ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ
Σχολή Επιστημών Υγείας
Πανεπιστήμιο Θεσσαλίας

# ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

## «ΜΕΘΟΔΟΛΟΓΙΑ ΒΙΟΙΑΤΡΙΚΗΣ ΕΡΕΥΝΑΣ, ΒΙΟΣΤΑΤΙΣΤΙΚΗ ΚΑΙ ΚΛΙΝΙΚΗ ΒΙΟΠΛΗΡΟΦΟΡΙΚΗ»

**Διπλωματική Εργασία**

# «Ο Στατιστικός Έλεγχος Διεργασίας ως εργαλείο έρευνας και βελτίωσης της υγειονομικής περίθαλψης:

# Συστηματική βιβλιογραφική ανασκόπηση εφαρμογών του Στατιστικού Ελέγχου Διεργασίας στη βελτίωση της περίθαλψης του παιδικού άσθματος»

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# POSTGRADUATE PROGRAMME

## «RESEARCH METHODOLOGY IN BIOMEDICINE, BIOSTATISTICS AND CLINICAL BIOINFORMATICS »

**Thesis**

## «Statistical Process Control as a Tool for Research and Healthcare Improvement:

## A systematic literature review of Statistical Process Control application in pediatric asthma care improvement»

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**ΠΕΡΙΛΗΨΗ**

Εισαγωγή:

Η εφαρμογή του Στατιστικού Ελέγχου Διεργασίας στον τομέα της υγείας επιτρέπει την παρακολούθηση της απόδοσης ενός οργανισμού, πχ. νοσοκομείου και τον προσδιορισμό της διακύμανσης εντός μίας συνεχούς διαδικασίας. Το διάγραμμα ελέγχου αποτελεί τη γραφική απεικόνιση των δεδομένων μίας διεργασίας ταξινομημένων στο χρόνο εντός προκαθορισμένων ορίων και προσδιορίζει τυχαίες ή ειδικές μεταβολές πριν και μετά την πραγματοποίηση μίας υγειονομικής παρέμβασης. Το άσθμα είναι η πιο συχνή χρόνια ασθένεια στα παιδιά και σχετίζεται με σημαντική νοσηρότητα και υψηλό ποσοστό νοσηλείας, αναδεικνύοντας την ανάγκη βελτίωσης της παρεχόμενης υγειονομικής φροντίδας.

Σκοπός της μελέτης ήταν η συστηματική ανασκόπηση της βιβλιογραφίας όσον αφορά την εφαρμογή των διαγραμμάτων ελέγχου σε παρεμβάσεις υγείας με στόχο τη βελτίωση της περίθαλψης παιδιών με άσθμα.

Μεθοδολογία:

Πραγματοποιήθηκε συστηματική αναζήτηση τριών ηλεκτρονικών βάσεων δεδομένων: MEDLINE, Cochrane Database και Web of Science, της βάσης δεδομένων του περιοδικού Pediatrics της Αμερικανικής Ακαδημίας Παιδιατρικής καθώς και των αντίστοιχων βιβλιογραφικών αναφορών. Η ανασκόπηση πραγματοποιήθηκε την 1η Σεπτεμβρίου 2020, βάσει των κατευθυντήριων οδηγιών PRISMA. Τα κριτήρια επιλογής τέθηκαν ώστε να προσδιοριστούν οι μελέτες που εφάρμοσαν τα διαγράμματα ελέγχου, οι παρεμβάσεις που υιοθετήθηκαν και αξιολογήθηκαν σε αυτές καθώς και οι περιορισμοί κατά την εφαρμογή του Στατιστικού Ελέγχου Διεργασίας.

Αποτελέσματα:

Η έρευνα κατέληξε σε 14 δημοσιεύσεις από το 2015 έως σήμερα. Εφαρμογές διαγραμμάτων ελέγχου εντοπίστηκαν σε διάφορους υγειονομικούς χώρους ενδο-νοσοκομειακά και εξω-νοσοκομειακά. Τα X-bar και s-διαγράμματα καθώς και τα p-διαγράμματα ελέγχου χρησιμοποιήθηκαν ως επί το πλείστον. Όλες οι μελέτες ανέφεραν βελτίωση μετά την εφαρμογή των παρεμβάσεων. Ωστόσο, οι ετερογενείς προσεγγίσεις στο σχεδιασμό της μελέτης, οι διαφορετικές συνθήκες εφαρμογής των μελετών και οι διαφορετικοί συμμετέχοντες επιβάλλουν προσεκτική ερμηνεία, προσαρμογή και γενίκευση των αποτελεσμάτων των μελετών.

Συμπεράσματα:

Τα διαγράμματα ελέγχου αποτελούν σημαντικό εργαλείο στην έρευνα και βελτίωση της υγειονομικής περίθαλψης. Καθώς η εφαρμογή τους καθιερώνεται σε όλο και περισσότερους τομείς της υγειονομικής περίθαλψης, οι περιορισμοί και τα εμπόδια του Στατιστικού Ελέγχου Διεργασίας θα πρέπει να διερευνώνται με προσοχή κατά την αξιολόγηση των αποτελεσμάτων.

## ABSTRACT

Background:

Statistical Process Control is widely applied in the healthcare sector for monitoring hospital performance and determining process variability. Control chart, the major SPC tool, provides a visual illustration of time ordered data within predefined limits and identifies types of variation (common or special cause) within a process. Asthma is the most common chronic childhood illness, associated with significant morbidity and a high hospitalization rate; indicating that there is always room for improvement.

The purpose of this study was to systematically review the literature and examine control charts application in quality improvement interventions in pediatric asthma healthcare.

Methodology:

A search of 3 electronic databases MEDLINE, the Cochrane Database, and Web of Science database, the database of Pediatrics official journal of American Academy of Pediatrics and reference lists was performed on 1rst September 2020. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Studies were assessed to determine the use of control charts, the healthcare interventions and limitations of SPC implementation in pediatric asthma care improvement.

Results:

SPC application has been reported in 14 publications since 2015. Literature survey showed that control charts were applied to different settings (inpatient and outpatient). X-bar charts paired with s-charts and p-charts were mostly preferred to assess changes over time. All studies reported improvement in standardizing asthma criteria and adherence to guidelines. However, the heterogenous approaches on QI design methods, the different study settings and various intervention-stakeholders imply careful interpretation, adaptation and generalization of the results across the studies.

Conclusion:

SPC control charts are a useful tool in healthcare improvement methodology. As their application is establishing across healthcare sectors, limitations and barriers of SPC methodology should be assessed with caution.



KEYWORDS:

quality improvement, statistical process control, control chart, asthma, pediatric, intervention, asthma-care

**TABLE OF CONTENTS**

**Tables**



**Figures**

## ABBREVIATIONS

| | |
|---|---|
| AAIRS | Acute Asthma Intensity Research Score |
| AE | Adverse Event |
| ALOS | Average Length of stay |
| CARAT-R | Childhood Asthma Risk Assessment Tool–Revised |
| CL | Centerline |
| CPG | Clinical Practice Guideline |
| CQI | Continuous Quality Improvement |
| CUSUM | Cumulative Sum Chart |
| CXR | Chest Radiographs |
| EB-CPM | Evidence-based asthma care process model |
| ED | Emergency Department |
| EMR | Electronic Medical Record |
| EWMA | Exponential Weighted Moving Average Chart |
| ICU | Intensive Care Unit |
| ITS | Interrupted time series analysis |
| LOS | Length of stay |
| LCL | Lower Control Limit |
| LWL | Lower Warning Limit |
| MPIS | Modified Pulmonary Index Score |
| NHS | National Health Service, UK |
| PASS | Pediatric Asthma Severity Score |
| PDSA | Plan-Do-Study-Act |
| PICO | Pediatric Intensive Care Unit |
| QC | Quality Control |
| QI | Quality Improvement |
| QI-MQCS | Quality Improvement Minimum Quality Criteria Set |
| RT | Respiratory therapist |
| SABA | Short-acting b-agonist |
| SLR | Systematic Literature Review |
| SQC | Statistical Quality Control |
| SQUIRE | Standards for Quality Improvement Reporting Excellence |
| SPC | Statistical Process Control |
| UCL | Upper Control Limit |
| UWL | Upper Warning Limit |

# 1. INTRODUCTION

## 1.1 Background

Performance improvement comes through changing the corresponding procedure. Any process has characteristics that can be measured, analyzed, improved, and controlled. Based on these characteristics, the capability of the process can be assessed and improved. Hence, we can evaluate healthcare systems, improve or change their outcomes, design policies and programs, by thinking of them as continuous processes (Berwick 1996; Benneyan et al. 2003).

Poor in-hospital quality, divisions from evidence-based treatments, the increasing occurrence of adverse events and in-hospital infections impose the implementation of healthcare interventions; aiming to a safer, patient-centered, timely and more effective, efficient and equitable healthcare provision (Institute of Medicine 2001). But not any change leads to better outcomes. Distinguishing changes that yield to improvement and those that do not, is mandatory to determine and implement new interventions (Berwick 1996; Benneyan et al. 2003).

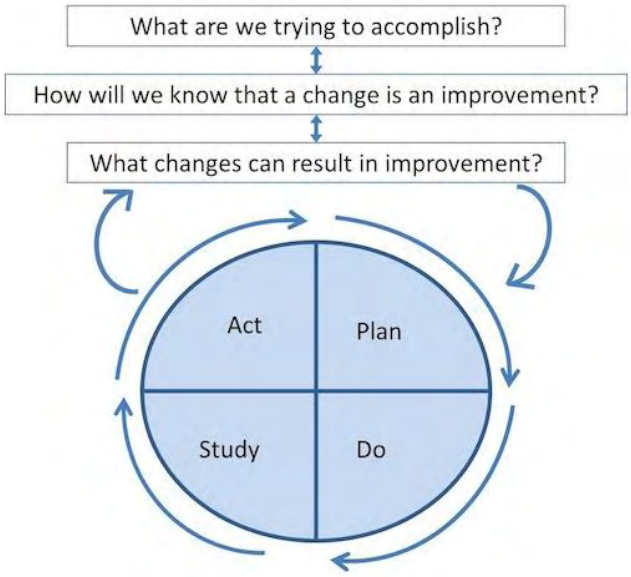
## 1.2 Quality Improving (QI) Interventions

Quality Improvement (QI) methodology is applied to detect this beneficial change, that implies stable and predictable results for patients and the healthcare system. QI is a systematic and continuous process; an enhanced effort to analyze the performance and improve outcomes. A QI program uses the established knowledge and clinical practice within the healthcare organization and develops multiple changes in-site. Implementing QI methods in healthcare requires primarily to well-define the healthcare gap, develop a focused goal, determine the possible improvement tool and select the measure outcomes (Institute of Medicine 2001).

QI studies include before-after intervention studies (controlled or uncontrolled), time series analysis (interrupted or not), and stepped wedge designs (Fan et al. 2010). Before and after studies measure the performance and possible differences between prior and post-implementation of an intervention in the same setting. A controlled before and after study enrolls a control population with similar baseline characteristics or performance to the study population (Grimshaw et al. 2000). In interrupted time series (ITS) design data are collected at multiple time points (e.g. weekly, monthly, or yearly) before and after an intervention (Hudson et al. 2019).

QI application involves several techniques such as, continuous quality improvement (CQI), six sigma studies, plan-do-study-act (PDSA) cycles or statistical quality control (SQC) (Nicolay et al. 2012; Portela et al. 2015). Running multiple PDSA cycles is the most common QI strategy. PDSA allows continuous testing and evaluating incremental changes in small cycles in order to successfully address three key questions related to the objective of the intervention (**Figure 1**) (Knudsen et al. 2019).

**Figure 1: The model of Improvement based on Plan-Do-Study-Act (PDSA) cycles approach**




*Source: (Langley et al. 2009)*

The key aspect of determining the beneficial change is to analyze and interpret the data and data variation (M A Mohammed 2004). Hence, a critical point on a QI study is to identify the variation within a clinical process. Every process includes inherited variation, but sometimes unexpected variation occurs, which may result in errors, clinical harm or poor outcomes for the patient. Determining performance variation can reveal the outcome of a process; the implementation's success or failure, or even the standardization of the procedure (Portela et al. 2015).

## 1.3 Statistical Process Control (SPC)

### 1.3.1 Methods and philosophy of SPC

Statistical process control (SPC) is the application of several statistical methods, in order to measure the performance, evaluate process productivity or modify the process for optimal results (Keller et al. 2015). SPC was originally used in industrial manufacturing processes. However, in 2000s SPC was adopted in the NHS (National Health Service, UK). Nowadays, its methodology is widely embraced in healthcare sector. SPC provides insights to researchers, clinicians and policymakers, so that they can observe, monitor and record process variability, evaluate the impact of applied interventions and achieve continuous improvement (Matthes et al. 2007; NHS 2017).

In 1928, Walter Shewhart developed a simple graphical method, the first SPC charts, in order to improve the quality of manufactured telephones at Bell Laboratories in the USA. He observed that

repeated measures of the same parameter did not always produce the same results; but the outcomes varied. Shewhart identified two types of variation within a process (Shewhart 1931).

i. Common Cause Variation; which is the natural (random) and inherent variation in a process on a regular basis. It can be predictable and indicates a completely stable process.
ii. Special Cause Variation; which is occurred due to unexpected events, unplanned situations, interventions under examination. These assignable causes imply that the process is unstable (Deming 1986; Benneyan et al. 2003).

The basic principles of SPC extracted from Benneyan *et al*. are presented in the following **Table 1**:

**Table 1: The basic principles of SPC**

| The basic principles of SPC |
|---|
| • Individual measurements from any process will exhibit variation. |
| • If the data come from a stable common cause process, their variability is predictable within a knowable range that can be computed from a statistical model such as the Gaussian, binomial, or Poisson distribution. |
| • If processes produce data with special causes, measured values will deviate in some observable way from these random distribution models. |
| • Assuming the data are in control, we can establish statistical limits and test for data that deviate from predictions, providing statistical evidence of a change |
| Source: (Benneyan, Lloyd, and Plsek 2003) |

Variation exists everywhere. Processes with common cause variation are stable and predictable within statistical limits; while procedures with special cause variation should be investigated. SPC provides signals when the entire process is out of control or variability between sample sets has increased. During improvement initiatives, understanding and exploring these causes of variation is the key aspect to assess how effectively changes affect a process. A special cause variation might be the result of a successful intervention in the organization or it might indicate a lower performance. Moreover, SPC advantage is that data are taken over time in an on-going process and so, it can easily determine the process sustainability after implementing the intervention (Harries et al. 2019; Hansen 2005).

There are seven basic SPC tools for process improvement (7 quality control tools, 7-QC):

1) Check sheet
2) Stratification
3) Scatter diagram
4) Histogram or Steam-and-Leaf Plot
5) Pareto chart
6) Cause and effect diagram
7) Control chart (Ishikawa 1982).

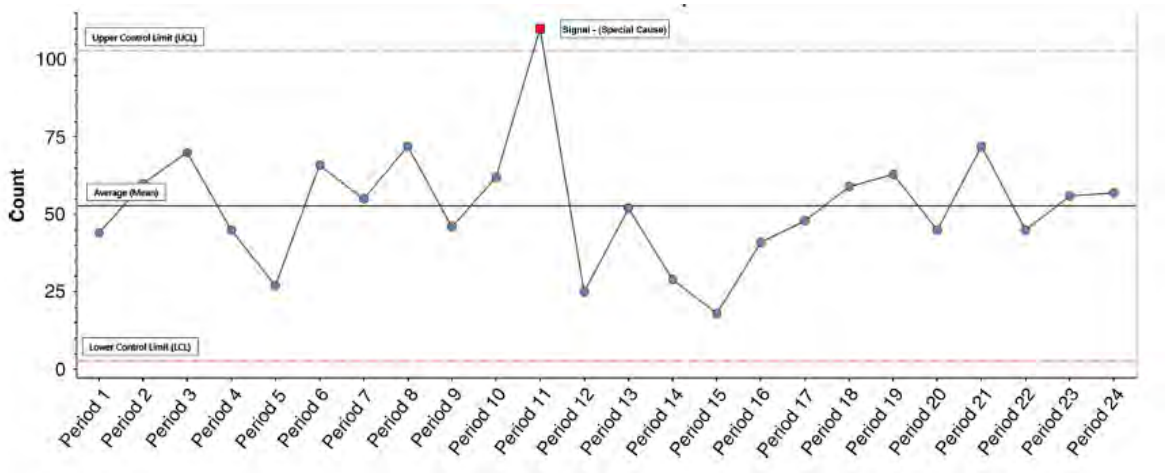
### 1.3.2 Shewhart Control Chart

The primary tool of SPC is the “Control Chart” (**Figure 2**) (also known as Shewhart chart), and it is a robust tool for distinction between two types of variation. A control chart is a simple graph with time ordered data, indicating the type of variation in an on-going process, presenting errors or deviations in the ongoing process and recognizing sectors that may need further investigation (Suman and Prajapati 2018).

The core elements of a control chart are:

a) Data displayed over time
b) A centerline calculated by the mean value (CL)
c) Two other horizontal lines, the upper and lower control limit (UCL, LCL) (**Figure 2**)

**Figure 2: Control Chart Example**




*Source: (Harries, Filiatrault, and Abu-Laban 2019)*

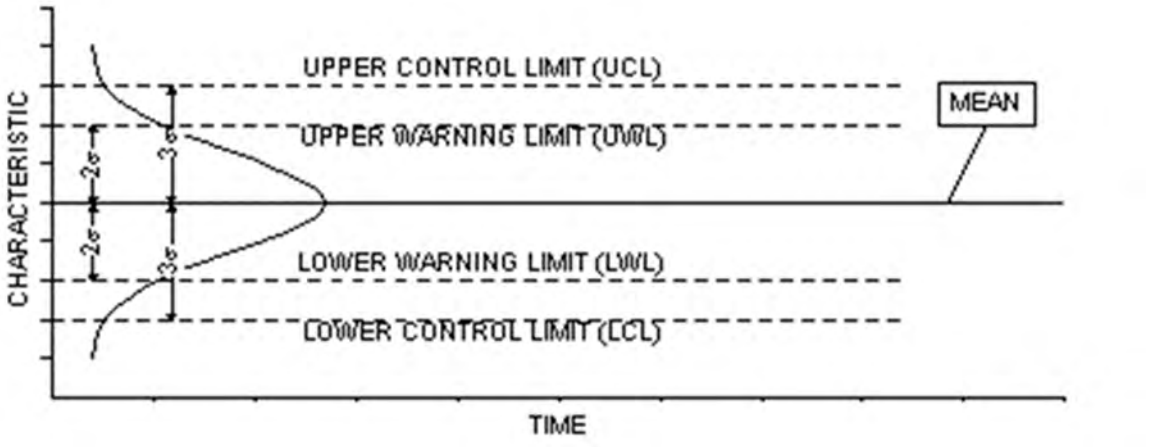
Control chart construction:

The two axes represent the time period (x: horizontal) and the unit of measurement (y: vertical). Data points refer to mean values of the sample taken at specific time points. Usually, 20 to 30 measurements are required to set the upper and lower control limits. Data is collected into sample sets in order to detect if the process is stable and controlled. The upper and lower control limits are calculate based on the standard deviation (SD) of the sample, depending on the type on the variable. The standard deviation describes the amount of variation in a measured characteristic.; how much a value measured is expected to deviate from the mean on average (Benneyan et al. 2003).

Shewhart and other SPC researchers recommended that control limits should be set at ± 3SD (three sigma limits) (Shewhart 1931). Although, control charts do not require normally distributed data. if data follows a normal distribution and the process is under statistical control, then 99.73% of the values should be between upper and lower limits. Moreover, it is optional to use additional warning limits set at ± 2SD; which are inside the control limits and define that when a process in on target, 95.0% of the values will lie within them. Hence, the limits are set as follows:

- Upper Control Limit (UCL): Average + 3 * Standard Deviation
- Upper Warning Limit (UWL): Average + 2 * Standard Deviation
- Centerline: Mean – Average
- Lower Warning Limit (LWL) – Average - 2 * Standard Deviation
- Lower Control Limit (LCL) – Average - 3 * Standard Deviation (**Figure 3**)

**Figure 3: Control Chart with Control and Warning Limits**




*Source: Technical manual on Quality Control; extracted from IAEA/FAO Co-ordinated Research Project*

Data points between ± 3SD of the mean centerline, ie. within UCL and LCL limits, demonstrate that the process is stable and in statistical control. Data points lying outside the upper or down control limit signalize special cause variation (red signal) (**Figure 2**). These signals may reveal the positive or negative impact of a particular intervention or change introduced to the standard process (Harries et al. 2019).

Notably, correctly applying the control chart on the ongoing process is critical. If the limits are set wrong, we will indicate false special cause variation. Particularly, by setting too narrow limits, there is a risk of ‘‘type I error’’ indicating that the process is out of control when in reality is in control (false positive special cause variation). On the contrary too wide limits might lead to a ‘‘type II error’’ and

the risk of claiming that a process is in control when it is not really in control (false negative special cause variation) (Benneyan et al. 2003).

There is a common set of rules to interpret a control chart and determine if the process is out of control:

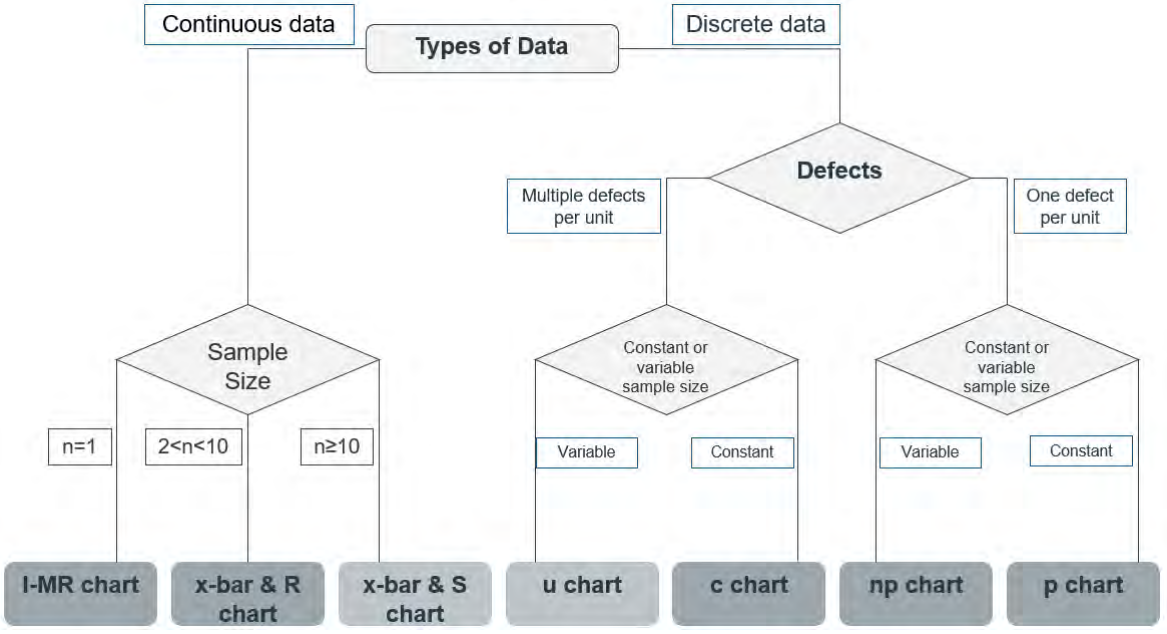
- if any point is beyond the specified ± 3SD (3 σ, three sigma) control limits
- if two out of three consecutive points are beyond the (± 2SD (2 σ two sigma) control limit on the same side of the center line
- if four out of five consecutive points fall beyond the ± 1SD (one sigma) control limit on the same side of the center line
- if a run of eight consecutive points is on the same side of the center line
- if six consecutive points are increasing or decreasing (a trend) and
- if there is an obvious cyclic behavior in consecutive points (Benneyan et al. 2003; Provost and Murray 2011).

### 1.3.3 Types of Control Charts

There is a range of control chart based on the characteristic analyzed:

- Control charts for variables (data on a continuous scale): x-bar and R, x-bar and S, I-MR
- Control charts for attributes (data as discrete distinctions or percentages): p, np, u, c

**Figure 4: Classification of control charts**



Controls chart are also classified based on sample size; control chart for rationally defined subgroups if there is more than one observation per subgroup (n > 1) and control chart for individual observations if there is only one observation (I-MR chart) (**Figure 4**). The study presents control charts formulas given that upper and lower control limits are at a distance of three standard deviations from the center line (Woodruff 2012).

**Control Chart for Continuous Data**

- X bar control chart

An *X-bar control chart* is used for continuous data to control the change in average value. It represents the mean value (or average) of a set of samples at a given time, plotted in order (hours, in hospital days, etc.). Each set of samples taken at regular intervals constitutes a subgroup. We can calculate the mean value and the three standard-error (3SD); and then estimate the control limits for the mean of each subgroup.

Centre line: Average X = $\sum_{i=1}^{k} \bar{x}$

UCL= Average X + 3SD (X)

LCL= Average X - 3SD (X)

where: average X=mean value of the subgroups average, x̄=mean value of each subgroup, k=the number of subgroups and SD=the standard deviation of the subgroup averages (Gejdo 2015).

- R control chart

An *R control chart* is used to control the change in variability. The R-chart indicates the variation of a process based on samples taken from the process at given times. It accompanies an X bar control chart and represents the sample-range, by calculating the minimum and maximum values. It is usually applied when the sample size is relatively small (n < 10). An *I-MR chart* (moving range) is applied when there is only one subgroup.

x-bar UCL= $X + A_2R$

x-bar LCL= $X – A_2R$

R central line: Average R = $\frac{(R_1+R_2+\cdots R_k)}{k}$

UCL= $D_4R$

LCL= $D_3R$

where: X= mean value of the subgroups average; R=average range of subgroup observations; k=number of subgroups; $A_2$: constant that depends on the sample size; $D_3$, $D_4$: constants

- S control chart.

An *S control chart* accompanies an X bar chart when monitoring variable data. It is applied paired with an *x-bar* chart, when there is a large set recorded (subgroup size ≥ 10) and represents the standard deviation within a sample set. The S-chart indicates the variation of the sample, by using the standard deviation of all data and not just the minimum and maximum values. A reduction in variability points out a more stable process.

Standard Deviation, SD= $\sqrt{\frac{\sum(x-\bar{x})^2}{n-1}}$, in each sample set

x-bar UCL= $X + A_2 * SD$

x-bar LCL= $X - A_2 * SD$

s-UCL= $B_4 * S$

s-LCL= $B_3 * S$

where: X= mean value of the subgroups average; SD=average standard deviation of subgroup observations; $\bar{x}$=mean value of each subgroup; $A_2$, $B_4$, $B_3$: constants

**Control charts for Discrete Data**

- p and np control charts

A *P control chart* is used for dichotomous variables, ie. when there is a pass/ fail (or yes/ no) data determination. It represents the defective unit proportion within a process over a period of time, indicating the portion of successes. In a p chart the sample size can be constant or variable over time (ie. the proportion of discharges from the hospital within 30 days).

Central line: $p = \frac{\sum n*p}{\sum n}$

UCL= $p + 3\sqrt{\frac{p*(1-p)}{n}}$

LCL= $p - 3\sqrt{\frac{p*(1-p)}{n}}$

where: p=Defective units over a period of time; n=subgroup size

An *np control chart* is similar to p-chart monitoring the number of defective units and it is applied when the sample size is constant over the sampling period. Both charts are based on binomial analysis theory.

Central line: np = $\frac{\sum n*p}{k}$

UCL= np + $3\sqrt{np*(1-p)}$

LCL= np - $3\sqrt{np*(1-p)}$

where: np=number of defective units; p=defective units over time; n=subgroup size; k=number of subgroups.

- c and u control charts

A *c control chart* is used when there are multiple types of defects in a unit (counting type), in order to indicate the number of defects as presented over the study period (ie. the adverse events). The sample size needs to be constant over a period of time.

Central line: c = $\frac{\sum c}{k}$

UCL= c + $3\sqrt{c}$

LCL= c - $3\sqrt{c}$

where: c=number of defects; k=number of subgroups

Accordingly, a *u control chart* monitors the number of defects per sample unit, while the number of samples may vary over sampling period. They are based on Poisson distribution theory (M A. Mohammed et al. 2013).

Central line: ū = $\frac{\sum c}{\sum n}$

UCL= ū + $3\sqrt{\frac{\bar{u}}{n}}$

LCL= ū + $3\sqrt{\frac{\bar{u}}{n}}$

where: c= number of defects; u=number of defects per unit; n= subgroup size.

In addition to the above charts, there are also other types of Shewhart control charts that can be used depending on available data. G control charts are applied for opportunities between rare events, presenting the number of events between infrequent events, but they are generally less preferable. Accordingly, T Charts are used for rare events between infrequent continuous data (NHS 2017).

Besides these, there are two charts for continuous data: CUSUM (Cumulative Sum Chart) and EWMA (Exponential Weighted Moving Average Chart); which are more sensitive for detecting a small or moderate shift in the process (Suman and Prajapati 2018).

Run charts are applied to display time ordered sequence of data with a median line, to monitor the process and demonstrate a central tendency. Although, run charts are useful tools to indicate upward or downward trends or unusual patterns in a process, they do not have any upper or lower threshold limits. As a result, they incorporate the element of subjectivity when interpreting the results (NHS 2017; Anhøj and Bjørn 2009).

### 1.3.4 Application of Statistical Process Control in Healthcare Improvement

The SPC methods can be applied to numerous processes such as manufacturing processes, finance, marketing, customer support and engineering development. Accordingly, it can be implemented on any healthcare process; including biological processes like blood pressure; clinical events such as adverse events from antibiotics and in-hospital infections; or organizational processes for instance length of stay in hospital and percentage of discharges. SPC can also be used to investigate pharmaceutical product compliance to GMP (Good Manufacturing Practice) (Eissa 2018).

According to Thor *et al*., SPC can be implemented in different fields of healthcare (specialties), such as, cardiology, allergology, nursing, pediatrics, emergency medicine, surgery, anesthesia and intensive care, urology, orthopedics, mental health or clinical chemistry. Moreover, it can also be applied directly to health indicators (asthma scores, diabetes index) and allows patients to manage their own health (Thor et al. 2007). Ten years later, Suman & Prajapati reported wide implementation of control charts in emergency, surgery, epidemiology, radiology, pulmonary, cardiology, administration and pharmaceutical departments (Suman and Prajapati 2018).

The purpose of the present study was to examine the literature for SPC application in QI interventions in pediatric asthma healthcare. Asthma is the most common chronic childhood illness, associated with significant morbidity and a high hospitalization rate. Unfortunately, the evidence-based asthma care endorsed by guidelines differs from the actual care provided to hospitalized children. According to the American Academy of Pediatrics there is an unmet need for improving interventions and research in pediatric asthma-healthcare (AAP 2009). We systematically reviewed the literature to find different settings of SPC control charts applications on QI interventions associated with pediatric asthma; the implementation, types and frequency of control chart used as well as the interventions that these studies have been conducted for.

# 2. SYSTEMATIC LITERATURE REVIEW

## 2.1 Search Strategy

This systematic literature review (SLR) was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al. 2009).

### 2.1.1 Research Question

Research question was structured by following the PICO model (Schardt et al. 2007):

- Can Statistical Process Control (SPC) methodology be applied to evaluate asthma-related healthcare interventions in pediatric population?
- How are SPC and control charts implemented to measure the impact of an asthma-related related intervention intended to improve pediatric asthma?

### 2.1.2 Inclusion and Exclusion Criteria

All included studies were conducted at pediatric population (newborns, infants, children and adolescents; aged 0 to 18 years old) with a primary asthma diagnosis, asthmatic status or asthma exacerbations. We reviewed any quality improvement study reporting interventions aiming to improve asthma care in-patient, out-patient and at community settings. We undertook the usage of control charts for special cause variation in an on-going process and process standardization. The analysis of all eligible studies was based on SPC methodology and appropriate control charts to interpret asthma-related interventions and determine the success of the QI process.

Studies without SPC control charts application were excluded from the review. Publications that did not evaluate interventions in patients with asthma as a primary diagnosis, such as pneumonia, bronchiolitis, and in pediatric population (aged 0-18 years old); as well as tutorials, letters, book reviews and dissertations were excluded.

### 2.1.3 Search Strategy

A literature research was performed in order to detect journal articles related to statistical process control applications on pediatric asthma care interventions. To identify eligible studies, the research was conducted in three electronic databases PubMed (Medline), Cochrane Library and Web of Science on 1rst September, 2020, using the following string: ((((statistical process control) OR (SPC)) OR (control chart)) AND ((asthma) OR (asthma*))) AND ((((children) OR (child*)) OR (pediatric)) OR (adolescen*)).

Text availability included abstracts, full texts and free full texts, with no limitation regarding the publication date. Additional filters applied were “human species” and “English language”. Moreover, we screened all QI studies for asthma in the database of Pediatrics official journal of American

Academy of Pediatrics, for grey literature. Bibliographies of included studies were searched for further relevant studies.

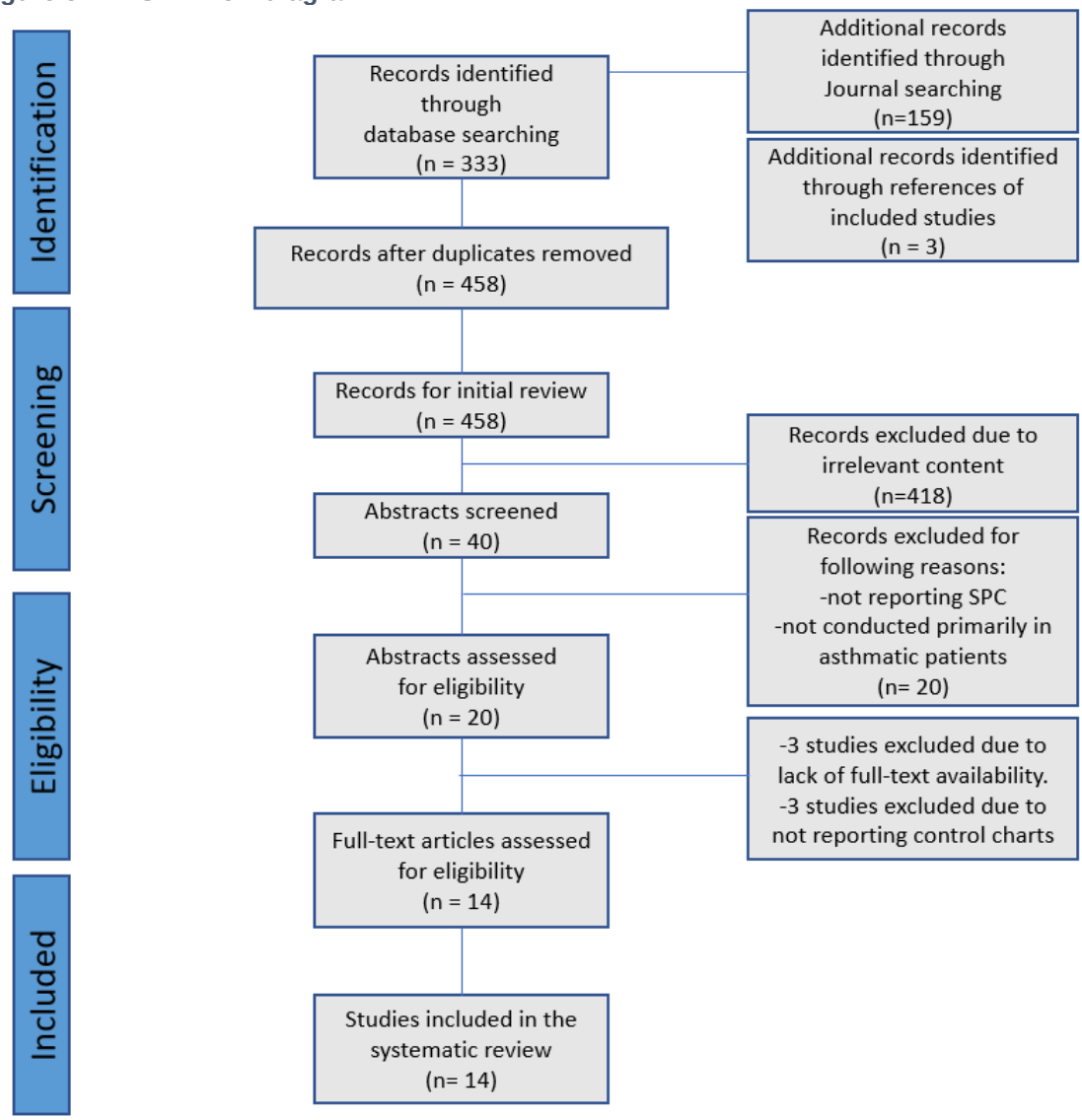
All retrieved references were managed by using Zotero as reference manager.

## 2.2 Studies Identification

### 2.2.1 Study Selection

**Figure 5** presents the PRISMA flow diagram illustrating studies selection (Moher et al. 2009).

**Figure 5: PRISMA flow diagram**



Initially 333 potentially relevant articles were identified through electronic database and 159 through pediatric journal searching. After duplicates were removed, 458 records were screened for relevance on title. 418 papers were excluded due to irrelevant content (ie. cost-effectiveness studies, randomized trials, genetic association studies, asthma management, asthma risks and biomarkers). We screened 40 abstracts and 20 were eligible for full study. Three of them were excluded because they did not report the application of control charts; and three studies due to lack of full text availability.

As a result, 14 QI studies were included in the SLR.

### 2.2.2 Quality Assessment of QI Studies

Reporting guidelines impose a specific form and structure of publication for quality improvement studies (Portela et al. 2015). SQIRE 2.0 (Standards for QI Reporting Excellence) provides standardized criteria for reporting QI interventions, which are available on the EQUATOR Network. The reporting quality of the 14 included studies was determined by SQIRE 2.0 checklist and it is presented in **Table 6 in Appendix** (Ogrinc et al. 2008; Ogrinc et al. 2016).

Subsequently, studies were appraised using the Quality Improvement Minimum Quality Criteria Set (QI-MQCS) framework. The QI-MQCS tool was developed on top of SQUIRE framework and it is a critical appraisal instrument that can be applied to healthcare QI intervention publications. It includes 16 domains that must be addressed by a dichotomous answer: Criteria met or not (**Table 2**) (Hempel et al. 2015).

**Table 2: Domains evaluated with QI-MQCS tool**

| | |
|---|---|
| **1. Organizational motivation** | It refers to a specific healthcare problem, reason or situation that requires the intervention (study's purpose or objective) |
| **2. Intervention rationale** | A short description of the current situation that requires the specific improvement, based on empirical medical evidence or relevant bibliography |
| **3. Intervention description** | A detailed description of the intervention applied at the healthcare organization (hospital, ED, ICU, outpatient care, community setting). |
| **4. Organizational characteristics** | Intervention setting, hospital size, patient population (ie. table with study population characteristics). It is necessary for evaluation study's generalizability. |
| **5. Implementation** | It includes the steps or phases of implementing the healthcare changes (ie. using the Plan-Do-Study-Act cycle approach). It refers to the staff involved (a group of physicians, a multidisciplinary team) and the key components to introduce the intervention in the healthcare organization. |
| **6. Study design** | The type or approach of QI evaluation (e.g., time series analysis, retrospective or prospective analysis, before and after- comparison). |
| **7. Comparator** | It describes the existing situation (standard of care) or patient group, prior to implementation |
| **8. Data source** | Data collection, Hospital data, electronic health records (EHRs) and the collection method |
| **9. Timing of intervention and evaluation** | A clear indication of baseline and intervention period |
| **10. Adherence/ fidelity** | It describes the compliance with the intervention over the study period and acknowledges the data lack or availability to indicate adherence to the intervention. It is necessary to evaluate the reason of the study's failure or success. |
| **11. Health outcomes** | Patient health-related outcomes as part of the evaluation (ie. mortality therapy safety and tolerance, re-admissions and length of stay, quality of life) |
| **12. Organizational readiness** | Culture and resources (e.g., QI committee, leadership commitment, education) or barriers, supporting or preventing the implementation |
| **13. Penetration/ reach** | The study reports information on the proportion of all eligible units who actually participated and acknowledges that not all patients identified met the inclusion criteria. |
| **14. Sustainability** | It includes a statement for positive evidence of the intervention or an extended duration of the intervention period as evidence of sustainability. |
| **15. Spread** | It described the potential that the study can be generalizable or replicated |
| **16. Limitations** | The authors report study's limitations |

Source: (Hempel et al. 2015).

# 3. RESULTS

## 3.1 Characteristics of QI studies included in the review

After systematically reviewing the available literature, fourteen studies with available full text were indicated; reporting SPC control charts application in pediatric asthma healthcare improvement. All included studies were conducted in the USA, from 2015 onwards. **Table 3** presents the characteristics of the QI studies, arranged based on study design, population, primary intervention, setting and data source, as well as primary outcome and results.

The studies were designed to compare the changes in asthma care between two time periods. Regarding the study design, most studies were before-and-after intervention studies; assuming that any observed difference in control charts was due to the intervention. Data was collected retrospectively from two separate time periods, extracted from hospital records (electronic medical records) or administration and billing data, to form the pre- and postintervention study populations. In Maue *et al.*, the subjects in the pre-intervention group and in the post-intervention group were obtained by different data sources (Maue et al. 2019), while Nkoy *et al*. collected retrospectively pre-intervention data and prospectively post-intervention data (Nkoy et al. 2015). On the contrary, Hatoun *et al*. conducted a longitudinal study following one cohort of 102 children over time (Hatoun et al. 2016). The sample could also be randomly selected (Brown et al. 2016)

Time-series (interrupted or not) analysis was conducted in most studies, to investigate if the observed outcome differs between post-intervention and pre-intervention period. Gray *et al.* applied time series-analysis to evaluate single interventions and SPC charts to assess changes over time (Gray et al. 2016). Plan-do-study-act cycles were implemented to test changes over time. Three studies provided sufficient documentation on PDSA cycles; describing the objective of each cycle and the changes tested (Bartlett et al. 2017; Lo et al. 2018; Hatoun et al. 2016), while Lo *et al.* conducted also an initial feasibility pilot prior to PDSA cycles (Lo et al. 2018). Six studies declared a specific quantitative aim and reached it (Hatoun et al. 2016; Gray et al. 2016; Brown et al. 2016; Bartlett et al. 2017; Watnick et al. 2018; Lo et al. 2018)

SPC methods had been applied in a wide range of settings. Five studies examined pediatric asthma in emergency department (ED) (general, pediatric-specific or community), two concerned children with asthma exacerbations in the intensive care unit (ICU) and one in a pediatric ward, three were conducted throughout the entire hospital; two studies also included the outpatient setting and one study investigated an evidence-based clinical practice guideline in 8 different hospitals.

### Table 3: Characteristics of QI studies included in the review

| Reference | Study Design | Population – Sample size | Intervention | Data Source and Collection | Study Setting | Primary Outcome measured | Results |
|---|---|---|---|---|---|---|---|
| **(Maue et al. 2019)** | QI study (before-after comparison) | 221 children >2 years old admitted to the pediatric intensive care unit (PICO) with status asthmaticus; requiring continuous albuterol administration | Establishment of a continuous albuterol weaning protocol in the PICU based on respiratory-therapists (RT) opinion, along with usage of a pediatric asthma severity score (PASS) | Electronic medical records extracted from billing software<br><br>Baseline period: September 2015 to August 2016 Vs. Implementation period: September 2016 to October 2017 | Single center, a PICU of a children's hospital with 36-bed capacity | Health outcome: The length (duration) of continuous albuterol administration to children admitted in the PICU | The duration of continuous albuterol and the length of PICO stay were not statistically significant different between the baseline and the post-intervention period.<br><br>According to X-bar control charts using means, both measures were stable without indication of special-cause variation presence.<br><br>A standardized RT-driven protocol based on PASS score can be applicable in a PICU without increasing length of continuous albuterol and changing the rate of adverse events (AEs). |
| **(Johnson et al. 2018)** | QI before-after comparison study | 7,115 children ≥2 years old with asthma diagnosis and without chronic comorbidity | Implementation of an asthma clinical practice guideline (CPG) to standardize asthma care | Electronic data warehouse and Pediatric Health Information Systems database<br><br>Pre-implementation period: May 2012 to April 2014 Vs. Post-implementation period: May 2014 to June 2016 | A quaternary-care children's hospital with 271-bed capacity | -ED and inpatient length of stay (LOS), percent<br>-In patient LOS including ICU<br>-Percentage of ED admitted patients<br>-Percentage of patients requiring ICU<br>-Total charges per case and ED TR cases | Standardizing a pediatric asthma CPG across hospital units (inpatient, ED, ICU) improved asthma healthcare and resource use outcomes.<br><br>LOS for ED TR patients was reduced from 3.9 hours to 3.3 hours, with special cause variation indication; and it was stable for 15 months.<br><br>Also, the CPG implementation reduced the average total charges per asthma case from $4457 to $3652; it was associated with special cause variation and was sustained for 2 years post-implementation. |
| **(Lo et al. 2018)** | QI study with a feasibility pilot study and 4 plan-do-study-act cycles | 2,909 children with median age 6 years old (Preintervention, N=1,530 Vs. Postintervention, N=1,379) | Changing the short-acting b-agonist (SABA) frequency discharge criteria from every 4 to every 3 hours to | Enterprise data warehouse<br><br>Pre-intervention Period: October 2011 to April 2013 Vs. post- | A quaternary pediatric hospital with 650-bed capacity, US | -In-hospital length of stay (LOS) in hours | The mean LOS decreased after changing the criteria for SABA frequency administration (39.9 hours compared to 47.9 hours pre-intervention). |

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| | | | reduce the in-hospital length of stay by 4 hours | intervention period: October 2013 to April 2015 | | | Control charts indicated special cause variation during the postintervention period.<br><br>Changing discharge criteria for SABA administration frequency decreased LOS for hospitalized asthma patients; and it was stable for 5 years beyond the intervention period. |
| **(Teufel et al. 2018)** | Interrupted time series QI study | 677 discharges of children 2 to 17 years, discharged with asthma diagnosis | Performing hospital discharge phone calls to to caregivers of children who were recently hospitalized for asthma. | Hospital administrative, phone call data and Medicaid data<br><br>Baseline period: January 2010 to September 2011 Vs. Intervention period: October 2011 to March 2014 | A single site, a tertiary referral medical center, US and out-patient setting | Proportion of children with a revisit to the ED or hospital within 90 days of discharge | The proportion of children revisiting ED or hospital within 90 days of discharge decreased during the intervention period (8% compared to 15%).<br><br>Based on control charts the children proportion was stable after phone-calls initiation.<br>However, there was no improvement in the preventive care outcomes. |
| **(Watnick et al. 2018)** | Nonresearch QI study | 6,680 children ≥2 years old with acute asthma exacerbations, without other chronic comorbidities | Implementation of targeted asthma clinical practice guidelines (CPGs) to decrease the percentage of chest radiograph (CXRs) from 29.3% to <20% | Electronic medical record system with asthma discharges<br><br>Baseline period: May 2013 to April 2014 Vs. Intervention period: May 2014 to April 2017 | A children's hospital with 271-bed capacity, Tennessee, US | Proportion of children with an acute asthma exacerbation who received a CXR | The implementation of an asthma CPG was associated with an overall reduction in CXR use from 29.3% to 16.0% in pediatric patients with acute asthma exacerbations; that maintained over the study period. However, this reduction was not associated with decreased antibiotic use.<br><br>The sub-analyses indicated that specific interventions produced different outcomes. |
| **(Bartlett et al. 2017)** | Time series QI study using Plan–Do–Study–Act cycles approach | 297 hospitalized children 2 to 18 years old with diagnosis of asthma exacerbation | Implementation of an asthma pathway in the electronic medical record (EMR) to reduce the length of stay from 2.9 days to | Electronic Health Records<br><br>-Baseline period: May 2013 to April 2014 | A tertiary care hospital with 190 bed capacity, Durham, NC | Average length of stay (ALOS) of pediatric patients with asthma exacerbations | After the implementation of the respiratory therapists–driven treatment protocol, ALOS decreased from 2.9 days at baseline to 2.3 days; the X-bar chart demonstrated the greatest decrease due to special cause variation, in June 2014. |

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| | | | 2.6 days within 12 months | -Intervention period: May 2014 to March 2016 | | | Accordingly, the paired S-chart for ALOS indicated a stable process after the implementation of the new asthma pathway.<br>The financial analysis resulted at savings of inpatient pediatric asthma care direct cost. |
| **(Kercsmar et al. 2017)** | QI study with time series analysis | 36,000 children 2 to 17 years old with asthma diagnosis | Implementation of a set of interventions combining medical and non-medical strategies at inpatient, outpatient, and community settings. | Medicare billing data<br><br>Baseline period: May 2008 to December 2009 Vs. Post-Intervention period: January 2010 to December 2015 | A children's hospital at Ohio with 628-bed capacity, in combination with outpatient and community settings | The percentage of asthma-related hospitalizations and ED visits. | Asthma-related hospitalizations and ED visits decreased significantly after implementing a variety of strategies from the hospital to the community level.<br><br>Based on SPC analysis the Improvements were stable for 12 months. |
| **(Walls et al. 2017)** | QI study | 724 children 2 to 17 years old asthma, bronchospasm, or wheezing; 64% of children were given an asthma score record | Implementation of an evidence-based pediatric asthma guideline | Patient's charts in paper forms and electronic health records<br><br>Pre-implementation period: August 2012–July 2013 Vs Post-implementation August 2013–February 2015 | Community ED with 55,000 patients annually, US | Children proportion needing transfer from community ED to additional care. | The proportion of children who transfer to additional care decreased after the asthma pathway implementation (10% compared with 14%); with a special cause variation noted in February 2015.<br><br>The mean time to steroids decreased from 196 minutes to 105 minutes. The X-bar chart indicated a special cause variation in April 2014.<br><br>The improvements were stable for more than one year and two respiratory seasons. |
| **(Brown et al. 2016)** | QI interrupted time series analysis | 684 children aged 1 to 18 years old | Implementation of a new pediatric nurse-driven protocol to standardize corticosteroid therapy to dexamethasone | Patients' scanned paper charts and electronic tracking board.<br><br>Baseline period: 01 February 2006 to | Academic pediatric ED, in a tertiary children's hospital (Washington) with almost | Time to corticosteroid administration | The mean time to corticosteroid administration decreased from 98 minutes in the baseline period (Prednisone) to 59 minutes in the intervention (Dexamethasone) phase. |

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| | | | and decrease administration by 15 minutes | 31 January 2007 Vs. Intervention: 01 March 2007 to 28 February 2008 | 87,000 patients per year | | The X-bar chart noted a special cause variation in the second month after the onset of the intervention, and the changes were sustained for one year. |
| **(Gray et al. 2016)** | Time series analysis, QI study | 5,552 children aged 2 to 18 years old in the ED receiving at least 1 SABA | To standardize timely and repetitive SABA administration by using asthma severity scores. | May 2012 through November 2015 Phase 1: July 2012 to | A tertiary pediatric ED with 36 ED beds | -PASS scoring compliance<br>-Time to first SABA (T1)<br>-Time to third SABA (T3)<br>-LOS in ED<br>-Admission rate | -X-bar chart indicated improvement to T1 for patients after implementation of asthma clinical pathway.<br>-By using PASS compliance scoring, SABA administration was standardized, while length of stay decreased, and admission rates improved. |
| **(Hatoun et al. 2016)** | QI study with three plan–do–study–act cycles | Children aged 4 days to 22 years | To increase the proportion of asthmatic children discharged with their medication from a baseline of 0% to >75%. | Retrospective data collection: Insurance Medicaid data | One pediatric ward of Boston Medical Center (BMC) | The proportion of patients discharged from an asthma admission with their medication (meds in hand) | In the end of the study, 75% of the eligible patients were discharged with meds-in-hand.<br><br>The p-chart noted a point of special cause variation with low performance; mainly due to winter holiday period. |
| **(Rutman, Migita, et al. 2016)** | Retrospective QI before-after intervention study using Plan–Do–Study–Act cycles approach | 3,688 children 1 to 18 years old with asthma exacerbation in the ED | Implementation of standardized score-based criteria for asthma admissions in pediatric ED after one hour of treatment to improve ED efficiency | Retrospective data collection: Administrative and billing databases<br><br>Baseline period: June 2010 to August 2011 Vs. Post-modification period: September 2011 to December 2012 | ED of a tertiary pediatric hospital with 350-bed capacity | -Length of stay in the ED for admitted children<br>-Time to bed request order by a physician | After the implementation of standardized admission criteria, LOS and time to bed request for decreased by 30 minutes (statistically significant decrease).<br><br>According to control charts for the percentage of admitted asthmatics, inpatient LOS and percentage of PICU admissions, there was no special cause variation from the pre- to post-implementation period, indicating that the applied admission criteria were appropriate. |
| **(Rutman, Atkins, et al. 2016)** | QI before-after intervention study using Plan–Do–Study–Act | 5,584 children 1 to 18 years old with asthma exacerbations | Modification of an Established Pediatric Asthma Pathway in ED and inpatient units | Retrospective data collection: EMRs and hospital administrative records | A tertiary, 323-bed pediatric hospital | -Length of stay in the ED<br>-Length of stay in hospital | The study included SPC and ITS analyses to assess the efficiency and adherence of the modified asthma pathway. |

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| | cycles approach | | | Before modification period: September 2009 to August 2011 Vs. Post-modification period: September 2011 to September 2013) | | | Modifying the asthma pathway enhanced patient-adherence and reduced length of stay and costs. SPC carts indicated that improvement was sustained for the 2-year post-modification period. |
| **(Nkoy et al. 2015)** | QI study with retrospective and prospective phases | 3,510 children aged 2 to 17 years old with a primary diagnosis of asthma | Implementation of an evidence-based asthma care process model (EB-CPM) at PCH (tertiary hospital) and 7 community hospitals | Healthcare enterprise data warehouse, physician and nursing documentation and EMRs<br><br>PCH: Baseline period: January 2003 to March 2009 Vs. Post-implementation: April 2009 to December 2013.<br>Community hospitals: January 2003 to June 2011 and July 2011 to December 2013, respectively | Multiple Hospitals: 1 tertiary children's hospital (PHC) and 7 community hospitals | 6-month asthma ED and hospital readmission rates | The average readmission rates at PCH were reduced after EB-CMP implementation, and the reduction was stable based on p-control chart.<br><br>The reduction of 6-month asthma readmission rates was not statistically significant in the community hospitals.<br><br>On the contrary, there was a slight increase in resource use at community hospitals, and it maintained stable at PCH. |

AEs: Adverse Events; ALOS: Average Length of stay; CPG: Clinical Practice Guideline; CXR: Chest Radiographs; EB-CPM: Evidence-based asthma care process model; ED: Emergency Department; EMR: Electronic Medical Record; ICU: Intensive Care Unit; ITS: Interrupted time series analysis; LOS: Length of stay; MPIS: Modified Pulmonary Index Score; PASS: Pediatric Asthma Severity Score; PICO: Pediatric Intensive Care Unit; QI; Quality Improvement; RT: Respiratory therapist; SABA: Short-acting b-agonist

**Table 4: Quality assessment of QI studies included in 16 domains**

| Reference | Organizational motivation | Intervention rationale | Intervention description | Organizational characteristics | Implementation | Study design | Comparator | Data source |
|---|---|---|---|---|---|---|---|---|
| (Maue et al. 2019) | Met | Met | Met | Met | Met | Met | Met | Met |
| (Johnson et al. 2018) | Met | Met | Met | Met | Met | Met | Met | Met |
| (Lo et al. 2018) | Met | Met | Met | Met | Met | Met | No | Met |
| (Teufel et al. 2018) | Met | Met | Met | Met | Met | Met | No | Met |
| (Watnick et al. 2018) | Met | Met | Met | Met | Met | Met | No | Met |
| (Bartlett et al. 2017) | Met | Met | Met | Met | Met | Met | No | Mer |
| (Kercsmar et al. 2017) | Met | Met | Met | Met | Met | Met | No | Met |
| (Walls et al. 2017) | Met | Met | Met | Met | Met | No | No | Met |
| (Brown et al. 2016) | Met | Met | Met | Met | Met | Met | Met | Met |
| (Gray et al. 2016) | Met | Met | Met | Met | Met | Met | No | No |
| (Hatoun et al. 2016) | Met | Met | Met | Met | Met | Met | No | Met |
| (Rutman, Migita, et al. 2016) | Met | Met | Met | Met | Met | Met | No | Met |
| (Rutman, Atkins, et al. 2016) | Met | Met | Met | Met | Met | Met | No | Met |
| (Nkoy et al. 2015) | Met | Met | Met | Met | Met | Met | Met | Met |
| | **Timing** | **Adherence/ fidelity** | **Health outcomes** | **Organizational readiness** | **Penetration/ reach** | **Sustainability** | **Spread** | **Limitations** |
| (Maue et al. 2019) | Met | No | Met | No | No | Met | Met | Met |
| (Johnson et al. 2018) | Met | Met | Met | Met | Met | No | No | Met |
| (Lo et al. 2018) | Met | No | Met | Met | Met | Met | Met | Met |
| (Teufel et al. 2018) | Met | Met | Met | Met | Met | No | No | Met |
| (Watnick et al. 2018) | Met | No | Met | Met | Met | Met | Met | Met |
| (Bartlett et al. 2017) | Met | No | Met | Met | No | Met | Met | Met |
| (Kercsmar et al. 2017) | Met | No | Met | Met | Met | Met | Met | Met |
| (Walls et al. 2017) | Met | Met | Met | Met | Met | Met | Met | Met |
| (Brown et al. 2016) | Met | No | Met | Met | Met | Met | Met | Met |
| (Gray et al. 2016) | Met | No | Met | Met | No | Met | Met | Met |
| (Hatoun et al. 2016) | Met | No | Met | Met | Met | No | Met | Met |
| (Rutman, Migita, et al. 2016) | Met | Met | Met | No | Met | No | Met | Met |
| (Rutman, Atkins, et al. 2016) | Met | Met | Met | Met | No | Met | Met | Met |
| (Nkoy et al. 2015) | Met | Met | Met | Met | Met | Met | Met | Met |

## 3.2 Quality of QI studies included in the review

**Table 4** presents the critical appraisal of the included studies using the QI-MQCS tool.

Most of the studies failed to describe the comparator, ie the post-intervention situation or the standard of care provided prior to the intervention. Moreover, not all studies reported the sustainability of the intervention or the long-term impact of QI implementation, by either stating if the results could be stable over long period after implementation or what next steps would be needed to maintain the optimal performance. Additionally, many studies lacked the rational of the eligible population estimation. The impact of organizational changes, the maintenance of adherence and compliance with the intervention (adherence/ fidelity) was rarely reported and difficult to estimate.

On the contrary, studies reported factors contributing to the success of the project or possible barriers to successful implementation of intervention, the estimated external validity and the potential of generalizable outcomes.

## 3.3 Results of individual studies

### 3.3.1 SPC application and methodology

SPC was used to analyze the data before and after implementation of the examined intervention and specific control charts were utilized to evaluate variation in processes over time. SPC charts showed special cause variation in study's measurement or stabilization by indicating a sustained shift in the process. **Table 5** illustrates the outcome, process and balancing variables, the types of control charts and SPC rules applied to each study.

SPC control charts were constructed in accordance with *Provost & Murray* published guidelines in healthcare improvement studies (Provost and Murray 2011). Five studies reported the rational for the estimation of the control limits and declared 3 standard deviations from the mean for setting upper and lower control limits. Eight studies reported the rules of interpretation of special cause variation. Three of them considered only the 8 consecutive points above or below the control limit as a special cause variation indication. However, not all studies provided explicit rules for interpreting changes figured in control charts.

Even though all studies described the outcome measures, most of the studies failed to report process or balancing measures. Reported SPC variables included clinical management variables: average length of inpatient' stay or in the ED, the time for drug administration, the proportion of children with a specific health outcome as primary outcomes; ICU admission time, re-admission rate mainly as balancing measure and financial resources variables such as direct cost per case.

In most studies SPC was utilized to analyze outcome measures before and after implementation of the examined intervention and indicate changes in process measures over time. Rutman, Atkins *et at*. utilized SPC to analyze process measures and performed ITS analysis for outcome measures (Rutman, Atkins, et al. 2016). Kercsmar et al. selected control charts in order to handle potential effects of seasonality (Kercsmar et al. 2017).

Control charts were constructed and annotated the examined interventions; providing directly insights on impact and outcomes of the interventions of interest. P charts for percentages, X-bar and S-charts for continuous variables were mostly preferred in QI studies. P charts usually were applied to track the proportion of children or rates between baseline and implementation period. X-bar charts demonstrated the variation in LOS. S charts paired with the X-bar charts showed the reduction in the variability over time, indicating process stability. Additionally, there were two studies using g-charts for infrequent events (Johnson et al. 2018; Gray et al. 2016); no study illustrated c, np and u charts.

SPC control charts were generated by using Minitab 17 Statistical Software or QI-Charts (Version 2.0) or displayed using Excel.

**Table 5: Variables and SPC statistical analysis applied to each study included in the review**

| | Variables | | | Statistical Analysis | |
|---|---|---|---|---|---|
| **Reference** | **Outcome measure** | **Process measure** | **Balancing measures** | **Determination of special cause variation** | **Control Chart Application** |
| **(Maue et al. 2019)** | -Mean duration of continuous administration albuterol in intensive care unit (ICU)<br>-Length of ICU stay | Not available | -Rate of adverse events (AEs) | -A run of 8 consecutive data points on the same side of the center line.<br><br>-The upper and lower control limits were calculated as 3σ above and below the center line. | -A X-bar chart illustrated the median duration of continuous albuterol administration in pediatric ICU duration<br>-A X-bar chart for median ICU length of stay<br>-Criteria for special-cause variation did not meet. |
| **(Johnson et al. 2018)** | -Monthly mean emergency department treat-and-release length of stay (ED- TR- LOS)<br>-In patient LOS including ICU<br>-Percentage of ED admitted patients<br>-Percentage of patients requiring ICU care<br>-Total charges per case<br>-Total charges for ED TR cases | Proportion of patients receiving dexamethasone (not in ICU) | -Proportion of asthma cases returning to the ED within 72 hours after primary discharge<br>-Asthma discharges between 30-days (including all-cause re-admissions after discharge) | -A single data point outside of the control limits<br>-A run of 8 consecutive data points on the same side of the center line<br><br>No statement of how upper and lower control limits were set | -X-bar charts to monitor LOS for asthma ED TR visits and LOS for all asthma admissions (inpatient and ICU)<br>-P-charts were used for the proportion of asthmatic patients in the ED and inpatient admissions requiring ICU care<br>-X-bar charts for the average charges per asthma case and ED-TR case<br>Balancing measures:<br>-G-chart of asthma discharges between 30-day all-cause readmissions<br>-P-chart for the percent of 72-hour asthma return ED visits |
| **(Lo et al. 2018)** | -In-hospital length of stay | Not available | -ED revisits<br>-Hospital readmissions at 3, 7, and 14 days from discharge for related diagnosis | No statement on which rule is indicating special cause variation.<br><br>No statement of how upper and lower control limits were set. | -X-bar and S-chart were applied throughout the study period to monitor monthly average LOS in hours and standard deviation, respectively.<br><br>Special cause variation was indicated during the post-intervention period. |
| **(Teufel et al. 2018)** | -The proportion of children revisiting the ED setting or hospital with a primary diagnosis of asthma within 90 days of discharge | The number of successful contacts with any follow-up call | Preventive care outcomes:<br>-Proportion of controller refills<br>-Ambulatory visits up to 90 days | No statement on which rule is indicating special cause variation.<br><br>No statement of how upper and lower control limits were set. | -P-control chart was used to monitor the percent of ED or hospital revisits within 90 days post-discharge.<br>-P- chart for the percent of inhaled corticosteroids refills<br>-P-chart for the percent of ambulatory visits |
| **(Watnick et al. 2018)** | -Proportion of children with an acute asthma | Not available | -Percentage of children with a 3-day | -A single data point outside of the control limits | -A p-chart tackled the percentage of children receiving a CXR |

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| | exacerbation who received a chest radiograph (CRX)<br>-Proportion of children receiving systemic antibiotics during their visit | | return visit to ED<br>-Proportion of children with a primary pneumonia diagnosis | -A run of 8 consecutive data points on the same side of the center line | -A p-chart was used for the percentage of children receiving systemic antibiotics |
| **(Bartlett et al. 2017)** | Average length of stay for asthma cases (ALOS).<br><br>Secondary: Direct cost of in hospital asthma care | Proportion of inpatient asthma order set use | Seven days and one-month readmission rate | A run of 8 consecutive data points on the same side of the center line.<br><br>Upper and lower control limits were set at 3-σ. | -A X-bar chart demonstrated the ALOS of pediatric patients with asthma (sample set: one month)<br>-A paired S-chart was used for standard deviation for ALOS<br>-A p-chart for the proportion of asthma order set use |
| **(Kercsmar et al. 2017)** | The percentage of asthma-related hospitalizations and ED visits.<br><br>Secondary:<br>-Patient proportion with rehospitalization or ED revisit within 30 days of discharge<br>-The percentage of in-hospital primary care patients with well-controlled asthma | -Percentage of patients with medications-in-hand | -Hospital admissions<br>-ED admissions per 10,000 Medicare patients | -A run of 8 consecutive points above or below the center line<br>-A run of 6 consecutive increasing or decreasing points<br>-Single points outside control limits | -A p-chart was applied to monitor the proportion of patients with asthma-related hospital re-admission and ED re-visit within 30 days after discharge<br>-Control charts for hospital admissions rate and ED admissions rate per 10,000 Medicare patients |
| **(Walls et al. 2017)** | -The proportion of children who needing transfer from community ED to an additional care unit<br><br>. | -Proportion of children with an asthma score<br>-Proportion of children receiving steroids<br>-Time period from triage arrival to steroid administration | -Patients proportion revisiting the community ED within 7 days of the initial ED visit, with an asthma related case. | No statement on which rule is indicating special cause variation.<br><br>Upper and lower control limits were set at 3 SD from the mean | -A p-chart to tackle the proportion of children who were transferred from the community ED.<br>-P-chart to monitor the proportion of children receiving steroids at the community ED.<br>-A x-bar chart to describe the time period to steroid administration before and after asthma pathway implementation. |
| **(Brown et al. 2016)** | -Time from triage to patient arrival to corticosteroid administration | -Emesis rate<br>-ED LOS for children not admitted in the hospital<br>-Admission rate | -ED re-visits for asthma care within five days<br>-ED re-admissions | -1 point outside control limits<br>-8 points in a row on same side of center line<br>-6 points in a row, all increasing or decreasing | -A Shewhart X bar control chart to tackle the mean times to corticosteroid administration during the baseline and intervention period. |

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| | | | -Follow up visits for asthma to hospital's primary care | -2 of three consecutive points that are >2 standard deviations from center line.<br><br>Upper and lower control limits were set at 3 SD from the mean. | |
| **(Gray et al. 2016)** | -PASS scoring in triage<br>-1 repeat PASS scoring within 2 hours of triage<br>-Time to first SABA (T1)<br>-Time to third SABA (T3)<br>-LOS in ED<br>-Admission rate | Total SABA administration | Asthma re-visits within 48 hours resulting in re-admissions (infrequent measure) | No statement on which rule is indicating special cause variation.<br><br>No statement of how upper and lower control limits were set. | -A P-chart was used to demonstrate scoring compliance bases on PASS record.<br>-A X-bar chart for monitoring T1, T3 and length of stay for all patients.<br>-A p-chart for tracking admission rate<br>-A g-chart for return visits resulting in re-admissions |
| **(Hatoun et al. 2016)** | -Proportion of patients with asthma discharged with their medications<br>-ED re-visitation<br>-Re-admission within 30 days | Not available | Mean length of stay (LOS) | No statement on which rule is indicating special cause variation.<br><br>No statement of how upper and lower control limits were set. | -A p-chart demonstrated the proportion of patients with asthma discharged with their medications during all 3 cycles of intervention<br>- X-bar chart for ED-LOS |
| **(Rutman, Migita, et al. 2016)** | -Length of stay in the ED for admitted children<br>-Time to bed request order by a physician | Not available | -The overall proportion of admitted asthmatics<br>-The inpatient length of stay<br>-The pediatric intensive care unit admissions | -A single point outside the control limit<br>-A run of 8 or more points in a row above or below the centerline<br>-6 points in a row, all increasing or decreasing<br>-2 of three consecutive points that are >2 standard deviations from center line<br>-15 consecutive points close to the centerline<br><br>Upper and lower control limits were set at 3 SD from the mean. | -A X-bar chart and the respective S-chart for monitoring mean ED length of stay for admitted patients with asthma<br>-X-bar chart and S-chart for mean time to bed request for admitted patients with asthma and standard deviation, respectively.<br>-P-charts were used for balancing measures: percentage of admitted asthmatics and asthma admissions to PICU over time.<br>-X-bar and s-chart for mean and SD inpatient LOS for asthmatics |
| **(Rutman, Atkins, et al. 2016)** | -Length of stay in the ED<br>-Length of stay in hospital | -Proportion of patients with asthma order set activated<br>-Proportion of patients receiving IV magnesium sulfate in ED<br>-Proportion of patients | -Proportion of patients with asthma admitted to the hospital<br>-Re-visits to the ED and in hospital<br>-Direct cost per case | -8 points in a row on same side of center line<br><br>No statement of how upper and lower control limits were set. | SPC was used to monitor all process measures.<br><br>Hence, P-charts were applied to monitor over time the proportion of patients having asthma order set activated, receiving IV magnesium sulfate in the ED or ipratropium bromide in |

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| | | receiving ipratropium bromide in hospital<br>-Proportion of patients recommended to steroids at discharge | | | hospital and receiving the appropriate steroid prescription at discharge. |
| **(Nkoy et al. 2015)** | -6-month ED rate<br>-6-month in-hospital asthma readmission rate<br><br>-Length of stay (LOS)<br>-Costs and hospital resource use<br>-ICU transfer after inpatient admission<br>-Deaths | Not available | Not available | No statement on which rule is indicating special cause variation.<br><br>No statement of how upper and lower control limits were set. | -A p-chart was used to monitor 6-month asthma readmission rates and LOS between the pre-implementation and post-implementation periods. |

AEs: Adverse Events; ALOS: Average length of stay; CXR: Chest Radiographs; ED: Emergency Department; ED-TR-LOS: Emergency department treat-and-release length of stay; ICU: Intensive Care Unit; LOS: Length of stay; PASS: Pediatric Asthma Severity Score; PICO: Pediatric Intensive Care Unit; SABA: Short-acting b-agonist; SD: Standard Deviation; SPC: Statistical Process Control; T1: Time to first SABA; T3: Time to third SABA

### 3.3.2 Interventions implemented in QI studies

All fourteen studies implemented several initiatives and changes in different inpatient and outpatient settings, aiming to improve the standard pediatric asthma care, ameliorate the outcomes and lower the costs (see **Table 7 in Appendix**). The improvement activities focused on reducing healthcare variability, increasing adherence to national guidelines and producing sustained outcomes over time. The authors examined the implementation of evidence-based clinical practice guidelines (CPGs) or modifications on well-established asthma care pathways; more specifically, the involution of respiratory therapists (RTs) and nurses to decision making process, medication and management modifications, increase of self-management, scoring systems, the establishment of well-defined criteria, as well as organizational education, training and support.

Regarding the impact of evidence-based asthma CPGs and new pathways, Rutman, Migita *et al*. implemented a modified asthma clinical pathway by adding early objective admission criteria, based on respiratory score (RCS scoring tool) in the ED of a tertiary hospital. As a result, clinicians were able to make earlier decisions and the ED length of stay was decreased (Rutman, Migita, et al. 2016). Subsequently, Rutman, Atkins *et al.* evaluated a modified asthma clinical pathway in ED and inpatient setting, conducting simultaneously a cost-analysis. Standardized admission criteria and specific recommendations on medication use improved the compliance to the guidelines and brought sustainable results over time; without increasing hospital costs (Rutman, Atkins, et al. 2016). In addition to this, Johnson *et al.* assessed the impact of a pediatric asthma CPG in all units of a hospital, including ED, inpatient care and the ICU in a larger sample. The authors observed significant reductions in LOS, re-admissions, ICU services, and costs (Johnson et al. 2018).

In terms of various hospital settings, Nkoy et al, examined the implementation and distribution of an evidence-based care process model (EB-CPM) to seven community hospitals, demonstrating better clinical and quality-provision outcomes (Nkoy et al. 2015). Likewise, Walls *et al*. effectuated a pediatric asthma pathway adapted from a tertiary hospital, in a community ED. The authors highlighted the need of practice guidelines for children with asthma, even in a community ED (Walls et al. 2017). Over and above, Kercsmar *et al*. performed numerous interventions in 3 phases: inpatient, outpatient, and community-based, underlying that similar multidisciplinary models could also be feasible in other chronic diseases (Kercsmar et al. 2017).

Moreover, few studies evaluated changes in treatment administration, by modifying the prescription medication, dosage and dose frequency or by intervening in the patients' access to treatment medication. Hence, Gray *et al*. implemented a clinical care pathway in a pediatric ED focusing on timely improvement of administration of short-acting b-agonist (SABA); without increasing LOS and readmission rates. The authors used PASS as standardized asthma severity assessment tool in relation to treatment administration (Gray et al. 2016). Accordingly, Lo *et al*. based on CRS to assess respiratory acuity, implemented discharge criteria throughout the hospital including the reduction of

SABA administration frequency discharge requirement from every 4 hours to every 3 hours (Lo et al. 2018). On the other hand, Hatoun *et al*. changed the delivery of healthcare by implementing a Meds-in-Hand project. They developed a medication delivery service engaging hospital physicians, nurses, pharmacists and caregivers, improved the adherence to discharge treatment and decreased asthma re-admissions (Hatoun et al. 2016). In 2018, Teufel *et al*. evaluated a potential preventive asthma care by using post-discharge follow-up phone-call to children's caregivers. Although, ED and hospital re-visits decreased, there was no improvement in preventive care measures, such as ambulatory visits (Teufel et al. 2018).

Regarding more targeted interventions, Bartlett *et al*. developed a new electronic health record system and assessed an asthma care pathway. The implementation of asthma objective criteria based on MPIS scoring tool with EMRs improved the adherence to guidelines and indicated future sustainability (Bartlett et al. 2017). Watnick *et al*. examined interventions to decrease the use of chest radiographs (CXRs) for pediatric patients with acute asthma exacerbations (Watnick et al. 2018). Moreover, Brown *et al.* targeted the lack of nurse's initiatives by implementing a new ED asthma care nurse-driven pathway based on standardizing corticosteroid medication and dosage. Time to steroid administration and hospital admissions decreased, while changes were sustainable for one year (Brown et al. 2016), and consistent with Walls *et al*. results in a community ED (Walls et al. 2017). Maue *et al*. recommended the development of a protocol in ICU, based on RTs' expertise, PASS severity scores and reduction of continuous albuterol treatment, without increasing adverse events (Maue et al. 2019).

### 3.3.3 Limitations within QI studies

All studies denoted important limitations and barriers (see **Table 7 in Appendix**).

Regarding the study design and data source the following limitations were reported: Most studies were conducted at a single institution, which might limit the generalizability of the results. Two studies reported a small sample size, which lowers the statistical power of the study to detect a statistically significant difference. Patients were identified primarily by using ICD-9 and ICD-10 codes, billing codes or insurance data; thus, there may have been inaccuracies and misclassifications between groups. Retrospective studies with data extracted from two separate time periods and different data sources led to disparities between the two groups. Other studies stated that there was an unbalanced distribution of characteristics, demographic considerations mainly, between population groups; that might further limit the generalizability. Also, the use of electronic medical records as data source could lead to missed re-admissions or bias in LOS determination. Regarding re-admission rates, the authors noted that they could only capture re-visits within the institution of the study, missing out patients readmitted to other hospitals.

Moreover, there was heterogeneity in inpatient pediatric services across different hospitals. Several studies utilized an asthma scoring tool in order to assess clinical severity, monitor the treatment response and determine adherence to the guidelines or the new pathway. However, different studies used different asthma scores, such as the Respiratory Clinical Scoring tool (RCS) (Rutman, Migita, et al. 2016; Lo et al. 2018), the Pediatric Asthma Severity Score (PASS) (Gray et al. 2016; Maue et al. 2019), the Modified Pulmonary Index Score (MPIS) (Bartlett et al. 2017), the Acute Asthma Intensity Research Score (AAIRS) (Johnson et al. 2018), the Childhood Asthma Risk Assessment Tool–Revised (CARAT-R) (Kercsmar et al. 2017). This variety in scoring tools to standardize asthma scoring and treatment between different institutions might decrease the generalizability of the study.

In addition to this, the different levels of infrastructure and organization of institutions, as well as the different levels of support or barriers imposed by intervention-stakeholders, might limit the generalizability of the results. Notably, organizational changes occurred during implementation of QI interventions might affect adherence and compliance. Furthermore, studies were subjected to the Hawthorne effect. Since patients and physicians were aware of being studied, they might adjust accordingly their behavior. Not all studies conducted a simultaneously financial analysis; involving the risk of under or over estimation of the beneficial outcomes. Finally, all fourteen studies declared the variety of other cofounders or real-time changes that could be measured during study design and might have affected the outcomes of the implemented interventions.

# 4. DISCUSSION – LIMITATIONS

Three bibliographic databases, articles extracted from one pediatric journal and the reference lists of relevant studies were systematically searched. After reviewing the available records, the full text of fourteen studies was indicated. Studies' quality was appraised using the Quality Improvement Minimum Quality Criteria Set (QI-MQCS) framework. According to the inclusion criteria, we included studies reporting the application of control charts in pediatric asthma healthcare improvement. The main objective was to standardize asthma care and improve clinical and performance outcomes throughout inpatient and outpatient settings. SPC control charts were implemented to monitor process changes and distinguish special from common cause variation.

All studies were published from 2015 onwards; denoting a relatively limited application but progressively increasing trend of SPC methodology in QI interventions. In addition, all 14 studies were conducted in US, consistent with Thor *et al.* findings in 2007; but limiting the generalization to other systems (Thor et al. 2007). That is probably due to the strong private healthcare sector that imposes QI studies for continuous monitoring and evaluation. However, the implementation of SPC methodology in different healthcare sectors in different countries, such as Greece, remains a challenge.

Control charts allowed rapidly detecting variation or stability before and after intervention periods, which were clearly predefined. The use and interpretation of x-bar charts for continuous variables and p-charts for percentages was preferred; accordant with Suman & Prajapati findings in 2018 (Suman and Prajapati 2018). By plotting continuous time-ordered data on control charts, investigators were able to ascertain the impact of an intervention or predict the future performance of a stable process and improve the upcoming results (Clark et al. 2018). For example, the authors noted that based on control charts observations, they were able to make decisions earlier, either to maintain the current asthma care treatment or to modify the regimen, the dosage or the entire healthcare pathway.

In all studies, SPC application was carried out by multidisciplinary teams, including physicians, respiratory therapists (RTs), nurses, pharmacists, and outcomes analysts; demonstrating the need for collaboration and communication between different disciplines or professional specializations in all hospital sectors (Thor et al. 2007). Furthermore, SPC results empowered the role of respiratory therapists and nurses in the decision-making process; denoting compliance to the guidelines and quality improvement of healthcare services. All QI studies emphasized the need for in-site educational interventions and trainings to all participated members, as important components of the process.

Most studies collected data retrospectively through accessible data sources; hospital databases, electronic medical records, insurance and billing record. However, retrospective studies are

subjected to recall bias, inherited limitations and difficulties in determining causality (Thor et al. 2007). In addition, QI studies were subjected to observation bias. When the performance of individuals in hospitals is under observation, it might alter his behavior and therefore the observed results, a bias known as the Hawthorne effect (McCambridge et al. 2014).

As the included QI studies involved heterogenous approaches on design methods, their outcomes need to be interpreted with conscious. SPC methodology was applied at different hospitals and outpatient settings, so caution is needed in determining the generalizability and disseminating the results. All fourteen studies examined the implementation of several interventions at successive time intervals or at the same time. Control charts provide this flexibility; testing several changes occurring simultaneously. However, this imposes a structural constraint of SPC methodology. When multiple interventions are occurring together, it is impossible to determine the single change that led to the optimal performance.

Moreover, control charts can indicate abnormal signal during a process, but there is no guarantee that it was an interventional outcome. Not obvious confounding factors may affect the results., Before and after-intervention studies were prone to changes in the underlying study setting or population over time periods. Also, not real-time obtained data might confuse the observation of special cause signals. As a result, it was difficult to detect whether the outcome was produced by the examined intervention or it would have occurred anyway in the process period. (Harries et al. 2019). In addition, an indication of “special-cause variation” does not imply necessarily an optimal clinical outcome or performance improvement. Literature recommends the simultaneous use of decision trees to help investigators interpret the results (M. A. Mohammed et al 2008).

Finally, the studies highlighted the requirement for strong leadership support and employees’ commitment, to ensure compliance to the intervention and accurate implementation of QI methodology. Healthcare management should incorporate this methodology in order to improve care quality and constrain resources and costs. Thus, it is necessary for QI studies to be accompanied by economic evaluations. Cost-analysis applied to clinical interventions or healthcare programs and policies, could inform of resources’ allocation, estimate the incremental cost of a new intervention and validate its benefit (Roberts et al. 2019).

The present study provides insights to researchers about the application of SPC control charts in pediatric asthma care. Also, it provides useful information on asthma-care interventions implemented in different settings, including various of potential targets for improvement and the corresponding limitations that should be considered.

Our study has several limitations. The main limitation of this review was the exclusion of three publications due to lack of full text availability (see **Table 8** in the Appendix). In addition, the systematic review was performed by only one reviewer, so it might have subjective bias in the

research and selection of the finally included studies. We must acknowledge potential publication bias, since projects that do not document improvements might not have been published.

## 5. CONCLUSION

Even if SPC method was initially implemented by Shewhart in 1920, it is still a useful and simple tool to healthcare improvement. The application of control charts enables a continuous monitoring of the impact of an intervention on outcomes of interest. It connects the inherited random variation within a process with real-time changes, identifies process outliers, known as “special-cause variation” and alerts QI investigators. It provides a rational for predicting future performance or indication of areas within a process that could be further investigated.

SPC application in pediatric asthma-care improvement is a simple and useful tool for researchers to assess new asthma pathways, establishment of new criteria or modifications on standard of care, so that they can standardize the provision of asthma care and improve adherence to guidelines.

However, implementation of control charts does not automatically lead to process improvement and a “special-cause variation” signal does not necessarily imply a better clinical or performance outcome. Therefore, control charts must be applied and interpreted wisely, with careful consideration on the local context.

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# APPENDIX

**Table 6: Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) in the 14 studies included in the review**

| Text Section and Item reported | (Maue et al. 2019) | (Johnson et al. 2018) | (Lo et al. 2018) | (Teufel et al. 2018) | (Watnick et al. 2018) | (Bartlett et al. 2017) | (Kercsmar et al. 2017) | (Walls et al. 2017) | (Brown et al. 2016) | (Gray et al. 2016) | (Hatoun et al. 2016) | (Rutman, Migita, et al. 2016) | (Rutman, Atkins, et al. 2016) | (Nkoy et al. 2015) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **TITLE AND ABSTRACT** | | | | | | | | | | | | | | |
| **1. Title** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **2. Abstract** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **INTRODUCTION** | | | | | | | | | | | | | | |
| **3. Problem description** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **4. Available Knowledge** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **5. Rationale** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **6. Specific aims** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **METHODS** | | | | | | | | | | | | | | |
| **7. Context** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **8. Interventions** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **9. Study of Interventions** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **10. Measures** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **11. Analysis** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **12. Ethics considerations** | | X | X | | X | X | | X | X | X | X | X | X | |
| **RESULTS** | | | | | | | | | | | | | | |
| **13. Results** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **DISCUSSION** | | | | | | | | | | | | | | |
| **14. Summary** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **15. Interpretation** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **16. Limitations** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **17. Conclusion** | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| **OTHER INFORMATION** | | | | | | | | | | | | | | |
| **18. Funding** | | | | | | | X | | | | | | | |

**Table 7: Interventions implemented and limitations within QI studies**

| Reference | Study setting | Study Objective | Intervention | Key Components | Study Limitation |
|---|---|---|---|---|---|
| **(Maue et al. 2019)** | Pediatric Intensive Care Unit (PICO) | To decrease the duration of continuous albuterol by using the expertise of respiratory therapists (RTs), but without increasing the adverse events | Establishment of an RT-driven continuous albuterol weaning protocol in the PICU | -Implementation of pediatric asthma severity score (PASS)<br>-Development of as continuous albuterol order-set in the electronic medical records (EMR)<br>-In-person education to clinicians and involved staff | -It was a single center study and the results cannot easily be generalizable to other hospitals.<br>-Other confounders not considered in the analysis may affect the results.<br>-The usage of electronic medical records might confuse the estimation of exact inpatient length of stay. |
| **(Johnson et al. 2018)** | Pediatric asthma care in ED, ICU and inpatient care | To standardize pediatric asthma-related care from the arrival to the emergency department (ED) through discharge | Implementation of an asthma clinical practice guideline (CPG) | -Usage of Acute Asthma Intensity Research Score (AAIRS)<br>-Specific treatment and dosing modifications in ED, ICU and in hospital | -Patient misclassification<br>-Lack of data indicating adherence to the intervention<br>-Limits on the generalizability of the results due AAIRS scoring tool<br>-Uncertainty about full compliance with specific intervention procedures |
| **(Lo et al. 2018)** | Pediatric asthma in hospital | To reduce the length of stay (LOS) <4 hours for children with asthma exacerbations | Treatment modification: Changing the short-acting b-agonist (SABA) administration frequency discharge requirement | -Updating guidelines<br>-Modifying SABA administration frequency discharge from every 4 hours to every 3 hours<br>-Development of EMR order sets and a specific asthma history and physical template documentation<br>-In-site education<br>-Interaction between respiratory therapists and physicians | -Small sample size without statistical power to detect difference in readmission rate<br>-Readmission rate was estimated only by the patients readmitted in the study hospital. |
| **(Teufel et al. 2018)** | Pediatric asthma in ED, hospital and outpatient setting | To decrease asthma-related re-visits to the ED or hospital by improving the preventing care | Performing hospital discharge phone calls to caregivers of children who were recently hospitalized for asthma | -Brief follow-up telephone call to educate and support caregivers<br>-Collection of real time claims data on patients' adherence to therapy<br>-Structured phone calls regarding caregivers' knowledge on child's medications | -Low percentage (34%) of patients having available claims data<br>-The study's design excluded other confounders to intervention's effectiveness |
| **(Watnick et al. 2018)** | Pediatric asthma in hospital and ED | -To decrease chest radiographs (CXRs) to children with acute asthma exacerbations<br>-To assess if this change reduces antibiotic use | Implementation of targeted asthma clinical practice guidelines (CPGs) with general recommendations on CXR use | -Treatment standardization<br>-Specific recommendations for CXR use<br>-Including CXRs in the inpatient electronic order set<br>-In-person education to clinicians | -Patient misclassification<br>-No data on the indication for antibiotic administration<br>-It was a single center study and the results cannot be easily generalizable to other hospitals. |

| | | | | | |
|---|---|---|---|---|---|
| **(Bartlett et al. 2017)** | Pediatric asthma exacerbations in hospital | -To decrease the average length of stay of pediatric patients with asthma from 2.9 to 2.6 days within one year | Implementation of an asthma pathway and development of a new electronic medical record | -Introducing an asthma score MPIS (Modified Pulmonary Index Score)<br>-Usage of asthma- specific order sets in a new EMR<br>-Establishment of a respiratory therapy–driven albuterol treatment protocol<br>-Targeted education to clinicians | -It was a single center study and it cannot be generalizable to other hospitals.<br>-The study's design did not consider other possible confounders to intervention's effectiveness |
| **(Kercsmar et al. 2017)** | Pediatric asthma at inpatient, outpatient, and community setting | To reduce asthma-related hospitalizations and ED visits for children and adolescents | Implementation of a multidisciplinary approach combining medical and non-medical strategies at inpatient, outpatient, and community settings | Hospital-based care (phase 1):<br>-Implementation of medication-in-hand project<br>-Adaptation of Childhood Asthma Risk Assessment Tool Revised (CARAT-R).<br>-Standardizing asthma criteria<br>-Usage of EMR, checklists, templates<br>Outpatient-based care (Phase 2):<br>-5 in-home nurse visits<br>Community-based initiatives (Phase 3):<br>-Collaboration with Medicaid managed care organizations and public schools | -Lack of a formal economic evaluation<br>-The study's design did not consider other possible confounders to intervention's effectiveness<br>-Uncertainty about the specific benefit of each change |
| **(Walls et al. 2017)** | Pediatric asthma in a community ED | -To improve asthma care<br>-To decrease the proportion of children who needed transfer from community ED to additional care. | Implementation of an evidence-based pediatric asthma pathway | -Introduction of an asthma score to standardize the procedure<br>-Provision therapies by nurses, such as bronchodilators and corticosteroids.<br>-Continuous nursing education and training | -Only 64% of children included had an asthma score recorded during the implementation period.<br>-Inconsistency in asthma severity definition<br>-Overestimation of the number of children who should have received corticosteroids |
| **(Brown et al. 2016)** | Pediatric asthma exacerbations in ED | To decrease the time to corticosteroid administration initiation for patients in the ED with asthma exacerbations | Implementation of a new pediatric protocol standardizing corticosteroid therapy | -Nurse initiated orders for dexamethasone replacing oral prednisolone.<br>-Standardizing dexamethasone as corticosteroid choice<br>-Standardizing the dose calculations<br>-Patients' discharge with their medicine | -Limited available time and resources<br>-It was a single center study and it cannot be generalizable to other hospitals.<br>-The study's design excluded other confounders to intervention's effectiveness |
| **(Gray et al. 2016)** | Pediatric asthma in ED | To improve patient asthma-related care in ED | Updating national guidelines including timely SABA administration | -Recording a Pediatric Asthma Severity Score (PASS) within electronic medical records (phase 1)<br>-Education and training for clinicians and nurses | -It was a single center study and it cannot be generalizable to other hospitals.<br>-Lack of a formal economic evaluation |

| | | | | | |
|---|---|---|---|---|---|
| | | | and usage of asthma severity scores. | -Standardizing protocol for SABA administration | |
| **(Hatoun et al. 2016)** | A pediatric ward | To increase the proportion of asthmatic patients discharged with their medication from 0% (baseline) to >75%. | A set of interventions to develop a medication delivery service | -The clinicians wrote the discharge prescriptions before the day of patient's discharge<br>-Caregivers were encouraged to take those medications before discharge<br>-Delivery of those medications at patient's room by the hospital pharmacy<br>-Continuous education for clinicians and caregivers | -Non-randomized sample with unbalanced distribution<br>-The study's design excluded other confounders to intervention's effectiveness |
| **(Rutman, Migita, et al. 2016)** | Pediatric ED | To investigate the impact of applying standardized ED-admission criteria on patient care<br>-To decrease ED Length of stay <4 hours<br>-To improve ED efficiency | Implementation of the modified pathway with new criteria and key-recommendations after one hour of treatment | -Inclusion of objective, respiratory score–based admission criteria for all eligible asthmatic children after 1 hour of providing the standard treatment in the ED.<br>-Use of the Respiratory Clinical Score<br>-Web-based education and training for clinicians | -Limits on the generalizability of the results due to Respiratory Clinical Score tool<br>-Unbalanced sample might affect study's external validity<br>-It was a single center study and it cannot be generalizable to other hospitals.<br>-The study examined only one pathway modification. |
| **(Rutman, Atkins, et al. 2016)** | ED and inpatient units | To evaluate the efficiency of the modified asthma pathway on children receiving asthma care with an asthma order set activated | Modification of an evidence-based asthma pathway and adopting new electronic order sets | -Use of the Respiratory Clinical Score<br>-Modifying the electronic order sets<br>-Adapting new prescription patterns<br>-On-site education and training for clinicians | -Patient misclassification based on ICD-10 codes<br>-Limits on the generalizability of the results due to Respiratory Clinical Score tool for assessing asthma severity<br>- In-organizational changes and culture might affect study's protocol compliance |
| **(Nkoy et al. 2015)** | Multiple Hospitals 1 tertiary hospital and 7 community hospitals | To evaluate the outcome of implementing an evidence-based asthma care process model (EB-CPM) and standardizing asthma-care criteria in a tertiary hospital and in seven community hospitals | Implementation of an evidence-based asthma care process model (EB-CPM) | -Standardizing diagnosis criteria for acute and chronic asthma<br>-Introducing algorithms for evaluation<br>-Criteria for specialist consultation,<br>-Specific criteria for pediatric ICU transfer or discharge<br>-Use of checklists<br>-On-site education and training for clinicians and involved staff | -Small sample size at community hospitals<br>-The usage of EMRs might lead to missed re-admissions<br>-Unbalanced sample<br>-In-organizational changes might affect study's protocol compliance |

AAIRS: Acute Asthma Intensity Research Score; CARAT-R: Childhood Asthma Risk Assessment Tool Revised; CPG: Clinical Practice Guideline; CXR: Chest Radiographs; EB-CPM: Evidence-based asthma care process model**;** ED: Emergency Department; EMR: Electronic Medical Record; ICU: Intensive Care Unit; LOS: Length of stay; MPIS: Modified

Pulmonary Index Score; PASS: Pediatric Asthma Severity Score; PICO: Pediatric Intensive Care Unit; RT: Respiratory therapist; SABA: Short-acting b-agonist

### Table 8: Characteristics of QI abstracts not included in the review

| Reference | Study Design | Study Objective | Study Setting-Population-Data Source | Interventions of interest | Statistical analysis and Outcomes | Results |
|---|---|---|---|---|---|---|
| **(Foradori et al. 2020)** | QI study with serial Plan-Do-Study-Act cycles | To increase the influenza vaccination rate from 13% to 80% over a 4-year period. | Children hospitalized with asthma<br><br>Data source: Electronic health records | -Modifications to the electronic health record (EHR)<br>-Educating families and clinicians<br>-Development of a hospital-vaccination tracking tool<br>-Nurse-driven vaccine protocol | -Rate of inpatient influenza vaccination<br><br>-Control charts were performed to analyze data | According to control charts, special cause variation was achieved, and the inpatient influenza vaccination rate increased from 13% to 57% in the postintervention period. |
| **(Parikh et al. 2019)** | QI study with Plan-Do-Study-Act cycles | To increase the percentage of children discharged with their medication in-hand from 15% to 80% | Children with asthma exacerbations, median aged 6.7 years | Interventions:<br>-Standardizing discharges<br>-Iterative meetings<br>-Bedside delivery of medications<br>-Initiating multidisciplinary daily discharges | -The proportion of patients discharged with their medications in-hand<br><br>-Control charts were used to assess the primary outcome | The percentage of patients with asthma who received their medications in-hand increased from 15% to >80% for all eligible children and >90% for children with public insurance. |
| **(Schondelmeyer et al. 2015)** | QI study | To reduce time on continuous pulse oximetry (CPOx) in room air | Children with wheezing.<br><br>1 unit of a children's hospital | -Standardized criteria for CPOx use<br>-In-site education,<br>-Nurse's checklist<br>-Order sets | -Time per week on CPOx<br><br>-Control charts tracked the impact of the interventions | Median time per week on CPOx decreased from 10.7 hours to 3.1 hours after the intervention. |

CPOx: continuous pulse oximetry; EHR: electronic health record