

**Recognizing Chemotherapy Induced Neurotoxicity: The Use of a Standardized Pathway by
Nurses**

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Abstract

As pediatric oncologic medicine evolves, chemotherapy-induced neurotoxicity is becoming more prevalent with certain medications. A delay in recognizing neurotoxic effects from medication can lead to detrimental patient health outcomes. Pediatric bedside nurses are at the forefront of recognizing clinical changes in these patients. Moderate-level evidence-based literature shows that education regarding patient decline paired with the proper use of a standardized neurotoxicity grading scale by nurses increases confidence in assessment skills and early recognition of neurotoxic effects leading to better outcomes. Applying Lippitt's theory of change with consideration of the results of the evidence reviewed, a need for education and the formation of a standardized chemotherapy-induced neurotoxicity pathway was developed and is to be initiated to a population of pediatric oncology nurses (Lippitt et al., 1958). The framework for implementing education using the new standardized follows Deming's plan, do, check, act model (Taylor et al., 2014).

Keywords: Chemotherapy, Neurotoxicity, Chemotherapy induced neurotoxicity, Recognition, Standard Grading Scale, Assessment, Nursing Education

Chemotherapy Induced Neurotoxicity Recognition

Bedside nurses have a vital role in the recognition of clinical changes in patients and reporting the change to a provider to initiate interventions promptly. As new medication regimens emerge for the treatment of pediatric oncologic disorders, more adverse effects are being reported. Many of the medications incorporated within these regimens can cause varying degrees of neurotoxicity in patients. The neurotoxic effects of the medications are central, peripheral, or both nervous systems which may cause rapid clinical deterioration and lasting neurological damage. As bedside nurses are at the forefront in recognizing acute clinical changes, education on proper grading of neurotoxicity effects is crucial to initiate appropriate interventions. The implementation of a standardized chemotherapy-induced neurotoxicity (CIN) pathway for grading neurotoxicity should be administered by pediatric hem/onc/BMT nurses to ensure early recognition and the initiation of proper interventions for patients at an increased risk of developing neurotoxic effects from medications.

Problem Statement

As oncologic treatment regimens continue to change as pediatric cancer research evolves, it is realistic to infer that the prevalence of neurotoxicity will continue to rise. For example, leukemia accounts for the majority of childhood cancers and the five-year survival rate is high, but the treatment to prevent central nervous system involvement can result in neurotoxic effects (American Cancer Society, 2023; Bhojwani et al., 2021). The effects of neurotoxic chemotherapy medications can be acute, such as seizures or alteration in mental status, or chronic, as seen in chemotherapy-induced peripheral neuropathy (Baer et al., 2019). Oncology nurses are responsible for recognizing and reporting these neurological changes to complete interventions before the patient's deterioration. There are inconsistent neurotoxicity rates and

interventions because of multiple neurotoxicity grading systems and the differences in the grading scales (Pennisi et al., 2020).

Purpose and Rationale

There is a great need for proper nursing use of neurotoxicity grading scales since neurotoxic adverse effects are becoming more prevalent with new oncologic treatment modalities. The grading scales traditionally have been used to grade neurotoxic effects in patients receiving Blinatumomab infusions and chimeric antigen receptor t-cell therapy (CAR-T) but apply to other oncologic medications that have been associated with neurologic changes. To apply this grading scale to patients at a higher risk for neurotoxicity, the implementation of a standardized chemotherapy-induced neurotoxicity pathway will allow nursing staff to recognize the degree of potential neurotoxicity and alert providers to intervene earlier. Early interventions based on proper neurotoxic assessment and the use of a standardized grading pathway can assist in helping initiate interventions before neurotoxic effects become detrimental to the patient. Proper use and charting of the neurotoxic grading scales by nurses in the electronic medical record will lead to better patient outcomes. Early intervention will help achieve better patient outcomes, less traumatic patient care, and reduce the overall transfers to the intensive care unit for neurological changes.

Background and Significance

A recent literature review shows that acute and chronic neurotoxic symptoms are common in patients actively being treated for malignancy. Neurotoxicity is commonly recognized in stem-cell therapies as a symptom of cytokine release syndrome (Baer et al., 2019). Along with stem-cell therapies, certain medications and chemotherapy can lead to symptoms of neurotoxicity that include encephalopathy, altered mental status, and seizures. For example,

Ifosfamide and Aprepitant, chemotherapy, and antiemetic drugs, both very common in treatment protocols, have been shown to cause neurotoxic symptoms in 30% of patients receiving them (Vazirian et al., 2022). The correct use of neurotoxicity grading scales and neurologic assessment education is essential to identify early signs of neurotoxicity to intervene and improve patient outcomes.

Pediatric Oncology Nurses (P)

Nurses are at the frontline of reporting assessment findings to the healthcare team to initiate interventions when needed. As the United States continues to have approximately 10,000 new cases of pediatric cancer diagnosed each calendar year, the number of oncology nurses continues to grow as well (American Cancer Society, 2023). Providers rely on knowledgeable nursing staff and assessment skills to identify neurotoxic symptoms in patients and understand the patients at great risk for developing neurotoxicity (Baer et al., 2019). Mandatory oncology nursing education sessions, interprofessional collaboration with physicians, and using a chosen standard neurotoxicity grading scale are beneficial in boosting nursing confidence and understanding chemotherapy adverse effects, leading to better assessment and recognition of patient decline (Gallegos et al., 2019).

Standardized CIN Grading Scale and Pathway (I)

Oncology nurses need to be competent in how to grade and assess neurotoxicity using a standardized CIN grading scale and intervention pathway. Competence in implementing a standardized grading scale on identified patients at high risk of neurotoxicity can be obtained through nursing education. Education presented to oncology nurses regarding chemotherapy administration has been shown to decrease nursing anxiety related to the recognition of adverse effects (Gallegos et al., 2019). Gaining knowledge of the medications that place a patient at

greatest risk for neurotoxicity along with nursing use of a standardized age-appropriate grading scale for immune effector cell-associated neurotoxicity syndrome (ICANS) leads to proactive management of neurotoxicity (Lee et al., 2019). The grading scales that assess ICANS traditionally are the immune effector cell-associated encephalopathy (ICE) score for patients over the age of twelve or the Cornell assessment of pediatric delirium (CAPD) score for patients under the age of twelve (Brown et al., 2021).

Current Practice (C)

Despite two neurotoxicity grading scales developed for patients going through CAR-T cell therapy, these scales are not validated for use on other medications due to more research needing to be done. The grading scales to assess ICANS related to CAR-T cell therapies can be applied to other oncologic medications that place patients at high risk of developing neurotoxicity; thus, the grading scales can still serve as a helpful guideline to identify risks and subtle changes in a patient's neurologic status (Jordan et al., 2020). The current practice of recognizing neurotoxicity relies heavily on the bedside nurses' understanding of neurotoxic medications and the ability to recognize, document, and report changes in assessment promptly.

Increase Recognition of Neurotoxicity in Patients (O)

Early recognition of neurotoxic symptoms is crucial to prevent severe nervous system damage. Early signs of neurotoxicity that can be educated on and are represented on the ICANS grading scale are inattention, personality changes, and inability to do simple tasks (Burton et al., 2021). If caught in earlier stages, pharmacologic measures are implemented to potentially reverse the neurotoxic effects. Proper understanding of the grading scales by the nursing staff helps tailor the pharmacologic intervention as the intervention differs with the severity of toxicity (Lee et al., 2019). The goal of education on proper assessments is to increase overall recognition of

neurotoxicity and determine more medications that place these patients at higher risk of developing toxicity.

Internal Data

A pediatric hematology/oncology unit within a children's hospital in the southwestern United States found that neurotoxicity screening tools are available for use, but are not being utilized effectively by the nursing staff to identify neurologic changes early in patients at greatest risk. In casual conversations with the nursing staff and providers, along with a documented rise in rapid response or code blue calls, there has been an increase in patients being transferred to the intensive care unit due to signs of late-stage neurotoxicity (seizure, altered mental status, stroke-like symptoms). The severe signs of progressive neurotoxicity can be detrimental to patient outcomes and difficult for the family to witness. While education has been conducted on this unit in a previous quality improvement project regarding components of the neurotoxicity grading scales and identified medications that place patients at high risk for CIN, the scales are rarely administered to patients. The grading scales are consistently used with Blinatumomab infusions and CAR-T cell therapy but should include patients who are receiving high-risk CIN medications. The additional high-risk chemotherapies identified by the institution include methotrexate, ifosfamide, cytarabine, peg asparaginase, and nelarabine. Patients with any elevation in immunosuppressive therapy levels or who experience posterior reversible encephalopathy syndrome (PRES) are also considered at high risk for neurotoxicity. Patients receiving these medications are to be graded using the appropriate scale by nursing staff and proper provider ordering of the appropriate standardized neurotoxic grading scale.

This project will take place on the oncology unit where nurses report a concern about their ability to recognize subtle neurologic changes and are unable to identify which medications

place a patient at higher risk. The goal of this project is to measure compliance and accuracy in using and documenting a standardized CIN grading scale pathway. This project includes expanding neurotoxicity education, that BMT nurses received in a previous quality improvement project to all hem/onc nurses. The additional education will include how to chart the new CIN pathway scale and the interventions associated with each grade. The goal is for nursing staff to identify neurological changes in high-risk patients through proper assessment and documentation of the correlating neurotoxicity grade in the electronic medical record, thus improving recognition and patient outcomes.

PICOT Question

For pediatric oncology nurses, does (I) accurate use and adherence of a standardized chemotherapy-induced neurotoxicity screening pathway versus (C) current practice (O) increase the recognition of neurotoxicity in patients who are at an increased risk due to medication treatment?

Search Strategy

A review of current literature took place to answer the PICO question. Three databases were extensively searched: PubMed, Cumulative Index of Nursing Allied Health Literature (CINAHL), and ProQuest Medline. These databases were selected for their relevance to the PICO question. Keywords included: *standardized scale, nursing education or teaching, cancer, oncology, neurotoxicity or chemotherapy toxicities, cytokine release syndrome, ICANS or ICE grading, evaluation, assessment, recognition, pediatrics*. The search was completed in order of the PICO question. *Oncology and cancer* were frequently combined to yield more results. *Oncology* on all databases tended to have articles with more adult patient populations as opposed to pediatrics, so the addition of the term *pediatric* was added. The Boolean phrase “or” was

utilized to assist in finding articles relevant to the intervention of education on the use of standardized pathways. The intervention was defined as *education or teaching or assessment or recognition*. The phrases *standardized assessment, grading scale, documentation, neurotoxic or chemotherapy toxicities*, were also used to support the intervention in nurse utilization of a standardized scale to improve recognition of toxicity.

On PubMed, peripheral neuropathy was excluded from the search to tailor the focus to more central nervous system toxicity, as not excluding this term resulted in 4,231 articles, after exclusion there were 100 articles to review. Articles including the education or incidence of posterior reversible encephalopathy syndrome (PRES) were included as the project organization includes this syndrome as a form of neurotoxicity from chemotherapy. CINAHL and ProQuest Medline provided my search with practice guidelines and more research on how to educate healthcare on the ICANS score. The average number of articles within all databases was 60, multiple articles discussed neuropathy as opposed to neurotoxicity and were excluded from the search. The Boolean phrase “NOT” neuropathy was added as a result.

Limitations, Inclusion, and Exclusion Criteria

The majority of the studies were qualitative, the results were based on pre and post education questionnaires or how nursing staff described the quality of education received. Thus, the majority of studies were excluded from the exhaustive search because of the low quality of evidence. Grey literature was scarcely used to develop background and significant and included many practice guidelines or ongoing trials of various assessment tools being utilized. Studies that were earlier than five years ago were excluded from the exhaustive search.

Critical Appraisal and Synthesis of Evidence

The rapid critical appraisal and level of evidence for literature included in this paper were guided by the Melnyk and Fineout-Overholt (2019) guidelines. A combination of both qualitative and quantitative studies was included and reviewed. Overall, most of the studies included followed a similar design with pre- and post-intervention questionnaires provided to the participants of the studies to see if the ideal outcome was achieved (See Appendix A, Tables A1, and A2). The level of evidence varied slightly between studies, with the average level of evidence being four (See Appendix A, Table A3). The sample characteristics of the studies included were relatively similar, with the majority being oncology nurses with varying experience levels. Three studies included physicians, patients, and other healthcare professionals in the sample (See Appendix A, Table A3).

All studies included educational sessions as the primary intervention to assess staff members' knowledge, management strategies, and confidence levels in treating neurotoxic effects or clinical deterioration of patients (See Appendix A, Table A3). Approximately half of the studies highlighted interprofessional education sessions and saw reduced medical errors and quicker management strategies to improve patient outcomes. The results of these studies showed an increase in knowledge and confidence in the management of patient conditions. The Jensen (2020) study was the only one to utilize healthcare professionals working in the adult oncology population rather than pediatrics. However, the overall design utilizing a questionnaire and education session regarding standardized questionnaires applies to the research question in this project.

Discussion

There is evidence in the literature reviewed that healthcare professional education sessions lead to an increase in knowledge and confidence in terms of patient management. In

addition, interprofessional education sessions showed reduced medication errors and quicker medical decision-making in patient decline. Overall, the literature supports that education sessions make a difference in more confident and proper assessment or scoring based on patient clinical appearance, leading to more optimal management of disease process and better outcomes overall.

Specific to the oncology population, nurses who received education about the neurotoxic effects of chemotherapy or other cellular therapies are more confident in recognition, reporting, and early initiation of management in patient decline. A standardized tool used to assess patient adverse effects that both nurses and other healthcare providers understand results in less error and better management of the patient to avoid poor patient outcomes. Although there are many variations of the scale to assess neurotoxic effects, the literature concludes that a healthcare system should educate staff on a one standardized grading scale and base interventions on those scores to improve early recognition and treatment of neurotoxic effects.

Theoretical Framework Application

The Lippitt theory of change model, an expanded version of Lewin's theory of change, applies to this project's goals and desired outcomes. Lippitt's theory outlines the process of creating, implementing, and sustaining change through seven phases that correlate with the three phases of Lewin's theory (see Appendix B, Figure 1). The core concepts of Lippitt's theory of change are identifying the issue that needs to be changed, developing a relationship with the organization, establishing routes to change, implementing change, and sustaining the change (Lippitt et al., 1958).

The concepts of this theory provide a framework to guide this quality improvement project. The identification is that nurses need to accurately score and document the standardized

CIN grading scales to initiate appropriate interventions. In addition, a relationship has been established with the organization through a previous quality improvement project with the same stakeholders. Relationships with the hem/onc nurses and stakeholders allow the expansion of education sessions to include all hem/onc nursing staff on a new pathway to recognize neurotoxicity in high-risk patients. The new education and compliance of pathway use through documentation align with Lippitt's (1958) implementation of change and sustaining of change. The new CIN pathway used by nurses will allow for ongoing feedback and data collection to evaluate how documentation compliance is maintained. Consideration of feedback and adjustment of interventions will allow the change to be sustainable within the target population of nurses. Once the education and pathway are adequate, termination, the last phase of Lippitt's theory, can occur.

Implementation Framework

The plan, do, check, *or* study, act (PDCA or PDSA) method developed by William Deming in the 1950s is a well-known method utilized to guide healthcare quality improvement projects (Taylor et al., 2014). The PDCA method is often used for quality improvement because the application begins on a small scale and adapts to feedback while implementing changes that result in favorable outcomes for a particular patient population (See Appendix B, Figure 2). The PDCA will guide the steps of implementation of this project.

This framework builds upon each other and continues to adapt and change as feedback is gathered during the intervention. This framework's cycle begins with a plan to identify a need for change and establishes a team of qualified individuals to investigate current practices and brainstorm ideas for improvement (See Appendix B, Figure 2). As a team is assembled and current practices are reviewed, the next step is to create evidence-based interventions with

measurable outcomes (Taylor et al., 2014). The intervention is selected by the team and initiated within a specific population, data is collected, and unexpected challenges with the intervention are recorded during this period. After collecting data throughout the “do” stage of the PDCA, the data is analyzed to evaluate the outcomes of the implemented change (See Appendix B, Figure 2). Through the interpretation of findings, plans on improving the initial intervention and ideas on how to carry the intervention out on a larger scale are developed, thus repeating the PDCA cycle (Taylor et al., 2014).

Implications for Practice Change

The evidence has shown that nursing education about neurotoxicity and using a standardized scale to evaluate for toxicity has led to increased recognition and management of this disorder. In a previous project, nursing education regarding neurotoxicity assessment and grading scales was conducted with pediatric BMT nurses on the unit, excluding nursing staff that are not oriented to BMT care yet. The education provided was regarding which patients are at high risk of neurotoxicity development and how to add neurotoxicity scoring the electronic medical record on these patients.

Since that initial education was completed, a new pathway was developed to be utilized by both providers and nurses to standardize the assessment and scoring of chemotherapy-induced neurotoxicity. Education sessions need to be conducted with all hem/onc nurses on the unit to ensure understanding of the new pathway, accurate documentation, and initiation of appropriate interventions.

The literature analyzed shows that interprofessional education sessions have been proven to increase confidence, knowledge, and management of patient conditions (See Appendix A, Table A3). This intervention is within the “Do” phase using the PDCA framework for

implementation. A review of charts and assessment confidence levels post previous education sessions will be reviewed before the new pathway education. Education regarding the pathway will be introduced to the nurses during mandated education sessions. The new neurotoxicity grading scale will be added to patients deemed high-risk electronic medical records. Post-education regarding this new CIN pathway will be assessed for compliance via chart review on identified high-risk patients. The ideal outcome is improving nursing compliance and appropriate use of the CIN pathway after expanded education sessions and protocol rollout on the unit.

Methods

Setting and Stakeholders

The project site is a standalone children's hospital system in the southwestern United States. The hospital system consists of a main campus, multiple outpatient clinics, and two smaller satellite campuses. The project will take place within the inpatient pediatric hematology/oncology/bone marrow transplant unit (hem/onc/BMT) located on the main campus. The unit has 46 inpatient beds that are utilized by numerous patients for the treatment and management of hematologic or oncologic disorders. The stakeholders for this project include the hem/onc/BMT inpatient nurses, the unit educator, the unit manager, hem/onc/BMT providers, neurocritical care providers, and patients who receive one of the identified medications that place them at a greater risk for neurotoxicity.

Recruitment Participation

The participants of this project include inpatient hem/onc/BMT patients being cared for by the chemotherapy service receiving one of the identified medications that increase the risk of neurotoxicity or patients that experience posterior reversible encephalopathy syndrome (PRES) during the hospital stay. The high-risk medications include Cytarabine, Methotrexate,

Blinatumomab, Ifosfamide, Peg Asparaginase, Nelarabine, or CAR-T cell therapy. Patients who are under 28 days of age, patients who did not receive identified high-risk neurotoxic medications or develop PRES, and patients re-admitted after discharge for treatment complications are to be excluded from this project. Recruitment of these participants will occur by identifying admitted patients who meet inclusion criteria during this project timeframe. The consent to participate in this project is obtained through assuring each patient has a completed HIPPA release form documented in the electronic medical record.

Intervention Plan

The evaluation question for this project is: will the implementation of a standardized chemotherapy-induced neurotoxicity protocol lead to at least 50% of pediatric oncology patients receiving high-risk chemotherapy having a documented neurotoxicity score in the electronic medical record? Education regarding neurotoxicity and associated scoring has been done with the hem/onc/BMT nursing staff within the first stage of the project. This evaluation question was developed by discussing the timeline and need for a standardization of evaluating interventions associated with neurotoxicity by the project stakeholders. Institutional board review (IRB) approval was obtained through Arizona State University and the project site IRB waiver was obtained before chart audits were conducted.

The presentation of the standardized chemotherapy-induced neurotoxicity (CIN) pathway occurred at multiple mandatory hem/onc/BMT staff education meetings throughout August/September 2023. The pathway will be implemented for use by the chemotherapy service in December 2023. Data gathered via chart auditing will evaluate the primary outcome of adherence to nursing administration and documentation of neurotoxicity screening scores. The data was gathered between December 2023 and February 2024. Additional outcomes are

recorded in the chart audit form that pertains to the use of the CIN pathway. The chart audit tool (See Appendix C, Figure 1) developed by a group of hem/onc/BMT and neurology providers is utilized to evaluate the documentation of neurotoxicity scoring and if interventions were implemented per protocol. Chart auditing has been proven to be beneficial in evaluating patient care, improving quality of care, and continuous improvement of clinical practice (Azzolini et al., 2019).

Results

Descriptive Statistics

Introduction

The project included n=55 patient charts audited within the two-month time frame. The patient charts that were included were followed by the chemotherapy service providers and received an identified neurotoxic medication. Descriptive statistics and comparison between variables are used to describe the results of this project as the chart audit form is not validated.

Table 1 lists the six medications/combinations administered to patients within the chart auditing period. The most frequently administered medication is Methotrexate (n=22).

In evaluating the primary outcome of this project, nursing adherence to documentation of CIN grading scores greater than 50% of the time, scores were documented 80% of the time overall (n=44). Approximately 16% (n= 9) of patients had incomplete scores documented, which means that one or more shifts did not have a score documented during the seven days after chemotherapy administration. Thus, overall exceeding the original goal of 50% adherence by the nursing staff.

As the adherence was well beyond what was expected, Table 2 shows that four instances of neurotoxicity were identified via screening. Two were related to the developmental level of the patients in which nurses were variable in scoring depending on the patients' actions each

shift, but two did require interventions per the CIN pathway. The two instances of true neurotoxicity did not require transfer to the ICU.

As this is a multidisciplinary effort, the chart audit tool included secondary outcomes that evaluated the provider's orders and interventions. Orders were placed by providers on 89% of the patients, but baseline assessments were done only 50% of the time by the nursing staff. A trend in the data collection that was not recorded directly in the chart audit form is that the orders were placed the day after starting chemotherapy in some cases, this could have impacted the baseline assessment amount.

Table 1

Medication Distribution

Variable	<i>n</i>	%
Medication		
High Dose Methotrexate	22	40.00
Ifosfamide	17	30.91
Cytarabine	6	10.91
High Dose Methotrexate, Cytarabine	3	5.45
Blinatumomab	6	10.91
Peg- asparaginase	1	1.82

Table 2

Outcome frequencies

Variable	<i>n</i>	%
Baseline Assessment (before chemotherapy)		
Yes	28	50.91
No	27	49.09
Neurotoxicity Order Placed		
Yes	49	89.09
No	6	10.91
Nursing documented CIN grade (every shift x7 days or d/c)		
Yes	44	80.00
Incomplete	9	16.36
No	2	3.64
Supportive measure initiated (if a change in neuro status)		

Yes	2	3.64
No	2	3.64
No change	51	90.91

Limitations

Limitations occurring through the implementation phase of this project include inconsistency in screening scores, order placement by providers, and documentation of both scores and associated grades of toxicity. Although orders were placed on 89% of patients receiving neurotoxic medications, some orders were placed the day after medication administration, thus nursing forgot to document a baseline screening score, which unless caught on the following shift, resulted in incomplete screening documentation. Also, without a baseline score, there were variations in scoring by nurses. The variable scores represent a neurotoxicity grade change, but in most cases, the score reflected the patients' developmental levels that would have been reflected on the baseline assessment.

Another barrier is that nurses not only had to add in the parameter to document screening scores but after calculating the total score, had to separately document a neurotoxicity grade. The providers look at the neurotoxicity grade changes to introduce interventions per the CIN clinical pathway. Nurses received reminders via email and flyers to document the grade as well. The information technology (IT) team is going to be contacted to see if grades can be automatically calculated to avoid this limitation.

Summary and Future Recommendations

The goal of 50% adherence to screening score documentation and administration by nurses was exceeded. After the education sessions and CIN pathway rollout, the data gathered reflected that 80% of patients had scores properly documented, reaching 100% adherence in the last two weeks of data collection. The two cases of CIN recognized did not require emergent

intensive care unit transfer, therefore adherence to screening ensures that CIN is caught promptly. The education sessions regarding neurotoxicity recognition are aimed at being sustainable and available for use in future pediatric oncology nurses.

Due to the success of the project, it is recommended to expand the CIN pathway and screening requirements to the other services on the hem/onc/BMT unit. It is recommended that the IT department assists in automatically calculating grades and adding the neurotoxicity order to the high-risk chemotherapy order sets, to avoid a delay in order. Continue to use the PDSA model to evaluate the implementation of the other services and revise education as updates are presented.

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Appendix A

Evaluation and Synthesis Tables

Table A1
Evaluation Table for Qualitative Studies

Citation	Theory/ Conceptual Framework	Design/ Method/ Sampling	Sample/ Setting	Major Themes Studied/ Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Themes	Level/ Quality of Evidence; Decision for/ Application to practice; Generalization
<p>Harden et al., (2020), CAR-TEAM: A Simulation-Based Interprofessional Education Intervention for Management of CAR Toxicities</p> <p>Country: United States</p> <p>Funding: Jazz Pharmaceuticals grant</p> <p>Bias: None stated by authors.</p>	<p>Not stated</p>	<p>Design: Retrospective Study</p> <p>Method: Interprofessional members were chosen at random and looked at cases of NT along with didactic lectures</p> <p>Purpose: Development and implementation of an educational module to address evidence-based management and recognition of CRS.</p>	<p>Sample: (n= 70). 47/70 responses to the pre- and post-survey were obtained.</p> <p>Demographics: Various health care roles and areas of oncologic specialty. 41% were staff nurses.</p> <p>Setting: 57% inpatient faculty; the other portion is either outpatient or unknown</p> <p>Attrition: Not all members responded to the pre/post questionnaire</p>	<ul style="list-style-type: none"> Do inter-professional education sessions improve knowledge and confidence regarding CAR-T therapy adverse effects? Authors: Hypothesis that education sessions would assist in: Assessment of NT Interprofessional Collaboration Management of CRS <p>Definitions: CRS: Cytokine Release Syndrome</p>	<p>Data Collection: Pre and post-educational module confidence assessment tools.</p> <p>Data Dependability: Data is dependable as this study could be repeated and the guidelines discovered can be followed.</p>	<p>No statistical analysis was stated, but it can be inferred that the pre-post test results were analyzed using a paired sample t-test to compare pre and post education answers.</p> <p>Pre and post confidence and knowledge assessments after education modules, simulations, and didactic content.</p>	<p>(1) Improved knowledge: 90 days after education 22/24 respondents expressed that the education sessions improved knowledge and clinical practice of CAR-T therapy CRS</p> <p>(2) CRS recognition: over 90% of the respondents expressed more confidence in CRS clinical recognition and interventions</p> <p>(3) Use of ICANS grading for CRS management: ></p>	<p>LOE: 6</p> <p>Strengths: Interprofessional communication, QR code at the beginning and end of educational sessions, various modalities of education</p> <p>Weakness: Not all members completed the survey, lower level of evidence</p> <p>Application: Interprofessional education improves recognition of CRS</p>

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Citation	Theory/ Conceptual Framework	Design/ Method/ Sampling	Sample/ Setting	Major Themes Studied/ Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Themes	Level/ Quality of Evidence; Decision for/ Application to practice; Generalization
				Car-T: Cellular infusion therapy utilized to treat malignant disease			90% of respondents expressed comfortability in interpreting ICANS scores and how that relates to CRS management	
Knoerl, R. (2023) Exploring Clinicians' Perspectives of Barriers to Chemotherapy-Induced Peripheral Neuropathy Assessment and Management in Oncology Practice: A Qualitative Analysis of Semi-structured Interviews.	None Stated	<p>Design: Qualitative longitudinal study</p> <p>Method: 30-minute structured interviews with clinicians involved in the study</p> <p>Purpose: explore clinician perspectives on CIPN assessment, management, and the use of a</p>	<p>Sample: 15 eligible doctors interviewed (oncology unit)</p> <p>Attrition: 24 physicians due to lack of time or responses to the initial email</p>	<p>What are the barriers to recognition, assessment, and management of CIPN in oncology patients?</p> <p>Healthcare providers were interviewed to recognize:</p> <p>-Neurotoxic medications</p> <p>-Personal barriers to screening for CIPN</p> <p>-Management of neurologic-related side effects</p>	Data Collection: Audio-recorded interviews with the participants of this study	<p>Statistical Analysis: No tool is stated in the study; It is stated that an inductive content analysis is utilized to identify and code themes within the interviews.</p> <p>Due to the coding of themes, multiple statistical tools can be applied to this data.</p> <p>Interviews were coded into a</p>	<p>CIPN Management Practice Patterns and Barriers were identified and addressed through the interviews. Physicians differed in their approach to assessing and managing CIPN.</p> <p>Utilization of the CIPN Clinician Decision Support Tool was reported to not support the</p>	<p>LOE: 5</p> <p>Strengths:</p> <p>Interview structure and barrier identification for proper neuro assessment</p> <p>Weakness:</p> <p>Lack of communication about neurotoxicity (peripheral neuropathy) between providers and patients</p>

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Citation	Theory/ Conceptual Framework	Design/ Method/ Sampling	Sample/ Setting	Major Themes Studied/ Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Themes	Level/ Quality of Evidence; Decision for/ Application to practice; Generalization
<p>Country: United States</p> <p>Funding: CARTOX program at MD Anderson</p> <p>Bias: No conflict of interest reported</p>		CIPN decision tool				codebook by research assistants summarized in a framework matrix with themes and sub-themes with subsequent quotes from the interviews	physician’s current practice as the utilization of the tool did not alter the course of treatment for CIPN. If used, the physicians recommended that the tool be integrated into the electronic medical record with recommendations that correlated with a score on the tool.	<p>Limitations in which interviews only involved physicians</p> <p>Application:</p> <p>Continue to utilize a standardized screening approach in patients at risk for neuro-related side effects.</p>
<p>Jensen et al., (2020), Involving patients and nurses in choosing between two validated questionnaires to identify chemotherapy-induced peripheral</p>	Phenomenological hermeneutic approach	<p>Design: Qualitative exploitative study</p> <p>Method: Interviews with cancer patients and two focus groups of nurses</p> <p>Purpose:</p>	<p>Sample: (n=23) 15 patients, 8 oncology nurses</p> <p>Demographics: All nurses female with a mean years of experience of 6.5 years, patients were receiving</p>	<p>Screening tool applicability</p> <ul style="list-style-type: none"> • Application to practice • The usefulness of tools in practice from a healthcare and patient perspective 	<p>Data Collection: Semi-structured interviews</p> <p>Data Dependability: Dependable data, the interviews were recorded and the study could be repeated in the</p>	Phenomenological hermeneutic approach: describe the translation of quotes. General concepts from interviews coded into themes/sub-themes for interpretation of participants' answers	<p>The tool is useful in assessing urgent versus non-urgent levels of peripheral NT and how this impacts nursing care</p> <p>(2) Need for a precise description of NT—tool</p>	<p>LOE: 5</p> <p>Strengths:</p> <p>Continued interviews and follow-up throughout the study process</p> <p>Weakness: interpretation of quotes from a</p>

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Citation	Theory/ Conceptual Framework	Design/ Method/ Sampling	Sample/ Setting	Major Themes Studied/ Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Themes	Level/ Quality of Evidence; Decision for/ Application to practice; Generalization
<p>neuropathy before implementing in clinical practice—A qualitative study.</p> <p>Country: Denmark</p> <p>Funding: Novo Nordic Fund</p> <p>Bias: None stated.</p>		<p>To evaluate from nurse and patient perspectives which tool is better to assess peripheral NT to guide treatment</p>	<p>chemotherapy—those with cognitive impairments excluded</p> <p>Setting: Oncology outpatient clinic</p> <p>Attrition: One nurse unable to participate due to illness</p>	<p>Definitions: Peripheral NT: neuropathy developing due to chemotherapy infusions</p>	<p>future following the same format,</p>		<p>provides more clarity and guidance</p>	<p>research consumer perspective or researcher reviewing information</p> <p>Feasibility:</p> <p>Application: involving the users of the tool (nurses and patients) is essential for proper treatment to be initiated</p>
<p>Winacoo et al., 2019 Implementing Immune Effector Cell Education for Nursing Staff</p> <p>Country: USA</p> <p>Funding: None reported</p> <p>Bias: None reported</p>	<p>NA</p>	<p>Design: Utilizing class evaluations (pre and post lecture) to evaluate nursing knowledge</p> <p>Method: Review underpinnings of toxicities associated with IECT through</p>	<p>N= 100</p> <p>Demographics: Inpatient, outpatient, and triage nurses</p>	<p>Themes: Nursing knowledge around cellular therapy toxicity recognition</p> <p>Definitions: IECT: Immune effector cell therapy</p>	<p>Data Collection: Post education session survey filled out by the participants of the course.</p>	<p>No specific analysis tool was stated. Can infer that a form of a t-test would be utilized to compare pre and post intervention questionnaires</p>	<p>Majority of the nurses reported an increase in knowledge of CAR-T cell treatment and common toxicities</p>	<p>LOE: 5</p> <p>Strengths:</p> <p>Large sample size with good participation rates</p> <p>Applicable to current nursing practice</p> <p>Increased knowledge</p>

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Citation	Theory/ Conceptual Framework	Design/ Method/ Sampling	Sample/ Setting	Major Themes Studied/ Definitions	Measurement/ Instrumentation	Data Analysis	Findings/ Themes	Level/ Quality of Evidence; Decision for/ Application to practice; Generalization
		classes and modules Purpose: Oncology nurses play a crucial role in the identification of cellular therapy toxicity, thus the need for education for early intervention and treatment						Course content met participant's needs Weaknesses: Time constraint All nurses may not have replied to post survey Applicability: The study applies to hem/onc nursing practice and could be recreated with the same information

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Table A2:

Evaluation Table for Quantitative Studies

Citation	Theory/ Conceptual Framework	Design/ Method/ Purpose	Sample/ Setting	Variables	Measurement/ Instrumentation	Data Analysis	Results/Findings	Level of Evidence; Application to practice; Generalization
<p>Crowe et al., (2018). The impact of simulation-based education on nursing confidence, knowledge and patient outcomes in general medicine units</p> <p>Funding: University of British Columbia</p> <p>Country: Canada</p> <p>Bias: None</p>	Not stated	<p>Design: Pre and post-analytic study with survey given at three separate points in time</p> <p>Purpose: Implementation of simulation to improve nurse knowledge, confidence, and communication with a focus on clinically declining patients</p>	<p>N= 161 nurses completing the pre and post-survey</p> <p>Inpatient hospital: all nurses of various genders and experience levels are invited to attend an education session on patient decompensation.</p> <p>Attrition: only 79/161 nurses completed the 3-month follow-up survey</p>	<p>IV1: Simulation Course for clinically declining patient</p> <p>DV1: Nursing self-report of confidence</p> <p>DV2: Nursing recognition of patient deterioration</p> <p>DV3: Nursing knowledge</p> <p>Definitions: N/A.</p>	Pre and post analytic survey after the 4-hour simulation education session	<p>Statistical analysis: Paired t-tests for evaluating knowledge and confidence questionnaires</p>	<p>DV1: Increased self-reporting of confidence</p> <p>Increased recognition of patient decline</p> <p>Knowledge retention evaluated by the survey given 3 months post intervention</p>	<p>LOE: 4</p> <p>Strengths: Large sample</p> <p>Weakness: Not all completed surveys at 3 months. Only given to nurses at one facility; questionnaire not used in other studies.</p> <p>Application: Education sessions with pre & post tests increase confidence & assessment all skill levels.</p>
<p>Fisher et al., 2017 Impact of a Pharmacist-Led Chemotherapy Education Program on the Knowledge of Pediatric</p>		<p>Design: 3-session educational program with a pre-test before the first session and a post test after each</p>	<p>N= 30</p> <p>Demographics: 30 inpatient oncology nurses; 78%</p>	<p>IV1: Educational Sessions</p> <p>DV1: Chemotherapy medication errors</p>	<p>Tools: Pre and post multiple choice tests with a final cumulative post education program test</p>	Paired t-test	<p>Statistically significant improvement in knowledge (P <0.0001) as evidenced by a 14.1% score</p>	<p>LOE: 4</p> <p>Strengths: Knowledge gained through education</p>

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Citation	Theory/ Conceptual Framework	Design/ Method/ Purpose	Sample/ Setting	Variables	Measurement/ Instrumentation	Data Analysis	Results/Findings	Level of Evidence; Application to practice; Generalization
<p>Hematology/Oncology Nurses</p> <p>Country: USA</p> <p>Funding: Children’s Colorado</p> <p>Bias: None to disclose</p>		<p>educational session.</p> <p>Purpose: Do education sessions by a chemotherapy pharmacist increase nurses’ knowledge and confidence in identifying adverse effects and safe administration of chemo?</p>	<p>with a bachelor of nursing degree; mean of 7.8 years experience; 21 with APHON credentials</p> <p>Setting: one inpatient oncology unit</p> <p>Exclusion: None</p> <p>Attrition: Not reported</p>	<p>DV2: Nursing chemotherapy knowledge</p> <p>Definitions: APHON: Association of pediatric hem/onc nurses</p>	<p>Validity/ Reliability: This study could be repeated utilizing the same format.</p>		<p>improvement on posttests overall; individual sessions were 6%, 22%, and 16% respectively.</p> <p>Reduction in medication errors from 8 per month to 4 per month post education session attendance by nurses</p>	<p>Good rate of survey completion</p> <p>Error reduction was measured</p> <p>Weaknesses:</p> <p>Attendance not required</p> <p>Application:</p> <p>Could be applicable to practice if attendance and participation were mandated. The same questions and information could be valuable to be presented and gauge nursing knowledge.</p>
<p>Gallegos et al. (2019). Chemotherapy Education An interprofessional approach to standardizing processes and improving nurse and patient satisfaction.</p>	<p>None stated.</p>	<p>Design: Pre and post intervention questionnaire</p> <p>Purpose: Evaluating the utilization of a standardized educational tool regarding chemo and side effects</p>	<p>Sample: N=55</p> <p>Demographics: Nurses who are chemotherapy-certified</p> <p>Setting: Outpatient cancer infusion clinic</p>	<p>IV1: Standardized education tool</p> <p>DV1: Nursing knowledge</p> <p>DV2: Nursing Satisfaction</p>	<p>Data Collection: Pre and post questionnaire before utilizing a standardized education tool regarding chemotherapy and side effects.</p>	<p>Paired t-tests to evaluate the difference in mean between the pre and post tests of both nurses and patients.</p>	<p>Improvement in nursing and patient knowledge regarding medication and side effects</p> <p>Improved nursing</p>	<p>LOE: 4</p> <p>Strength: ability to measure both patient and nurse satisfaction and confidence due to setting</p> <p>Weakness: Small hospital, outpatient</p>

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Citation	Theory/ Conceptual Framework	Design/ Method/ Purpose	Sample/ Setting	Variables	Measurement/ Instrumentation	Data Analysis	Results/Findings	Level of Evidence; Application to practice; Generalization
Country: United States Funding: none reported Bias: none reported		(such as NT) increases nurse knowledge and overall patient satisfaction.	Exclusion: Attrition:	DV3: Patient satisfaction Definitions: None to report.	Data Validity: The study could be repeated using the same standardized education tool and survey.		satisfaction with increased confidence and knowledge of chemo and side effects	facility, standardized tool not utilized in other studies Application: education and utilization of standardized screening tools increase nursing confidence and satisfaction
Moreira et al. (2021). Creation of a successful multidisciplinary course in pediatric neuro-oncology with a systematic approach to curriculum development Country: USA/International Funding: American Lebanese Syrian Associated Charities Disclosures: No conflicts of interest or	Not Stated	Design: Pre and post test in the form of questionnaires before and after the course curriculum was completed Purpose: Create educational modules to improve healthcare provider knowledge on central nervous system tumors	N= 36 Demographics: Various healthcare roles in 8-9 different medical institutions Setting: Online course and in-person course	IV1: Course curriculum DV1: Comprehension of central nervous system tumors and adverse effects	Data Collection: Pre and post questionnaire regarding new knowledge, management, and recognition of central nervous system tumors and adverse effects Data Validity: The study could be repeated using the same educational curriculum in the healthcare worker community.	Wilcoxon single-rank tests. Analysis of results performed with GraphPad computer software.	DV1: Clinical outcomes of patients with central nervous system tumors are improved	LOE: 4 Strengths: Interdisciplinary and international outreach. Participants were satisfied with the program. Clinical outcomes of patients are improved. Weakness: Limited to budgeting constraints.

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disclosures were reported.								Complexities of a multidisciplinary team with answers to questionnaire Tailoring of content (too specific to area) Feasibility: Application: This study is applicable to practice as it outlines how education can be utilized across professions and countries.
Pergert et al. (2015) Confidence and authority through new knowledge: An evaluation of the national educational programme in paediatric oncology nursing in Sweden Country: Sweden		Design: Study specific questionnaire with open and closed questions (both quantitative and qualitative elements) Purpose: Evaluate a national pediatric oncology nurse education program to enhance the	N= 66 Demographics: Pediatric Oncology inpatient Nurses; Ages 24-77; 3 Male; Mean experience (years): 11-20	IV1: Education Program DV1: Working situation after the program DV2: Nurse perception of educational program influence on practice	Study specific questionnaires with open and close-ended questions.	Descriptive statistics for the structured portion of the questionnaire. Open-ended questions were abstracted into codes and a comparative analysis was performed.	DV1: 65% of nurses changed into a higher level of work (manager, charge nurse, educator) DV2: 98% shared information with coworkers and 67% reported utilizing the new	LOE: 4 Strengths: Network across the country Consensus reached that there is a need for educational programs Weaknesses:

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Citation	Theory/ Conceptual Framework	Design/ Method/ Purpose	Sample/ Setting	Variables	Measurement/ Instrumentation	Data Analysis	Results/Findings	Level of Evidence; Application to practice; Generalization
<p>Funding: Swedish Childhood Cancer Foundation</p> <p>Bias: No disclosures or conflict of interest reported</p>		<p>quality of care in the pediatric oncology units</p>		<p>DV3: Nursing confidence in caring for clinically ill oncology patients</p>			<p>education in their personal practice as a nurse</p> <p>DV3: Reported that nurses felt better equipped to care for pediatric oncology patients</p>	<p>Targeted oncology nurses with a lot of experience, need to include newer nurses</p> <p>Applicability:</p> <p>This study applies to practice in that it can be recreated in any pediatric hem/onc nursing unit</p>
<p>Peterson et al. (2017) An Online Educational Program Improves Pediatric Oncology Nurses' Knowledge, Attitudes, and Spiritual Care Competence</p> <p>Country: USA</p> <p>Funding: American Cancer Society Doctoral Degree Scholarship</p> <p>Bias: No conflicts of interest to report</p>		<p>Prospective, longitudinal study</p> <p>Purpose: to evaluate the effect of educational sessions on improving nursing knowledge and core competence</p>	<p>N= 112</p> <p>Demographics: Oncology Nurses, 29% of participants with 11-20 years of experience</p>	<p>IV1: Education Sessions</p> <p>DV1: Nursing knowledge</p>	<p>Three questionnaires were administered to participants as a baseline, immediately after the program, and three months post education</p>	<p>RM- ANOVA</p>	<p>DV1: Increased nursing knowledge about the use of scale and shows that education sessions do work to increase and retain knowledge on patient care topics</p>	<p>LOE: 3</p> <p>Strengths:</p> <p>Strong sample size</p> <p>Online educational program success</p> <p>Weakness:</p> <p>Self-report bias</p> <p>Lack of control group</p>

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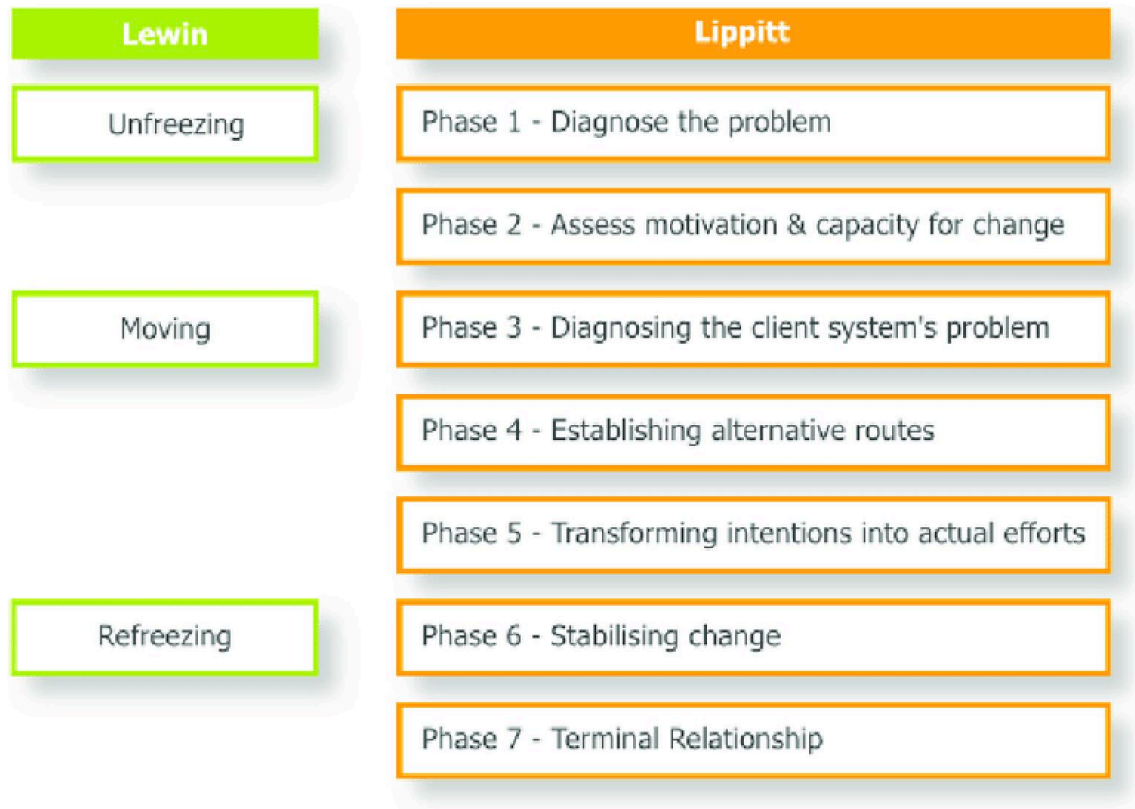
Table A3
Synthesis of Evidence Table

Study (Author, year)	Crowe et al., 2018	Fisher et al., 2017	Gallegos et al., 2019	Harden et al., 2020	Knoerl et al., 2023	Jensen et al., 2020	Moreira et al., 2021	Pergert et al., 2015	Peterson et al. 2016	Winacoo et al., 2019
Design LOE	Pre and post analytic study LOE: 4	3-session educational program with a pre- and post-test LOE: 4	Pre and post intervention questionnaire LOE: 4	Retrospective LOE: 6	Qualitative longitudinal study LOE: 5	Qualitative exploitative study LOE: 5	Pre and posttest in the form of questionnaires LOE: 4	Study specific questionnaire with open closed questions LOE: 4	Prospective longitudinal study LOE: 3	Pre and post course evaluation questionnaires LOE: 5
Sample Demographics										
<i>Number of Participants</i>	161	30	55	47	15	23	36	66	112	100
<i>Profession</i>	Nurses	Nurses	Nurses	41% Nurses	Physicians	Nurses/Patients	VAR	Nurses	Nurses	Nurses
<i>Mean Experience</i>								11-20 yrs	11-20 yrs	
Setting										
<i>Work Environment</i>	INPT	INPT	OPT	51% INPT Other UNKN	INPT/OPT	OPT	INPT/OPT	INPT	INPT/OPT	INPT/OPT
Interventions										
<i>Educational Course</i>	X	X	X	X	X	X	X	X	X	X
<i>Pre and Post Knowledge Test</i>	X	X	X	X		X	X	X	X	X
<i>Interprofessional Collaboration</i>		X		X		X	X			
Outcomes/ Themes										
<i>Knowledge</i>	+	+	+	+	+		+		+	+
<i>Confidence</i>	+	+	+					+	+	
<i>Management</i>	+	+		+		+	+	+		
<i>Medication related</i>		-medication errors		+ adverse effect recognition						
<i>Standardized Scale Use</i>				+		+			+	

Key: **ED** Education, **LOE** Level of Evidence **Prof:** profession, **PPQ:** Pre and post questionnaire, **IP:** Interprofessional, **INPT:** Inpatient, **OPT:** Outpatient, **KNW:** Knowledge, **UNKN:** unknown, **VAR:** varies, **+** : increased, **-** : decreased

Appendix B**Models and Frameworks****Figure 1**

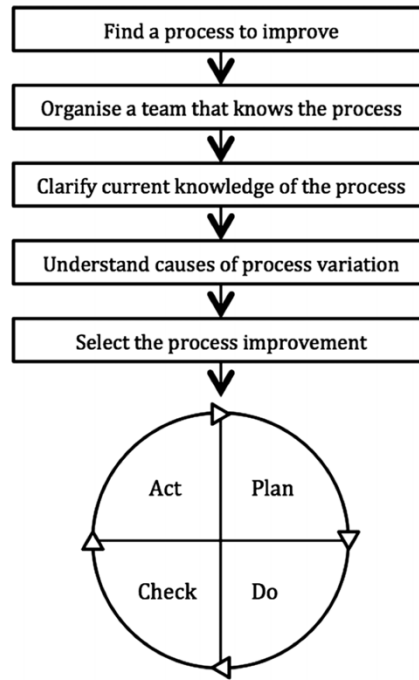
Lippitt Change Theory (Expansion on Lewin's Theory of Change in 1951)



(Lippitt, Watson, & Wesley, 1958)

Figure 2

Deming's Plan, Do, Check, Act (PDCA) Model for Quality Improvement



(Taylor et al., 2014)

