Order Sets in Healthcare:

An Evidence-based Analysis

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Executive Summary

This study was prepared for OHTAC by the Healthcare Human Factors Team based at the Centre for Global eHealth Innovation at the University Health Network, Toronto.

The goals of this study were:

1) To determine whether order sets are effective tools in improving guideline adherence, diagnosis and treatment outcomes, processes of care, efficiency, or cost
2) To enable Ontario Hospitals to derive optimal benefit from the development and implementation of order sets

To accomplish this, a multi-disciplinary team was assembled, including experts from the following areas; medicine, healthcare IT, human factors, biomedical engineering and clinical epidemiology.

A systematic review of evidence in the literature was undertaken, to determine the extent and quality of evidence related to the two key goals of this study. Inclusion and exclusion criteria were developed, and a comprehensive literature search was performed in OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, The Cochrane Library for studies published between January 01, 1999 and April 18, 2009. As a result of this process, a total of 22 publications were selected for inclusion in this review.

The assessment of quality of evidence was conducted using the STROBE checklist and GRADE Working Group criteria.

No randomized controlled trials were found. One paper described a non-randomized study with contemporaneous controls, and the remaining 21 papers described non-randomized studies with historical controls.

Generally, the studies reported positive outcomes in terms of increased levels of compliance for both diagnosis and treatment through the use of order sets, but the quality of evidence was graded as very low. Only a few of the papers contained any economic analysis of the impact of order sets, and these were limited in scope. It should be pointed out that in other areas such as aviation and the nuclear industry, the methodical use of checklists has been associated with improved compliance and safety outcomes, and in part, this general assumption about the intrinsic benefits of checklists, or order sets, explains why more rigorous studies have not been undertaken in the clinical setting, coupled with the intrinsic difficulty of conducting a true randomized controlled trial.

There are currently three main approaches to the generation and propagation of order sets in medicine; 1) the traditional paper form developed by in-house clinicians, 2) the electronic form that is downloadable and is sometimes developed from input from a number of institutions, and 3) the list that is integrated into a (Computerized Physician

Order Entry) CPOE system. Of these three approaches, the last has the clear advantage that it allows the institution to assess the level of compliance with the order set, which provides important information about the degree of acceptance of the tool, and potentially its usefulness as well. Most hospitals in Ontario are either not using order sets or are using paper order sets developed by in-house clinicians. Some are using shared, electronic forms, and still others are actively working toward order sets that are embedded in the CPOE system.

An additional factor to consider is the need to review and update order sets based on fresh evidence. Systems are now available that "push" evidence to hospitals, and this can be used to review and revise order sets, to keep them current. This continual reviewing and updating is important, to avoid having order sets in place that no longer represent best practice.

The question of physician adoption is also important. It is clear that physicians do not welcome the introduction of order sets that slow down their workflow or otherwise interfere with their ability to care for their patients in a timely way. Anecdotal comments from users indicate that successful adoption depends on selecting order set processes that integrate well with physician workflow, and that staff consultation and involvement is an essential step in the development and implementation process. Order sets cannot simply be imposed from outside with an expectation that they will be widely adopted and followed.

Based on these findings, the following recommendations are made:

1) **Given the fact that there is very low quality evidence that order sets improve the rate of guideline adherence, processes of care, treatment outcomes, efficiency and cost, it is recommended that order sets for diagnosis and/or treatment become an important focus for further development through a formal evaluation of existing models.**

2) **It is recommended that any future commitment to order sets should be:**

    - **Developed from a common starting framework across Ontario for as many applications as possible which includes all end users in the formative process**

    - **Overseen and coordinated by a third party**

    - **Customized by each institution with broad participation by potential institutional and professional end-users**

    - **Adaptable to paper, electronic form, or embedded in CPOE systems with linked real-time evidence support**

- **Gradually incorporated into CPOE systems and linked in real-time to evidence from the literature assessed by end-users, to ensure that compliance can be monitored and that fresh evidence is constantly made available**

Objective

3) To determine whether order sets are effective tools in improving guideline adherence, diagnosis and treatment outcomes, processes of care, efficiency, or cost
4) To enable Ontario Hospitals to derive optimal benefit from the development and implementation of order sets

Background

Clinical Need

Order sets are conveniently grouped medical orders that work to standardize diagnosis and treatment following pre-established clinical guidelines. Order sets are believed to make ordering more efficient (1) and represent a significant opportunity to decrease variation in care and enhance compliance with treatment guidelines. By grouping orders that should be placed together for diagnosis and treatment, order sets address the needs of both patients and clinicians by making the "right thing" easier to do (2). The groups in standardized order sets are based on standard practice guidelines and are normally extensively reviewed prior to implementation in clinical settings. The use of paper order sets has been reported to improve legibility, ensure the completeness and unambiguousness of orders, increase efficiency by reducing the need to verify and/or clarify orders, and standardize patient care (3). In addition, the expected benefits of standardized order set embedded in Computerized Physician Order Entry (CPOE) systems include increased user time-efficiency, improved completeness and accuracy of orders (4), reduced ordering of unnecessary tests (5), and improved patient outcomes.

Some unintended, negative outcomes of order sets have been identified as issues relating to maintenance and standardization (2). Clinical knowledge advances rapidly, and as such, it is a challenge to keep up with demands for the update of old, and creation of new, order sets. Standardization issues may also arise due to this speed of advancement, as existing order sets may not be properly maintained and/or order sets may be implemented without organizational standards and clinical review. This can quickly lead to inconsistencies with recommended practices and the widespread practice of outdated medicine.

Technology Overview of Order Sets

The use of standardized order sets is not a new concept. Order sets have been in use in hospitals since the 1980's (6), and they have evolved both in format and in the source of their content since their inception.

Order sets were first created as paper order forms for standardized treatment listing orderable items with adjacent pre-checked boxes for mandatory standard orders, blank checkboxes for optional orders, and spaces for providers to write additional orders. The use of these order sets showed an initial improvement in patient care, but as paper order set use became more prevalent in hospitals, so did their limitations. Paper order sets were found to provide a significant maintenance challenge to hospitals due to difficulties in keeping them up-to-date and monitoring them for compliance to ever changing practice guidelines (2). However, despite these challenges, the simplicity and low development costs of paper order sets have led to their continued use to this day.

Standalone electronic order sets were subsequently created as an improvement on paper order sets. These order sets usually resemble their paper order set counterparts with the exception of allowing users to fill-in the order set form on the computer before printing and placing it in the patient's chart. This format provides clinicians with basic decision support (e.g. use of drop-down menus to fill-in fields) and the ability to ensure orders are complete and legible. These standardized and pre-printed order sets have been linked with reductions in the occurrence of medication errors and the amount of additional support work required by ancillary departments (e.g. pharmacy, nursing) (3).

Finally, order sets embedded within Computerized Physician Order Entry (CPOE) systems were developed most recently in efforts to address many of the limitations presented by paper and standalone electronic order sets. The layout of CPOE-embedded order sets varies depending on the CPOE user interface design, which often differs between systems. These order sets can provide the added benefits of automated order checking and electronic communication of orders to ancillary services. Although maintenance of CPOE-embedded order sets are still a challenge, they are less so in comparison to paper order sets, where older versions may still be available for use after forms have been updated. CPOE-embedded order sets also allow clinicians to easily determine if the orders had been followed. However, CPOE-embedded order sets possess higher implementation and development costs, require user training, and are not always accepted by clinicians due to usability issues (7).

The evolution of the source content of order sets has also enhanced their benefits. Source content for order sets began with a narrow focus with in-house development, then moved to shared development between hospitals, and finally to a broader, more advanced system that can be automatically updated by an evidence-based medicine database. In the beginning, order sets were developed in-house by multidisciplinary clinical teams that decided what orders would be necessary for standard practice within their facility. Most hospitals in Ontario use this method of creating their own order sets. These in-house order sets have been shown to improve patient care within the specific hospital for a particular use, but the results of their use cannot be generalized to other facilities since their design is specific to the institution.

This resulted in a move towards the sharing of information between hospitals and medical governing bodies to further standardize the order sets. The Open Source Order Set approach is an example of this type of shared order set development. This is an

Ontario-based company comprised of clinicians (e.g. physicians, nurses, and pharmacists) who are dedicated to the creation of standardized, evidence-based paper order sets across a collaborative network (8). Currently, their network includes over 78 hospitals and health centres and 47 health offices/units across Canada, including CAMH, Central East LHIN, Niagara Health System, Toronto East General and Trillium Health Centre among others. The collaboration of these organizations ensures that the developed order sets are more compliant with standard clinical practice than an order set developed in isolation, and allows the sharing of implementation knowledge. However, the order sets shared may not be strictly evidence-based, and challenges to maintain and update order sets still exist.

More advanced systems have been developed where order sets may be automatically updated with an evidence-based medicine database. Vendors that provide these systems include: Zynx Health (9), Thomson Reuters (10), Wolters Kluwer (11) and TELUS Health Solutions (12). Using these systems, users are alerted of the most current evidence, which can then be incorporated into order sets and used as standard practices. Computerized order sets are also conveniently linked to the relevant evidence for easy access. Often, an order set management tool is provided for institutes to organize and customize order sets based on their needs. However, these advanced systems are not widely adopted due to their significant cost and implementation difficulties.

Evidence-Based Analysis of Effectiveness

Research Questions

1. Are order sets effective in improving guideline adherence, diagnosis and treatment outcomes, processes of care, efficiency, or cost?

2. How should Ontario Hospitals proceed with the development and implementation of order sets, to achieve optimal benefit?

Methods

Inclusion and Exclusion Criteria

Inclusion Criteria

- ➢ Population: Any patients treated in a hospital setting
- ➢ Intervention: Order set must be the primary intervention
- ➢ Intervention: Studies that used order sets as the only tool to implement a new guideline or clinical pathway are included, provided that the primary focus is on the order set
- ➢ Control: Not using any standardized order sets

- ➢ Publication type: Randomized controlled trials, non-randomized controlled trials, observational studies
- ➢ Publication date range: January 01, 1999-April 18, 2009

Exclusion Criteria

- ➢ Studies with educational interventions other than the use of order sets and/or new guidelines are excluded
- ➢ Studies with other interventions (e.g. patient education, implementation of other new forms or charts, change in workflow not related to using the order sets) are excluded
- ➢ Studies that improved on their existing order sets (i.e. the control is an old order set) are excluded
- ➢ Retrospective studies where both the study and control group were selected in the period after the implementation of an order set, with the control group defined post-data collection as cases where the order set was not used by physicians.
- ➢ Studies published in a language other than English

Outcomes of Interest

- ➢ Adherence to guidelines
- ➢ Changes in processes of care
- ➢ Treatment outcomes
- ➢ Efficiency
- ➢ Cost

Method of Review

A comprehensive literature search was performed in OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, The Cochrane Library for studies published between January 01, 1999 and April 18, 2009. The literature search strategy is available in Appendix 1.

Abstracts were screened and studies meeting the inclusion criteria outlined above were obtained. Studies were then reviewed in full text, and two reviewers agreed on the inclusion or exclusion of each study.

In addition, bibliographies of relevant papers were searched for additional references that may have been missed. A search was also conducted for publications in the grey literature, including the Gartner reports and studies registered in clinicaltrial.gov.

Assessment of Quality of Evidence

The quality of each individual study was determined with criteria based on the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist (13) since a majority of the included studies were observational studies. The

checklist was modified to make it more appropriate for the research question at hand (see Appendix 2).

The overall quality of the evidence was examined according to the GRADE Working Group criteria (14). The consistency, directness and precision of evidence, as well as any study limitations and publication bias were evaluated to assign a quality rating. Table 1 outlines the definitions used in grading the quality of the evidence (15).

  ➢ Consistency refers to the similarity of effects across the studies.
  ➢ Directness refers to the extent to which the interventions and outcome measures are similar to those of interest.
  ➢ Precision refers to the level of confidence in the overall effects reported.

Table 1: Definitions of quality of evidence

High	Further research is very unlikely to change confidence in the estimate of effects.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low	Any estimate of effect is very uncertain

Qualitative Analysis of Outcomes

The outcome measures of the included studies were summarized qualitatively. Quantitative analysis was not performed since the studies involved population and outcome measures that varied greatly.

Qualitative Analysis of Development and Implementation Guidelines

Aside from determining the effectiveness of order sets from the literature, a qualitative analysis was conducted to derive common challenges and strategies for the implementation of order sets from the included studies. Interviews with experts in the field were also conducted to gain further understanding of issues concerning the use of order sets. These experts included: Dr. Chris O'Connor of Trillium Health Care, who is the founder of Open Source Order Set; Dr. Jeremy Theal, who is the leader of the order set project at North York General Hospital; and Dr. Valerie Palda of St. Michael's Hospital, who is an expert in evidence-based medicine.

Results of Evidence-Based Analysis

The literature search identified 1931 citations published between January 1, 1999 to April 22, 2009. Of these 1931 citations, 152 were retrieved in full text, and 22 non-RCTs were identified for inclusion in this review. The level of evidence of each of the included

studies is displayed in Table 2. No systematic reviews that are conducted specifically on order sets were found.

Table 2: Quality of Evidence of Included Studies*

Study Design	Level of Evidence	Number of Eligible Studies
Large RCT, systematic reviews of RCTs	1	0
Large RCT unpublished but reported to an international scientific meeting	1(g)	0
Small RCT	2	0
Small RCT unpublished by reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls	3a	1
Non-RCT with historical controls	3b	21
Non-RCT presented at international conference	3(g)	0
Surveillance (database or register)	4a	0
Case series (multisite)	4b	0
Case series (single site)	4c	0
Retrospective review, modelling	4d	0
Case series presented at international conference	4(g)	0

* Adapted from the Oxford Centre for Evidence (16)
An additional designation "g" was added for preliminary reports of studies that have been presented at international scientific meetings.
Abbreviations: RCT, randomized controlled trial; Non-RCT, non-randomized controlled trial

Summary of Findings of Literature Review

Twenty-two studies met the inclusion criteria and were included in this review (17-38). Table 3 summarizes study design, population, and quality characteristics for these studies.

Summary of Study Design/Quality

Of the 22 studies, twenty were observational before-after studies with a historical group (17-20,22-29,29-37). One study was an observational before-after study with both a historical control group from the same site and a control group from other hospitals (38), and only one study was a non-RCT with a contemporaneous control group (21).

The non-RCT by Noschese *et al* (21) was the only study with a contemporaneous control group. They enrolled 35 diabetes patients from two hospital units, one as the control unit and the other the intervention unit. A paper diabetes order set was implemented for 4 months in the intervention unit, and 3 days of data were collected within the implementation period. However, due to physician crossover, the order set was also used in some of the patients in the control unit, thus resulting in serious limitations in the study.

Moreover, the studies conducted by Kanji *et al*, Elsasser *et al*, Chisolm *et al*, and Biviano *et al*, did not compare all patients in the intervention arm to the historical controls (23,26,28,35). Rather, the intervention arm was retrospectively divided into a group with the order set used, and a group with no order set used. Comparison was made between the intervention group with order set used and the historical controls, and also between the two intervention groups.

Summary of Demographics

The population sample varied greatly across the studies. It included patients with diabetes (21,24), pneumonia (17,23), sepsis (19,27), anemia (25,32), acute coronary disease (29), ischemic stroke (33), chest pain (35), asthma (28), and cancer (38). Most of the studies did not exclude any patients based on age (17,18,20-22,24,25,27,29,32-38). Two studies were conducted with adult patients only (i.e. >18 years) (23,26), and one was conducted with pediatric patients only (28). The setting of the studies also varied from academic hospitals (19,24,27), community hospitals (17,18,23) to tertiary care centers (21,34).

Summary of Intervention Characteristics

The interventions described in the studies included all three formats of order sets: paper-based, electronic, and CPOE-embedded. Seventeen studies investigated paper-based order sets (17-19,21-27,32-38), two studies investigated electronic order sets (30,31), and two studies investigated CPOE-embedded order sets (20,28). The study conducted by Asaro *et al* (29) evaluated both the paper-based version and CPOE-embedded versions of an order set. It was conducted over four periods of time: Phase 1 was before the introduction of any order sets; Phase 2 began after the introduction of paper acute coronary syndrome order sets; Phase 3 began after CPOE implementation; Phase 4 began after promotion of the CPOE-embedded order set. Therefore, The first 2 phases acted as a before-after study of the paper-based order set, and the latter 2 phases was used to evaluate the CPOE-embedded order set.

While the order sets found in the included studies were mostly used for treatment purposes (18-22,24-30,32-38), the order sets described by O'Connor *et al* and Kanji *et al* also included some diagnostic components (17,23), and the order sets described by Vardy *et al* consisted of diagnostic tests only (31). Despite the differences in format and content, all of the order sets seemed to be developed in-house by clinicians at the study location.

In most studies, the order sets was not used for all patients in the intervention arm (17,20-23,25,26,28,29,29,34,35,37), and only two studies clearly stated that the order set was used for all patients in the intervention arm (24,38). The rest of the studies did not measure the adoption rate of the intervention, and thus the extent of its adoption was unknown (18,19,27,30-33,36).

Summary of Control Characteristics

All of the control groups consisted of patients with no order set used for their prescriptions. However, the study conducted by Asaro *et al* was varied slightly (29). As mentioned, they evaluated both the paper-based version and CPOE-embedded version of an order set consecutively. Aside from comparing the two intervention arms to a control arm with no order set used, the intervention group with paper-based order set also acted as a control for the intervention group with the CPOE-embedded order set.

Summary of Outcome Characteristics

The outcome measures of the included studies varied considerably. The only similar outcome that was commonly reported was the rate of adherence to guideline. Other outcomes related to treatment outcomes, changes in processes of care, cost, and efficiency were also reported. However, due to the different population and patient conditions that were involved, it is difficult to compare these outcomes across studies.

Qualitative Summary of Outcome Measures

The outcome measures differed considerably across the studies. Table 4 summarizes the outcomes measured for each study. One similar measure was the rate of adherence to recommended guidelines:

- ➢ Both Thiel *et al* and Micek *et al* reported a significant increase in sepsis patients that receive appropriate initial antibiotic therapy (19,27).

- ➢ Garrelts *et al* found a significant increase in the guideline-supported uses of epoetin alfa, but no significant difference in patients receiving guideline-approved dosage (25).

- ➢ Sano *et al*, whose study involved 64 standardized chemotherapy order forms, reported a significant reduction in prescription errors (30).

- ➢ The study conducted by the California Acute Stroke Pilot Registry found a significant increase in patients receiving optimal treatment for ischemic stroke (33).

- ➢ Debrix *et al* reported a significance increase in proportions of prescriptions in compliance with guideline for patients receiving colony-stimulating factors as part of cancer treatment (38).

- ➢ Koplan *et al* found an increase in the proportion of smokers who received some form of guideline-recommended smoking cessation therapies, although the significance was not determined by statistical tests (20).

- Clark *et al* also reported an increase in patients receiving appropriate initial dose for chemo-induced anemia, patients who had their dose decreased or held appropriately, and patients who received appropriate erythropoietic therapy for greater than 12 weeks; however, the significance of these results was not determined by statistical tests (32).

- On the other hand, Noschese *et al* did not find any significant difference in the portion of orders that are appropriate between the control and intervention groups of diabetic patients (21).

- Asaro *et al,* whose study evaluated both a paper-based version and CPOE-embedded version of an acute coronary syndrome order set, also did not report any improvement in compliance with guidelines for either order set (29). However, both of these studies were rated to be of low quality due to serious limitations.

- When comparing historical controls to part of the intervention group with order set used, Elsasser *et al* reported a significant increase in patients with prophylaxis provided according to guidelines (26), and Biviano *et al* found a significant increase in the rate of adherence for various therapies for patients with chest pain (35).

- Kanji *et al* also reported an increase in the selection of the appropriate empiric antibiotics; however, its significance was not determined by statistical tests (23).

Overall, the use of order sets showed a positive effect on the rate of adherence to the recommended guidelines. There were no important inconsistencies between the results reported by studies involving different types of order sets, whether it be paper-based, electronic, CPOE-embedded, for treatment or for diagnostic purposes.

Aside from that, many studies also reported significant improvements in processes of care (17,19-21,25-28,34), treatment outcomes (19,24,27), efficiency (19), and cost (30), as shown in Table 4.

Only two studies have reported any undesirable outcomes associated with the use of order sets. O'Connor *et al* found that order set use was associated with a significant decrease in dating of orders and with an unintended effect of overall increased ordering of nighttime sedation (17), and Noschese *et al* reported a significant increase in diabetic patients experiencing hyperglycemia on the intervention unit than the control unit (21).

In summary, order sets seemed to be beneficial with little or no undesirable outcomes reported. However, due to the lack of common outcome measures, it is difficult to perform qualitative analysis and draw conclusions on the magnitude of each effect.

Table 3: Characteristics of the included studies

Study, Design	Setting and duration of study[†]	Population	Intervention	Source of guideline	Adoption rate	Quality of evidence
O'Connor *et al*, 2009 Non-RCT with historical control	Trillium Health Centre, Mississauga ON, Canada Period 1 (Control): Oct-Nov 03 Period 2 and 3 (Intervention): Apr-Dec 04 and Feb-Mar 05	n(Period 1) = 113 n(Period 2) = 291 n(Period 3) = 283 General medical patients admitted to hospital	Paper-based: A general admission order set and six diagnosis-specific order sets (community acquired pneumonia, chronic obstructive pulmonary disease, febrile neutropenia, soft tissue infection, upper gastrointestinal bleeding and urinary tract infection)	Evidence-based where possible and informal consensus methods, without explicitly grading evidence	Period 2: 32.3% Period 3: 51.6%	High
Cronin *et al*, 2009 Non-RCT with historical control	Glen Cove Hospital, Glen Cove NY, USA Control: 2005 Intervention: 2006	n(Control) = 953 n(Intervention) =1003 Total-joint arthroplasty patients	Paper-based: A thromboprophylaxis risk factor assessment and prescriber order sheet	American College of Chest Physicians (ACCP) guidelines	Unknown	Very low - Adoption rate not reported - Statistical analysis not performed - Characteristics between control and intervention groups not compared
Thiel *et al*, 2009 Non-RCT with historical controls	Barnes-Jewish Hospital, St. Louis MO, USA Control: Dec03-May05 Intervention: Jun05-Dec06	n(Control) = 200 n(Intervention) = 200 Bacteremic patients with severe sepsis, except for: - patients with refractory septic shock dying within 12h of the onset of severe sepsis shock - patients with an alternative	Paper-based: Bacteremic severe sepsis order set	Derived from the Surviving Sepsis Campaign	Unknown	Moderate - Adoption rate not reported

			diagnosis accounting for the shock state - patient with a pre-existing do not resuscitate order			
Koplan *et al*, 2008 Non-RCT with historical controls	Brigham and Women's Hospital, Boston MA, USA Control: Nov05-Jan06 Intervention: Feb06-May06	n(Control) = 17024 n(Intervention) = 17530 Any admitted patients	CPOE-embedded: Smoking cessation order set for acute myocardial infarction, congestive heart failure and pneumonia	Unclear	14.50%	Low - Characteristics between control and intervention groups not compared - Low adoption rate - Statistical test not performed for all results
Noschese *et al*, 2008 Non-RCT with contemporaneous controls at another hospital unit	University of Pittsburgh Medical Center, Pittsburgh PA, USA Contol/Intervention : Nov05-Feb06	n(Control) = 35 n(Intervention) = 35 Patients that: - had an order for a diabetes medication - had at least 3 days of glucose data on the control or intervention unit	Paper-based: Diabetes order set	Consensus-based	Control unit: 10% Intervention unit: 71%	Low - Physician crossover - Characteristics between control and intervention groups not compared
Weber *et al*, 2008 Non-RCT with historical controls	University of Minnesota Medical Center, Minneapolis MN, USA Control: Jan-Jun04 Intervention: Jan-Mar05	n(Control) = 336 n(Intervention) = 243 Patients receiving patient-controlled analgesia	Paper-based: Standard order set for patient-controlled analgesia	Unclear	85%	Very low - Statistical analysis not performed - Characteristics between control and intervention groups not compared
Kanji *et al*, 2008 Non-RCT with historical controls	Lion's Gate Hospital. Vancouver BC, Canada Control: May-Aug00 Intervention:	n(Control) = 51 n(Intervention) =103 Patients that: - had community acquired pneumonia	Paper-based: Community Acquired Pneumonia Order set	Infectious Disease Society of America and American Thoracic Society 2007 guidelines	42%	Very low - Statistical analysis not performed - Characteristics between control and intervention groups

	Jan-Dec2002	- greater than 18 yrs old - were not immuno-suppressed - were not transferred from another institution				not compared - Low adoption rate - Historical controls not compared to all patients in intervention arm
Thielen *et al*, 2008 Non-RCT with historical controls	Barnes-Jewish Hospital, St Louis MO, USA Control: Sep04-Apr05 Intervention: Sep05-Apr06	n(Control) = 26 n(Intervention) = 26 Patients admitted to vascular surgery service with underlying diabetes, except if: - no bedside blood glucose monitoring was available - the planned hospital stay was projected to be less than 24 hrs - diabetic ketoacidosis was present - the patient was receiving glucocorticoids -consent was not provided - the patient was receiving total parenteral nutrition in conjunction with intravenously administered insulin - the patients' outpatient dose of insulin exceeded 2.0U/kg	Paper-based: Order set for glycemic control on a vascular surgery service	Unclear	Mandatory	Moderate - Very small sample size
Garrelts *et al*, 2007 Non-RCT with historical controls	Wesley Medical Center, Wichita KS, USA Control: Jan04 Intervention: Jan05	n(Control) = 45 n(Intervention) = 44 Parients with orders for epoetin alfa	Paper-based: Epoetin alfa preprinted order for erythropoiesis	Unclear	88%	Moderate - Very small sample size
Elsasser *et al*, 2007	Creighton University Medical Centre, Omaha	n(Control) = 100 n(Intervention) = 180	Paper-based: Risk assessment and	American College of Chest	23.30%	Low - Very low adoption

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			prophylaxis order form	Physicians (ACCP) guidelines		rate
Non-RCT with historical controls	NE, USA Control: Mar04-May04 Intervention: Mar05-May05	All admitted, non-obstetric adult patients, except if: - length of stay was less than 24 hrs - the admission was initiated by a service other than family medicine - the patient's age was less than 19 years - the patient was receiving full therapeutic anticoagulation - the patient was admitted for labour and delivery				- Historical controls not compared to all patients in intervention arm
Micek *et al*, 2006 Non-RCT with historical controls	Barnes-Jewish Hospital, St Louis MO, USA Control and Intervention combined: Dec04-Nov05	n(Control) = 60 n(Intervention) = 60 Patients with a clinical diagnosis of septic shock, except for: - patients with refractory septic shock dying in the emergency department despite vasopressor administration - patients with an alternative diagnosis accounting for the shock state - patients with a preexisting do-not-resuscitate order	Paper-based: Order set for management of septic shock	Derived from the Surviving Sepsis Campaign	Unknown	Low - Adoption rate not reported - Small sample size
Chisolm *et al*, 2006 Non-RCT with historical controls	Columbus Children's Hospital, Columbus OH, USA Control: Nov01-Aug02 Intervention:	n(Control)=261 n(Intervention)=529 Asthma patients who are: - between the age of 2 and 20 year - not admitted to the pediatric	CPOE-embedded: Asthma order set	Unclear	88%	Moderate - Historical controls not compared to all patients in intervention arm

	Oct02-Nov03	intensive care unit				
Asaro *et al*, 2006 Non-RCT with historical controls	Washington University, St Louis MO, USA Phase 1 (No order set): 1 month Phase 2 (Paper order set): 1 month Phase 3 (CPOE implementation): 1 month Phase 4 (Promotion of CPOE-embedded order set): 1 month	n(Phase 1) = 45pts n(Phase 2) = 66pts n(Phase 3) = 48pts n(Phase 4) = 49pts Patients seen in the ED with an ED diagnoses of unstable angina, acute oronary syndrome, or acute myocardial infarction	Paper-based and CPOE-embedded: Acute coronary syndrome order set	American College of Cardiology-American Heart Association Task Force on Practice Guidelines	Phase 2: 15% Phase 3: 40% Phase 4: 55%	Low - Characteristics between control and intervention groups not compared - Adoption rate not reported - Small sample size
Sano *et al*, 2005 Non-RCT with historical controls	Walter Reed Army Medical Center, Washington DC, USA Control: Mar-Jun03 Intervention: Jul-Oct03	n(Control) = unknown n(Intervention) = unknown Patients from the medical and gynaecologic oncology services	Electronic: 64 standardized chemotherapy order forms	NCCN, ASHP and ASCO anti-emetic regimens. Evidence based guidelines and phase II and III clinical trial data	Unknown	Low - Adoption rate not reported - Characteristics between control and intervention groups not compared
Vardy *et al*, 2005 Non-RCT with historical controls	Clalit Health Service - southern district, Israel Control: Nov02-Feb03 Intervention: Nov03-Feb04	n(Control) = unknown n(Intervention) = unknown All patients of participating primary care practices	Electronic: Diagnostic laboratory routines	Consensus-based	Unknown	Very low - Adoption rate not reported - Statistical analysis not performed - Characteristics between control and intervention groups not compared
Clark *et al*, 2005	DCH Regional Medical Center, Tuscaloosa AL, USA	n(Control) = 42 n(Intervention) = 21	Paper-based: Order set for treatment of chemo-	National comprehensive cancer network	Unknown	Very low - Statistical analysis not performed

Non-RCT with historical controls	Control: May-Jun03 Intervention: Feb-Mar04	Patients that: - had a non-myeloid malignancy with chemotherapy induced anemia - recieved erythropoietic therapy - were treated with darbepoetin for at least 6 weeks or with erythropoietin for at least 4 weeks - did not have chronic renal failure, non-Hodgkin lymphoma, myelodysplasia, myeloid leukemia, promyelocytic leukemia, myclomonocytic leukemia, HIV-associated anemia, or essential thrombocytosis	induced anemia	guidelines and manufacturer's recommendations		- Adoption rate not reported - Characteristics between control and intervention groups not compared - Very small sample size
California Acute Stroke Registry, 2005 Non-RCT with historical controls	6 Hospitals in California, CA, USA Control: Nov02-Jan03 Intervention: Nov03-Jan04	n(Control) = 187 n(Intervention) = 226 All patients discharged with diagnosis of suspected stroke or transient ischemic attack, at admission or discharge	Paper-based: Ischemic stroke standard orders	Consensus among stroke champions for the CDC CDC Coverdell pilot stroke project	Unknown	Moderate - Adoption rate not reported
Treece *et al*, 2004 Non-RCT with historical controls	Harborview Medical Center, Seattle WA, USA Control: Jun-Aug00 Intervention: Jul-Nov01	n(Control) = 41 n(Intervention) = 76 Patients who died at trauma center, except for: - patients who were brain dead - patients who were not on ventilators - patients who died while receiving cardiopulmonary	Paper-based: Comfort care orders for withdrawal of life support	Based on a textbook ("Principles and practice of withdrawing life-sustaining treatments in the ICU" by Rubenfeld GD and Crawford F)	71%	Moderate - Small sample size

		resuscitation				
Biviano *et al*, 2003 Non-RCT with historical controls	New York Presbyterian Hospital, New York NY, USA Control: Mar-May00 Intervention: Mar-May01	n(Control) = 60 n(Intervention) = 60 Patients presented to the emergency department with: - chest pain and an elevation of troponin I level to >2.0ng/ml by 24 hrs after initial triage - have a history of chest pain or anginal equivalent or at least one of the following primary diagnosis: cardiac arrest, recent internal defibrillator placement, abdominal aortic aneurysm rupture, rhabdomyolysis, sepsis, acute cerebrovascular accident, gastrointestinal bleed or vaginal bleed requiring blood transfusion, pulmonary embolus, acute asthma exacerbation, pneumonia, or endocarditis	Paper-based: Chest pain protocol order set	Established guidelines from American College of Cardiology, etc. and personal treatment preference	65%	Low - Small sample size - Historical controls not compared to all patients in intervention arm
Hughes *et al,* 2001 Non-RCT with historical controls	Medical University Hospital Authority, Charleston SC, USA Control: Jan94-Jun97 Intervention: Jul97-May01	n(Control) = 722 n(Intervention) = 775 PICU patients receiving mechanical ventilation, except for: - patients who were acutely unstable - patients who were long-term chronically ill	Paper-based: Standardized physician orders for PICU ventilator weaning practice	Incorporated proven research from literature	Unknown	Very low - Adoption rate not reported - Characteristics between control and intervention groups not compared - Statistical analysis not performed for all results

Jordan *et al*, 2001 Non-RCT with historical controls	Saint Agnes Medical Center, Fresno CA, USA Control: Unknown Intervention: 2 months	n(Control) = 48 n(Intervention) = 29 Carotid endarterectomy patients	Paper-based: Post-Anesthesia Care Unit Carotid Order Set	Unclear	80%	Very low - Statistical analysis not performed - Very small sample size
Debrix *et al*, 2001 Non-RCT with historical controls and controls from other hospitals	Hopial Tenon. Paris, France Control: Oct-Nov96 Intervention: Oct-Nov 97 Controls from other hospitals (before): Feb-Mar96 Controls from other hospitals (after): Feb-Mar97	n(Control) = 105 n(Intervention) = 82 n(Controls from other hospitals, before) = 51 n (Controls from other hospitals, after) = 55 Patients who received colony stimulating factors as part of cancer treatment	Paper-based: Hematopoietic colony stimulating factors order form for cancer treatment	American Society of Clinical Oncology guidelines for use of hematopoietic colony stimulating factors on cancer care	Mandatory	Low - Characteristics between control and intervention groups not compared - Small sample size

† Control - Time period for data collection for historical controls; Intervention - Time period for data collection for intervention group

Table 4: Summary of outcome measures of the included studies investigating paper order sets

Study, Design	Intervention	Adoption rate	Rate of Adherence to guideline	Other outcomes	Undesirable outcomes
O'Connor *et al*, 2009 Non-RCT with historical control	Paper-based: A general admission order set and six diagnosis-specific order sets	Period 2: 32.3% Period 3: 51.6%	None	Processes of care Admitted patient receiving orders for deep vein thrombosis prophylaxis increased from 10.9% to 35.6 % ($p<0.001$) to 44.0% ($p<0.001$) Monthly DVT prophylaxis utilization in medical inpatients increased from 12.8% to 25.8% ($p<0.0001$) Many other secondary outcomes were improved by order set use	Dating of orders decreased from 93.9% to 84% with order set use ($p=0.0067$)* The ordering of nighttime sedation increased from 1.0% to 45.7% ($p<0.0001$)*
Cronin *et al*, 2009 Non-RCT with historical control	Paper-based: A thromboprophylaxis risk factor assessment and prescriber order sheet	Unknown	None	Treatment outcome Rate of venous thromboembolism decreased from 4.6% to 2.4% (Significance unknown) Rate of pulmonary embolism decreased from 0.9% to 0.4% (Significance unknown)	None
Thiel *et al*, 2009 Non-RCT with historical controls	Paper-based: Bacteremic severe sepsis order set	Unknown	More patients received appropriate initial antibiotic treatment (65.5% vs. 53.0%, $p=0.01$)	Efficiency Patients in after group had a shorter time to appropriate antibiotic coverage (737min vs 995min, $p=0.04$) Processes of care Patients in the after group received more IV fluids in the first 12 hours after onset of hypotension (2054mL vs 1627mL, $p=0.04$) No significance in the number of patients with steroids given in 24 hours	None

				Treatment outcome In-hospital mortality was decreased (39.5% vs 55.0%, $p<0.01$) Length of stay decreased (22.4d vs 28.7d, $p<0.01$) Reduction in occurrence of renal failure (36.0% vs 49.0%, p<0.01) and cardiovascular failure (57.0% vs 70.5%, $p<0.01$) Less likely to require vasopressors after initial fluid resuscitation (52.5% vs 68.5%, $p<0.01$)	
Koplan *et al*, 2008 Non-RCT with historical controls	CPOE-embedded: Smoking cessation order set for acute myocardial infarction, congestive heart failure and pneumonia	41.50%	Smoking cessation quality measure (proportion of smokers who received smoking advice, counseling or medication) increased from 86% to 95% (Significance unknown)	Processes of care Orders for nicotine replacement therapy increased from 1.6% to 2.5% ($p<0.0001$); Orders for smoking consultations rose from 0.8% to 2.1% ($p<0.0001$)	None
Noschese *et al*, 2008 Non-RCT with contemporaneous controls at another hospital unit	Paper-based: Diabetes order set	Control unit: 10% Intervention unit: 71%	No significant difference in proportion of orders that are appropriate	Processes of care More orders for basal/bolus insulin therapy ($p<0.001$) No significant difference for SSI monotherapy orders Basal/bolus insulin was more frequently prescribed ($p=0.008$) Frequency of corticosteroid therapy was higher ($p=0.019$) Treatment outcome	More patients experienced hyperglycemia (60% vs 35%, p=0.015)

				No significant difference in the number of patients with an episode of mild hypoglycemia, or severe hypoglycemia	
Weber *et al*, 2008 Non-RCT with historical controls	Paper-based: Standard order set for PCA	85%	None	Treatment outcome A proportion of patients with severe respiratory depression decreased from 8% to 0% (Significance unknown)	None
Kanji *et al*, 2008 Non-RCT with historical controls	Paper-based: Community Acquired Pneumonia Order set	42%	Increased appropriateness of admission (8% vs 16%, Significance unknown)** Increased rates of performing guideline-recommended blood and sputum culture within 24h of admission (63% vs 47%, Significance unknown)** Increased selection of appropriate empiric antibiotics (74% vs 53%, Significance unknown)**	Medical outcomes Mean length of stay decreased from 9.9d to 7.1d (Significance unknown)**	None
Thielen *et al*, 2008 Non-RCT with historical controls	Paper-based: Order set for glycemic control on a vascular surgery service	Mandatory	None	Medical outcome Mean blood glucose level was lower (149.4mg/dL vs 165.2mg/dL, $p<0.005$) Incidence of hypoglycemia decreased by 50% More patients stayed within the target range of blood glucose level (75% vs 61%, $p<0.005$)	None
Garrelts *et al*, 2007 Non-RCT with historical controls	Paper-based: Epoetin alfa preprinted order for erythropoiesis	88%	A significant increase in the guideline supported uses of epoetin (73% vs 44%, $p=0.0089$) No significant difference in	Processes of care More patient's ferritin and transferrin saturation values were measured (39% vs 16%, $p=0.0176$) Cost	None

			patients receiving guideline-approved dosage	Decreased by $6518 or 26.6% (Significance unknown)	
Elsasser *et al*, 2007 Non-RCT with historical controls	Paper-based: Risk assessment and prophylaxis order form	23.30%	Patients with prophylaxis provided according to the ACCP guidelines increased from 9% to 36% ($p<0.05$)**	<u>Processes of care</u> More patients had some form of prophylaxis provided (83% vs 32%, $p<0.05$)**	None
Micek *et al*, 2006 Non-RCT with historical controls	Paper-based: Order set for management of septic shock	Unknown	More patients received appropriate initial antibiotic treatment (86.7% vs 71.7%, $p=0.043$)	<u>Processes of care</u> More patients received antibiotic administration within 3 hrs of ED arrival (86.7% vs 60%, $p=0.001$) Patients in received more IV fluids (3789ml vs 2825ml, $p=0.002$) Patients were more likely to receive IV of >20mL/kg body weight before vasopressors administration (88.3% vs 58.3%, $p<0.001$) <u>Treatment outcome</u> Patients were less likely to require vasopressor administration (71.7% vs 100% , $p<0.001$) Patients had a shorter length of stay (8.9d vs 12.1s, $p=0.038$), and a lower risk of 28-day mortality (30.0% vs 48.3%, $p=0.04$)	None
Chisolm *et al*, 2006 Non-RCT with historical controls	CPOE-embedded: Asthma order set	88%	None	<u>Processes of care</u> More uses of systematic corticosteroid (94.4% vs 75.1%, $p<0.001$), metered-dose inhaler (55.6% vs 47.9%, $p=0.019$), and pulse oximetry (90.8% vs 78.9%, $p<0.001$)** <u>Treatment outcome</u> No significant difference in length of	None

				stay**	
				Cost No significant difference in total or pharmacy charges**	
Asaro *et al*, 2006 Non-RCT with historical controls	Paper-based and CPOE-embedded: Acute coronary syndrome order set	Phase 2: 15% Phase 3: 40% Phase 4: 55%	No overall improvement in compliance with guideline recommendations for beta-blockers, heparin or aspirin/clopidogrel across the phases of the study	None	None
Sano *et al*, 2005 Non-RCT with historical controls	Electronic: 64 standardized chemotherapy order forms	Unknown	Reduction in prescribing errors from 1.4% to 0.3% (p<0.0001)	Cost Reduction in acquisition cost ($70.92/order vs $65.42/order, p<0.037)	None
Vardy *et al*, 2005 Non-RCT with historical controls	Electronic: Diagnostic laboratory routines	Unknown	None	Processes of care Reduction of 2% in total number of lab test orders (Significance unknown)	None
Clark *et al*, 2005 Non-RCT with historical controls	Paper-based: Order set for treatment of chemo-induced anemia	Unknown	Receipt of appropriate initial dose increased from 38% to 76% (Significance unknown) No improvement seen in the percentage of patients who received an appropriate dose increase after no response was seen Increase in percentage of patients who had their dose decreased or held appropriately when Hgb was greater than or equal to 12g/dL (50% vs 0%, Significance	Cost Decreased cost of erythropoetin meds ($85,000 vs $115,500, Significance unknown)	None

			unknown)		
			More patients received appropriate erythropoeitic therapy for greater than 12 weeks (60% vs 19%, Significance unknown)		
California Acute Stroke Registry, 2005 Non-RCT with historical controls	Paper-based: Ischemic stroke standard orders	Unknown	Patients were more likely to receive optimal treatment (Mean score with 6=perfect: 5.5 vs 5.1, *p*<0.0001) Rates of optimal treatment improved significantly for DVT prophylaxis (96% vs 85%, *p*=0.001) , lipid-lowering medications at discharge (78% vs 64%, *p*=0.002), and antithrombotic medications within 48hrs (98% vs 93%, *p*=0.02) and at discharge (96% vs 89%, *p*=0.01) No improvement in rates of optimal treatment for thromolysis or smoking cessation counseling	None	None
Treece *et al*, 2004 Non-RCT with historical controls	Paper-based: Comfort care orders for withdrawal of life support	71%	None	Processes of care Increased use of narcotic (18.5mg vs 8.6mg, *p*=0.001) and benzodiazepines (4.9mg vs 0.6mg, *p*=0.0002) 1 hours before death Increased use of narcotics (7.6mg vs 3.36mg, *p*=0.03)and benzodiazepines (1.5mg vs 0.1mg, *p*=0.02) 1 hr before withdrawal of ventilator Increased use of narcotics (12.3mg vs	None

				5.2mg, p=0.03) and benzodiazepines (3.2mg vs 0.4mg, p=0.02) 1 hr after withdrawal of ventilator Treatment outcome No significant changes in quality of death scores or median time to death after ventilator withdrawal	
Biviano *et al*, 2003 Non-RCT with historical controls	Paper-based: Chest pain protocol order set	65%	Higher rates of adherence for statin therapy (88% vs 54%, p=0.001), beta-blocker therapy (100% vs 85%, p=0.02), aspirin therapy (100% vs 90%, p=0.04)** No significance difference for rate of adherence for ACE inhibitor therapy**	None	None
Hughes *et al*, 2001 Non-RCT with historical controls	Paper-based: Standardized physician orders for PICU ventilator weaning practice	Unknown	None	Processes of care 50% of patients were weaned off the ventilator in 48 hours in after group as compared to 60.5hr in before group (Significance unknown) Cost $357,072 reduction in patient costs (Significance unknown)	None
Jordan *et al*, 2001 Non-RCT with historical controls	Paper-based: Post-Anesthesia Care Unit Carotid Order Set	80%	None	Processes of care The variation of drug used to treat hypertension decreased from 7 to 4 (Significance unknown) Number of patients requiring an ICU bed decreased from 15% to 12% (Significance unknown) Treatment outcomes Reduction in the percentage of patients	None

			experiencing a postoperative neurologic deficit (8.3% to 6.9%, Significance unknown), excessive bleeding (6.3% to 3.4%, Significance unknown). More stable length of stay in PACU (Significance unknown) No change in average length of stay <u>Cost</u> Estimated annual savings of $17500 from the decrease in ICU usage (Significance unknown)		
Debrix *et al*, 2001 Non-RCT with historical controls and controls from other hospitals	Paper-based: Hematopoietic colony stimulating factors order form for cancer treatment	Mandatory	Significance increase in proportion of prescriptions in compliance with guideline (before: 39%, after: 61%, *p*=0.003) Significant increase in compliance in secondary prophylactic administration (52% to 93%, *p*=0.007) No significant changes in compliance with primary prophylactic administration, and therapeutic CSF administration	None	None

* Comparison between intervention group with order set used, and intervention group with no order set used
** Comparison between intervention group with order set used and historical controls

Quality of Evidence

Table 5 shows a summary of the overall quality of the included studies. The overall GRADE assessments of the evidence were graded as very low.

Since most of the included studies were observational studies, the overall quality of the evidence is initially assessed as low, even without any serious limitations to study design. However, since most of the studies were found to have some serious limitations, the overall quality was downgraded to very low. These limitations include missing tests of significance, not measuring adoption rate of the intervention, having a very small sample size, and not comparing the population characteristics of intervention and control group.

In general, there is a lack of high-quality evidence surrounding the use of order sets, but due to the nature of the intervention, it is unlikely that any randomized controlled trials will be conducted. Issues such as physician crossover and blinding would be very difficult to address.

Table 5: GRADE assessment of overall quality of the included studies

No. of Studies (# participants)	Study Limitations	Consistency	Directness	Precision	Publication Bias	Summary of findings	Quality
22 (21554)[†]	Serious limitations (-1)[‡]	No important inconsistency	Direct	No important imprecision	Unlikely	Overall, studies indicated order sets have positive effects on guideline adherence, treatment outcomes, cost, and different processes of care.	+, Very low

[†] Two studies reported the number of orders instead of the number of patients involved, and thus was not included in the overall population sample size

[‡] Test of significance missing, intervention adoption rate not reported, population characteristics of intervention and control group not compared, small sample size used

Overview of Development and Implementation Guidelines

Despite it being a simple tool, successful development and implementation of order sets must involve careful planning and customization based on institutional needs. According to Dr. Chris O'Connor, "The process of developing and implementing order sets is anything but trivial. It is crucial for each organization to assess the technology, analyze its impact on current workflow and engage physicians before implementing it. One cannot force the technology onto users and expect it to work." Therefore, this section will

explore some of the challenges and implementation strategies that studies have reported, so that other institutions considering the use of order sets can benefit from them.

The major challenge that many studies have reported is the lack of motivation from physicians to adopt this tool (17,23,30). As stated by Noschese *et al* (2008) (21), "The use and success of [an] order set depends on medical staff being aware of it, understanding it and liking it enough to use it correctly and consistently." Without support from physicians, it would be very difficult to realize the benefits of order sets. Based on the included studies, some of the key factors that can greatly affect physicians' adoption of an order set include 1) the quality of the order set, 2) efficiency in using the order set, 3) awareness of the order set, and 4) accessibility of the order set.

Firstly, it is obvious that the perceived quality of an order set, in terms of its correctness and completeness, is crucial to its successful implementation. According to the focus groups conducted by Chisolm *et al* (2006) (28), this was one of the two major factors that affected residents' decisions to use an order set. Since the content of an order set can greatly affect the standard of care that patients are receiving, it is not surprising that this factor plays an important role. Hence, extra attention should be given when deciding which items/orders should be included or excluded. Dr. Jeremy Theal also emphasized that institutes should make an effort to incorporate the best evidence into order sets where possible. As a current user of an advanced order set system with an evidence-based database, Dr. Theal believed the best way to ensure high quality content is to engage an evidence-based medicine vendor, even though it would be associated with a high cost and possibly other implementation challenges.

Secondly, it is essential that using the order set does not impede the workflow of physicians. This is particularly important when it comes to CPOE order sets where users have to get accustomed to using a new software system. As stated by Asaro *et al* (2006) (29), "Although the general push for CPOE related primarily to patient safety and quality of care, the chief concern of clinicians is their ability to accomplish the tasks at hand efficiently." Hence, both paper and electronic order sets should be designed intuitively such that they are easy to understand and navigate. Order sets should also be sorted in an efficient manner such that users can easily find the order set of interest.

Thirdly, in order to gain support from physicians, it must be first ensured that they are aware of the order sets. Many studies have involved education programs, clinician visitations and on-going reminders to raise awareness of the order sets (18,20,24,26,30,34). According to the focus groups conducted by Chisolm *et al* (2006) (28) that were mentioned earlier, this was the other major factor that affected residents' decisions to use an order set.

Lastly, the accessibility of an order set also plays an important role in the extent of its adoption. This includes making the order set physically available at the appropriate locations, and also at various points of the treatment process. For example, Elsasser *et al* (2007) (26) did not have their [order set] form readily available throughout the hospital, and thus residents had to carry the form with them when admitting a patient. Hence, they

have realized that having "a form distributed throughout the hospital may be more extensively used by [their] residents and faculty." Koplan *et al* (2008) (20) also suggested that "allowing [their order set] to be accessible after admission would likely further improve smoker identification". Therefore, in order to implement an order set successfully and achieve a high rate of adoption, careful attention must be given to the quality, efficiency, awareness and accessibility of an order set.

To ensure that these four key factors are addressed, many of the included studies have employed similar strategies in the development and implementation process. These included 1) formation of a multidisciplinary team, 2) establishment of a feedback system, and 3) continual maintenance and monitoring of order sets.

First of all, many of the studies involved the formation of a multidisciplinary team when developing and implementing an order set (18,19,21,22,27,29,32,35-38). These multidisciplinary teams typically included at the very least physicians, nurses and pharmacists. By engaging different healthcare professionals, the needs and concerns that are unique to each group may be taken into consideration. Physicians are also more willing to support the order set if their peers are involved in the development and implementation process.

Aside from having a number of physicians on the multidisciplinary team, many of the studies also engaged the rest of the physicians by establishing a feedback system (17,21,28,31). This ensures that individual concerns from physicians can be heard, and more importantly, feedback from physicians can help improve the order set.

Finally, many studies acknowledged that the implementation of order sets requires an on-going effort (17,23,32,36,37). Since order sets are mostly based on existing evidence or best practice guidelines, they should be evaluated and updated regularly to include the most current evidence/guidelines. It is also essential to continually monitor the treatment outcomes and adoption rate associated with each order set to determine the sustainability of the improvements and the need for any modifications (17,37). Hence, many of the included studies have revised their order sets post-implementation based on study results and/or new guidelines (23,32,36).

In summary, successful implementation of order sets is not a simple task. The guidelines presented here serves as a high-level overview, and are certainly not exhaustive. Each institution should take measures to engage its staff in the development and implementation process, to address key factors that affect their decisions to adopt order sets, to customize order sets based on institutional needs and goals, and to put in place methods to ensure that their order sets reflect current evidence from the medical literature.

Recommendations

1) **Given the fact that there is very low quality evidence that order sets improve the rate of guideline adherence, processes of care, treatment outcomes, efficiency and cost, it is recommended that order sets for diagnosis and/or treatment become an important focus for further development through a formal evaluation of existing models.**

2) **It is recommended that any future commitment to order sets should be:**

- **Developed from a common starting framework across Ontario for as many applications as possible which includes all end users in the formative process**

- **Overseen and coordinated by a third party**

- **Customized by each institution with broad participation by potential institutional and professional end-users**

- **Adaptable to paper, electronic form, or embedded in CPOE systems with linked real-time evidence support**

- **Gradually incorporated into CPOE systems and linked in real-time to evidence from the literature assessed by end-users, to ensure that compliance can be monitored and that fresh evidence is constantly made available**

Acknowledgements

Appendices

Appendix 1: Search Strategies

Search date: April 22nd, 2009
Database searched: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library (all via OVID); Ebsco CINAHL

Database: OVID MEDLINE (R) <1996 to April Week 3 2009>
Search Strategy:
----
1. Medical Order Entry Systems/ (624)
2. (order set* or order-set* or template* order* or pre-printed order* or preprinted order* or preconstructed order* or pre-constructed order* or pre-formed order* or preformed order* or default* order* or order form* or order sheet* or pre-defined order* or predefined order* or standard* order* or set* of order* or pre-selected order* or preselected order*).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (502)
3. 1 or 2 (1082)
4. limit 3 to english language (1044)
5. limit 4 to yr="1999 -Current" (978)

Database: OVID EMBASE <1980 to 2009 Week 16>
Search Strategy:
----
1. Medical Order/ (82)
6. (order set* or order-set* or template* order* or pre-printed order* or preprinted order* or preconstructed order* or pre-constructed order* or pre-formed order* or preformed order* or default* order* or order form* or order sheet* or pre-defined order* or predefined order* or standard* order* or set* of order* or pre-selected order* or preselected order*).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (551)
7. 1 or 2 (629)
8. limit 3 to english language (591)
2. limit 4 to yr="1999 -Current" (406)

Database: Ebsco CINAHL <1981- 2009>
Search Strategy:

S1. MM Medical Orders [Search modes - Boolean/Phrase]   (763)
S2. order set* or order-set* or template* order* or pre-printed order* or preprinted order* or preconstructed order* or pre-constructed order* or pre-formed order* or preformed order* or default* order* or order form* or order sheet* or pre-defined

order* or predefined order* or standard* order* or set* of order* or pre-selected order* or preselected order* [Search modes - Boolean/Phrase]   (333)

S3. S1 or S2 [Search modes - Boolean/Phrase]   (1060)

S4. S3 [Search modes - Boolean/Phrase; Limiters - English Language] (1052)

S5. S4 [Search modes - Boolean/Phrase; Limiters - Publication Year from: 1999-2009] (733)

Appendix 2: Checklist for Quality Assessment

The following checklist descriptors were adapted from the STrengthening the Reporting of OBservational studies in Epidemiology（STROBE）checklist (13):

Objectives
Were the aims and rationale of the study clearly described?

Setting
Were the setting, location, relevant dates, including periods of exposure (i.e. use of order set), and data collection (i.e chart review), clearly stated?

Participants
Were the eligibility criteria, sources and methods of selection of participants (both before and after group) clearly stated?

Was the study size justified?

Were the characteristics (e.g. demographic, clinical) for the participants (both before and after group) described? If yes, are there any significant differences?

Intervention
Was the source of guideline/development process clearly described?

Was the format of the order set clearly described (either by picture or description)?

Were there any potential confounders (e.g. education intervention, changes in hospital directives, media attention, differences in characteristics b/w before and after group)?

Measurement of Outcomes
Were all outcomes clearly defined?

Was the adoption rate measured?

For each outcome, were the sources of data and methods of measurement clearly stated and justified (i.e. data were verified)?

Was statistical analysis performed? If so, were all statistical methods clearly described and justified?

Results
Was the adoption rate high enough (say >50%)?

Were all outcome measures analyzed and compared between groups?

Was the statistical significance of the results known? Were the results precise (confidence level=95%)?

Were there other serious limitations and potential bias that affects the quality of the study?

Were the results generalisable? (i.e. How similar is the study population/setting to patients/hospitals in Ontario?)

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