ahmed stated that NICU pharmacist input was significant during the prescribing and manufacture of parenteral

nutrition for infants.^[42] Pharmacists were reported as being commonly involved in the calculation of the daily calorie and protein requirements, preparing total parenteral nutrition (TPN) protocols, prescribing TPN regimens, reviewing TPN orders as well as identifying and resolving errors in nutrition orders.^[29, 20, 38] A UK study identified that 47% of NICU pharmacists surveyed were prescribers and mainly ordered parenteral nutrition and supplements (75%).^[26] Mulholland added that pharmacist prescribing of TPN promoted patient safety, reduced communication errors and reduced pharmacy costs.^[29, 26] An older prospective interventional study performed by Dice et.al. (1981) in a NICU that involved 28 patients, reported that pharmacist monitoring of individualised TPN regimens had significantly increased the mean weight gain and protein intake of infants ($p = < 0.02$), compared to those neonates on standardised TPN formulations with no pharmacist monitoring.^[19] Pharmacist monitoring involved calculating the neonate's required fluid and calories, recording changes in weight, documenting laboratory results and recommending changes to TPN solution.^[19] Furthermore, pharmacist monitored TPN programs led to greater amounts of nutrients being provided to neonates, fewer medication errors and lower overall pharmacy costs.^[19, 29] Prescribing pharmacists in British NICUs felt they were more integrated into the multidisciplinary treating team in the NICU after becoming a non-medical prescriber.^[26]

1.2 REVIEW OF ORDER

The majority of the literature reported that NICU pharmacists were involved in the review of patient medication charts.^[14, 15, 17, 20, 21, 27, 30, 32-38, 40, 39, 41, 23] As a service uniquely performed by pharmacists, the medication chart review process within the NICU was described in older literature as being a 'standard' practice for the advancement of medication safety.^[19, 29] The characteristics of the role involved the evaluation of medication charts for medication appropriateness, correct dosages according to the weight of the neonate, drug-drug/drug-laboratory value/drug-nutrient interactions, allergies, medication duplication, timing of administration (particularly with concurrent IV fluids or supplements), route of administration, adherence to clinical protocols and procedures, as well as the review of relevant patient progress notes, diagnostic tests and laboratory values.^[14, 15, 17, 20, 21, 30, 32, 33, 37, 38, 40, 39, 41, 23] In reviewing the patient's medication chart, NICU pharmacists also performed interventions to rectify medication safety issues which included correcting doses and modifying the route of administration.^[16, 19, 21, 24, 28, 31, 40, 41, 37] The benefits of a pharmacist-led

chart review were reported in one prospective study conducted in 2004 by Simpson et.al. who found that the implementation of daily pharmacist review in NICU led to a significant reduction in the incidence of medication errors ($p = <0.001$).^[32]

Several position descriptions require NICU pharmacists to perform patient medication reviews on at least a daily basis, with the BAPM recommending that pharmacists dedicate at minimum 10 – 20 minutes of time per patient.^[36-38, 40, 39, 41, 13] Observational research conducted in a South African NICU, found that 73% of pharmacist time was spent on patient review.^[31] In contrast, a study performed by Prot-Labarthe et.al. in four French-speaking countries determined that only 10 – 15% of clinical pharmacist time was spent on clinical activities.^[28] This study was conducted in paediatric intensive care units (PICUs), however as it also included neonatal patients (ages ranging from 0 – 6 days) within their study population, it was deemed relevant to this review. It is unknown what proportion of pharmacists' time in providing pharmaceutical services was spent on neonates in comparison to generalised paediatric patients.

1.3 MEDICATION PREPARATION

The extemporaneous compounding service was acknowledged in older articles as being a traditional pharmacist role often undertaken in the care of NICU patients.^[14, 20, 33] Pharmacotherapy in neonates often requires the preparation of dosage forms that are not commercially available and the Australian position description requires NICU pharmacists to be able to accurately perform duties in non-sterile and aseptic manufacturing when required.^[14, 34] The role was described within two older studies based in the USA (1985) and Australia (1991) respectively, as involving the routine compounding of novel medication formulations as well as specifically adapting adult medications for neonatal patients, including diluting existing products to ensure suitable concentrations for neonates as well as to improve accuracy of dosage measurement.^[14, 20] In a study from 1991, Dunkley found that pharmacists at the time most commonly prepared eye drops, topical creams and antiseptics.^[20]

1.4 PROVISION OF MEDICATION INFORMATION

A major responsibility of the NICU pharmacist was reported as the provision of a medication information service. The role comprised two components which involved the provision of

NICU specialised medication information to other health professionals on the ward. Part of the role required the pharmacist to be readily available at point of care, addressing spontaneous queries from nurses and doctors that arose during care.^{[13, 16, 23, 24, 27, 31, 32, 34-37, 40,}

^{41]} These queries pertain to a wide-range of medication-related issues, including: medication administration, side-effects, correct calculation of dosages and adherence to medication protocols and disease management procedures.^[16, 23, 24, 31, 32] Additionally, the Australian position description and BAPM service standards state that one of the main duties of the NICU pharmacists was to provide accurate information on off-label and unlicensed medicines, which are frequently utilised in the NICU.^[34, 13] Pharmacists often offered responses to information requests in written as well as verbal form to ensure comprehensibility.^[16, 23, 24, 31, 32] Two articles reported that through the provision of accurate and relevant information, pharmacists have the potential to minimise medication errors and adverse medication events.^[23, 32] The other part of the medication information role involved pharmacists as primary medication educators to the NICU therapeutic team, providing training and in-services on therapeutic updates in neonatal pharmacotherapy.^[42, 14-16, 18, 20, 24, 27, 33-35, 39] An in-service is defined as 'a professional training or staff development effort, where professionals are trained and discuss their work with others in their peer group. It is a key component of continuing medical education for clinicians, pharmacists and other medical professionals.'^[43] It is recommended in the older literature, that as a part of their clinical role, NICU pharmacists provide in-services for doctors, nurses, pharmacists, students and other health professionals encompassing: rational medication use, introducing new medications and the latest publications and updates on medications, revising medication administration principles, dose calculations, and classes of medicines most likely to be associated with error in the NICU.^[14, 20, 33, 15, 27]

The pharmacist is identified as being the first-line health professional to consult when medication-related issues arise.^[16, 23, 24, 31, 32] One South African study conducted a needs analysis of NICU staff on the medication information service provided by a pharmacist and concluded that the surveyed NICU doctors (n = 17) required a pharmacist to be present on the ward to respond to any medication-related questions.^[31] Furthermore, the provision of medication information involved 20% of pharmacist time in the South African NICU.^[31]

Pharmacists were also actively involved in reviewing, updating and developing NICU-specific medication protocols, guidelines, policies and formularies for the therapeutic team to use to improve drug safety.^[14, 15, 20, 33-36, 40, 42, 13] Chedoe et.al. supported these findings by stating

that pharmacists should work in multi-disciplinary teams to develop formularies and guidelines that summarise information on medication compatibilities, reconstitution, rates of infusion etc.^[15] It is considered in older literature that the provision of detailed medication protocols by pharmacists allows NICU health professionals to become better equipped for prescribing medications and managing pharmacotherapy regimens in neonatal patients.^[14, 33]

The pharmacist is responsible for counselling parents and carers on all aspects of medications used for their child.^[14] Upon admission, throughout the hospital stay, and at discharge, the pharmacist is required to consult with parents/caregivers on the medications being used for their child, advise on the role of the pharmacist in the care of patients and provide clear and comprehensive information on each aspect of therapy.^[14, 20, 33-38, 42, 27] The older literature highlighted that the type of information provided by pharmacists at that time included: indication for therapy, administration intervals, time to pharmacological effect, risks and benefits of therapy, adverse events and possible adverse reactions.^[14, 20, 33] It is also reported that pharmacists prepare written instructions on the storage and proper use of the medication for parents upon hospital discharge.^[14, 37, 38] Whilst it is apparent that parents and carers of neonates have considerable information needs during the time that their child is admitted to the NICU, there is insufficient evidence to suggest that the NICU pharmacist in contemporary practice fulfils this information provider role.

1.5 DISTRIBUTION AND STORAGE

Two sources discussed that, along with clinical roles, the NICU pharmacist had a specific set of ward 'house-keeping' responsibilities, ensuring the appropriate distribution and storage of medications.^[31, 41] This role involved ensuring the timely delivery of required medicines, stock-take, ordering of relevant items required on the ward, checking the medication fridge temperature and ensuring its cleanliness, checking storage conditions for product stability (for vaccines, blood products, and parenteral formulations), and stocking the emergency trolley.^[31, 41]

1.6 MONITOR FOR RESPONSE

Overall, NICU pharmacists were highly involved in monitoring drug serum levels in neonatal patients with the most commonly monitored medications identified from older literature as

including aminoglycosides, antibiotics, theophylline, chloramphenicol and vancomycin.^[14, 20] It must be highlighted that these articles are over 10 years old and as such some of the agents listed may not be as widely used in the NICU in modern practice, i.e. chloramphenicol, however they are still therapeutic agents that if used, require monitoring by pharmacists. The provision of a therapeutic drug monitoring (TDM) service by pharmacists was identified, in eight articles, as an important practice in ensuring optimal neonatal patient outcomes.^[14, 15, 20, 31, 28, 16, 24, 13] The role has been described as comprising the provision of correct dosing information from the interpretation of blood levels and recommending appropriate timing intervals for the collecting of blood serum samples.^[14-16, 20, 24, 28, 31]

Adverse event surveillance was identified as an important role for NICU pharmacists.^[13-15, 20, 21, 37-39, 41] Aside from the standard processes of monitoring, including laboratory tests and observation of physical signs, this also encompassed the development and utilisation of medication error reporting systems, requiring the thorough documentation of any medication errors as well as adverse drug events, followed by pharmacist-led interventions to rectify medication issues including dose adjustments and medication changes.^[13-15, 37-39, 41]

EXTENDED ROLES

Extended roles possessed specific objectives that did not correspond to one specific stage of the medication use process, but rather encompassed various steps of the M M P.

Vaccination

There are other potential roles for NICU pharmacists, with two articles identifying pharmacist involvement in implementing immunisation programs for neonatal patients.^[22, 25] An American article reported that a pharmacist stationed in the NICU was the primary resource responsible for the identification of eligible infants for routine childhood immunisations.^[22] Another US based interventional study by Mills et.al investigated pharmacist involvement in a tetanus toxoid, reduced diphtheria toxoids, and acellular pertussis (Tdap) immunisation program for close contacts of neonates by providing pharmacist-led education of parents and carers of neonates. This program had clear benefits for neonates, and significantly increased rates of vaccinations for the pertussis vaccine, from

1.3 vaccinations/month pre-study to 85.2 vaccinations/month in the study period ($p < 0.001$).^[25] These studies did not specify whether the pharmacists involved within these interventions were NICU pharmacists, or general hospital pharmacists. However, the studies demonstrate the potential value of NICU pharmacist involvement in vaccinations.

Research

NICU pharmacists were also active participants in clinical trials and research.^[18, 20, 24, 28, 34, 38, 40, 41, 44] Two sources stated that NICU pharmacists are encouraged to perform drug use evaluation studies, publish innovations in pharmacy and should facilitate investigational drug studies to improve rational and safe use of medicines.^[34, 38] An Australian study dated in 1991 highlighted that roles associated with clinical trials at the time specifically involved organising drug supply, maintaining patient records, randomising patients and preparing protocols.^[20] A study revealed that in Belgium as much as 50% of pharmacist working time was dedicated to research, however it did not specify roles associated with this practice.^[28]

Quality Use of Medicines Strategies

Several position statements required NICU pharmacists to be involved in ensuring medicines used in the NICU were cost-effective and being used rationally.^[27, 34, 38, 41] Key duties of the pharmacist included: monitoring the use of expensive medicines, developing cost-saving initiatives for the NICU, involvement in antimicrobial stewardship programs, documenting clinical interventions and cost-avoidance methods as well as performing target drug programs to decrease irrational use of medicines.^[38, 41, 34] NICU pharmacists were also tasked with ensuring the quality of pharmaceutical services being provided on the NICU, with increased emphasis on documenting clinical interventions, ensuring all medicine provision services are compliant with legislation and hospital policies and developing safety initiatives.^[27, 34, 37-39, 41]

Furthermore, in improving the quality use of medicines, the Irish model of care highlights that pharmacists should have input in implementing and maintaining medication safety technology in NICU practice.^[27] These technologies included e-prescribing, barcoding and smart pump technology.^[27]

INTERNATIONAL COMPARISON OF PHARMACIST ROLES

Articles from thirteen countries were included in this review, with the largest number from the USA (13 of 30 articles). Table 2 provides an overview of the different roles performed in each country, as identified in the literature. Although a wide-range of pharmacist roles have been identified within the literature, there are discernible differences in practice between certain regions worldwide. Literature gathered from the USA, UK, Australia and South Africa suggest that patient-oriented clinical activities such as patient medication chart review, participation in ward rounds, therapeutic drug monitoring and medication information services make up the majority of the role in NICU. Alternatively, the multi-national study incorporating data from PICUs in Belgium, France, Switzerland and Quebec, did not report on roles in ward rounds and TDM practices. However, pharmacists in these countries were found to be strongly involved in clinical research, provision of medication information and patient medication review. Overall, involvement in immunisations, ward-based housekeeping activities and extemporaneous compounding were not as frequently reported. The apparent lack of current and published literature does not allow for a good understanding of current pharmaceutical services provided worldwide. Furthermore, the literature does not yield any information about practices in South America or Asia. As such, there are inconsistencies and gaps in the literature about the level of practice in each country with respect to NICU pharmacy practice.

4. DISCUSSION

To our knowledge, this is the only review to compare the roles of NICU pharmacists between countries on an international scale. Whilst the amount of international research documenting clinical pharmacist practices in the NICU is limited, there was sufficient literature to map the pharmacist role against the MMP.^[9] A total of 16 different pharmacist roles were identified as being reported globally in published and grey literature. However, we are unable to ascertain if these services are currently provided or offered to NICUs worldwide, due to the lack of recently published literature.

Overall, it is difficult to ascertain the true extent of pharmacy practice in each country as relevant literature from Asia, South America and a large proportion of Africa and Europe was not available. The majority of the literature that was sourced was dated more than 10 years

ago, and it is difficult to determine whether the data gathered still reflect current practice. Furthermore, due to the lack of available research, several paediatric studies were included in the review that included a sub-section of neonatal patients in their evaluation. As such, it is unknown what proportion of pharmacy services described in these papers referred to neonatal patients. Relevant studies may have been excluded from the review because they were not available in the English language. Grey literature searches sought to identify service standards and guidelines from different countries, however many were not accessible as they were not publicly available or were published in languages other than English.

The findings of the review demonstrate that the value of pharmacists in USA, UK, South Africa and Australia lies in an interactive type of practice with literature identifying a broad range of roles extending from therapeutic drug monitoring and patient medication chart review through to immunisations, counselling of parents and extemporaneous compounding. The European countries reported roles in TPN prescribing, provision of medication information and patient medication chart review, however, however did not have such an extensive scope of practice. These difference in practice may be attributed to cultural, educational, legislative and funding differences in healthcare systems from country to country, impacting upon the level of pharmacist integration into NICU teams.^[45] Diversity in practice may have varying impacts upon patient outcomes. According to WHO, one of the main priorities for healthcare systems worldwide is the promotion of equity within and between healthcare facilities.^[46, 47] Health equity is a shared responsibility of all nations worldwide, and it is a fundamental right of each human being to receive the highest standard of healthcare.^[46, 48] As such, the RIO Political Declaration on Social Determinants of Health endorses global collaboration and benchmarking between countries to identify good practices and adopt coherent policies to promote consistent practices.^[48]

WHO identifies that the most effective pharmaceutical care is provided when clinical pharmacists become integrated into the healthcare team and play an active role in patient care.^[1] Pharmacists possess the relevant skills, knowledge and expertise to make valuable contributions to the quality use of medicines and medication safety.^[49] The review highlights that NICU pharmacists can provide both a medication support system for other NICU health professionals as well as a patient care role. The majority of the literature reported that the most important features of a NICU pharmacy service involved the physical presence of a

pharmacist on the ward, clinically reviewing the parameters of pharmacotherapy and providing medication information. Specifically, the most commonly reported roles are centred on patient medication chart review, therapeutic drug monitoring, provision of education services and prescribing of TPN therapy. By focussing upon these services, NICU pharmacists improve the rationalisation of therapy, reduce costs associated with therapy, promote collaboration with other healthcare professionals and decrease the incidence of avoidable harm.^[19, 23, 26, 32] Furthermore, these roles promote the individualisation of patient pharmacotherapy according to patient needs which is integral to achieving optimal neonatal outcomes.^[19] Other roles, relating to participation in ward rounds, adverse drug event monitoring, implementation of quality use of medicines strategies, immunisations, and parent counselling have been less commonly reported however are also important to the management of neonates. The Department of Health in Australia states that one of the current issues within its health system is the promotion of immunisations which are integral to the health of children and the wider community.^[50] These roles are potential areas of practice that require improvement and focus.

Clinical pharmacists have long established roles in specialised areas of practice such as in oncology, intensive care and emergency medicine.^[51-57] The development of these roles has demonstrated the pharmacist's contribution to the health care system, particularly in improving patient safety and rationalising the use of medication.^[58, 59, 14] However, whilst the roles of clinical pharmacists have been well described, when looking at the vulnerable neonatal population, who are at the start of the age-spectrum and are at greater risk of medication errors and significant resulting consequences, there is a lack of detail on current pharmacist contributions to the quality use of medicines.^[57] Furthermore, there is limited literature that identifies the impact of pharmacist practice on neonatal outcomes. Most of current research focuses upon pharmacist roles in adult populations, with relatively less exploring roles in paediatric practice and even less in neonatal care.^[60, 8, 23, 61] Given the challenges and risks of pharmacotherapy in neonates, the role of the pharmacist within the NICU therapeutic team is important. As such due to the limited research undertaken in this area, there is need to conduct investigations to establish what roles are being performed today as well as to develop standards of NICU pharmacy practice that clearly define pharmacist roles that meet the specific needs of the neonatal population. Further research needs to be conducted to identify opportunities to increase pharmacist engagement in each country's healthcare system and improve the level of involvement in the NICU.

5. PRACTICE IMPLICATIONS

The role of the pharmacist in the NICU has the potential to greatly improve patient outcomes as well as decrease incidence of medication error and associated harm. It is important to understand the differences in practice between each country, as it allows for the benchmarking of our own current service delivery system and promotes practice improvement to meet the standards of other settings. As such, this review has identified that the model of NICU pharmacist practice in USA, UK, Australia and South Africa appears to be patient-centred and promotes pharmacist integration into the NICU team. Furthermore, the findings of the review have allowed for the identification of areas of practice (i.e. parent counselling, immunisations) that can be improved upon and have the potential to be further developed into roles that are integral to the quality of medication management in NICU. This review may provide a foundation for future research, including subsequent reviews of the literature, and has the potential to act as a useful comparison of pharmacist practice in NICU to other patient groups, i.e. older paediatric patients and adults, to determine where differences in pharmacist roles lie.

6. CONCLUSION

The literature identifies that there is insufficient evidence to describe what roles are currently performed in NICUs worldwide. This is due to the low quantity of published literature, most of which was out-dated. Given the diversity of practice, it is important to establish clear definitions of pharmacist roles within the NICU and compare roles across different clinical settings and countries. Further research, comprising systematic, rigorous surveys are required if the current international roles of the NICU pharmacist are to be understood.

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Table 1 List of studies that were included in the review

STUDY	TYPE OF LITERATURE	COUNTRY YEAR SETTING	KEY FINDINGS
Ahmed M ^[42]	Descriptive Article	UK 2008 NICU	The main aspects of a pharmacist's role in the NICU are: educating staff and parents, developing a formulary, providing input into parenteral nutrition, advising on drug choice and attending weekly multidisciplinary ward rounds.
British Association of Perinatal Medicine (BAPM) ^[13]	Service Standard	UK 2010 Hospitals providing neonatal care	Neonatal pharmacists play a role in the optimisation of pharmacotherapy in neonates. They are required to perform a number of clinical roles including: monitoring of prescriptions, therapeutic drug monitoring as well as provision of advice on off-label and unlicensed medicines.
Bryant BG ^[14]	Report	USA 1985 NICU	Pharmacists perform daily patient medication reviews for medication appropriateness and any interactions, respond to information requests from medical and nursing staff, prepare dosage formulations suitable for babies and counsel parents.
Cambridge University Hospital ^[36]	Position Description	UK NICU	The neonatal pharmacist visits the NICU daily and performs the following services: prescription chart review, provides advice to the doctors and nursing team, reviews policies and guidelines and checks TPN orders.
Chedoe I et.al. ^[15]	Literature review	The Netherlands 2007 NICU	Pharmacist interventions, namely participation in ward rounds and review of medication orders prior to dispensing and distribution, were found to be the most common pharmacist interventions suggested to improve medication safety in the NICU.
Condren M et.al. ^[16]	Prospective descriptive study	USA 2004 Paediatric ward	The most common services performed by a pharmacist were drug therapy change, pharmacokinetic monitoring, medication information and medication histories. Also identified roles including; patient medication review, adverse drug event monitoring, and provision of medication information.
Conway C et.al. ^[17]	Literature review	Ireland 2012 NICU	The most important pharmacist roles for maintaining patient safety in NICU included medication chart checking and participation in physician consultations.
De Jager et.al. ^[18]	Literature review	South Africa 2014 NICU	Clinical pharmacists in NICUs should be involved in the following services; attending daily ward rounds, TDM, parenteral nutrition, patient education and research into safety and efficacy of medications.
Dice JE et.al. ^[19]	Prospective intervention al study	USA 1981 NICU	Pharmacist monitoring of an individualised TPN in neonates had greater mean daily weight gain, introduced a greater amount of nutrients to the infant and was more cost-effective than a standardised program.
Dunkley M K ^[20]	Prospective study	Australia 1991 NICU	Australian pharmacists provided strong support in extemporaneous manufacturing, parenteral nutrition, provision of medication information, TDM and adverse drug reaction monitoring. Standards of clinical pharmacy service in the NICU need to be developed to promote service equality between hospitals.
Folli H et.al. ^[21]	Prospective descriptive study	USA 1987 Paediatric hospitals	Pharmacist involvement in reviewing patient medication orders significantly reduced potential harm resulting from erroneous medication orders.

Gold Coast Hospital and Health Service ^[35]	Position Description	Australia 2015 NICU	The key duties of the neonatal pharmacist include: performing clinical reviews of medication therapies, monitoring patient outcomes and revising treatment strategies accordingly, delivering specialist educational presentations for pharmacists and other health professionals in the hospital and providing information obtained through research to optimise pharmaceutical care provided to complex neonatal patients.
Intermountain Healthcare ^[41]	Position Description	USA 2015 NICU	The essential duties of the NICU pharmacist include: providing accurate drug information, monitoring physician orders, training and supervising new pharmacy technicians and actively participating in department cost savings initiatives.
Johnson C et.al. ^[22]	Report	USA 1993 NICU	A pharmaceutical care system was established within NICU. The most important elements of this service included; monitoring of drug dosing, reporting adverse drug reactions, detecting medication interactions, immunisations and counselling of parents.
Kelishadi R et.al. ^[23]	Literature review	Iran 2012 Paediatrics	Pharmacist-physician-patient collaboration is important in maintaining medication safety in NICU. Pharmacist roles including medication chart checking, participation in multi-disciplinary meetings, parent interviews and clinical interventions were the most effective in medication management in the NICU.
Lobas N et.al. ^[24]	Descriptive article	USA 1991 NICU	NICU pharmacists participate in ward rounds, TPN therapy, medication information services and pharmacokinetic consultations.
Medical University of South Carolina ^[37]	Rotation Description	USA 2015 NICU	The pharmacist is expected to participate in daily ward rounds with the inter-professional team, evaluate each patient's drug therapy at least daily, communicate with patient's family or caregiver and provide timely responses to requests for drug information.
Mills B et.al. ^[25]	Prospective and descriptive study	USA 2014 Pharmacy in women's hospital	Vaccination rates increased after the implementation of a pharmacist-led intervention program for family members of neonates. The pharmacist was recognised as an important source in promoting immunisation for the safety and health of infants. Unknown whether the pharmacists involved were NICU pharmacists or general hospital pharmacists.
Mulholland P ^[26]	Prospective survey	UK 2012 NICU	40% of surveyed pharmacists were prescribers and 70% of these pharmacists were prescribing in the NICU. The main medications being prescribed were parenteral nutrition (75%), supplements (75%), antibiotics and caffeine (50%). Benefits of pharmacist prescribing included reductions in communication errors and timely corrections of wrong prescriptions.
Murphy J et.al. ^[27]	Model of Care	Ireland 2015 Hospitals providing neonatal care	The role of the neonatal pharmacist involves: ensuring the safe use of medicines in NICUs, prescription monitoring, ordering and monitoring parenteral nutrition, providing information on medicines and educating other health professionals as well as parents.
New South Wales Government ^[34]	Position Description	Australia 2013 NICU	The NICU pharmacist is responsible for reviewing medicines prescribed and optimising pharmacotherapy in critically ill neonates, ensuring the appropriate ordering and preparation of parenteral nutrition, actively participating in daily ward rounds as well as advising parents on medicine related issues.

Prot-Labarthe S et.al. ^[28]	Multi-centre, prospective and descriptive study	France, Quebec, Belgium and Switzerland 2013 PICU	Pharmacists recorded a break-down of their various activities in PICUs throughout each day, and the roles included student training, clinical research, drug distribution and clinical activities. Over the 6 month study period, the total duration of pharmaceutical care offered by pharmacists was reported as; 550 – France, 416 – Quebec, 410 – Switzerland and 124 – Belgium patient days.
Ragab M et.al. ^[29]	Literature review	Saudi Arabia 2014 NICU	Pharmacists are involved in initiating the neonatal TPN orders and are actively involved in assisting prescribers in the prescribing process, including participating in ward rounds and meetings
Sanghera N et.al. ^[30]	Systematic literature review	UK 2006 Paediatrics	Reviewing patient charts was deemed to be the most effective pharmacist role in improving medication safety in NICUs
Schellack N et.al. ^[31]	Prospective study	South Africa 2011 NICU	The majority of pharmacist time was spent on patient care and ward functions. Pharmacists also participated in ward rounds and clinical meetings. Doctors and nurses identified that the role of the pharmacist in NICU is a necessity to improve services provided to neonates.
Simpson JH ^[32]	Prospective Observational Study	UK 2004 NICU	Close liaison with a ward-based clinical pharmacist is an effective way of reducing medication errors. The role of the pharmacist in staff feedback and education as well as reviewing medication orders was identified as effective in reducing dose calculation and prescribing errors
St David's North Austin Medical Center ^[39]	Position Description	USA 2016 NICU	NICU pharmacist is responsible for: accurately and effectively providing medication therapy, providing medication counselling, assisting in training and educational programs, providing drug information upon request and reporting medication errors and adverse drug reactions.
University of Kentucky Hospital ^[38]	Position Description	USA 2009 NICU	The major responsibilities of the NICU pharmacist are: the provision of pharmaceutical care to patients including participation in daily ward rounds, monitoring drug therapy, counselling parents and caregivers and reviewing medication orders for accuracy and appropriateness, as well as facilitating investigational drug studies and providing education to trainees and other health professionals.
Website ^[40]	Position Description	USA 2015 NICU	The key duties of a NICU pharmacist include: daily multi-disciplinary patient rounds, daily medicine profile review, providing drug information, documenting all interventions performed and training and educating pharmacy students.
Zenk KE ^[33]	Report	USA 1980 NICU	Every neonatal ward needs a pharmacist who specialises in neonatal pharmacology. Ward-based clinical pharmacists are involved in all aspects of medication in the NICU, and perform specialised compounding and dilutions of medications, and are actively involved in determining TPN formulations, patient medication review, provision of medication information, education of NICU staff, participation in ward rounds, TDM, counselling of parents and preparing drug monographs.

Table 2 Internationally reported roles of pharmacists within the NICU

COUNTRY	LISTED ACTIVITIES
United States of America	TPN monitoring/ordering, patient medication review, education sessions with medical staff, participation in ward rounds, involvement in clinical research, parent counselling, TDM, provision of information to medical staff requests, manufacturing capabilities, participation in immunisation programs, establishing/updating policies and protocols, reporting ADE's and medication errors, monitoring the use of expensive medicines, documenting cost saving interventions
Australia	Review of patient charts, responding to information requests, ordering TPN, TDM, clinical trials/research, contributing to the manufacture of medications, counselling of parents, education for staff, developing drug protocols, reporting ADE's, ensuring adherence to legislation and hospital policies, ward rounds, participating in antimicrobial stewardship
South Africa	Responding to requests for information, ward activities, educational duties in training relevant medical staff, monitoring medication usage, monitoring pharmacokinetic parameters in TDM
France	Clinical activities - review of patient charts, student training, participation in clinical research, medication distribution, responding to medication information questions
Quebec	
Switzerland	
Belgium	
United Kingdom	Reviewing medication orders, staff feedback and education, responding to information requests, prescribing TPN, ADE reporting, attendance at ward rounds and clinical meetings, input into guidelines and policies, developing a formulary, advice on off-label/unlicensed medicines
Ireland	Prescription monitoring, documenting ADE's, ordering TPN, education of other health professionals, counselling of parents, provision of medication information on existing and new therapies, implementing technology into practice i.e. e-prescribing, barcoding, developing cost-effective and safety initiatives

ADE = Adverse Drug Event

TPN = Total Parenteral Nutrition

TDM = Therapeutic Drug Monitoring

Figure 1 Review of the search strategy employed to find relevant literature

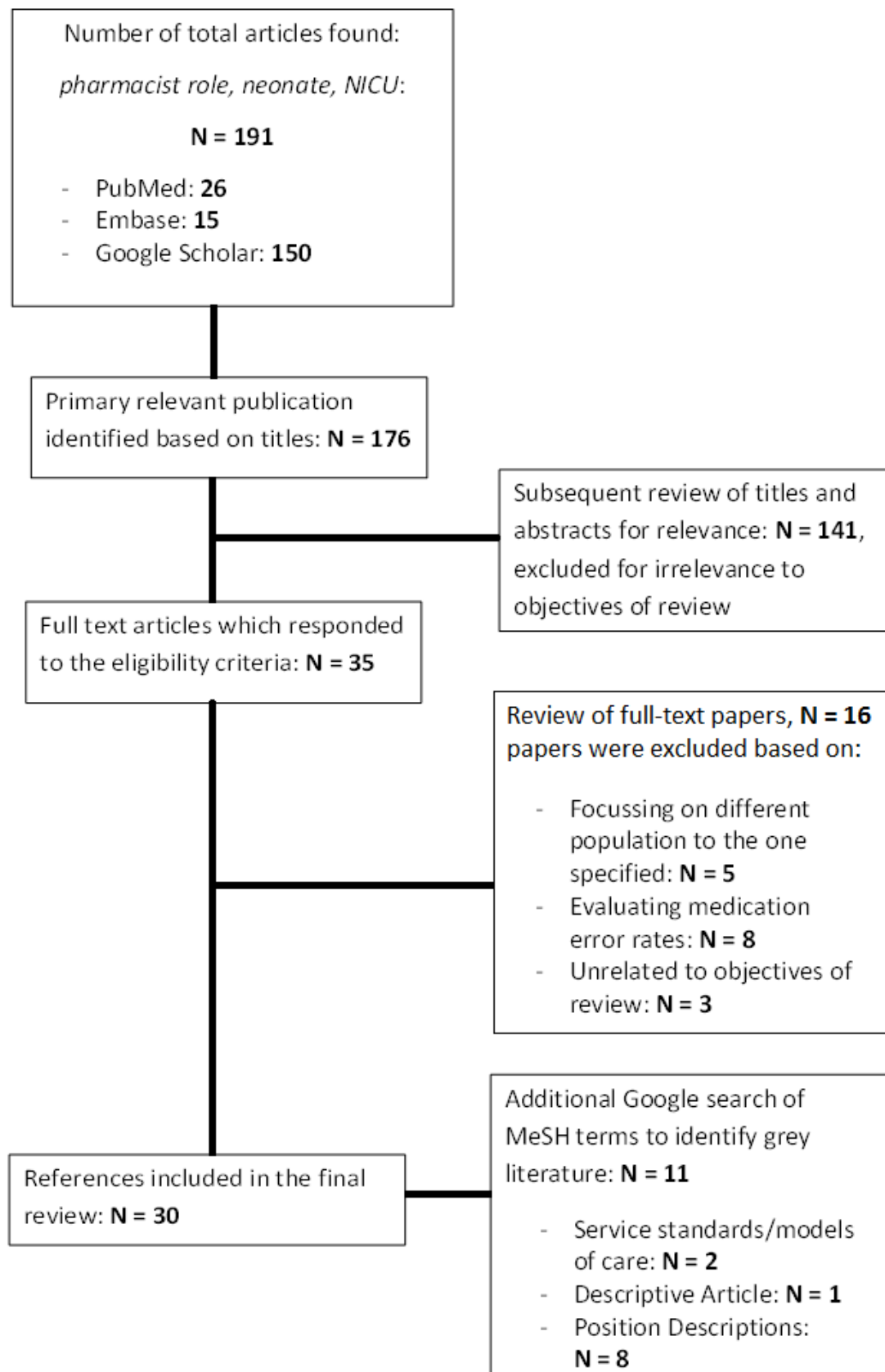


Figure 2 Pharmacist practice in the NICU mapped against the Medicines Management Pathway

Figure adapted from :Stowasser DA, Allinson YM, O'Leary KM, 'The Medicines Management Pathway', J Pharm Prac Res 2004; 34: 293-6 ^[9]

