

CADTH RAPID RESPONSE REPORT:  
SUMMARY WITH CRITICAL APPRAISAL

# Clinical Decision Support Systems for Appropriate Medical Imaging: Clinical Evidence and Cost- Effectiveness

Service Line: Rapid Response Service  
Version: 1.0  
Publication Date: January 14, 2019  
Report Length: 28 Pages

**Authors:** Rob Edge PhD, Caitlyn Ford

**Cite As:** Clinical decision support systems for appropriate medical imaging: clinical effectiveness and cost-effectiveness. Ottawa: CADTH; 2019 Jan. (CADTH rapid response report: summary with critical appraisal).

**ISSN:** 1922-8147 (online)

**Disclaimer:** The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein are those of CADTH and do not necessarily represent the views of Canada's federal, provincial, or territorial governments or any third party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

**Questions or requests for information about this report can be directed to [Requests@CADTH.ca](mailto:Requests@CADTH.ca)**

## Abbreviations

CDS	clinical decision support
CPG	clinical practice guideline
CT	computed tomography
CTPA	computed tomography pulmonary angiography
DS-RES	decision support and risk education system
ED	emergency department
mSv	millisievert
OAR	Ottawa Ankle Rules
PE	pulmonary embolism
PERC	Pulmonary Embolism Rule-Out Criteria
RCT	randomized controlled trial
SR	systematic review
US	ultrasound imaging

## Context and Policy Issues

Clinical decision support (CDS) systems for appropriate medical imaging are designed to provide guidance to healthcare providers who request diagnostic imaging for their patients. Integrated CDS systems provide feedback or require confirmation of patient symptoms as part of normal electronic image ordering workflow. CDS systems for appropriate medical imaging aim to increase appropriate imaging investigations that comply with evidence-based clinical practice guidelines (CPG).<sup>1</sup> Canadian statistics suggest that between 15% to 30% of medical imaging ordered for patients presenting to the emergency department (ED) with lower back pain (LBP) are unnecessary.<sup>2</sup> Diagnostic yields as low as 5% also suggest an opportunity to reduce unnecessary computed tomography pulmonary angiography (CTPA) investigations for patients with suspected pulmonary embolism (PE).<sup>3</sup> Due to concerns of ionizing radiation exposure of computed tomography (CT) imaging and the utility of ultrasound (US) in the diagnosis of appendicitis there has been an increasing consensus to limit CT use for this indication, especially for pediatric populations.<sup>4,5</sup> Inappropriate imaging results in unnecessary radiation exposure, potential contrast-related reactions, and results in economic and opportunity costs.<sup>6,7</sup>

The purpose of this report is to retrieve and review the existing evidence on the clinical benefit, safety, harms, and cost-effectiveness of CDS system for appropriate medical image ordering.

## Research Questions

1. What is the clinical effectiveness of clinical decision support systems for appropriate medical imaging?
2. What is the cost-effectiveness of clinical decision support systems for appropriate medical imaging?

## Key Findings

Overall, the clinical evidence regarding the use of clinical decision support systems for appropriate medical imaging is mixed. Evidence from two randomized controlled trials that supported the clinical benefit and safety of clinical decision support systems for appropriate medical imaging. Together the confidence in these findings is mixed as one randomized controlled trial presented evidence of attrition bias in addition to other methodological quality concerns. Low-quality evidence from 3 of 14 'before and after' studies was also identified that reported increased diagnostic yield along with no increased adverse events, however mixed evidence of clinical efficacy for clinical decision support systems was also reported in the low-quality evidence. Findings of the 'before and after' studies were limited by a study design that failed to control for potential temporal effects unrelated to the intervention. None of the identified evidence reported statistically significant decreases in diagnostic yield, increases in inappropriate imaging, or increases in adverse events that followed implementation of clinical decision support systems for appropriate medical imaging. Additional high-quality evidence of clinical benefit and safety of clinical decision support systems for appropriate medical imaging would increase the confidence in the evidence identified in this report. Ideally, future studies would provide sufficient intervention information for replication and aim to identify factors that lead to a successful implementation of clinical decision support systems. No evidence of the cost-effectiveness of clinical decision support systems for appropriate imaging was identified.

## Methods

### Literature Search Methods

A limited literature search, with concepts appearing in title, abstract and major subject headings, was conducted on key resources including PubMed, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2013 and December 6, 2018.

### Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

**Table 1: Selection Criteria**

<b>Population</b>	Patients presenting with symptoms that may require medical imaging
<b>Intervention</b>	Clinical decision support systems
<b>Comparator</b>	Usual care, control (no support system), before-and-after
<b>Outcomes</b>	Q1: Clinical benefit, safety, harms (e.g. exposure to radiation, psychological harms) Q2: Cost-effectiveness (e.g. QALYS)
<b>Study Designs</b>	HTA/Systematic Reviews/Meta-Analyses, RCTs, non-randomized studies, and economic evaluations

HTA = health technology assessment; QALYS = quality adjusted life years; RCT = randomized controlled trial

### Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, they were included in a systematic review that was itself included in this report, or were published prior to 2013. Studies that reported outcomes of guideline adherence and/or imaging use without also reporting clinical benefit, safety, or harms did not meet the literature selection criteria.

### Critical Appraisal of Individual Studies

One reviewer conducted critically appraisal using the Assessing the Methodological Quality of Systematic Reviews II (AMSTAR II)<sup>8</sup> to guide quality assessment of included systematic reviews, and Downs and Black<sup>9</sup> to guide quality assessment of clinical studies. Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of the included evidence is described narratively.

## Summary of Evidence

### Quantity of Research Available

A total of 533 citations were identified in the literature search. Following screening of retrieved titles and abstracts by one review, 507 citations were excluded and 26 potentially relevant reports from the electronic search were retrieved for full-text review. No additional potentially relevant publications were identified in the grey literature search for full text review. Of the total 26 potentially relevant articles, 17 publications were excluded for various reasons, and 9 publications met the inclusion criteria and were included in this report. These publications were comprised of one systematic review,<sup>3</sup> one randomized controlled trial,<sup>7</sup> and seven non-randomized studies.<sup>2,4-6,10-12</sup> Appendix 1 presents the PRISMA<sup>13</sup> flowchart of the study selection.

### Summary of Study Characteristics

#### *Study Design*

A single SR, published in 2018, was identified and included in this report.<sup>3</sup> The SR had a broader focus than this Rapid Response report and included all interventions that were aimed at reducing diagnostic imaging use for PE diagnosis. The SR identified two RCTs, one comparative study, three prospective 'before and after,' and 11 retrospective 'before and after' studies published between 1998 and 2017. Eight of these studies included

evidence relevant to CDS interventions.<sup>14-21</sup> These eight studies consisted of one RCT,<sup>18</sup> one prospective 'before and after',<sup>20</sup> and six retrospective 'before and after' studies.<sup>14-17,19,21</sup>

Identified primary clinical studies consisted of one RCT,<sup>7</sup> three prospective 'before and after',<sup>2,4,11</sup> and four retrospective 'before and after'.<sup>5,6,10,12</sup> The RCT took place at a single urgent care center where medical doctors and physician assistants were randomized to either receive the CDS intervention or not.<sup>7</sup> All 'before and after' studies used historical controls to examine the impact of implementing CDS systems.<sup>2,4-6,10-12</sup>

### *Country of Origin*

The SR was conducted by authors in Canada. English and French publications were included in the SR while country of origin was not used in the literature selection criteria. Of the eight identified studies in the SR relevant to this report, seven were conducted in the USA and one was conducted in Spain.

The RCT was conducted in the USA,<sup>7</sup> as were five of the 'before and after' studies.<sup>4,5,10-12</sup> One retrospective 'before and after' study was conducted in a resource-limited setting in a South African public-sector tertiary-level teaching hospital.<sup>6</sup> One prospective 'before and after' study was conducted at the St. Paul's ED in Vancouver, British Columbia, Canada.<sup>2</sup>

### *Patient Population*

The population of interest for the SR was patients that received a diagnostic workup for PE in EDs and inpatient services of adult tertiary and quaternary care hospitals.<sup>3</sup>

Two retrospective 'before and after' studies focused on patients with suspected appendicitis.<sup>4,5</sup> These studies included pediatric cases between the ages of 3 and 18 years old that presented to the ED with right-sided or diffuse abdominal pain,<sup>5</sup> or presented to the ED with suspected appendicitis.<sup>4</sup> Hendrickson et al. excluded patients with metabolic disease, active cancer, current pregnancy, abdominal surgery history, or a history of abdominal trauma within 7 days.<sup>4</sup> Karbanda et al. also excluded patients with metabolic disease, pregnancy, active cancer, pain preceded by trauma, and history of abdominal surgery. In addition this study excluded patients with immunodeficiency, diabetes, cystic fibrosis, sickle cell anemia, inflammatory bowel disease, acute pain greater than 96 hours, or patients for whom US or CT imaging was ordered at another center.<sup>5</sup>

Two 'before and after' studies examined adult patients, over 18 years old, with suspected PE.<sup>6,11</sup> Murthy et al. retrospectively included all requested adult computed tomography pulmonary angiograms (CTPAs) excluding pregnancy or post-partum.<sup>6</sup> Drescher et al. prospectively included all patients with suspected PE and excluded pregnancies, contradiction to CTPA, renal insufficiency, and allergy to imaging contrast material.<sup>11</sup>

Two clinical studies examined patients with acute injuries; an RCT that examined unique patients that presented to urgent care with a foot or ankle complaint related discharge diagnosis,<sup>7</sup> and a retrospective 'before and after' study that examined adults (18 years or older) presenting to the ED with blunt ankle injury within the past 10 days.<sup>12</sup>

One retrospective 'before and after' study examined unique ED patients that were then not subsequently admitted to hospital. Patients with abdominal pain, chest pain, fever in children, headache, head injury, laceration, lower and upper extremity injury, neck injury, shortness of breath, and vaginal bleeding as chief complaints were included.<sup>10</sup>

One prospective 'before and after' study examined diagnoses related to lower back pain (LBP) and included patients with fractured lumbar vertebra(e) cord injury – closed, fractured lumbar vertebra(e) cord intact – closed, epidural abscess, intraspinal abscess, radiculopathy with no other symptoms, lumbosacral strain, and sciatica.<sup>2</sup>

### *Interventions and Comparators*

#### **Systematic Review**

The SR included all interventions aimed at reducing diagnostic imaging use for PE diagnosis.<sup>3</sup> In addition to the relevant CDS interventions the SR identified both voluntary and educational interventions, performance and feedback reports, as well as policy interventions. CDS interventions were classified by the SR as either voluntary participation systems or mandatory participation systems. The evidence identified by the SR included one RCT,<sup>18</sup> and four retrospective 'before and after' studies that examined a voluntary participation CDS.<sup>14,15,19,21</sup> Evidence regarding the clinical effectiveness of mandatory participation CDS interventions was identified in one prospective 'before and after' study,<sup>20</sup> and two retrospective 'before and after' intervention studies.<sup>16,17</sup>

#### **Randomized Controlled Trial**

The RCT identified in this report described a CDS system software intervention based upon the Ottawa Ankle Rules (OAR) that was integrated into the physician order entry system (Percipio; Medicalis, San Francisco, CA). Four successive screens were presented to the ordering physician or physician assistant that captured data to determine the utility of any potential imaging according to OAR. If the utility of imaging was determined to be low an educational screen explaining the low utility and an opportunity to cancel or continue with the imaging order was presented to the ordering physician or physician assistant.<sup>7</sup>

#### **Non-randomized Studies**

The seven non-randomized before and after studies compared a CDS system intervention to image ordering during an interval of time prior to implementation of the CDS system.<sup>2,4-7,10-12</sup> Murthy et al. also included an intermediate intervention prior to CDS implementation where the relevant diagnostic algorithm was distributed to physicians.<sup>6</sup> Compliance to CDS system recommendations was optional in all studies.<sup>2,4-7,10-12</sup> Two studies did not require use of the CDS system to order imaging, therefore CDS use itself was optional.<sup>5,10</sup>

Two of the seven non-randomized 'before and after' studies examined the impact of CDS systems for patients with indications of appendicitis.<sup>4,5</sup> Hendrickson et al. implemented a CDS system that used the low-risk appendicitis rule, and the Pediatric Appendicitis Score Appendicitis as an evidence base for decision support.<sup>4</sup> Kharbanda implemented a voluntary CDS system based upon an in-house developed CPG for patients with suspected appendicitis.<sup>5</sup>

Two studies examined the impact of CDS systems for patients with indications of PE.<sup>6,11</sup> Both CDS interventions utilized the Wells score, and D-dimer testing for input. Dresher et al. also utilized the Pulmonary Embolism Rule-Out Criteria (PERC) for the CDS diagnostic algorithm.<sup>11</sup>

Based upon software screenshots and the description of the software provided in the publication, it is likely that Silveira et al. used the same CDS system as the RCT by Tajmir et al., which was based upon the OAR integrated into the electronic image ordering system.

The descriptions however are insufficient to conclude that the interventions were identical.<sup>7,12</sup>

In addition to dissemination of physician educational material, Min et al. implemented a CDS system that utilized a 'red flag checklist' that required physicians to provide a reason to order imaging for individuals with LBP. The checklist consisted of the following options: "suspected compression fracture," "suspected epidural abscess or hematoma," "suspected cancer," "suspected cauda equina syndrome," "suspected infection," "severe progressive neurologic deficit," or "other." Selection of "other" required further explanation by the physician for CDS non-compliant image ordering. Compliance to this CDS intervention was therefore considered optional.<sup>2</sup>

Carnevale et al. used a CDS system described as an electronic decision support and risk education system (DS-RES) which was reported to be useful for a range of patient indications. The authors do not report a commercial software vendor or the evidence on which this decision support was based upon. In addition to DS-RES this study also implemented interventions supported by the software including online risk-reduction training and regular feedback to physicians and nurses regarding documentation performance using the system. Use of the DS-RES software was voluntary.<sup>10</sup>

None of the studies reported using a commercially or otherwise available CDS software intervention.

### *Outcomes*

Outcomes considered in this report as related to clinical benefit, safety, and harms reported by the identified studies included diagnostic yield,<sup>3,6,7,11,12</sup> missed diagnoses,<sup>2,4</sup> perforated appendicitis,<sup>4,5</sup> negative appendectomy,<sup>4</sup> radiation exposure,<sup>3</sup> rehospitalization,<sup>4,5,10</sup> medical imaging ordered within 30 days of initial visit,<sup>2</sup> any adverse event within 90 days,<sup>3</sup> and ED length of stay.<sup>5</sup> None of the identified evidence reported cost-effectiveness outcomes.

Diagnostic yield outcomes were deemed relevant to patient safety as they quantify patient group exposure to radiation. Diagnostic yield was unanimously defined in the identified evidence as the proportion of imaging investigations that yielded a positive diagnosis.<sup>3,6,7,11,12</sup> A higher diagnostic yield therefore exposed fewer patients to imaging radiation that did not result in a definitive diagnosis.

Two studies reported missed diagnoses.<sup>2,4</sup> Hendrickson et al. reported the percentage of missed appendicitis cases before and after CDS intervention,<sup>4</sup> while Min et al. narratively reported missed diagnoses without predefining this outcome in the methodology.<sup>2</sup>

Rehospitalization was reported by three identified primary clinical studies.<sup>4,5,10</sup> The rehospitalization timeframe differed by study with Hendrickson et al. reporting rehospitalization within 4 weeks,<sup>4</sup> Kharbanda et al. reporting return ED visits within 30 days,<sup>5</sup> and Carnevale et al. reported both return ED visits within 3 days and return ED visits within 7 days.<sup>10</sup> Rehospitalization within these timeframes was used by the authors as an indication of unmet patient needs and determined to be at least partially a function of diagnostic yield.<sup>10</sup> An acknowledged limitation of the data associated with rehospitalization outcomes included that rehospitalization had to occur within the same hospital system.<sup>4,5</sup>

Included studies reported at least one outcome from the literature selection criteria and in addition the identified evidence also reported imaging use,<sup>3-5,7,12</sup> imaging orders,<sup>2,11</sup> and compliance.<sup>7,10-12</sup>

Characteristics of the included studies are also summarized in Appendix 2, Table 2 and Table 3.

## Summary of Critical Appraisal

### Systematic Review

The included SR reported a methodology with some limitations that included a lack of an assessment of publication bias, conclusions that were not associated with the evaluated risk of bias, and no justification was provided for the study design selection. Otherwise the SR was of a high-quality and methodological strengths included prior protocol registration, study selection and data extraction executed in duplicate, a list of excluded studies, a critical appraisal of individual included studies, quantitative assessment of the appropriateness of meta-analysis, and a discussion of heterogeneity.<sup>3</sup>

One RCT was identified in the SR as being relevant to CDS,<sup>18</sup> which was appraised as being of good quality.<sup>3</sup> The body of evidence identified by the comprehensive literature search strategy of the SR was primarily comprised of 'before and after' studies. These studies were critically appraised as generally poor quality, subject to the biases associated with 'before and after' studies, and biases associated with the interaction between the intervention and its implementation context. The overall quantity and quality of the included studies included in the SR precluded associating a high degree of confidence in the results, this was similarly articulated by the authors of the SR.<sup>3</sup>

Critical appraisal of the SR is summarized in Appendix 3, Table 4.

### Randomized Controlled Trial

The RCT included in this report had important methodological strengths.<sup>7</sup> Despite a relatively small size (n = 26 providers saw 632 enrolled patients) an *a priori* statistical power calculation justified the sample size. The authors of the study provided clearly defined outcomes and reported no conflicts of interest (COI). Importantly, the authors also examined the role of intervention compliance, which increased the authors ability to account for the effect of the intervention itself. Methodological limitations of the RCT included a lack of description of the randomization methods, a lack of allocation concealment and blinding, and a lack of safety or diagnostic accuracy data. External validity was limited in this RCT in part due to the randomization being at the level of medical doctor and physician assistants at a single center. The co-existence of CDS and control in the same center may have overlooked important intervention impacts when implemented at the institutional level. The CDS intervention was not cited as being software that was available commercially or otherwise, potentially limiting replicability. Based on the results reported in the study it was also not clear if the randomization was successful; providers randomized to the intervention likely evaluated a patient group with a statistically significant greater presence of fractures than the control group. Additionally, the providers that diagnosed enrolled patients were a fraction of the total randomized providers, making the study subject to attrition bias. The ratio of medical doctors to physician assistants in the intervention and control group clearly indicated at least one aspect of attrition bias. The authors of this RCT transparently reported this potential for failed randomization and attrition bias and also provided a comprehensive discussion of these and other limitations of the study.<sup>7</sup> The RCT also studied the longest timeframe following implementation of a CDS system (20 months) in the identified evidence but it was not reported if the intervention effects increased or decreased over time as providers gained more experience with the CDS system.

### Non-randomized studies

The seven non-randomized studies included in this report share limitations associated with being 'before and after' studies.<sup>2,4-6,10-12</sup> 'Before and after' study designs employ historical controls and therefore are subject to uncontrolled chronological effects such as staff changes, training effects, and patient factors unrelated to the intervention. Additionally four of the seven non-randomized, 'before and after' studies were retrospective studies and were therefore subject to the biases associated with retrospective study design.<sup>5,6,10,12</sup> Other important limitations within the body of evidence from the identified 'before and after' studies included a lack of safety and diagnostic accuracy data,<sup>6,11,12</sup> a lack of information on CDS compliance,<sup>4-6,10</sup> a lack of sample size determination by an *a priori* statistical power calculation,<sup>2,4-6,10,11</sup> and limited information on patient populations.<sup>2,5</sup> Importantly, some studies included a multi-faceted intervention which limit the findings applicability to implementation of CDS as an intervention alone.<sup>2,5,6,10,11</sup> None of the studies described the CDS software sufficiently for a precise replication of the intervention. All studies provided a comprehensive discussion of the study limitations.<sup>2,4-6,10-12</sup> Silveira et al. reported a relevant COI,<sup>12</sup> while two other non-randomized studies did not provide a COI statement.<sup>6,10</sup> The remaining studies reported no conflicts of interest.<sup>2,4,5,11</sup> Common methodological strengths of the non-randomized studies include well defined, quantitative outcomes,<sup>2,4-6,10-12</sup> and tabulated patient characteristics.<sup>4-6,10,12</sup> Overall the non-randomized studies provide evidence that should be interpreted with caution due to the limited external validity and chronological biases associated with using historical controls.

A summary of the critical appraisal of the included primary studies is provided in Appendix 3, Table 5.

## Summary of Findings

### *Clinical Effectiveness of CDS Systems*

#### **Diagnostic Yield**

Diagnostic yield outcomes are a measure of the efficiency with which medical imaging was utilized and reflected the proportion of patients exposed to imaging radiation that did not lead to definitive diagnosis, however without additional safety data, diagnostic yield is not a safety outcome. The SR, RCT, and three non-randomized studies reported diagnostic yield outcomes.<sup>3,6,7,11,12</sup> The SR identified six retrospective 'before and after' studies, and one prospective 'before and after' study that reported diagnostic yield outcomes.<sup>3,14-17,19-21</sup> The highest quality evidence for diagnostic yield therefore was reported in the RCT which reported a statistically significant decrease in foot and total radiography yield but not for ankle radiography yield. The authors acknowledged this finding may have been a result of ineffective randomization that resulted in over twice as many fractures per patient visit in the intervention group.<sup>7</sup> Overall a statistically significant improvement in diagnostic yield was observed in four 'before and after' studies,<sup>6,14,19,21</sup> whereas six 'before and after' studies did not observe a statistically significant increased diagnostic yield following implementation of CDS.<sup>11,12,15-17,20</sup> The RCT examined a CDS system that was very similar or identical to the CDS intervention of one retrospective 'before and after' using OAR. The 'before and after' study was published prior to the RCT and did not observe a statistically significant improvement in diagnostic yield for this CDS intervention. These two studies shared the most similar intervention and the baseline diagnostic yield differs significantly between the two studies.<sup>7,12</sup>

Diagnostic yield results for studies examining PE were also mixed,<sup>3,6,11</sup> although the CDS intervention used was not the same in these studies. While the highest-quality study suggested an improved diagnostic yield for a CDS system intervention, the lack of any consistent impact on this outcome limited the confidence in this finding. It is likely that CDS compliance impacted the outcomes such as diagnostic yield, and Drescher et al. reported a CDS system compliance of 66% and a statistically significant improvement in diagnostic yield of PE only when CDS was followed as compared to when the protocol was violated.<sup>11</sup> Statistically significant improvements in compliance with CDS were associated with improved diagnostic yield in the RCT, and in Drescher et al., but not in Silveira et al.<sup>7,11,12</sup> Findings of statistically significant improvements in diagnostic yield and CDS interventions that were either mandatory or voluntary were also mixed.<sup>3,6,7,11,12</sup>

### Safety

Safety related outcomes reported in the identified evidence included rehospitalization.<sup>4,5,10</sup> None of three 'before and after' studies that reported this outcome identified a statistically significant change.<sup>4,5,10</sup>

Additional safety related outcomes included no statistically significant changes in missed diagnoses,<sup>2,4,7</sup> perforated appendicitis,<sup>4,5</sup> negative appendectomy,<sup>4</sup> and ED length of stay.<sup>5</sup> The RCT identified in the included SR reported a statistically significant decrease in the proportion of patients that received > 5 millisievert (mSv) of radiation from CTPA,<sup>3</sup> the full-text of this RCT also reports no significant difference in delayed diagnoses, return rate to hospital, or any adverse event within 90 days.<sup>18</sup> The SR also narratively reported the results of this RCT and found no differences in mortality, complications because of thromboembolic and bleeding events, or any other adverse events during 3 months of follow-up. Together these findings suggested the decreased radiation finding was relevant to patient safety.<sup>3,18</sup>

Kharbanda et al. examined trends in appendiceal perforation, return ED visits, and ED length of stay and did not identify any statistically significant impact of CDS implementation.<sup>5</sup> Consistent evidence of varying methodological quality identified here supported CDS interventions as not having presented any additional safety risk to patients.

### Clinical Effectiveness reported with safety data

Appropriate imaging related outcomes, such as diagnostic yield, reported in isolation do not account for potential missed diagnoses or other adverse events. Six included studies reported both an efficacy and safety outcome, two RCTs,<sup>7,18</sup> and three 'before and after' studies reported statistically significant evidence of increased diagnostic yield along with no significant increased safety risks with a CDS system intervention.<sup>2,5,10</sup> One 'before and after' study reported no statistically significant improvement in appropriate imaging.<sup>4</sup> Specifically, the SR identified RCT evidence that reported decreased radiation exposure and no statistically significant increased adverse events within 90 days.<sup>3</sup> The identified RCT, presented evidence of an increased diagnostic yield and no significant increase in adverse events.<sup>7</sup> Carnevale et al. also did not observe a statistically significant increase in 3-day or 7-day revisit rates to the ED associated with a statistically significant increase in appropriate imaging. The authors concluded that together these observations suggested greater diagnostic accuracy although they were unable to directly measure diagnostic accuracy. The authors state that this inability was despite the fact that diagnostic accuracy measures were an organization goal of CDS implementation.<sup>10</sup>

Two other 'before and after' studies reported no changes in safety related outcomes of appendiceal perforation,<sup>5</sup> return ED visits within 30 days,<sup>5</sup> ED length of stay,<sup>5</sup> or missed

serious diagnoses,<sup>2</sup> associated with evidence of increased appropriate imaging rates following CDS implementation. Hendrickson et al. reported no changes in rates of appendicitis diagnosis, performed appendectomy, perforated appendicitis, rehospitalization within 4 weeks, missed appendectomy, or negative appendectomy, and these outcomes were not associated with a more statistically significant appropriate usage of imaging.<sup>4</sup>

### Duration

The included studies had limited follow-up periods, and the long-term effectiveness of these CDS interventions was not examined.<sup>5</sup> The study with the longest follow-up period was the RCT that examined the effects of an OAR-based CDS system based for 20 months and reported a statistically significant improvement in diagnostic yield and adherence to OAR.<sup>7</sup> Trends in more appropriate imaging use (US over CT for suspected appendicitis) reported by Kharbanda et al. over a 13 month CDS intervention period demonstrated linear constant and continuing improvement. The authors did not hypothesize about how long the observed trend would last or at what point it might stop improving.<sup>5</sup>

Appendix 4, Table 6 and Table 7 present further detail regarding the findings of the included SR and primary clinical studies, respectively.

### *Cost-effectiveness of CDS*

No cost-effectiveness studies identified met the literature selection criteria, however the RCT included in the identified SR reported on some limited cost data for the healthcare system in the USA.<sup>3,18</sup> A statistically significant decrease in charges and estimated costs for medical care within 90 days of initial ED presentation (for suspected PE) in the investigated population was observed in the CDS intervention group. The authors of the SR stated that there was not enough evidence to make conclusions about the impact of CDS on healthcare costs.<sup>3</sup>

### Limitations

The findings of the identified body of evidence was associated with significant uncertainty due to a lack of clearly defined interventions and mixed findings. The ability to discern CDS intervention and implementation causal factors, and therefore generalizability to the Canadian context, in the mixed efficacy findings is limited. While some identified evidence examined patients with the same condition, the lack of consistently defined intervention also limited generalizability to patient condition. Most identified evidence was from 'before and after' studies which limit external validity of the findings. The included RCT may have biased findings due to a significant failure of randomization and attrition bias.

## Conclusions and Implications for Decision or Policy Making

This report identified one SR,<sup>3</sup> one RCT,<sup>7</sup> three prospective 'before and after',<sup>2,4,11</sup> and four retrospective 'before and after' studies relevant to the clinical effectiveness of CDS systems used to guide appropriate medical imaging.<sup>5,6,10,12</sup> The SR identified eight relevant studies that consisted of one RCT,<sup>18</sup> one prospective 'before and after',<sup>20</sup> and six retrospective 'before and after' studies.<sup>14-17,19,21</sup>

This report followed a similar CADTH assessment of CDS systems for Diagnostic Imaging published in 2012.<sup>1</sup> This previous report identified a lack of published evidence to support effective CDS systems on patient outcomes and a need for more comparative effectiveness research.<sup>1</sup> This current report identified such evidence published after 2012.<sup>7,18</sup>

The highest quality evidence identified was from the two RCTs,<sup>7,18</sup> one of which was included in the SR.<sup>3</sup> These studies reported decreased radiation exposure,<sup>3</sup> greater guideline adherence,<sup>7</sup> increased diagnostic yield,<sup>7</sup> and no increase in missed diagnoses<sup>7,18</sup> following CDS implementation. The decreased radiation exposure data was reported along with no increased adverse events for patients with suspected PE.<sup>3</sup> Lower-quality evidence of the clinical efficacy of CDS systems for PE was mixed.<sup>3,6,11</sup> The other RCT reported an increased diagnostic yield and no increased safety risks, however also reported results that indicated an acknowledged potential failure of randomization that greatly increased the uncertainty of these conclusions. This RCT examined an OAR-based CDS system for patients with possible ankle or foot fractures.<sup>7</sup> Lower-quality evidence of a similar OAR-based CDS system also reported increased adherence to OAR, but no statistically significant increase in diagnostic yield.<sup>12</sup> Neither the included RCT or the RCT identified by the SR provided sufficient intervention information to enable precise replication.<sup>3,7,18</sup>

Three 'before and after' studies also identified increased diagnostic yield without any increases in patient safety risk.<sup>2,5,10</sup> One of these studies was conducted in the Canadian healthcare system.<sup>2</sup>

The remainder of the identified evidence from 'before and after' studies had very limited consensus on outcomes of diagnostic yield or diagnostic imaging use, however none of the studies reported a statistically significant increase in inappropriate imaging use following a CDS system intervention. Additionally, all studies did not report any statistically significant increased patient safety risks following CDS implementation.<sup>2,4-6,10-12</sup> The SR, published in 2018, concluded that there was not enough data to make safety related conclusions.<sup>3</sup>

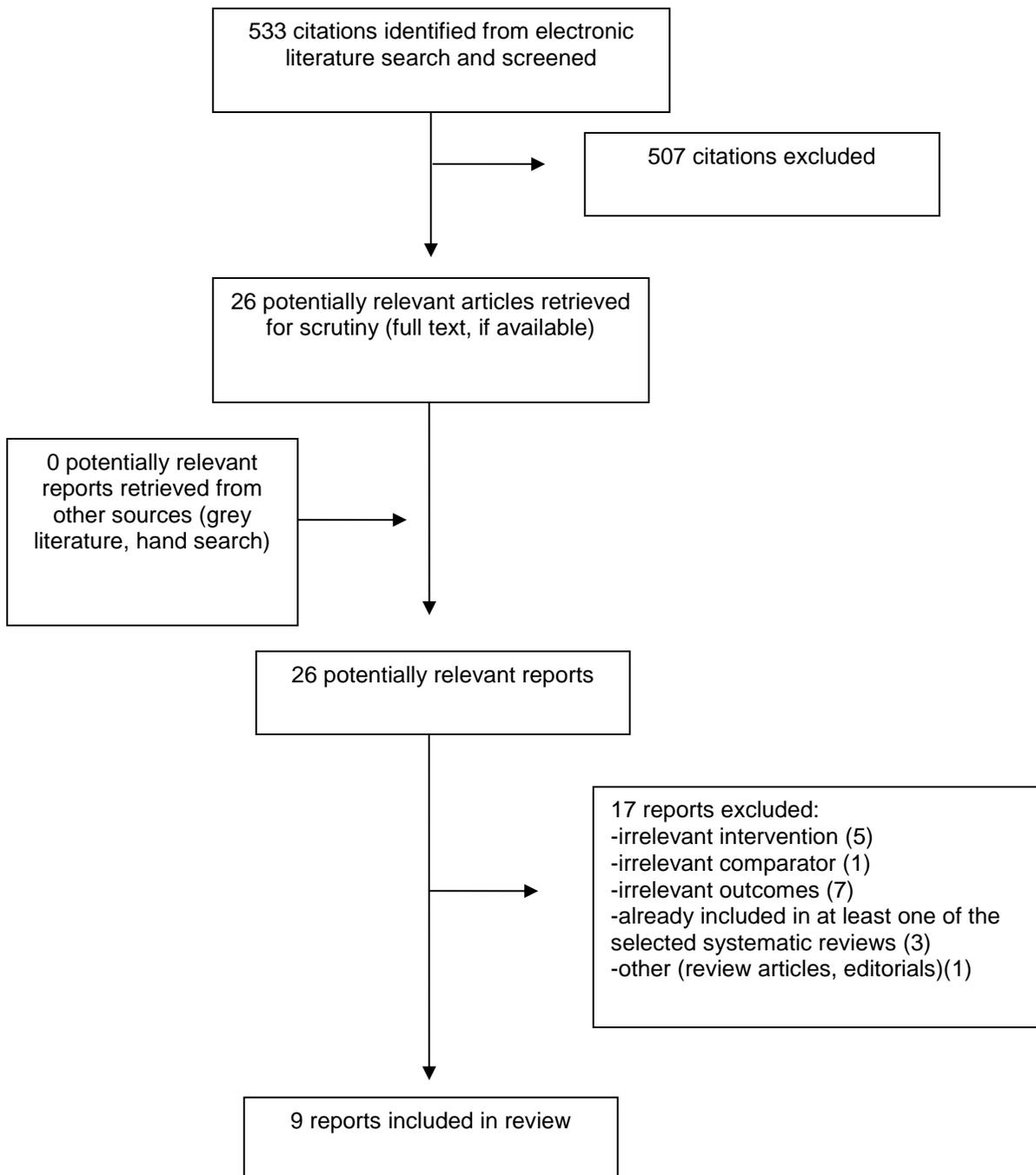
All identified studies provided limited information on CDS system details and implementation, no studies cited commercially or otherwise available software that would facilitate replication of similar CDS system implementation. The authors of the SR stated, "Future research should also aim at bringing answers to the knowledge gaps related to the factors of success and barriers associated with the implementation of the interventions."<sup>3</sup>

While this report identified evidence that supported the clinical efficacy and safe implementation of CDS systems, it also identified low-quality evidence of mixed efficacy results along with a lack of clarity associated with the intervention and implementation. Additional high-quality evidence of clinical benefit and safety of clinical decisions support systems for appropriate medical imaging would increase the confidence in the evidence identified in this report. Cost-effectiveness studies conducted in the Canadian healthcare system are also required to more comprehensively evaluate CDS systems for appropriate imaging.

## References

1. Clinical decision support systems for diagnostic imaging. (*CADTH issues in emerging health technologies no.177*). Ottawa (ON): CADTH; 2012: <https://www.cadth.ca/clinical-decision-support-systems-diagnostic-imaging-0>. Accessed 2019 Jan 11.
2. Min A, Chan VWY, Aristizabal R, et al. Clinical decision support decreases volume of imaging for low back pain in an urban emergency department. *J Am Coll Radiol*. 2017;14(7):889-899.
3. Deblois S, Chartrand-Lefebvre C, Toporowicz K, Chen Z, Lepanto L. Interventions to reduce the overuse of imaging for pulmonary embolism: a systematic review. *J Hosp Med*. 2018;13(1):52-61.
4. Hendrickson MA, Wey AR, Gaillard PR, Kharbanda AB. Implementation of an electronic clinical decision support tool for pediatric appendicitis within a hospital network. *Pediatr Emerg Care*. 2018;34(1):10-16.
5. Kharbanda AB, Madhok M, Krause E, et al. Implementation of electronic clinical decision support for pediatric appendicitis. *Pediatrics*. 2016;137(5).
6. Murthy C, Davis R, Koegelenberg CF, Irusen EM, Pitcher RD. The impact of an electronic clinical decision support for pulmonary embolism imaging on the efficiency of computed tomography pulmonary angiography utilisation in a resource-limited setting. *S Afr Med J*. 2015;106(1):62-64.
7. Tajmir S, Raja AS, Ip IK, et al. Impact of clinical decision support on radiography for acute ankle injuries: a randomized trial. *West J Emerg Med*. 2017;18(3):487-495.
8. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017;358:j4008. <http://www.bmj.com/content/bmj/358/bmj.j4008.full.pdf>. Accessed 2019 Jan 11.
9. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health*. 1998;52(6):377-384. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf>. Accessed 2019 Jan 11.
10. Carnevale TJ, Meng D, Wang JJ, Littlewood M. Impact of an emergency medicine decision support and risk education system on computed tomography and magnetic resonance imaging use. *J Emerg Med*. 2015;48(1):53-57.
11. Drescher MJ, Fried J, Brass R, Medoro A, Murphy T, Delgado J. Knowledge translation of the PERC rule for suspected pulmonary embolism: a blueprint for reducing the number of CT pulmonary angiograms. *West J Emerg Med*. 2017;18(6):1091-1097.
12. Silveira PC, Ip IK, Sumption S, Raja AS, Tajmir S, Khorasani R. Impact of a clinical decision support tool on adherence to the Ottawa Ankle Rules. *Am J Emerg Med*. 2016;34(3):412-418.
13. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009;62(10):e1-e34.
14. Drescher FS, Chandrika S, Weir ID, et al. Effectiveness and acceptability of a computerized decision support system using modified Wells criteria for evaluation of suspected pulmonary embolism. *Ann Emerg Med*. 2011;57(6):613-621.
15. Dunne RM, Ip IK, Abbett S, et al. Effect of evidence-based clinical decision support on the use and yield of CT pulmonary angiographic imaging in hospitalized patients. *Radiology*. 2015;276(1):167-174.
16. Geeting GK, Beck M, Bruno MA, et al. Mandatory assignment of modified Wells score before CT angiography for pulmonary embolism fails to improve utilization or percentage of positive cases. *AJR Am J Roentgenol*. 2016;207(2):442-449.
17. Jimenez D, Resano S, Otero R, et al. Computerised clinical decision support for suspected PE. *Thorax*. 2015;70(9):909-911.
18. Kline JA, Jones AE, Shapiro NI, et al. Multicenter, randomized trial of quantitative pretest probability to reduce unnecessary medical radiation exposure in emergency department patients with chest pain and dyspnea. *Circ Cardiovasc Imaging*. 2014;7(1):66-73.
19. Prevedello LM, Raja AS, Ip IK, Sodickson A, Khorasani R. Does clinical decision support reduce unwarranted variation in yield of CT pulmonary angiogram? *Am J Med*. 2013;126(11):975-981.
20. Raja AS, Gupta A, Ip IK, Mills AM, Khorasani R. The use of decision support to measure documented adherence to a national imaging quality measure. *Acad Radiol*. 2014;21(3):378-383.
21. Raja AS, Ip IK, Prevedello LM, et al. Effect of computerized clinical decision support on the use and yield of CT pulmonary angiography in the emergency department. *Radiology*. 2012;262(2):468-474.

## Appendix 1: Selection of Included Studies



## Appendix 2: Characteristics of Included Publications

**Table 2: Characteristics of Included Systematic Review**

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
<b>Deblois 2018,<sup>3</sup> Canada</b>	2 RCTs 1 Comparative 3 Prospective 'before and after' 11 Retrospective 'before and after' studies	Patients that received diagnostic workup for PE in EDs and inpatient services of adult tertiary and quaternary care hospitals	Interventions aimed at reducing diagnostic imaging use for PE diagnosis. Comparators of usual care or another intervention aimed at reducing diagnostic imaging.	<ul style="list-style-type: none"> <li>• Use of imaging</li> <li>• Diagnostic yield</li> <li>• Radiation dose</li> <li>• Guideline adherence</li> <li>• Safety</li> <li>• Costs</li> </ul>

ED = emergency department; PE = pulmonary embolism; RCT = randomized controlled trial

**Table 3: Characteristics of Included Primary Clinical Studies**

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes
<b>Hendrickson 2018,<sup>4</sup> USA</b>	Prospective comparative 'before and after' study  Before: 3 months After: 6 months	Pediatric (age 3 to 18 years) ED patients with suspected appendicitis (n = 327)  Exclusions: metabolic disease, active cancer, current pregnancy, previous abdominal surgery, history of abdominal trauma in the past 7 days	Intervention – post E-CDS implementation Comparator – pre E-CDS implementation  CDS was based upon an in-house CPG developed upon the low-risk appendicitis rule, and the Pediatric Appendicitis Score.  Compliance to CDS was not mandatory.	<ul style="list-style-type: none"> <li>• US use</li> <li>• CT use</li> <li>• Safety</li> <li>• Missed diagnoses</li> <li>• Perforated appendicitis</li> <li>• Negative appendectomy</li> <li>• Rehospitalization within 4 weeks</li> </ul>
<b>Drescher 2017,<sup>11</sup> USA</b>	Prospective comparative 'before and after' study  Before: 12 months After: 12 months	Adults (age over 18 years) for whom a diagnosis of PE is suspected (n = 199, 200)  Exclusions: pregnancies, contraindication to CTPA, renal insufficiency, allergy to imaging contrast material	Intervention – post E-CDS implementation with education component Comparator – pre E-CDS implementation  CDS based upon Wells score and PERC criteria  Compliance to CDS was not mandatory but overriding the protocol was recorded and reasons required.	<ul style="list-style-type: none"> <li>• CTPA orders</li> <li>• CTPA yield</li> <li>• Compliance</li> </ul>
<b>Min 2017,<sup>2</sup> Canada</b>	Prospective comparative 'before and after'	All patients with a diagnosis related to LBP (n = 4,562):	Intervention – post E-CDS implementation Comparator – pre E-CDS	<ul style="list-style-type: none"> <li>• Medical imaging tests ordered</li> <li>• Physician</li> </ul>

**Table 3: Characteristics of Included Primary Clinical Studies**

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes
	study  Before: 2 years After: 14 months	Fracture lumbar vertebra(e) cord injury – closed, epidural abscess, acute back pain (<2 weeks duration), lumbosacral strain, radiculopathy with no other symptoms, fracture lumbar vertebra(e) cord intact – closed, intraspinal abscess, sciatica	implementation  CDS developed in-house, LBP ‘red-flag’ checklist incorporated into image ordering.  Compliance to CDS was not mandatory but overriding the protocol was recorded and reasons required.	variation in medical image ordering ● Medical imaging ordered within 30 days of initial visit
<b>Tajmir 2017,<sup>7</sup> USA</b>	RCT – randomization was at the level of medical doctor or physician assistant  Duration 20 months	All unique patients presenting to urgent care with a discharge diagnosis code for foot or ankle complaint (n = 14,642)	Intervention – CDS based upon OAR integrated into image ordering system  Comparator – no CDS  Compliance to CDS was not mandatory but overriding the protocol was recorded and reasons required.	● Adherence to OAR ● Radiography use ● Radiography yield
<b>Kharbanda 2016,<sup>5</sup> USA</b>	Retrospective comparative ‘before and after’ study  Before: 11 months After: 13 months	Pediatric patients (age 3 to 18 years) presenting to the ED with right-sided or diffuse abdominal pain (n = 2,803).  Exclusions: active cancer, immunodeficiency, diabetes, metabolic disease, cystic fibrosis, sickle cell anemia, inflammatory bowel disease, acute pain > 96 hours, pain preceded by trauma, US or CT ordered at another center, pregnancy, history of abdominal surgery.	Intervention – post E-CDS implementation Comparator – pre E-CDS implementation  CDS based upon in-house CPG developed by multidisciplinary team E-CDS comprised of three components: a standardized pain order-set, Web-based risk stratification tool, and a BPA when imaging was ordered (compliance not mandatory)  CDS use was voluntary.	● CT use ● US use ● Immediate impact on imaging use ● Trends in imaging use ● Appendiceal perforation ● Return ED visits within 30 days ● ED length of stay
<b>Silveira 2016,<sup>12</sup> USA</b>	Retrospective comparative ‘before and after’ study  Before: 6 months After: 8 months	Adult (age ≥ 18 years) ED patients with acute (within 10 days) blunt ankle injury (n = 460)	Intervention – E-CDS based upon OAR Comparator – pre E-CDS implementation  Compliance to CDS was not mandatory but overriding the protocol was recorded and reasons required.	● Adherence to OAR ● Radiography use and yield

**Table 3: Characteristics of Included Primary Clinical Studies**

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes
<b>Carnevale 2015,<sup>10</sup> USA</b>	Retrospective comparative 'before and after' study  Before: 11 months After: 11 months	All unique ED patients not subsequently admitted to hospital with the following chief complaints:  Abdominal pain, chest pain, fever in children, headache, head injury, laceration, lower and upper extremity injury, neck injury, shortness of breath, and vaginal bleeding. (n = 25 690)	Intervention – post DS-RES system with online risk-reduction training, and regular feedback to physicians and nurses regarding documentation performance using DS-RES.  Comparator – pre DS-RES implementation  Use of DS-RES was voluntary	<ul style="list-style-type: none"> <li>• CT/MRI rate</li> <li>• Appropriate use</li> <li>• Return ED visits within 3 days</li> <li>• Return ED visits within 7 days</li> </ul>
<b>Murthy 2015,<sup>6</sup> South Africa</b>	Retrospective comparative 'before and after' study  Before: Unclear Pre CDS: 1 year After: Unclear	All requested adult (> 18 years) CTPAs excluding pregnancy, or post-partum (n = 424)	Intervention – post CDS system  Comparators – pre CDS implementation with PE diagnostic algorithm distribution and pre CDS implementation prior to distribution of PE diagnostic algorithm.  Compliance was voluntary.	<ul style="list-style-type: none"> <li>• CTPA yield</li> </ul>

BPA = best-practice advisory; E-CDS = electronic clinical decision support; CDS = clinical decision support; CGP = clinical practice guideline; CT = computed tomography; CTPA = computed tomography pulmonary angiogram; DS-RES = decision support and risk education system; ED = emergency department; MRI = magnetic resonance imaging; OAR = Ottawa Ankle Rules; PE = pulmonary embolism; PERC = Pulmonary Embolism Rule-Out Criteria; US = ultrasound imaging

## Appendix 3: Critical Appraisal of Included Publications

**Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR II<sup>8</sup>**

Strengths	Limitations
<i>Deblois, 2018<sup>3</sup></i>	
<ul style="list-style-type: none"> <li>• Elements of PICO sufficiently described</li> <li>• Review protocol registered prior to execution in PROSPERO</li> <li>• Comprehensive literature search strategy</li> <li>• Study selection and data extraction performed in duplicate</li> <li>• List of excluded studies provided</li> <li>• Tabulated characteristics of included studies provided</li> <li>• Critical appraisal of included studies in supplementary material</li> <li>• Quantitative reasoning provided for determination that meta-analysis was inappropriate</li> <li>• Discussion of heterogeneity</li> <li>• Conflict of Interest statement provided: no conflicts</li> </ul>	<ul style="list-style-type: none"> <li>• No justification provided for study design selection (experimental and observational)</li> <li>• Unclear specific risks of bias associated with some conclusions</li> <li>• No assessment of publication bias</li> </ul>

PICO = population, intervention, comparator, and outcome; PROSPERO = international prospective register of systematic reviews

**Table 5 Strengths and Limitations of Clinical Studies using Downs and Black<sup>9</sup>**

Strengths	Limitations
<i>Randomized Controlled Trials</i>	
<i>Tajmir, 2017<sup>7</sup></i>	
<ul style="list-style-type: none"> <li>• Discussion of study limitations provided</li> <li>• Clearly defined outcomes</li> <li>• Examines role of compliance</li> <li>• Conflict of interest statement provided: no conflicts</li> <li>• Statistical power calculation</li> <li>• Commented on safety outcomes</li> </ul>	<ul style="list-style-type: none"> <li>• Randomized at the level of provider (medical doctors and physician assistants)               <ul style="list-style-type: none"> <li>• Unclear if provider groups that actually saw enrolled patients had similar characteristics</li> <li>• This level of randomization may miss institutional impacts of intervention</li> </ul> </li> <li>• Results suggest ineffective randomization</li> <li>• Single center study</li> <li>• No blinding</li> <li>• Intervention software unclear</li> <li>• Randomization methodology not described</li> <li>• No allocation concealment</li> <li>• Small sample size (26 providers saw 632 enrolled patients)</li> </ul>
<i>Non-Randomized Studies</i>	
<i>Hendrickson, 2018<sup>4</sup></i>	
<ul style="list-style-type: none"> <li>• Patient inclusion/exclusion criteria described</li> <li>• Clearly defined outcomes</li> <li>• Patient enrollment flow-chart provided</li> <li>• Tabulated patient characteristics provided</li> <li>• Conflict of interest statement provided: no conflicts</li> <li>• Statistical methods described</li> <li>• Attempts to provide data on safety and accuracy</li> <li>• Discussion of study limitations</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study</li> <li>• No statistical power calculation</li> <li>• No compliance data</li> <li>• Historical controls used for 'before and after' study</li> <li>• Intervention software unclear</li> </ul>

**Table 5 Strengths and Limitations of Clinical Studies using Downs and Black<sup>9</sup>**

Strengths	Limitations
Drescher, 2017 <sup>11</sup>	
<ul style="list-style-type: none"> <li>● Prospective study</li> <li>● Compliance was mandatory – deviations from recommendations recorded</li> <li>● Patient inclusion/exclusion criteria described</li> <li>● Clearly defined outcomes</li> <li>● Conflict of interest statement provided: no conflicts</li> <li>● Statistical methods described</li> <li>● Discussion of study limitations</li> </ul>	<ul style="list-style-type: none"> <li>● Single center study</li> <li>● No patient enrollment flowchart</li> <li>● Limited patient characteristics provided</li> <li>● No safety or accuracy data reported</li> <li>● Multifaceted intervention – CDS not isolated</li> <li>● No statistical power calculation</li> <li>● Historical controls used for 'before and after' study</li> <li>● Intervention software unclear</li> </ul>
Min, 2017 <sup>2</sup>	
<ul style="list-style-type: none"> <li>● Prospective study</li> <li>● Compliance was mandatory – deviations from recommendations recorded</li> <li>● Attempts to provide data on safety and accuracy</li> <li>● Patient inclusion/exclusion criteria described</li> <li>● Conflict of interest statement provided: no conflicts</li> <li>● Clearly defined outcomes</li> <li>● Statistical methods described</li> <li>● Discussion of study limitations</li> </ul>	<ul style="list-style-type: none"> <li>● Single center study</li> <li>● No patient enrollment flowchart</li> <li>● Multifaceted intervention – CDS not isolated</li> <li>● Limited patient characteristics provided</li> <li>● No statistical power calculation</li> <li>● Historical controls used for 'before and after' study</li> <li>● Intervention software unclear</li> </ul>
Kharbanda, 2016 <sup>5</sup>	
<ul style="list-style-type: none"> <li>● Tabulated patient characteristics</li> <li>● Clear patient inclusion/exclusion criteria</li> <li>● Patient enrollment flow-chart provided</li> <li>● Clearly defined outcomes</li> <li>● Conflict of interest statement provided: no conflicts</li> <li>● Attempts to provide data on safety and accuracy</li> <li>● Statistical methods described</li> <li>● Discussion of study limitations</li> </ul>	<ul style="list-style-type: none"> <li>● Retrospective study</li> <li>● Multifaceted intervention – CDS not isolated</li> <li>● No measure of compliance</li> <li>● No statistical power calculation</li> <li>● Historical controls used for 'before and after' study</li> <li>● Intervention software unclear</li> </ul>
Silveira, 2016 <sup>12</sup>	
<ul style="list-style-type: none"> <li>● Compliance was monitored – deviations from recommendations recorded</li> <li>● Tabulated patient characteristics</li> <li>● Clear patient inclusion/exclusion criteria</li> <li>● Clearly defined outcomes</li> <li>● Discussion of study limitations</li> <li>● Statistical methods described</li> <li>● Statistical calculation <i>a priori</i> based on prior evidence</li> </ul>	<ul style="list-style-type: none"> <li>● Retrospective study</li> <li>● No patient enrollment flowchart</li> <li>● Authors report relevant conflict of interest</li> <li>● Historical controls used for 'before and after' study</li> <li>● No safety or accuracy data reported</li> <li>● Intervention software unclear</li> </ul>
Carnevale, 2015 <sup>10</sup>	
<ul style="list-style-type: none"> <li>● Tabulated patient characteristics</li> <li>● Clear patient inclusion/exclusion criteria</li> <li>● Effort to control for potential patient factor confounding</li> <li>● Attempts to provide data on safety and accuracy</li> <li>● Statistical methods described</li> <li>● Clear patient inclusion/exclusion criteria</li> <li>● Clearly defined outcomes</li> </ul>	<ul style="list-style-type: none"> <li>● Retrospective study</li> <li>● Multifaceted intervention – CDS not isolated</li> <li>● No statistical power calculation</li> <li>● Historical controls used for 'before and after' study</li> <li>● No patient enrollment flowchart</li> <li>● No conflict of interest statement provided</li> <li>● No information on compliance</li> <li>● Intervention software unclear</li> </ul>

**Table 5 Strengths and Limitations of Clinical Studies using Downs and Black<sup>9</sup>**

Strengths	Limitations
Murthy, 2015 <sup>6</sup>	
<ul style="list-style-type: none"> <li>● Tabulated patient characteristics</li> <li>● Clear patient inclusion/exclusion criteria</li> <li>● Statistical methods described</li> <li>● Clearly defined outcomes</li> </ul>	<ul style="list-style-type: none"> <li>● Retrospective study</li> <li>● Multifaceted intervention – CDS not isolated</li> <li>● No patient enrollment flowchart</li> <li>● No statistical power calculation</li> <li>● Historical controls used for 'before and after' study</li> <li>● No conflict of interest statement provided</li> <li>● No information on compliance</li> <li>● No safety or accuracy</li> <li>● Unclear timeframe for 'before and after'</li> <li>● Intervention software unclear</li> </ul>

CDS = clinical decision support; ITT = intention-to-treat; RCT = randomized controlled trial

## Appendix 4: Main Study Findings and Authors' Conclusions

**Table 6: Summary of Findings Included Systematic Review**

Main Study Findings	Authors' Conclusion
Deblois, 2018 <sup>3</sup>	
<p><b>CDS Results Only</b>  <b>Voluntary Participation systems</b>  <b>RCT (n=541) (Kline et al., 2014<sup>18</sup>)</b>  <u>Proportion of patients exposed to &gt; 5 mSv (P=0.038)</u>            CDS: 25%            Control: 33%</p> <p><u>Medical care costs within 30 days of initial ED presentation (Median US\$) (P=0.018)</u>            CDS: \$934            Control: \$1,274</p> <p><u>Medical care charges within 30 days of initial ED presentation (Median US\$) (P=0.004)</u>            CDS: \$6,281            Control: \$7,595</p> <p><i>"did not find significant differences between the intervention and the control groups with respect to ... any adverse event during the 3-months' follow-up" (pp. 58)</i></p>	<p><i>"The impact of CDS on diagnostic yield was mixed because 3 studies observed an increase in diagnostic yield postintervention, and 3 others monitored no significant impact." (p. 59)</i></p> <p><i>"There is limited evidence on the safety of appraised interventions. Only 6 studies appraised venous thrombotic events or mortality. However, no adverse events were noted in those studies evaluating possible complications or missed diagnoses. Additional research is needed to confirm the safety of the interventions appraised in this systematic review." (p. 59)</i></p> <p><i>"There is not enough data to conclude on safety and the impact on healthcare costs." (p. 60)</i></p>
<p><b>Retrospective 'Before and After' USA (n=434) (Drescher et al., 2011<sup>14</sup>)</b>  <u>Use of Imaging (/1000 patients) (P=NA)</u>            Before: 14            After: 12.8</p> <p><u>Diagnostic Yield (% (95% CI))</u>            Before: 8.3 (4.9,12.9)            After: 12.7 (8.6, 17.7)</p>	
<p><b>Retrospective 'Before and After' USA (n=5,862) (Dunne et al., 2015<sup>15</sup>)</b>  <u>Use of Imaging (/1000 patients) (P=0.008)</u>            Before: 26            After: 22.8</p> <p><u>Diagnostic Yield (%) (P=0.65)</u>            Before: 10.4%            After: 12.1%</p>	
<p><b>Retrospective 'Before and After' USA (n=2,891) (Prevedello et al., 2013<sup>19</sup>)</b>  <u>Use of Imaging (/1000 patients) (P&lt;0.02)</u>            Before: 26.5            After: 24.3</p> <p><u>Diagnostic Yield (%) (P&lt;0.01)</u>            Before: 9.2%            After: 12.6%</p>	
<p><b>Retrospective 'Before and After' USA (n=6,838) (Raja et al., 2012<sup>21</sup>)</b></p>	

**Table 6: Summary of Findings Included Systematic Review**

Main Study Findings	Authors' Conclusion
<p><u>Use of Imaging (/1000 patients)</u>            Before: 14.5 to 26.4 (<math>P&lt;0.0001</math>)            After: 26.4 to 21.1 (<math>P=0.0379</math>)</p> <p><u>Diagnostic Yield (%) (<math>P=0.0323</math>)</u>            Before: 5.8%            After: 9.8%</p> <p><b><u>Mandatory Participation systems</u></b>  <b><u>Retrospective 'Before and After' USA (n = 2,830) (Geeting et al., 2016<sup>16</sup>)</u></b>  <u>Use of Imaging (% ED visits with CTPA) (<math>P=0.13</math>)</u>            Before: 3.02%            After: 2.85%</p> <p><u>Diagnostic Yield (%) (<math>P=0.406</math>)</u>            Before: 6.89%            After: 7.53%</p> <p><u>Adherence to Guidelines (%) (<math>P=NA</math>)</u>            Before: 58%            After: 76%</p> <p><b><u>Retrospective 'Before and After' Spain (n=1363) (Jimenez et al., 2015<sup>17</sup>)</u></b>  <u>Use of Imaging (% of patients with CTPA) (<math>P=0.02</math>)</u>            Before: 55%            After: 49%</p> <p><u>Diagnostic Yield (%) (<math>P=NS</math>)</u>            Before: 31%            After: 33%</p> <p><b><u>Prospective 'Before and After' USA (n=2421) (Raja et al., 2014<sup>20</sup>)</u></b>  <u>Diagnostic Yield (%) (<math>P=0.88</math>)</u>            Before: 10.4%            After: 10.1%</p> <p><u>Adherence to Guidelines (%) (<math>P&lt;0.01</math>)</u>            Before: 56.9%            After: 75.6%</p>	

CDS = clinical decision support; CI = confidence interval; CTPA = computed tomography pulmonary angiography; ED = emergency department; NA = not available; NS = not significant;

**Table 7: Summary of Findings of Included Primary Clinical Studies**

Main Study Findings	Authors' Conclusion
<i>Randomized Controlled Trial</i>	
Tajmir, 2017 <sup>7</sup>	
<p><u>Ankle Workups consistent with OAR (n=632) (<math>P=0.0155</math>)</u>            CDS: 92.6%            Control: 61.8%</p>	<p><i>"The prevalence of significant fractures of ankle and foot differed significantly (near twofold) between control and intervention groups. Thus, our observed higher imaging yield of significant</i></p>

**Table 7: Summary of Findings of Included Primary Clinical Studies**

Main Study Findings	Authors' Conclusion
<p><u>Foot Workups consistent with OAR (n=632) (P=0.0001)</u>            CDS: 81.0%            Control: 63.6%</p> <p><u>Ankle Radiography use (n=632) (P=0.0002)</u>            CDS: 64.3%            Control: 48.9%</p> <p><u>Foot Radiography use (n=632) (P=0.95)</u>            CDS: 54.6%            Control: 54.0%</p> <p><u>Ankle Radiography yield (n=632) (P=0.195)</u>            CDS: 10.5%            Control: 5.6%</p> <p><u>Foot Radiography yield (n=632) (P=0.0099)</u>            CDS: 8.5%            Control: 3.7%</p> <p><u>All fractures Radiography yield (n=632) (P=0.0060)</u>            CDS: 19.0%            Control: 9.4%</p> <p><i>"we found no missed fractures re-presenting to the urgent care center." (p. 494)</i></p>	<p><i>fractures, and higher use of radiography in the intervention group may simply reflect the higher prevalence of fractures in the intervention group. This in turn suggests that our randomization might not have been effective, with the intervention group consisting of providers evaluating patients with more significant fractures." (p. 494)</i></p> <p><i>"We also found that implementation of CDS reduced unnecessary foot radiography. Although the prevalence of clinically significant foot fractures was 2.3-fold higher in the CDS group, foot radiography use was similar to the control group, resulting in a higher foot radiography yield in the CDS group." (p. 493)</i></p>
<i>Non-Randomized Studies</i>	
<b>Hendrickson, 2018<sup>4</sup></b>	
<p><u>US use (OR (95% CI)) OR&lt;1 favours CDS (P=NS)</u>            Children's ED (n=67): 0.7 (0.22, 2.25)            Community ED (n=260): 1.59 (0.9, 2.82)</p> <p><u>CT use (OR (95% CI)) OR&lt;1 favours CDS (P=NS)</u>            Children's ED (n=67): 0.85 (0.12, 6.05)            Community ED (n=260): 0.74 (0.44, 1.24)</p> <p><u>US use for imaged patients (OR (95% CI)) OR&lt;1 favours CDS (P=NS)</u>            Children's ED (n=67): NS            Community ED (n=260): 1.70 (0.91, 3.18)</p> <p><u>CT use for imaged patients (OR (95% CI)) OR&lt;1 favours CDS (P=NS)</u>            Children's ED (n=67): 0.95 (0.12, 7.33)            Community ED (n=260): 0.50 (0.25, 1.03)</p> <p><u>Appendectomy performed (P&gt;0.05)</u>            Before CDS: 24%            After CDS: 21%</p>	<p><i>"An E-CDS can effectively decrease CT scanning and increase use of ultrasound in children with suspected appendicitis in a community hospital ED." (p. 10)</i></p> <p><i>"Our measures for safety showed no statistical difference in the perforation rate, missed appendicitis rate, negative appendectomy rate, or 4-week rehospitalization rate over the study period" (p. 12)</i></p>

**Table 7: Summary of Findings of Included Primary Clinical Studies**

Main Study Findings	Authors' Conclusion
<p><u>Final diagnosis appendicitis (P&gt;0.05)</u>            Before CDS: 24%            After CDS: 20%</p> <p><u>Perforated appendicitis (P&gt;0.05)</u>            Before CDS: 11%            After CDS: 11%</p> <p><u>Rehospitalization within 4 weeks (P&gt;0.05)</u>            Before CDS: 7%            After CDS: 4%</p> <p><u>Missed appendicitis cases (P&gt;0.05)</u>            Before CDS: 2%            After CDS: 0.6%</p> <p><u>Negative appendectomy (P&gt;0.05)</u>            Before CDS: 0%            After CDS: 2%</p>	
Drescher, 2017 <sup>11</sup>	
<p><u>Use of CTPA (/1000 patients (95% CI)) (P&lt;0.001)</u>            Before CDS: 10.53 (9.9, 11.2)            After CDS: 8.81 (8.3, 9.4)</p> <p><u>Diagnostic Yield (%) (P=NS)</u>            Before CDS: 15.9%            After CDS: 15.2%</p> <p><u>Compliance = 66% of the time after implementation</u></p> <p><u>Diagnostic Yield (%) (P&lt;0.001)</u>            Following protocol: 18.4%            Protocol violations: 9.2%</p>	<p><i>“The present study demonstrated a significant decrease in utilization of CTPA when the principles of KT, in which a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically-sound application of knowledge, were applied to the diagnosis of PE using a novel CDS, which included PERC criteria to risk stratify along with Wells criteria for PE and D-dimer testing.” (p. 1095)</i></p> <p><i>“We did not find an overall increase in yield despite a decrease in utilization. This raises the question of whether the protocol resulted in more missed PEs along with the decrease in utilization of CTPA. However, we did find an increase in yield when the protocol was followed and a significant decrease in yield when the protocol was violated.” (p. 1095)</i></p>
Min, 2017 <sup>2</sup>	
<p><u>Medical imaging tests ordered (P=0.0002)</u>            Before CDS: 22%            After CDS: 17%</p> <p><u>Mean imaging rate among individual physicians (n=43) (P=NR)</u>            Before CDS: 24%            After CDS: 20%</p> <p><u>IQR imaging rate among individual physicians (n=43) (P=NR)</u>            Before CDS: 13%            After CDS: 13%</p> <p><i>“One minor thoracic spine compression fracture was missed postintervention, but management was likely not impacted. No serious diagnose affecting or altering clinical management were</i></p>	<p><i>“Point-of-care CDS effectively modifies the behavior of ED physicians with respect to their decision to order medical imaging for patients who present with LBP. Its use in the order entry form for lumbar imaging resulted in greater compliance with established professional guidelines, a safe reduction in the rates of inappropriate imaging, and improved cost-effectiveness of care.” (p. 898)</i></p>

**Table 7: Summary of Findings of Included Primary Clinical Studies**

Main Study Findings	Authors' Conclusion
<i>recorded.</i> "	
Kharbanda, 2016 <sup>5</sup>	
<p><u>CT use (P=NS)</u>            Before CDS: 38.8%            After CDS: 23.8%</p> <p><u>US use (P=NS)</u>            Before CDS: 45.7%            After CDS: 59.7%</p> <p><u>Change in CT use immediate impact (% (95%CI) (P=NS)</u>            -20 (-33.4, -3.6)</p> <p><u>Change in US use immediate impact (% (95%CI) (P=NS)</u>            -5.7 (-22, 14.9)</p> <p><u>Post implementation change in CT use/month (% (95%CI) (P&lt;0.05)</u>            -2.5 (-3.3, -1.7)</p> <p><u>Post implementation change in US use/month (% (95%CI) (P&lt;0.05)</u>            1.4 (0.8, 2.1)</p> <p><u>No statistical difference in total imaging use and trends</u></p> <p><u>Appendiceal perforation (P=NS)</u>            Before CDS: 27.6%            After CDS: 25.2%</p> <p><u>Return ED visits within 30 days (P=NS)</u>            Before CDS: 7.0%            After CDS: 5.1%</p> <p><u>ED length of stay (hours) (P=NS)</u>            Before CDS: 4.2            After CDS: 4.2</p> <p>No significant impact on trends of appendiceal perforation, return ED visit rate, or ED length of stay between before and after CDS implementation</p>	<p><i>"We have demonstrated that a multicomponent CDS, linked within the EHR, providing guidance for the management of patients with possible appendicitis can reduce the use of CT while maintaining safety and high quality care for patients." (p. e7)</i></p>
Silveira, 2016 <sup>12</sup>	
<p><u>Adherence to OAR (P&lt;0.001)</u>            Before CDS: 55.9%            After CDS: 95.7%</p> <p><u>Ankle radiography use (P=0.839)</u>            Before CDS: 78.1%            After CDS: 77.3%</p>	<p><i>"Implementation of the OAR into a CDS system tool automated the data capture and retrieval of key clinical data and was associated with an increase in documented adherence to OAR. Use and yield of ankle and foot radiography were not adversely affected." (p. 417)</i></p>

**Table 7: Summary of Findings of Included Primary Clinical Studies**

Main Study Findings	Authors' Conclusion
<p><u>Foot radiography use (P=0.352)</u>            Before CDS: 50.2%            After CDS: 45.9%</p> <p><u>Ankle radiography yield (P=0.679)</u>            Before CDS: 13.1%            After CDS: 11.7%</p> <p><u>Foot radiography yield (P=0.352)</u>            Before CDS: 8.7%            After CDS: 12.8%</p> <p><u>4.3% of imaging orders were nonadherent to the CDS</u></p> <p>For nonadherent imaging decisions the recommendation on the educational screen was ignored 36.6% of the time. Clinical judgement and specialist recommendation were reasons provided.</p> <p>31.8% of nonadherent imaging orders had CDS entries inconsistent with patient medical chart.</p> <p>The remainder (31.8%) of nonadherent imaging orders were due to software failure.</p>	
Carnevale, 2015 <sup>10</sup>	
<p><u>Adjusted CT/MRI rate (P&lt;0.0001)</u>            Before CDS: 26.0%            After CDS: 28.3%</p> <p><u>Change in CT/MRI use in low-risk (% (95%CI)</u>            -6.2% (-4.0, -8.5)</p> <p><u>Change in CT/MRI use in medium-risk (% (95%CI)</u>            -3.3% (-1.6, -5.0)</p> <p><u>Change in CT/MRI use in high-risk (% (95%CI)</u>            +5.6% (4.3, 7.0)</p> <p><u>Change in 3-day rebound visits (% (95%CI)</u>            -1.4% (0.7, -2.2)</p> <p><u>Change in 7-day rebound visits (% (95%CI)</u>            -0.7% (-1.5, 0.2)</p>	<p><i>"Implementation of an emergency medicine decision support and risk education initiative did not decrease overall CT/MRI rates in ED visits, but it was associated with a shift in utilization toward high-risk patients. We conclude that baseline imaging rates included components of both over- and underuse by risk group; concomitant decreases in rebound rates suggest greater diagnostic accuracy." (p. 56)</i></p> <p><i>"Decreased rebound rates suggest that fewer patients had unaddressed needs after an ED visit in the post period, which is likely to be a function, at least in part, of increased diagnostic accuracy. However, these data remain suggestive, and further study is required to understand the mechanisms underlying lower rebound rates and to identify any role played by increased diagnostic accuracy." (p. 56)</i></p>
Murthy, 2015 <sup>6</sup>	
<p><u>CTPA yield</u>            1. Prior to CDA – 17.4%            2. Prior to CDA with diagnostic algorithm dissemination – 22.4%            3. Post CDA – 31.7%</p> <p>1. vs 2. P=0.267</p>	<p><i>"In this first study of its kind in a resource limited environment, we have shown that the phased implementation of a computer prompted pre-test probability scoring system for PE almost doubled the efficiency of CTPA and significantly decreased the number of inappropriate scans." (p. 64)</i></p>

**Table 7: Summary of Findings of Included Primary Clinical Studies**

Main Study Findings	Authors' Conclusion
2. vs 3. $P=0.128$ 1. vs 3. $P=0.014$	<i>"Our substantial decrease in the proportion of inappropriate scans over time has considerable economic benefit, reflected in savings on consumables, and technician and radiologist time,[15] enhancing overall institutional cost-effectiveness and efficiency." (p. 64)</i>

CDS = clinical decision support; CTPA = computed tomography pulmonary angiogram; E-CDS = electronic clinical decision support; ED = emergency department; IQR = interquartile range; OAR = Ottawa Ankle Rules; NR = not reported; NS = not statistically significant; PE = pulmonary embolism; PERC = Pulmonary Embolism Rule-Out Criteria