

Running Title:

Lean Six Sigma, Root Cause Analysis and patient safety in Healthcare.

Lean Six Sigma, Root Cause Analysis to enhance patient safety in healthcare organizations: a narrative review, 2000-2016.

Abstract

Background: Lean Six Sigma [LSS] and Root Cause Analysis [RCA] are powerful quality business tools that cost-effectively improve efficiency and effectiveness of and client satisfaction in healthcare, academia and other industries. RCA, an iterative process helps in the identification of the root cause of an adverse medical incident and injuries and consequently prevents its recurrence provided RCA recommendations are properly implemented in the healthcare industry. **Objective:** This narrative review aims to describe the principles and objectives of LSS and RCA tools with a special focus on their diverse roles in healthcare organizations. **Methods:** A computer searches of PubMed, OvidSP, and Google Scholar (2000-2016) were made using keywords such as Lean, or Six Sigma or lean six sigma or medication errors (MEs) or adverse drug events or RCA which retrieved thousands of references but only 110 articles were included in this paper. **Results:** Lean, Six Sigma, LSS, and RCA are powerful quality improvement tools that prevent adverse events, produce better quality services and result in enhancing patient satisfaction and safety. These quality tools also decrease costs, work performance variance, waste and increase customer satisfaction and the work performance of healthcare professionals. **Conclusion:** The use of the quality improvement tools produce better quality healthcare services with greater efficiency, and good outcome and also prevents adverse drug events linked with significant morbidity, mortality and financial burden on the public health around the world.

Keywords: Lean, six sigma, lean six sigma, root cause analysis tools, medical incidents, medication errors, adverse drug events, client satisfaction.

Introduction

The safe use of medications with efficacy and efficiency and patient safety are the two prioritized objectives of healthcare and academic organizations around the world [1]. To address the two interconnected concerns, some qualitative tools, policies and programs were developed to facilitate the safe management of medications, prevent the adverse drug events

including adverse drug reactions and medical incidents and enhance patient safety with better healthcare services and outcome [2,3]. Regardless of types and severity of medical incidents (MEs and near misses) and adverse drug events, they are associated with substantial morbidity and mortality and increasing healthcare costs globally [4,5]. Nonetheless, most adverse drug events including ME are preventable [2,3,5]. Electronic health records, medication prescribing system, ME reporting systems, adverse drug reaction reporting system, pharmacovigilance, RCA and other quality improvement tools including Lean and Lean Six Sigma (LSS) have provided a platform for the reduction of occurrence of medical incidents and adverse events not only in healthcare and academic institutions but also in industrial organizations across the world [2,3,5-8]. Lean and lean six sigma methodologies are also used efficiently to reduce waste, time, and to increase production and customer satisfaction in non-health industries [6,8]. This narrative review will be supported by evidence-based data published in the relevant literature. The significance of this review is that it will disseminate important information about commonly used quality improvement tools among healthcare professionals and public especially in Saudi Arabia and the Middle East region where the related research is minimal [2,3,9]. Furthermore, the adverse drug events including MEs are reported to be decreasing in the Western world but are rising in the Eastern world and, therefore, this study will familiarize the concerned health professionals to take appropriate, preventive measures to control rising prevalence of events in low- and middle-income countries. This is only possible if the main causes of adverse drug events are recognized and rectified to ensure safe use of medications linked with enhanced patients' safety, good quality healthcare and better outcomes. Moreover, there is scanty literature on Lean, SS and LSS in Saudi Arabia [10]. The objective of this review is to describe the quality improvement tools including the lean, SS, LSS and root cause analysis that help efficiently to reduce waste, time, worker performance variance, to increase production and customer satisfaction and safety, and in the identification of root cause of adverse events.

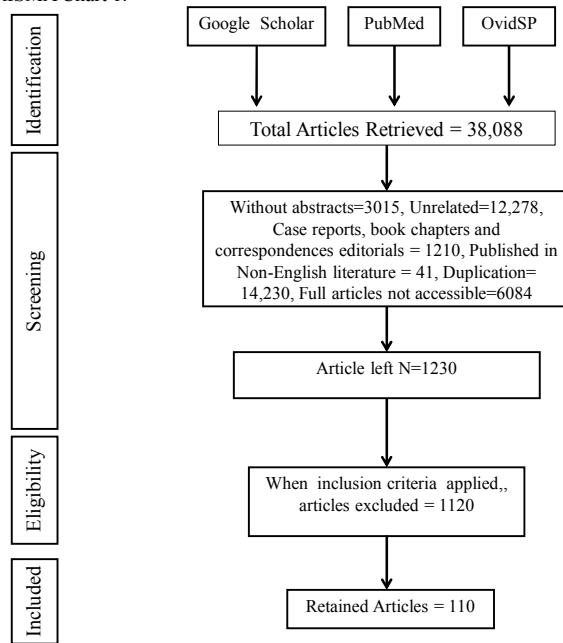
Methods

Search

Computer searches were made using keywords such as Lean, Sigma Six, Lean Six Sigma, adverse events, medication error, and root cause analysis. These words were combined with patient safety, quality care, pharmacy care, medication error reporting, computerized physician order entry, adverse events, adverse drug reactions, and outcome. We used PubMed, Google Scholar, and OvidSP search engines and retrieved more than 38,088

65 articles published over a period of 17 years, from 2000 to 2016. Two authors [NAQ & DSD]
 66 reviewed these articles in light of the following exclusion criteria; duplication (similar articles
 67 were found in two or three databases, n=14,230), no abstract available (n=3015), full articles
 68 unavailable (n=6084), unrelated articles (when keyword “root cause analysis” was used in
 69 searches, articles having “Cause” were retrieved but not related to RCA, n=12278), case
 70 reports, unavailable book chapters and correspondences (n= 1210) and published in non-
 71 English literature (n=41). The total number of retained article (n=1230) were subjected for
 72 intensive review using the following inclusion criteria; articles published in local and
 73 international English literature, available abstract or full article or both, articles’ focus on
 74 tools of root cause analysis, lean, sigma six, LSS and medication safety, and patient safety in
 75 healthcare settings, editorials, systematic reviews, and meta-analysis and randomized clinical
 76 trials (RCTs). Furthermore, 1120 articles were excluded due to small case series, English
 77 abstracts of important non-English papers not accessible, and papers published before the
 78 year 2000. Thus, a total of 110 sources (Prisma flow chart 1) were included for supporting the
 79 role of Lean, Sigma Six, LSS and RCA in the management of safe use of medication, and
 80 identification of root cause of MEs together with their prevention. In addition, the retained
 81 sources of information helped in the adaptation and development of policies, procedures,
 82 action plan and guidelines for conducting the root cause analysis in healthcare settings.
 83

PRISMA Chart 1:



84

85 Results

Lean and Lean Six Sigma

Lean is defined as a process strategy that uses less of everything including less human effort, space, investment in tools or information, and reduces the number of steps in the process cycle. Furthermore, it removes waste, time, non-value added processes and complexity. Lean also drives speed and increases capacity and efficiency compared with the traditional process [11]. Lean Six Sigma, the combination of two processes (Lean and Six Sigma) is reportedly a better quality improvement methodology (Figure1) compared to standalone lean or six sigma [6] and also helps in good returns on the investment [12]. The two main tasks of lean are eliminate waste and shorten cycle time whereas SS eliminates variations in the process and improves its capability. When they combine, they produce additional tasks including flawless execution of a project, and impact top and bottom line personnel together with enhanced client experience (Figure 1).

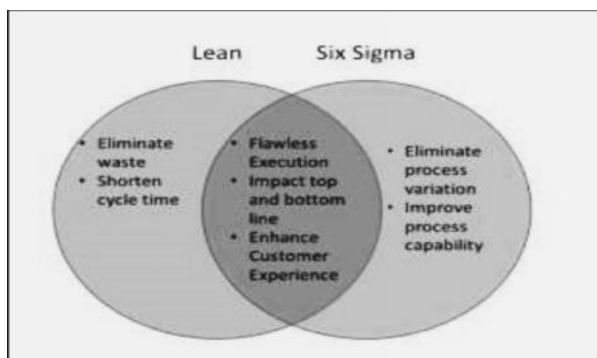


Figure 1 Integrated Lean Six Sigma; shows lean eliminates waste and shorten cycle time while SS eliminates process variations and improves its capability.

Lean temple diagram [Figure 2] reflects how lean helps organizations to improve continuously their production line by reducing wastage. Lean main principal begins with customer, ends with customer and customer satisfaction which is the prime goal in healthcare. By checking and comparing, lean focuses on eliminating and controlling waste such as over processing, motion, transportation, waiting, inventory overproduction, and defects. Thus, lean is centered on making obvious what adds value by reducing everything else including time and errors [13] with sustained quality and smooth workflow. Notably, continuous improvement in healthcare organization is dependent on multiple factors including workplace organization, visual management, standard work, smooth work flow and better quality and proper engagement of the healthcare professionals (Figure 2).

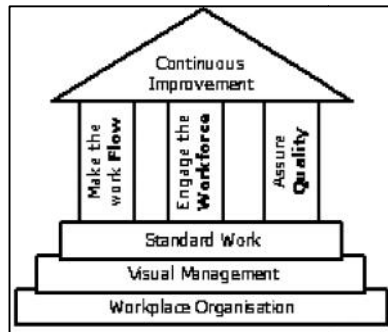


Figure 2 Lean Temple Diagram: Showing factors that determine the continuous improvement in an organization.

From healthcare perspective, the hospital is an ideal setting for using the lean methodology that efficiently impacts quality of care delivered to patient population [14], and lean has several applications in health industry [15]. In a simulation study, Setijono and colleagues reported that decision support system (embedded in electronic prescribing system) and lean tend to achieve considerable reduction in a patients' non value added time and total patients' time by assigning three physicians and three surgeons in emergency ward. The combination of physicians and surgeons leads to 13 percent reduction of patients' non-value-added time while maintaining the total time in system at approximately the same level [16]. Working from the view of client who consumes a product or service, value is any process or action that a customer would be willing to pay for the service [17]. Lean improves functioning of emergency departments (EDs) in terms of decrease in length of patients' stay, waiting times, and proportion of patients leaving EDs without being seen [18]. Furthermore, lean reduces infection rate and increases efficiency of operation room and trauma care in surgical healthcare settings [19, 20]. In a systematic review, Jadhav and colleagues have identified 24 barriers and lean success will not only depend on application of appropriate tools and techniques but also on the active participation of top management and leadership, workers' attitude, resources and the organizational culture [21]. In a case study from Sweden, many advantages of lean methodology were realized in the geriatric care concerning better communication, organization and workflow, though some challenges such as the difficulty to create long-lasting lean commitment were encountered [22]. Evidently, single case study is a sound approach as Six Sigma empirical researches are also reported to use single case study design [23].

Lean six sigma controls waste in healthcare or other industries. TIMWOOD (alternative WORMPIT) is an acronym for WASTE. Transportation (T) means does not transport something farther than necessary. Inventory (I) means do not have excess stock of anything. Motion (M) here means unnecessary motion to complete the task. Waiting (W) for anything is waste. Over-processing (O) is the processing what the customer does not want. Over-production (O) reflects making too much. Defects (D) indicate work that needs to be redone [24]. Concerning healthcare, lean approach is perceived variably by concerned staff in hospitals [25]; however it has a potential role in clinical laboratory [26], interventional radiology [27] and surgery [28]. It also guides quality management and improvement among in-patient population [29], improves emergency department workflow and delivery of services in line with severity index [30] and streamlines biomedical clinical and translational research [31]. Overall, LSS has multiple applications in healthcare industry including prevention of adverse events and MEs, reduction in inpatients' length of stay [32], costs and risks to nurses and physicians from cancer drugs [33]. However, more research needs to be done to evidence its impact on quality of healthcare [34]. In a prospective observational study with 131 patients, Font Noguera and colleagues reported that a proportion of patients with a medication error was reduced from 61.0% to 55.7% in four months. Furthermore, percentage of errors decreased in the different phases of the process including prescription (from 5.1% to 3.3%), preparation (from 2.7% to 1.3%) and administration (from 4.9% to 3.0%). Interestingly, nursing complaints decreased from 10.0% to 5.7% with considerable cost saving [35]. Currently, Luton and colleagues reported a blended quality improvement approach concerning milk in pharmacy practice [7]. This paradigm comprised of a model for improvement, Lean and Six Sigma methodologies, and principles of high reliability organizations to identify and drive short-to long-term developments concerning neonatal human and formula milk feeding to critically ill neonates in intensive care unit [7]. Besides improving entire dispensation system of human and formula milk, this blended technique reduced feeding errors by 83% [7] and, thus, enhancing safety of neonates. According to some researchers, Six Sigma and Lean requiring clear approach to integrate the two tools for overcoming their independent shortcomings are repackaged versions of two previously used quality methods, i.e., total quality management and just-in-time, respectively [6]. Accordingly a new method would be process-oriented that will bring organizational improvements [6, 36, 37] and innovations when LSS is integrated with other methods (holistic approach) that are better suited to breakthrough creativities, i.e., multiple disruptive innovations [38].

Six Sigma (SS) is a method to discover customer requirements and meets them with minimal variation. Alternatively, SS is a set of techniques and tools for process improvement and is used in industrial sector and more recently in healthcare to improve patient safety by eliminating life-threatening errors and other potential risks associated with repeated exposures to radiation in radiology setting [39]. In a study from Taiwan, Chan implemented SS methodology for reducing pharmacists' dispensing errors which is the second most common error. Furthermore, SS is needed to catalyze the combination of quality, cost, and patient safety. In addition, the results indicated reduction in costs and enhanced patient safety and their satisfaction [40]. In another study involving home-delivery pharmacies in USA, Castle and colleagues reported reduction in MEs concerning wrong-drug selection, wrong directions, and sound-alike and look-alike errors, and suggested that continuous quality improvement programs should be in place for providing pharmaceutical care to patient population at their homes [41]. In Saudi Arabia, Lean Six Sigma application in a tertiary care hospital was reported to improve pediatric care, costs reduction and sustained care [10].

Notably, in several studies SS derived control charts demonstrated evidence of sustained process improvement and actual reduction in specific ME elements [42, 43]. In addition, SS seeks to improve the quality of the output of a process by identifying and removing the causes of defects or errors and minimizing variability in manufacturing and business processes, and by extension in healthcare where a defect could reflect the difference between life and death. SS uses a set of quality management methods including empirical and statistical, and creates infrastructure of expert people within the organization. Overall, SS has a variety of interventions and applications in healthcare with effective outcome [42, 43, 44]. Like lean process, each Six Sigma project carried out within an organization follows a defined sequence of steps and has specific objectives and value targets including costs reduction and enhancement of customer satisfaction and safety (Figure 3 & 4). LSS organization structure has four belts including yellow belt responsible for lean six sigma awareness, green belt focuses on tools usage, DMAIC (definition, measurement, analysis, improvement and control) and lean principle application, black belt signifies full time project leader and master black belt (MBB) means black belt trained with at least two years experience and teaches lean six sigma (Figure 4). SS utilizes more than 18 established quality-management tools including 5 Whys, Fishbone diagram, Run Charts, Pareto chart, RCA, and SIPOC analysis (suppliers, inputs, process, outputs, and customers) [42]. The underlying concept of SS is $Y = f(x_1, x_2, \dots)$ introduced to drive focus on improving critical

process inputs rather than just outputs items of reports, services, deliveries, and sales, and determination of critical X's [$Y=f(x)$] for finding out the output responses (Y). Critical X's inputs (factors) include: operating and training budgets, system requirement, and number of people, operating hours, functional requirements, and customer interface and skills selection. These factors input into process (Info Systems Release) to know outputs responses (Y) related mainly to delivery time. LSS methodologies have diverse applications in healthcare and have five stages in terms of (Recognize) definition, measurement, analysis, improvement (design) and control (verify) [RDMAIC, DMAIC and DMADV/DFSS (design for Six Sigma)] and most commonly focused on improving an existing process [44,45]. SS meets failure in case there is lack of benefit quantification and management buy-in, no tangible results, lack of resources, seems too complicated and weak coaching and skills of human resources [44,45]. In a study to enhance patient safety outcomes, continuous quality improvement (CQI) and lean management initiatives (LMI) were significant in intervening hospital error sources. Six sigma initiatives (SSI) were not significant after accounting for the other two process improvement (PI) types. CQI and SSI were significant concerning organizational effectiveness improvement whereas LMI was not significant compared with other two PI types. Notably, SSI was significant for superior sustainable competitive advantage [46]. Overall, integrating all three PI tools will significantly impact medical errors. More studies are needed as there are significant gaps in the LSS healthcare quality improvement data and also to strengthen evidence that LSS improve health care quality [47] and safety.

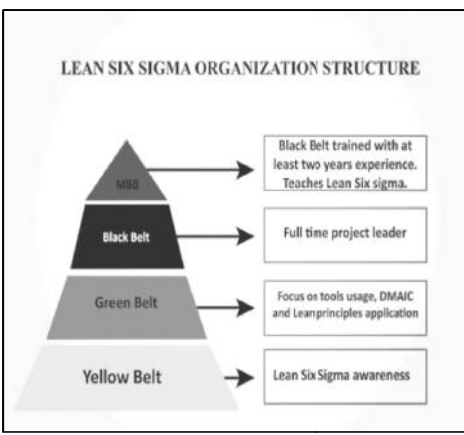
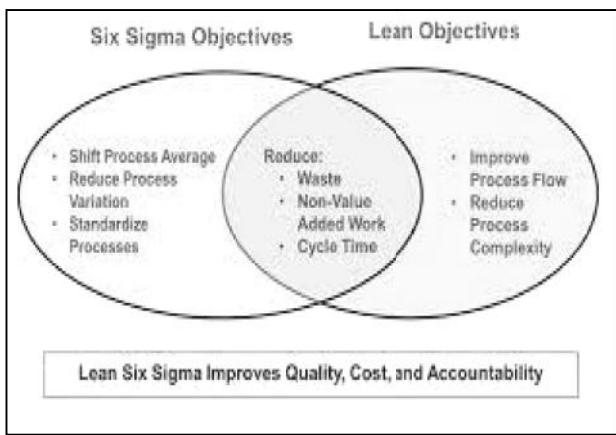


Figure 3 SS and Lean individual and sharing

Figure 4 Lean SS Structure with four belts:

objectives. yellow green, black, and master black .

Table 1 Lean Six Sigma Approaches and key principle

Approaches	
Concept	Remark
Lean	A culture using tools aimed at minimizing waste and creating more value while doing less work
Six Sigma	A data-driven approach to error reduction by improving processes and reducing process variability
Key principles of Lean Six Sigma	
Focus on customer- Patients as well as physicians (may include caregivers)	
Identify and understand how work is get done in hospital settings (the value chain)	
Manage, improve and make workflow more efficient	
Remove non-value-added steps and waste	
Manage the hospital data to reduce workflow variations	
Empower the people in the process (by involving and equipping them)	
Systematically undertake improvements in all activities	
Differentiation between Lean and Six Sigma	
Lean	Six Sigma
Requires a long term vision	Requires only a short term vision
Culture based	Project based
Requires input from all within the organization	Requires input from very few
Needs fact	Needs data
Is a system	Is a tool
Requires behaviors that demonstrate respect	Demonstrate a lack of respect
Accountability and engagement by all	Hierarchical belt system
Aims for flat organization structures	Builds in levels of distinction

Approaches and Principles of Lean Six Sigma

The approaches and principles of Lean Six Sigma help in the process improvement [Tables 1]. Lean Six Sigma is the integration of two powerful business improvement approaches in production organizations as well as in health industry [48]. Lean focuses on fast speed of finishing work and elimination of waste. Meaning thereby, it reduces waste and increases process speed in manufacturing industry and healthcare settings. Its focus is on implementation of waste reduction tools. Lean uses methods of improving events value stream mapping. Overall, Lean speed enables six sigma quality by faster cycles of experimentation or learning, thus it increases efficiency and leadership role changes [49]. On the other hand, SS improves quality and cost. The goal of SS is to improve performance on items critical to customer quality (CTQs), and focus on to use DMAIC with total quality management (TQM) tools to eliminate variation and its methods include management

engagement, infrastructure, and dedicated team effort [50]. The quality of SS enables Lean Speed in the form of fewer defects which means less time spent on rework. Thus, SS is closely linked with effectiveness and, in turn both efficiency and effectiveness as shown in healthcare setting [51]. Cycling operates simultaneously, and success is dependent upon the value of other inherent variables (data and data analysis and cause validation) in the function concerning the process and the quantifiable results are not readily apparent because the problem in using the SS Improvement Cycle is the length of time required which is three to six months to realize any benefits. Unlike SS improvement cycle (Figure 5a) of DMAIC, the cycle of LSS represented by Deming's Plan-Do-Check-Act Cycle (Figure 5, PDCA) is specifically associated with typical quality measures and continuous improvements. It differs from Plan-Do-Check-Act Cycle of value addition in which the difference between output and input prices and the critical roles of all functions in the process of value addition are evaluated and visualized [52]. More details of PDCA are available here [52, 53].

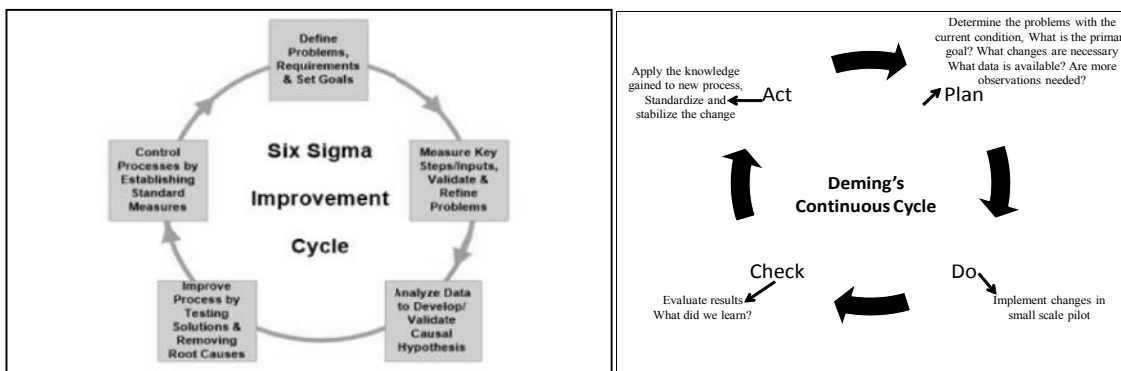


Figure 5a SS improvement cycle Figure 5bAdapted Deming's Plan-do-check-act cycle [26]

However, PDCA briefly refers to a continuous and ongoing effort to achieve measurable improvements in the efficiency, effectiveness, performance, accountability, outcomes, and other indicators of quality in services or processes which achieve equity and improve the health of the community. Notably, this definition is approved by Accreditation Coalition [53]. Other fundamental principles of lean approach (Table 1) are equal involvement of and equal respect for all staff members, standardization of work processes with improvement of flow, use of visual cues to communicate and inform, and use of specific tools to perform targeted data collection and analysis for the implementation and guide change [54,55]. Lean tools described in the literature facilitate a number of tasks including value stream mapping for visualizing the current state of a process and identifying activities that add no value. The RCA determines the fundamental cause of a problem or errors and

team charters plan guide, and communicate about change in a specific process. Furthermore, the management dashboards monitor real-time developments and a balanced scorecard oversights strategic planning in the areas of finance, customer service, internal operations, and staff development [55, 56]. Lean thinking and six sigma methodologies face some implementation challenges. The solutions include multidisciplinary team approach, involvement of all stakeholders, and the willingness of team members to change daily practice and to adapt new and innovative ways to deliver healthcare [57]. In another study of mid-sized hospitals, Esimai used lean six sigma strategies to change policy and practices as a solution for preventing MEs. Following implementation of solutions, there was a reduction in MEs, labor costs fell and patients were more satisfied and overall employees morale was high [58]. Using similar approach in a corporate hospital in India, Miglani reported a decrease in MEs, the complexity of the work flow simplified and systematized, nurses' work load was decreased, and the average time for drug administration was decreased by 55%. Thus LSS reduced MEs and simplified the work of nurses in ward and delivered patient care with high quality and efficiency [59].

As mentioned earlier, Like DMADV, DMAIC is a problem solving methodology that helps in the prevention of MEs [60-64]. DMAIC has 5 steps, and D- defines the opportunity from both business and customer perspectives. Measure - means to understand the process and its performance. Analyze - is for searching the key factors (critical X's) that have the biggest impact on process performance and determine the root causes. Improve - [Design related to DMADV] reflects to develop improvement solutions for the critical X's. Lastly, Control-[Verify related to DMADV] signifies to implement the solutions and control plan (for related questions see Table-2) [44,45]. Six Sigma uses these two methodologies (DMAIC and DMADV) for projects aimed at improving an existing business process rather than developing new process and projects aimed at creating new product or process designs, respectively [44,45, 62, 64]. According to some studies on lean methodology, client (patients) value-added is used to describe any activity such as easy access to healthcare service that contributes directly to satisfying the needs of the client, and non-value-added refers to any activity such as waiting in long queue that takes time, space or resources but does not contribute directly to satisfying client needs. Furthermore, new strategies such as successful engagement of staff and central focus on accessing services should strike a balance between value added and feeling valued [65]. In a study from Saudi Arabia, Almorsy and Khalifa analyzed the data derived from the Six Sigma DMAIC approach used to reduce over

utilization of resources in healthcare. There was a decrease in the unnecessary quality control (QC) runs from 13% to 4%, a reduction in the failed QC runs from 14% to 7%, and a drop of the QC to patient testing ratio from 24/76 to 19/81[66]. Thus, healthcare costs could be reduced if resources are used efficiently using six sigma DMAIC approaches and principles. More details of six sigma DMAIC tools, their roles, and as critical success factors are given here [67].

Table 2 Value Add – From the Customer Perspective

Customer Value Add (CVA) Questions	Business Value Add (BVA) Questions	Non-Value (NVA) Questions
Does the task add form, feature, or function to the process or service?	Does this task reduce owner financial risk?	If the customer knew we were doing this, would they request that we eliminate the activity so we could lower our prices?
Does the task enable a competitive advantage (reduced price, faster delivery, fewer defects)?	Does this task support financial reporting requirements?	Does the task fit into either of the other two categories?
Would the customer be willing to pay extra or prefer us over the competition if he or she knew we were doing this task?	Would the process of producing/selling the service break down if this task were removed?	Can I eliminate or reduce this activity?
Example CVA Activities: Improved Safety, Shorter Deliver Times, Fewer Errors and Accurate Reporting	Is this task required by law or regulation?	Typical NVA Activities: Over Inspecting, Transporting/Moving, Stocking/Storing, Rework Loops, Multiple Signoffs, and Document Handling
Overall solution– Optimization	Typical BVA Activities: Reconciliations, Internal Audits Invoice Processing, IRS/OSHA/EPA Reporting, and Internal Financial Reporting	Overall result - elimination
Overall, action– minimization		

IRS=Internal Revenue Service, OSHA= Occupational Safety and Health Administration, EPA=Environmental Protection Agency

Audit

Audit is a function of a finding for example medication errors that allows stakeholders to fully understand what occurred, how significant the occurrence was, and how the personnel may be able to effectively protect against its reoccurrence in a blame free

culture[68, 69]. According to some researchers, audits in real time ensure safety of patients in critical care. Audits are a useful tool for modifying clinical practice in line with provided guidelines, care processes, actions and minimizing errors in critical settings with high care load and acute diseases with severe degree [70,71]. Besides failure mode and effects analysis (FMEA), RCA and other quality improvement tools such as LSS, random safety auditing with feedback is an important tool for system analysis and redesign focused on providing safe delivery of care not only in the complex neonatal intensive care unit system [72] but also other health care settings including infection control units and outpatient clinics with better outcomes [73, 74]. More details of audit process in healthcare industry including end-of-life care are available here [75-78].

Root Cause Analysis

Root cause analysis is one of the elements of effective auditing and risk management strategies [79]. While conducting RCA [9], four questions need to be answered including what should be the criteria, what condition does exist, what effect related to the impact of the difference, why the difference exist to know the cause, and what is a possible remedy (ies) should be included in the list of recommendations. RCA has several critical steps [Figure 6] and is a process for identifying the most basic factor(s) underlying a variation in performance, such as detection and reporting of adverse drug reactions and events including medication errors by health professionals. Most importantly, RCA focus needs to be on systems and processes but not on individual healthcare workers [80-82]. In other words, RCA is a process of determining the causes of active and latent errors that led to a nonconformance, adverse event or undesirable condition [83]. RCA identifies corrective actions to prevent recurrence of events which, when solved restores the status quo or establishes a desired effect [83]. The Joint Commission Root Cause Analysis and Action Plan tool has 24 analysis questions that facilitate RCA in finding the main cause of the problem [84]. Furthermore, root cause analysis is a retrospective, structured method and involves thorough review of the problem in order to identify and verify the underlying prime cause of medication errors or symptoms and adverse drug events [83-85]. Thus, identified root causes are controlled by risk management team by specifying workable corrective measures, and allow for the generation of charts, recommendations and their implementation in healthcare industry. RCA is carried out in case of significant or consequential events, occurrence of repetitive human errors and system failures during a specific process, and low performance of workers contrary to desired quality standards. In addition, RCA prevents problems from

recurring, reduces injury to healthcare personnel, increases competitiveness and efficiency, promotes patient safety and outcome, improves communication about patient care, team work and stability of profession, and reduces cost [86]. Moreover, a thorough understanding of RCA is a key component in promoting safety within the healthcare, and risk reduction strategies used by healthcare professionals make RCA meaningful and efficient that impact safety of healthcare system [87]. Furthermore, several RCA-related tools useful in healthcare industry are identified and those are; 1) "five whys" approach, 2) cause-and-effect diagrams (Ishikawa), 3) causal tree mapping, 4) affinity diagrams, 5) interrelationship diagram, and 6) Pareto charts and 7) other tools [80,82] which are briefly described in subsequent sections.

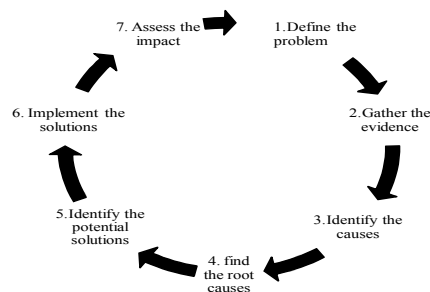


Figure 6 The adapted seven critical steps of RCA [81]

RCA- Root Cause Factor

Root cause is a harmful factor that results in the production of problem or adverse outcome in business organizations including health industry. Root cause is usually used to describe the depth in the causal chain where an intervention could be implemented to improve performance or prevent an undesirable outcome or event [88]. These adverse events may include medicinal incidents (i.e., MEs or close calls), injuries and adverse drug reactions. Causes or causal factors determine a condition or event that results in an effect reflecting cause-effect relationship (i.e., temporal) [89]. In RCA process, investigating team members should always see beyond obvious because the initial response surprisingly is usually the symptom, not the root cause of the problem [90]. To fix the problem, causal factor must be clearly defined using evidence-based RCA toolbox and corrected by implementing recommended solutions. Doggett (2004) compared 3 such tools, i.e., the cause-and-effect diagram, the interrelationship diagram, and the current reality tree to find out the differences but could not find the best tool for finding the underlying cause of the problem [88]. Notably, most times root cause turns out to be much more in terms of process or program failure,

system or organization failure, poorly written work instructions, and lack of training of healthcare professionals [91, 92]. Furthermore, Vincent (2004) criticized RCA based on its notion of single root cause and instead used the term system analysis [92].

Root Cause Analysis - Tools

There are many quality improvement tools for determining the root cause of adverse drug events including adverse drug reactions and medication errors. These tools are; 1) the “5 Whys” relates to 5 questions that need to be asked while doing RCA [Figure 7], 2) data collection and prioritization-Pareto statistical analysis identifies vital few (20%), and trivial many (80%), and the focus is mainly only critical few causes [Figure8], 3) brainstorming that allows team members to openly discuss comprehensively the cause and effect dimension, 4) flow charts or process mapping, 5) cause and effect diagram, 6) causal tree diagram, 7) affinity diagrams, 8) scattered diagrams, 9) event and causal factor analysis, 10) failure mode and effects analysis (FMEA), 11) change analysis, 12) barrier Analysis, and 13) management oversight and risk tree (MORT) analysis[93-95].

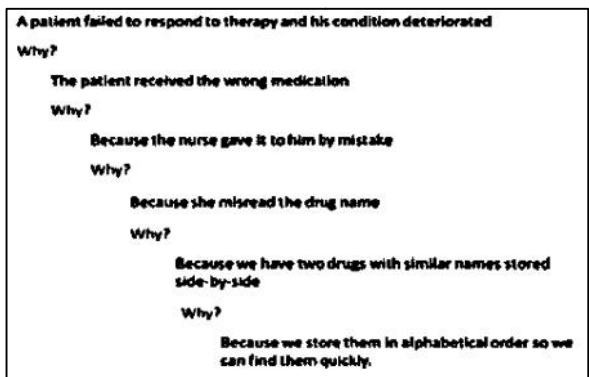


Figure 7 The "5" whys

After root cause is found, benchmarking which is the process of identifying, understanding, and adapting outstanding practices and processes for improving the performance of healthcare organization including reduction in adverse events is followed by recommendation generation and their implementation [80, 88, 96, 97]. Finally, the effectiveness of RCA is based on anecdotal evidence, a limitation and, hence, researchers called for more sophisticated studies to demonstrate that it overall improves patient safety and saves costs in healthcare industry [98]. It is wise to know that all aforesaid tools are not required in root cause analysis for finding a causal factor (s). Furthermore, more details how RCA is conducted in hospital setting are available here [9].

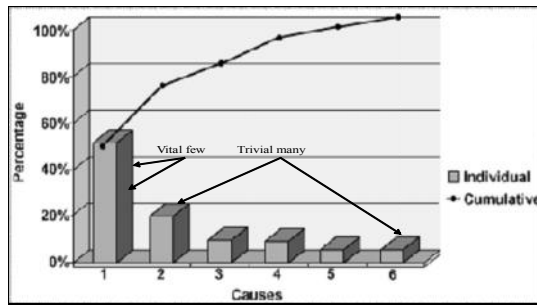


Figure 8 Pareto Charts 1(vital few) and 2-6 (trivial many)

1. RCA- the 5 whys

The “5 Whys” is an iterative question-asking technique (Figure 7). Its primary goal is to explore the cause-and-effect relationships underlying a serious problem. The serious events (and serious medicinal errors) are seen not only in manufacturing industry but also in healthcare organizations worldwide. The “5” in the name derives from an empirical observation on the number of iterations typically required to resolve the problem, which needs to be considered from three perspectives, i.e., physical, detection and systemic (Figure 9). However, RCA team may ask more than 5 questions to systematically organize and analyze data. The “5 Whys” help identify the root cause (s) of a problem, and determine a relationship between different root causes of a problem. This process is simple and easy to complete without personal opinion and statistical analysis. It is relatively more effective when problems involve human factors or interactions. Moreover, implementation of corrective steps mostly stops recurrence of the same problem in future [93, 99].

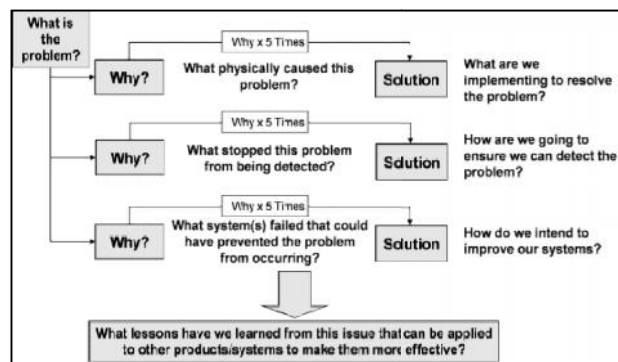


Figure 9"5 whys"

In addition to other quality management tools including flowchart, nominal group, matrix decision, decision table, the cause-effect diagram depicts visual display of possible causes, real causes and guesses, and cause categories which include materials, machines,

methods, and people, and reveals gaps in existing knowledge and systems [9, 95]. After cause-effect diagram (Figure10), RCA multidisciplinary team members identify likely candidates for root cause(s) by one of the actions. They look for causes that appear repeatedly within or across major cause or process categories. Members focus changes or other sources of variation in the process or environment. Team members use consensus decision-making to select a cause (s) and collect data to confirm a potential root cause as real and finally recommend risk reduction strategies for preventing error recurrence [95]. **Problem ranking** is an objective way to rank problems or root causes rather than simply picking the favorite option (Figure11). **Statistical process** controls variations related to common cause and special cause. Process needs to be stable, and if not, points outside lower control limit/upper control limit that warrant investigation and alert for problems (Figure 12).

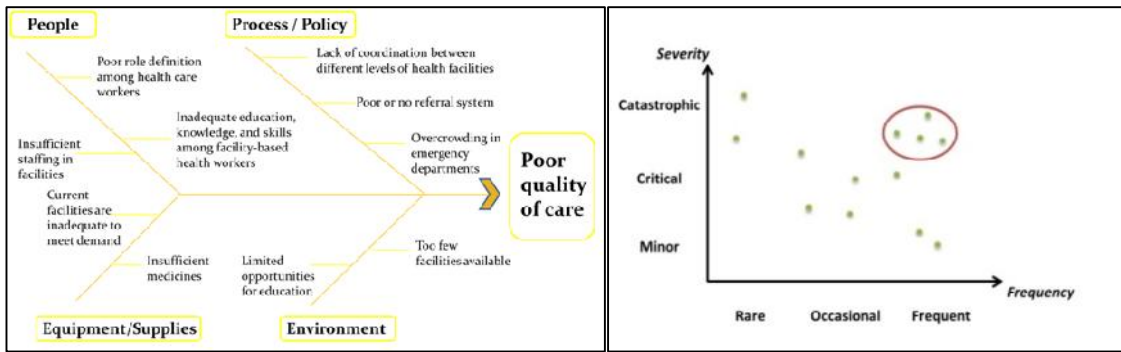


Figure10. Cause and Effect (Fishbone) **Figure 11.**Problem ranking

2. RCA- Decision Table and Scatter Diagrams Test

The Decision Table considers the severity levels of events and reflects whether the event was potentially life threatening or involved a serious injury. Furthermore, decision table also looks for its (event) potential for minimal harm or temporary injury, or no realistic potential for harm. The table also considers the probability of recurrence and the detectability of the event. Scatter diagrams test for possible cause and effect relationships with some variation. Relationships being tested must be logical and visually depicted (Figure 13) [82].

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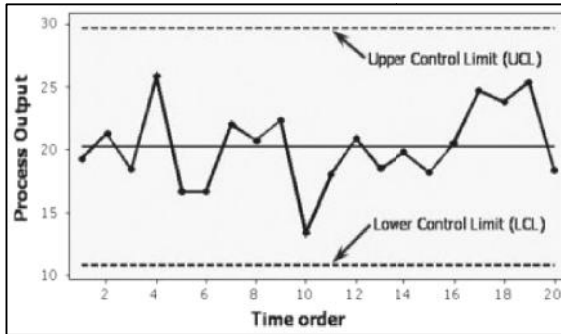


Figure 12Control chart

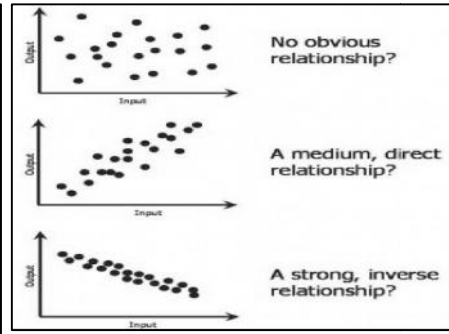


Figure 13 Scattered plot

3. RCA-Tree Diagram

Tree diagram (Figure14) states the problem and causes are listed as branches to the right of the problem with continuation to clarify causes, drawing additional branches to the right and repetition is continued until each branch reaches its logical end. In causal tree, the worst thing that happened or almost happened is placed at the top [82].

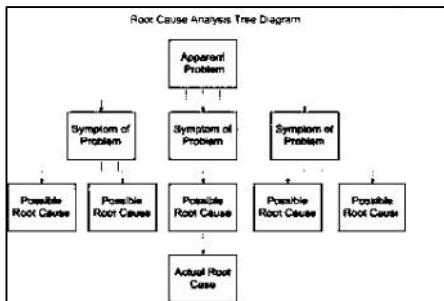


Figure14RCA – Tree diagram

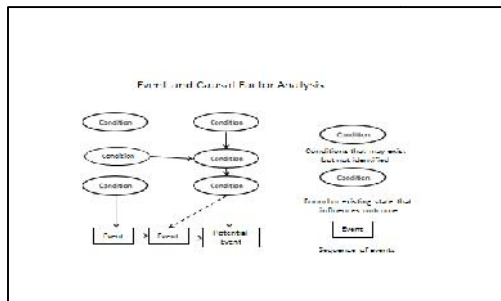


Figure 15 Event and Causal factor analysis

4. RCA- Event and causal factor analysis

Event and causal factor analysis is used for multi-faceted problems or long, complex causal factor chains and cause effect diagram usually describes time sequence (Figure 15). Furthermore, anything that shapes the outcome is recorded. It identifies what questions to ask to follow path to root cause. The results are displayed in an events and causal factor chart that gives a picture of the relationships of the events and causal factors.

5. RCA- and Change analysis

Change analysis is used when problem is obscure and generally used for single occurrence. It focuses on things that have changed and compares trouble-free process with occurrence to identify differences, and the latter are evaluated for contribution to occurrence. Change analysis steps include answer to the following questions that is what causes the change or event, when did happen, where did it occur, how it occurred and who contributed to the occurrence of the event.

6. RCA- and Barrier analysis

Barrier analysis is a systematic process to identify barriers or controls that could have prevented the occurrence and barriers may be associated with physical, administrative, procedural controls. It determines why these barriers or controls failed and what is needed to prevent reoccurrence.

6. RCA- and Management Oversight and Risk

Management Oversight and Risk Tree is used to prevent oversight in the identification of causal factors to physical, administrative, procedural controls and management factors that permit these factors to exist and questions for each factor on the tree are included [82].

7. RCA - Pareto Chart

A Pareto chart (Figure 8) is a graphical tool to prioritize multiple problems in a process so the team can focus on areas where the largest opportunities exist. Pareto charts are a type of bar chart in which the horizontal axis represents categories of interest. By ordering the bars from largest to smallest, a Pareto chart can help team determine which of the defects comprise the “vital few”, and which are the “trivial many.” The Pareto principle states that 80% of the effect is generated by 20% of the causes, and focus needs to be on the 20% [82].

8. RCA- Cause Charting and Process mapping

For identifying root cause, the Cause Charts and subject matter experts are used to gain a proper understanding of the event. Asking the right questions will help address the actual problem rather than focusing on the symptoms. Types of questions to ask are what is the scope of the problem?, how many problems are there?, what is affected by the problem?, and how often does the problem occur? The identification of root cause reduces the list of potential root causes through rank root causes using Pareto (Statistical) analysis, rank the

items in order of significance in term of organizational and identify the items with the most significant impact which include time, cost and manpower. Confirm potential root causes relate to the overall problem and verify that root causes identified have a causal relationship with the desired output, ensures the legitimacy of the measurement system as well as results are repeatable and reproducible. Notably, if the team cannot state the problem simply, team members do not fully understand the problem. It provides a structure for analyzing the information and identifying gaps and deficiencies in knowledge. Cause charting can also take the form of process mapping (Figure 16). The process map is simply an illustration that depicts the steps or events leading up to an occurrence. Finally, there are three basic steps to the Cause Mapping method which are define the issue (problem) by its impact to overall goals, analyze the causes by asking why did it happen in a visual map and prevent any negative impact on the goals by selecting the most effective solutions.

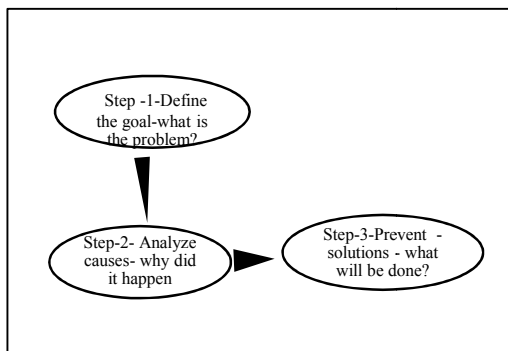


Figure 16 Cause Mapping,

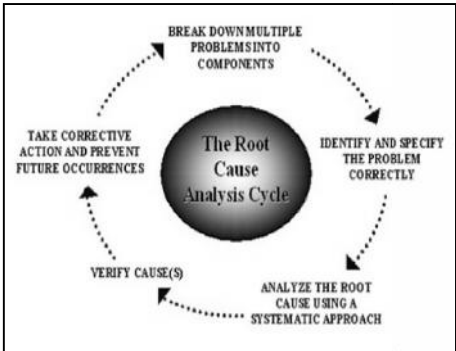


Figure 17 RCA cycle

9. RCA-Cause and Effect Diagram (Fishbone Diagram)

It is a tool to represent the relationship between an effect (problem) and its potential causes by category type and is carried out when a root cause needs to be determined. It helps ensure that a balanced list of ideas have been generated during brainstorming. Cause and effect diagram (Figure 10) determines the real cause of the problem versus a symptom and refines brain stormed ideas into more detailed causes. Cautionary note about cause and effect analysis is that it cannot get past existing knowledge - must have either observed (or considered) that the cause produced the effect in the past (retrospectively). More details of RCA toolbox and web-based tools including versions of BARCA based on the tenets of RCA for analyzing medical incidents are available here [82, 100, 101]. From ethical perspective, BARCA does not disclose the identity of medical incident report analyzer and relatively better technique as compared to other web-based tools.

9. RCA -Additional tools

Some additional RCA tools include fault tree analysis, current reality tree, Kepner-Tregoe technique or rational process with four phases including situation, problem, solution and potential problem analysis and rapid problem resolution [101,102,103,104], and all techniques including lean, lean sigma, SS and LSS help in finding the root cause of adverse events.

10. RCA-Data Collection

Data collection is must as it provides information and an understanding of causal factors. Good data collection techniques involve data types whether it is attribute or discrete and good or bad in terms of counts or percentages. The data should be collected in a planned way. For example about the event when it occurred and who reported it to incident reporting system. Furthermore, how the medical incident happened and how it is reported together with its stratification. In addition, recording sheets should be checked for consistency of data collection, and measurement system analysis ensures the data collection process is repeatable and reproducible [103,105].

11. RCA-Addressing root cause (s)-value added analysis

It is advisable to conduct value add analysis (Figure 18), a process in which a good or **poor** service is uncovered to its essential attributes or benefits. Those that contribute to the customer appeal are enhanced, and the others are reduced or eliminated. The investigating team must ensure that items identified will add value to the organization or customers as well as the items are required by regulation or policy makers. Overall, the team members confirm that the item does not add value and is not needed or required.

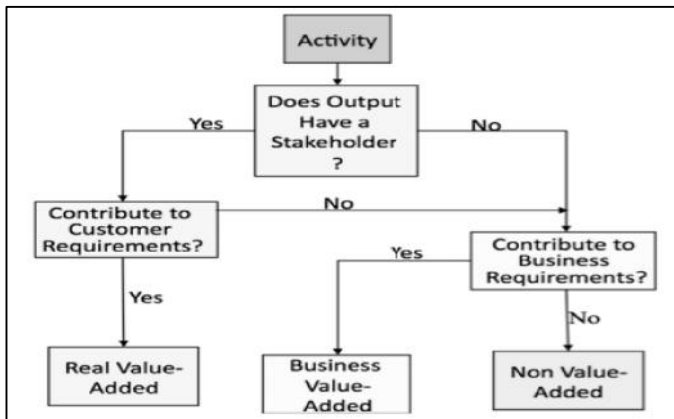


Figure 18 Value add analysis

12. RCA-Common Errors of Root Cause

Notably the investigating team members look for a single cause but often 2 or 3 contribute and may be interacting. The team often ends at a symptomatic cause. Furthermore, a common error is thus assigning symptomatic cause as the cause of the problem. This is but the “why” event that preceded the real cause. Successful application of the analysis and determination of the root cause should result in elimination of the problem and all stakeholders, i.e., patient, physician, nurse, pharmacist, administrator and team members should be satisfied. Concerning this, regular effective collaboration among various committees including Medication Safety Committee, Pharmacy and Therapeutic Committee and Patient Safety Committee is mandatory for performing a number of medication safe management tasks, developing annual action plan, conducting root cause analysis, and recommendation implementation [2,5,6,7,9]. Although RCA is a promising incident investigation technique, it has multiple problems including its name implying a singular, linear causal factor, questionable quality of many RCAs, their tendency to produce poor risk controls, investigating team not comprising of experts, and poorly functioning feedback reports. Lessons learned from RCAs and their effectiveness needs to be disseminated within and across healthcare organizations [106].

13. RCA-Recommendation Implementation

The team members should consider important things prior to implementation. First determine the impact the root causes will have on critical inputs (X) and estimate impact of the root cause on over-all output (Y). Second, from the perspective of management, implement recommendations based on significance to organizational goals and objectives, availability of personnel, finances or other essential resources, and complexity of the implementation. Finally, evaluate and monitor controls required to maintain corrective actions after implementation [103-105].

Discussion

Lean and six sigma methodologies are the best tools that streamline the quality and work performance of business industries and healthcare organizations [10-15, 26, 29, 30]. However, when the two methodologies are integrated, the end results in terms of efficiency, efficacy, production, customer satisfaction, waste and time management, costs, performance

variance and inconsistency, patients' safety and adverse drug events are reported to improve significantly [11, 13-16,36, 66]. Furthermore, lean and LSS has multiple interventional applications in all departments of healthcare industry including pharmacy, medical incidents, adverse events and medication errors [40,41,58,59,63], laboratory, radiology, medicine and surgery, geriatrics, trauma, inpatient and ambulatory clinical practice, and clinical and translational research [10, 12, 19-20, 23, 26-33,39], helps in the identification of root cause of any defect or adverse events [45,53,60-62,67], improves healthcare outcome [46] and create innovations in industry [38]. There are some barriers and challenges such as constrained budgets, training of novice professionals, resources and leadership, lack of strong evidence and cultural bottlenecks when lean, lean sigma and lean six sigma projects are introduced in business and healthcare organizations [21-23,34,37,50, 55-57]. The two problem solving techniques DMAIC and DMADV also used in LSS help in the prevention of adverse events including medication errors [60-64]. Lean six sigma also uses these approaches to improve an existing business process and create new product or process designs [44,45, 62, 64]. Furthermore, the application of lean methodology contributes to patients' value-added activity such as easy access to healthcare service linked with client satisfaction. Lean methodology also controls non-value-added activity such as long waiting time, space or resources but does not contribute directly to satisfying client needs [65]. However, successful engagement of staff and main focus on accessing services should strike a balance between value added to clients and feeling valued by healthcare staff [65]. LSS and SS mostly utilize a variety of quality improvement tools commonly employed in conducting root cause analysis of adverse events including medicinal incidents [45,53,60-62,67].

Root cause analysis, a retrospective, complex method uses a variety of quality and statistical tools to help in identifying the root cause of work performance variance and defects in business industry and adverse drug events in healthcare settings [107]. However, root cause analyses are reported to produce inconsistent benefits, negative responses, lack of strong evidence [85, 86] and, hence, needs further research. The "5 whys" technique commonly used in RCA for identifying root cause of adverse events including medicinal incidents is associated with multiple problems including investigating team comprising of inexperienced experts, focus on symptom rather than root cause, interactional issues, huge investment and looking for singular cause when the cause is more than one [86,108]. However, all above described powerful quality tools assist in improving a variety of health related issues such as waiting time, inconsistent performance of health workers, wastage,

601 medical incidents, adverse events, never events, efficiency, efficacy, injury, appointment
602 time, client satisfaction, quality of inpatient, outpatients, intensive care unit, and emergency
603 services and outcomes together with research accomplishments [13,102,107]. A
604 comprehensive guide for conducting RCA with performance improvement projects will assist
605 multidisciplinary investigating team to identify the root factor of adverse event, MEs, injury
606 and close calls [103,109]. Notably, like active errors, the root cause underlying latent errors
607 more often embedded in institution and regulation bodies, management, work environment,
608 team environment, health professionals, and task- and patient-related concerns [107]. The
609 implication of these results is that while conducting RCA using a variety of quality
610 improvement tools, investigating team must focus and explore these sources of medicinal
611 errors or adverse drug events in healthcare industry. In a related development, RCA software
612 tools are developed for finding out solutions of complex problems in medical and other
613 industries [110]. This narrative review has some limitations. Selection and publication biases
614 are the two limitations because there is huge literature on quality improvement tools and
615 programs in healthcare industry and some important publications might have escaped our
616 attention. Another limitation is healthcare industry is largely wider and we might have not
617 covered all relevant healthcare topics in this review. However, the strength of this paper is
618 that it provides important windows into most quality improvement tools including lean, lean
619 sigma, six sigma, lean six sigma, and root cause analysis and approximately 18 approaches
620 they use in improving the quality of diverse health perspectives in healthcare industry [42].

621 **Conclusion**

622 Lean six sigma methodology and RCA are now widely used in healthcare industry to
623 improve the quality of healthcare services, manage time and waste effectively, control and
624 prevent defects, injuries, adverse events including medication errors, close calls and adverse
625 drug reactions, improve patient safety, enhance patient satisfaction, reduces healthcare costs,
626 and improve health outcome. Further research is needed to overcome several identified
627 challenges and barriers for utilizing the full potential of these quality improvement
628 methodologies in healthcare industry.

629 **Consent:** not applicable

630 **Conflicts of Interest:** No conflicts of interest exist in this work.

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