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Title: Economic impact of electronic prescribing in the hospital setting:
a systematic review

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Abstract: Objective:

To examine evidence on the economic impact of electronic prescribing (EP)
systems in the hospital setting.

Method:

We conducted a systematic search of MEDLINE, EMBASE, PsycINFO,
International Pharmaceutical Abstracts, the NHS Economic Evaluation
Database, the European Network of Health Economic Evaluation Database and
Web of Science from inception to October 2013. Full and partial economic
evaluations of EP or computerised provider order entry were included. We
excluded studies assessing prescribing packages for specific drugs, and
monetary outcomes that were not related to medicines. A checklist was
used to evaluate risk of bias and evidence quality.

Results:

The search yielded 1,160 articles of which three met the inclusion
criteria. Two were full economic evaluations and one a partial economic
evaluation. A meta-analysis wasn't appropriate as studies were
heterogeneous in design, economic evaluation method, interventions and
outcome measures. Two studies investigated the financial impact of
reducing preventable adverse drug events. The third measured savings
related to various aspects of the system including those related to
medication. Two studies reported positive financial effects. However the
overall quality of the economic evidence was low and key details often
not reported.

Discussion

There seems to be some evidence of financial benefits of EP in the
hospital setting. However, it is not clear if evidence is transferable to
other settings. Research is scarce and limited in quality, and reported
methods are not always transparent. Further robust, high quality research
is required to establish if hospital EP is cost effective and thus inform
policy makers' decisions.

COVER LETTER

Submission date: 27/11/2014

To the Editors:

Charles Safran and Jan Talmon

International Journal of Medical Informatics

Dear Charles and Jan,

We are pleased to submit our manuscript entitled: "Economic impact of electronic prescribing in the hospital setting: a systematic review". This systematic review examines the evidence to establish if electronic prescribing systems use in the hospital setting is cost effective. We conducted a systematic search of seven databases from inception to October 2013 and included full and partial economic evaluations of electronic prescribing systems or computerised provider order entry.

We found some evidence of financial benefits of EP use. However, it is not clear if evidence is transferable to other settings. Our review also shows that studies exploring the economic impact of electronic prescribing systems in this context are scarce and limited in quality. Therefore we endorse further robust research to establish if electronic prescribing systems use in hospitals is good value for money.

This manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other peer-reviewed media. All authors listed have contributed sufficiently to the project to be included as authors, and all those who are qualified to be authors are listed in the author byline. To the best of our knowledge, no conflict of interest, financial or other, exists. We have included acknowledgements, conflicts of interest, and funding sources after the discussion

Sincerely,

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Economic impact of electronic prescribing in the hospital setting: a systematic review

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Discussion

There seems to be some evidence of financial benefits of EP in the hospital setting. However, it is not clear if evidence is transferable to other settings. Research is scarce and limited in quality, and reported methods are not always transparent. Further robust, high quality research is required to establish if hospital EP is cost effective and thus inform policy makers' decisions.

1. Introduction

Government policies are increasingly promoting the use of technology in healthcare. In May 2013, the English Health Secretary announced a £250 million “safer hospitals, safer wards” technology fund for English NHS trusts, aiming for technology delivery in 2015 [1]. This fund was doubled in September 2013 with the goal of facilitating greater access to information for healthcare professionals. These steps mirror US government legislation to spread meaningful use of healthcare information technology through the Medicare and Medicaid incentive program [2].

The use of electronic prescribing (EP) systems in English hospital is expanding [3]. EP systems can reduce medication errors [4-8] and increase efficiency [9]. However, similar to most technologies, they are also associated with substantial acquisition costs and on-going support costs; enormous organisational change is also likely to be required [10]. Estimates of up to \$8 million for implementation of computerised provider order entry (CPOE) in a 500-bed US hospital have been reported [11], where CPOE may be used for ordering other investigations and treatments as well as medication. The challenge that most healthcare organisations face under the current financial climate is reducing costs and increasing productivity while improving quality. Therefore, many healthcare institutions are seeking evidence about the economic impact of technology adoption to better inform decisions about the optimal choice and implementation strategy.

There are limited data about the cost effectiveness of adopting technology in healthcare settings [9]. This may be due to the complexity of estimating and identifying factors contributing to direct and intangible costs and benefits of technology use. Moreover, variations in study designs and systems used in the literature make it difficult to extrapolate data to other settings. Previous reviews in this area have explored the economic effects of a wide range of technological interventions in various healthcare settings [12-14]. In contrast, our review specifically focuses on EP and the medication-related aspects of CPOE in the hospital setting.

2. Objective:

To examine the available evidence about the economic impact of EP systems in the hospital setting.

3. Methods:

3.1 Search strategy:

We followed the PRISMA guidelines for reporting systematic reviews and meta-analyses [15]. A review protocol guide was developed. A structured electronic search strategy was developed and carried out in the following databases: The Cochrane Library, MEDLINE, EMBASE, PsycINFO, International Pharmaceutical Abstracts, the NHS Economic Evaluation Database, the European Network of Health Economic Evaluation Database and the Web of Science for conference proceedings up to Oct 2013. We searched for facets relating to (1) EP/CPOE and (2) economic evaluation. Details of the MEDLINE search strategy are available as supplementary material. References in relevant previous reviews were screened [12-14]. Five key journals were screened manually for papers published between 2006 and 2013: International Journal of Technology Assessment in Health Care, International Journal of Healthcare Technology and Management, Journal of the American Medical Informatics Association, Journal of Evaluation in Clinical Practice and Journal of Health Economics.

3.2 Inclusion and exclusion criteria:

We included any full or partial economic evaluation studies of EP and/or CPOE in hospitals published in English. Full economic evaluation was defined as the comparative analysis of alternative courses of action in terms of both costs and consequences [16]. Full economic evaluations thus included cost effectiveness analysis (CEA), cost utility analysis (CUA) and cost benefit analysis (CBA). Studies that reported costs (resource use) and/or monetary consequences but did not make explicit comparisons between alternative interventions in terms of both costs and consequences were considered partial economic evaluations [17].

1 To be included, studies had to assess electronic systems that allow healthcare professionals to order
2 or prescribe medication orders electronically. We were interested in systems used for prescribing a
3 wide range of drugs for either general hospital populations or specific populations such as
4 paediatrics. Therefore, we excluded studies assessing prescribing packages aimed at specific
5 group(s) of drugs. Where a system was used to order more than just medicines, monetary outcome
6 measures unrelated to medicines were excluded. Inclusion and exclusion criteria are summarised in
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17 **3.3 Study selection and data extraction:**

18 Article abstracts and titles were initially screened by one researcher (ZA) and assessed against our
19 criteria. For all papers which potentially met the inclusion criteria, or if there was any doubt, the full
20 text was obtained and evaluated using an assessment sheet. A 10% random sample of the abstracts
21 and titles screened, and of the full text articles screened, were reviewed by a second researcher
22 (SG). Data extraction from included papers was conducted independently by two researchers (ZA &
23 YJ) using an extraction template. Extracted data included setting, design, intervention, comparator,
24 population, outcome measures, and type of economic evaluation. For both study selection and data
25 extraction, disagreement was resolved by consensus and if necessary review by a third researcher
26 (BDF).
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43 **3.4 Study appraisal and analysis:**

44 Assessment of risk of bias and study quality was carried out using the checklist of Drummond et al
45 [18]. Studies were classified and organised according to design and type of economic evaluation.
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51 **4. Results**

52 The electronic search resulted in 1,160 unique articles after removing 205 duplicates (Figure 1).
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1 European Network of Health Economic Evaluation database). There was 91% (105 of 116) agreement
2 between reviewers for screening of title & abstract, and 100% (n=3) for full text review.
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5 **4.1 Study characteristics:** 6

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8 Three studies [19-21] (table 2) met our inclusion criteria, of which two were full economic
9 evaluations [19, 20] and one a partial economic evaluation [21]. One study was conducted in the US
10 [21], one in Canada [20] and one in the UK [19]. One [21] was based in a single tertiary care hospital
11 and one in a multi-site healthcare institution [20]. The remaining study had no actual setting and all
12 cost estimates were based on a theoretical model of a 400 bed acute UK hospital using a
13 hypothetical system [19]. Interventions and comparators also varied. Interventions included were
14 described as CPOE [19, 21] of which one was home grown [21], and a commercial medication order
15 entry system combined with medication administration records [20]. The clinical decision support
16 system capabilities of the interventions assessed were described fully in one study [20] partially in
17 another [21] and the remaining study did not provide any description [19]. Given the small number
18 of studies which met our inclusion criteria and their heterogeneity, meta-analysis was not possible.
19 We therefore undertook a narrative synthesis of the findings.
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38 **4.2 Economic impact assessment:** 39

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41 Methods used to assess the financial impact of the technology varied. The three studies all reported
42 monetary outcomes specifically related to medicines (table 2), of which two investigated the
43 financial impact of reducing preventable adverse drug events [19, 20]. The third measured savings
44 related to various aspects of a CPOE system and displayed a breakdown of savings associated with
45 different aspects including those related to medicines [21].
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54 Two studies showed favourable economic impact [19, 21]. Karnon et al [19] developed a decision
55 tree model to estimate the net benefits of three interventions (CPOE, ward pharmacists, and bar
56 coding) aimed at reducing medication errors using information obtained from a systematic review of
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1 the literature. Lower and upper estimates for implementation and maintenance costs of a
2 hypothetical CPOE system in a 400 bed hospital were used in the model including potential
3 efficiency savings (reduced medication costs, range: £75,000-150,000) from the deployment of
4 CPOE. Estimated resource requirements for the additional treatment of ADEs, and monetary
5 valuations of the health effects of ADEs on patients were also included in the analysis [19]. Karnon
6 and colleagues found CPOE to be associated with no probability of producing positive net financial
7 benefits when only health service costs were considered. However, a net benefit of CPOE with a
8 mean estimate of around £31.5 million over five years was predicted when monetary value of lost
9 health (due to preventable adverse drug events) was included in the analysis. In a separate study,
10 Wu et al reported incremental costs for the intervention compared with a conventional approach of
11 a total of USD\$ 3,322,000 over a 10 year horizon [20]. These authors also estimated an incremental
12 cost-effectiveness of \$12,700 per adverse drug event prevented after system implementation [20].
13 This was found to be sensitive to the adverse drug event rate, the effectiveness of the new system in
14 preventing adverse drug events, the cost of the system, and costs due to possible increases in doctor
15 workload. Authors estimated acquisition costs of USD \$1.4 million, implementation costs of \$1.7
16 million and operating costs of \$19,652 per year [20]. Estimates of the effect of the system were
17 obtained from the literature while cost data were obtained from a health care institution in Toronto,
18 Canada in which the study was based. The remaining paper was a partial economic evaluation which
19 reported savings in various outcome measures, with a breakdown of each outcome measure
20 separately [21]. Authors of this study estimated upfront costs of development and implementation
21 of a CPOE system to be USD\$ 11.8 million. Over ten years, the system saved \$28.5 million resulting in
22 a cumulative net savings of \$16.7 million and net operating budget savings of \$9.5 million. However,
23 the full financial effect of system implementation was not evaluated. Of the total system savings,
24 60% were medication related savings (17.1 million). About 65% (11.1 million) of medication related
25 savings were through decreased ADEs, while the remaining 35% (6 million) were cash savings due to
26 decreased drug use, frequency, or savings due to IV to oral medicine switch.
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4.3 Risk of bias and quality assessment and limitations of the studies:

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3 Overall, studies were found to vary significantly in the quality and transparency of the reporting of
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5 both methods and results. Although the research questions were clearly stated in all three studies,
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7 justification for the type of economic analysis performed was not given. Some details about data
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9 collection and analysis were lacking. Although details of the selected time horizon for benefits and
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11 the approach to price discounting (converting prices to present values) were reported, the choices
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13 were rarely justified. Many of the data used in the evaluations were also based on assumptions
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15 which were not clearly justified and generalisability issues were not always addressed. For example,
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17 Karnon et al [19] developed a decision model of a UK hospital but included data from the US that
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19 might not be appropriate for the UK context. In another study, costs and benefits were assumed to
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21 be equally affected by inflation although they were assessed at different points in the model [21].
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23 Results relating to quality assessment of the included studies are available as supplementary
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5. Discussion

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39 This is the first review of the financial effects of EP systems in secondary care. Despite widespread
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41 uptake of EP, it seems that there are few evaluations of the cost effectiveness of this technology
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43 within this context. In addition, one of the three included studies was not specifically designed to
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45 capture the full economic impact of EP system implementation as it was carried out retrospectively
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52 Our review findings are consistent with previous reviews in the area of health information
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54 technology [9, 12-14]. There are issues surrounding the reliability and quality of the methods used in
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56 published economic evaluations. The choice of economic evaluation type in relation to the research
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58 question was not justified by the authors in any of our included studies. Hidden costs and potential
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1 savings were not taken fully into account in all the studies. In some cases, costing data were
2 obtained from the literature and/or expert estimates which might not be appropriate for the setting
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4 concerned. The effect of inflation and currency value was not taken into account or assumed to be
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6 stable over time in one of the studies identified. Moreover, justification for the choices of currency
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8 rates and discounting was often not given. Generalisability issues were not appropriately addressed
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10 which makes extrapolating evidence from literature to other settings difficult.
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14 Our review also showed that level of clinical decision support system was often not described in
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16 published economic evaluations of EP and CPOE. Such information is important for any meaningful
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18 assessment of benefits as the level and maturity of clinical decision support system is likely to have
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20 an influence on costs and benefits achieved. Moreover, systems continue to evolve over time and
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22 consequently any benefits are likely to be incremental. Therefore the level of evidence is weak and
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24 not sufficiently robust to establish clear recommendations.
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28 29 **5.1 Implications for clinical practice**

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32 Adopting new technology such as EP systems in hospital setting needs to be driven by formal
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34 evaluations. Our review shows that the literature evaluating the economic impact of such systems is
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36 limited. There seems to be some suggestion of financial benefit when implementing EP in hospital
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38 settings. However, it is not clear if this evidence is consistent or generalisable. There is little research
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40 output addressing economic evaluations of technology implementation as these projects tend to
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42 raise unique local issues [22]. Furthermore, expected financial impact is likely to depend on several
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44 factors including successful implementation, training, and how the technology is used in practice.
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48 Moreover, EP economic evaluation studies are challenging due to the diffuse effect of EP on many
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50 clinical processes across an institution [23]. Our review shows that studies exploring the economic
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52 impact of EP in this context are scarce. This is further complicated by quality issues and the lack of
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54 transparency in reported methods as well as assessment of only a limited range of variables related
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56 to EP use. Further research is required to establish if EP use in secondary care is good value for
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1 money. Systems' software capabilities and costs continue to change, therefore providing details of
2 the systems evaluated including software versions and decision support capabilities is essential in
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4 this field. We argue that planning for concurrent prospective economic evaluations before system
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6 implementation is vital to capture expected benefits and to inform policy makers. Involvement of a
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8 health economist at an early stage is therefore advisable.
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10 11 12 **5.2 Limitation of this review**

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15 We only included articles published in English. We were not able to include some economic
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17 evaluations of CPOE where systems were used for ordering more than just medicines if studies did
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19 not report the financial impact related to medications separately [6, 24, 25]. There were also two
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21 recent papers that couldn't be included as it was not possible to separate the cost outcomes of EP or
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23 CPOE from those of a wider intervention such as an electronic health record [26, 27].
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31 **6. Conclusion:**

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34 In spite of the issues surrounding the quality and robustness EP economic evaluations, the very small
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36 pool of evidence seems to suggest that there may be potential financial benefits related to EP
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38 adoption in the hospital setting. Other benefits may provide value to patients through reducing
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40 errors, improving quality, and increasing efficiency. However, it is difficult to reach any definitive
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42 conclusion as to whether EP provides value for money due to uncertainty surrounding the costs and
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44 outcomes, as well limitations in study design. Ensuring better quality and reporting in future
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46 economic evaluations is necessary to fill the knowledge gap and inform policy makers' future
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51 decisions.
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16 study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in
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18 the decision to submit the article for publication. The researchers are independent from the funders.
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Economic impact of electronic prescribing in the hospital setting: a systematic review

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Objective:

To examine evidence on the economic impact of electronic prescribing (EP) systems in the hospital setting.

Method:

We conducted a systematic search of MEDLINE, EMBASE, PsycINFO, International Pharmaceutical Abstracts, the NHS Economic Evaluation Database, the European Network of Health Economic Evaluation Database and Web of Science from inception to October 2013. Full and partial economic evaluations of EP or computerised provider order entry were included. We excluded studies assessing prescribing packages for specific drugs, and monetary outcomes that were not related to medicines. A checklist was used to evaluate risk of bias and evidence quality.

Results:

The search yielded 1,160 articles of which three met the inclusion criteria. Two were full economic evaluations and one a partial economic evaluation. A meta-analysis wasn't appropriate as studies were heterogeneous in design, economic evaluation method, interventions and outcome measures. Two studies investigated the financial impact of reducing preventable adverse drug events. The third measured savings related to various aspects of the system including those related to medication. Two studies reported positive financial effects. However the overall quality of the economic evidence was low and key details often not reported.

Discussion

There seems to be some evidence of financial benefits of EP in the hospital setting. However, it is not clear if evidence is transferable to other settings. Research is scarce and limited in quality, and reported methods are not always transparent. Further robust, high quality research is required to establish if hospital EP is cost effective and thus inform policy makers' decisions.

1. Introduction

Government policies are increasingly promoting the use of technology in healthcare. In May 2013, the English Health Secretary announced a £250 million “safer hospitals, safer wards” technology fund for English NHS trusts, aiming for technology delivery in 2015 [1]. This fund was doubled in September 2013 with the goal of facilitating greater access to information for healthcare professionals. These steps mirror US government legislation to spread meaningful use of healthcare information technology through the Medicare and Medicaid incentive program [2].

The use of electronic prescribing (EP) systems in English hospital is expanding [3]. EP systems can reduce medication errors [4-8] and increase efficiency [9]. However, similar to most technologies, they are also associated with substantial acquisition costs and on-going support costs; enormous organisational change is also likely to be required [10]. Estimates of up to \$8 million for implementation of computerised provider order entry (CPOE) in a 500-bed US hospital have been reported [11], where CPOE may be used for ordering other investigations and treatments as well as medication. The challenge that most healthcare organisations face under the current financial climate is reducing costs and increasing productivity while improving quality. Therefore, many healthcare institutions are seeking evidence about the economic impact of technology adoption to better inform decisions about the optimal choice and implementation strategy.

There are limited data about the cost effectiveness of adopting technology in healthcare settings [9]. This may be due to the complexity of estimating and identifying factors contributing to direct and intangible costs and benefits of technology use. Moreover, variations in study designs and systems used in the literature make it difficult to extrapolate data to other settings. Previous reviews in this area have explored the economic effects of a wide range of technological interventions in various healthcare settings [12-14]. In contrast, our review specifically focuses on EP and the medication-related aspects of CPOE in the hospital setting.

2. Objective:

To examine the available evidence about the economic impact of EP systems in the hospital setting.

3. Methods:

3.1 Search strategy:

We followed the PRISMA guidelines for reporting systematic reviews and meta-analyses [15]. A review protocol guide was developed. A structured electronic search strategy was developed and carried out in the following databases: The Cochrane Library, MEDLINE, EMBASE, PsycINFO, International Pharmaceutical Abstracts, the NHS Economic Evaluation Database, the European Network of Health Economic Evaluation Database and the Web of Science for conference proceedings up to Oct 2013. We searched for facets relating to (1) EP/CPOE and (2) economic evaluation. **Details of the MEDLINE search strategy are available as supplementary material.**

References in relevant previous reviews were screened [12-14]. Five key journals were screened manually for papers published between 2006 and 2013: International Journal of Technology Assessment in Health Care, International Journal of Healthcare Technology and Management, Journal of the American Medical Informatics Association, Journal of Evaluation in Clinical Practice and Journal of Health Economics.

3.2 Inclusion and exclusion criteria:

We included any full or partial economic evaluation studies of EP and/or CPOE in hospitals published in English. Full economic evaluation was defined as the comparative analysis of alternative courses of action in terms of both costs and consequences [16]. Full economic evaluations thus included cost effectiveness analysis (CEA), cost utility analysis (CUA) and cost benefit analysis (CBA). Studies that reported costs (resource use) and/or monetary consequences but did not make explicit comparisons between alternative interventions in terms of both costs and consequences were considered partial economic evaluations [17].

To be included, studies had to assess electronic systems that allow healthcare professionals to order or prescribe medication orders electronically. We were interested in systems used for prescribing a wide range of drugs for either general hospital populations or specific populations such as paediatrics. Therefore, we excluded studies assessing prescribing packages aimed at specific group(s) of drugs. Where a system was used to order more than just medicines, monetary outcome measures unrelated to medicines were excluded. Inclusion and exclusion criteria are summarised in table 1.

3.3 Study selection and data extraction:

Article abstracts and titles were initially screened by one researcher (ZA) and assessed against our criteria. For all papers which potentially met the inclusion criteria, or if there was any doubt, the full text was obtained and evaluated using an assessment sheet. A 10% random sample of the abstracts and titles screened, and of the full text articles screened, were reviewed by a second researcher (SG). Data extraction from included papers was conducted independently by two researchers (ZA & YJ) using an extraction template. Extracted data included setting, design, intervention, comparator, population, outcome measures, and type of economic evaluation. For both study selection and data extraction, disagreement was resolved by consensus and if necessary review by a third researcher (BDF).

3.4 Study appraisal and analysis:

Assessment of risk of bias and study quality was carried out using the checklist of Drummond et al [18]. Studies were classified and organised according to design and type of economic evaluation.

4. Results

The electronic search resulted in 1,160 unique articles after removing 205 duplicates (Figure 1). Three databases didn't yield any relevant papers (PSYCHINFO, The Cochrane Library, and the

European Network of Health Economic Evaluation database). There was 91% (105 of 116) agreement between reviewers for screening of title & abstract, and 100% (n=3) for full text review.

4.1 Study characteristics:

Three studies [19-21] (table 2) met our inclusion criteria, of which two were full economic evaluations [19, 20] and one a partial economic evaluation [21]. One study was conducted in the US [21], one in Canada [20] and one in the UK [19]. One [21] was based in a single tertiary care hospital and one in a multi-site healthcare institution [20]. The remaining study had no actual setting and all cost estimates were based on a theoretical model of a 400 bed acute UK hospital using a hypothetical system [19]. Interventions and comparators also varied. Interventions included were described as CPOE [19, 21] of which one was home grown [21], and a commercial medication order entry system combined with medication administration records [20]. The clinical decision support system capabilities of the interventions assessed were described fully in one study [20] partially in another [21] and the remaining study did not provide any description [19]. Given the small number of studies which met our inclusion criteria and their heterogeneity, meta-analysis was not possible. We therefore undertook a narrative synthesis of the findings.

4.2 Economic impact assessment:

Methods used to assess the financial impact of the technology varied. The three studies all reported monetary outcomes specifically related to medicines (table 2), of which two investigated the financial impact of reducing preventable adverse drug events [19, 20]. The third measured savings related to various aspects of a CPOE system and displayed a breakdown of savings associated with different aspects including those related to medicines [21].

Two studies showed favourable economic impact [19, 21]. Karnon et al [19] developed a decision tree model to estimate the net benefits of three interventions (CPOE, ward pharmacists, and bar coding) aimed at reducing medication errors using information obtained from a systematic review of

the literature. Lower and upper estimates for implementation and maintenance costs of a hypothetical CPOE system in a 400 bed hospital were used in the model including potential efficiency savings (reduced medication costs, range: £75,000-150,000) from the deployment of CPOE. Estimated resource requirements for the additional treatment of ADEs, and monetary valuations of the health effects of ADEs on patients were also included in the analysis [19]. Karnon and colleagues found CPOE to be associated with no probability of producing positive net financial benefits when only health service costs were considered. However, a net benefit of CPOE with a mean estimate of around £31.5 million over five years was predicted when monetary value of lost health (due to preventable adverse drug events) was included in the analysis. In a separate study, Wu et al reported incremental costs for the intervention compared with a conventional approach of a total of USD\$ 3,322,000 over a 10 year horizon [20]. These authors also estimated an incremental cost-effectiveness of \$12,700 per adverse drug event prevented after system implementation [20]. This was found to be sensitive to the adverse drug event rate, the effectiveness of the new system in preventing adverse drug events, the cost of the system, and costs due to possible increases in doctor workload. Authors estimated acquisition costs of USD \$1.4 million, implementation costs of \$1.7 million and operating costs of \$19,652 per year [20]. Estimates of the effect of the system were obtained from the literature while cost data were obtained from a health care institution in Toronto, Canada in which the study was based. The remaining paper was a partial economic evaluation which reported savings in various outcome measures, with a breakdown of each outcome measure separately [21]. Authors of this study estimated upfront costs of development and implementation of a CPOE system to be USD\$ 11.8 million. Over ten years, the system saved \$28.5 million resulting in a cumulative net savings of \$16.7 million and net operating budget savings of \$9.5 million. However, the full financial effect of system implementation was not evaluated. Of the total system savings, 60% were medication related savings (17.1 million). About 65% (11.1 million) of medication related savings were through decreased ADEs, while the remaining 35% (6 million) were cash savings due to decreased drug use, frequency, or savings due to IV to oral medicine switch.

4.3 Risk of bias and quality assessment and limitations of the studies:

Overall, studies were found to vary significantly in the quality and transparency of the reporting of both methods and results. Although the research questions were clearly stated in all three studies, justification for the type of economic analysis performed was not given. Some details about data collection and analysis were lacking. Although details of the selected time horizon for benefits and the approach to price discounting (converting prices to present values) were reported, the choices were rarely justified. Many of the data used in the evaluations were also based on assumptions which were not clearly justified and generalisability issues were not always addressed. For example, Karnon et al [19] developed a decision model of a UK hospital but included data from the US that might not be appropriate for the UK context. In another study, costs and benefits were assumed to be equally affected by inflation although they were assessed at different points in the model [21].

Results relating to quality assessment of the included studies are available as supplementary material.

5. Discussion

This is the first review of the financial effects of EP systems in secondary care. Despite widespread uptake of EP, it seems that there are few evaluations of the cost effectiveness of this technology within this context. In addition, one of the three included studies was not specifically designed to capture the full economic impact of EP system implementation as it was carried out retrospectively [21].

Our review findings are consistent with previous reviews in the area of health information technology [9, 12-14]. There are issues surrounding the reliability and quality of the methods used in published economic evaluations. The choice of economic evaluation type in relation to the research question was not justified by the authors in any of our included studies. Hidden costs and potential

savings were not taken fully into account in all the studies. In some cases, costing data were obtained from the literature and/or expert estimates which might not be appropriate for the setting concerned. The effect of inflation and currency value was not taken into account or assumed to be stable over time in one of the studies identified. Moreover, justification for the choices of currency rates and discounting was often not given. Generalisability issues were not appropriately addressed which makes extrapolating evidence from literature to other settings difficult.

Our review also showed that level of clinical decision support system was often not described in published economic evaluations of EP and CPOE. Such information is important for any meaningful assessment of benefits as the level and maturity of clinical decision support system is likely to have an influence on costs and benefits achieved. Moreover, systems continue to evolve over time and consequently any benefits are likely to be incremental. Therefore the level of evidence is weak and not sufficiently robust to establish clear recommendations.

5.1 Implications for clinical practice

Adopting new technology such as EP systems in hospital setting needs to be driven by formal evaluations. Our review shows that the literature evaluating the economic impact of such systems is limited. There seems to be some suggestion of financial benefit when implementing EP in hospital settings. However, it is not clear if this evidence is consistent or generalisable. There is little research output addressing economic evaluations of technology implementation as these projects tend to raise unique local issues [22]. Furthermore, expected financial impact is likely to depend on several factors including successful implementation, training, and how the technology is used in practice. Moreover, EP economic evaluation studies are challenging due to the diffuse effect of EP on many clinical processes across an institution [23]. Our review shows that studies exploring the economic impact of EP in this context are scarce. This is further complicated by quality issues and the lack of transparency in reported methods as well as assessment of only a limited range of variables related to EP use. Further research is required to establish if EP use in secondary care is good value for

money. Systems' software capabilities and costs continue to change, therefore providing details of the systems evaluated including software versions and decision support capabilities is essential in this field. We argue that planning for concurrent prospective economic evaluations before system implementation is vital to capture expected benefits and to inform policy makers. Involvement of a health economist at an early stage is therefore advisable.

5.2 Limitation of this review

We only included articles published in English. We were not able to include some economic evaluations of CPOE where systems were used for ordering more than just medicines if studies did not report the financial impact related to medications separately [6, 24, 25]. There were also two recent papers that couldn't be included as it was not possible to separate the cost outcomes of EP or CPOE from those of a wider intervention such as an electronic health record [26, 27].

6. Conclusion:

In spite of the issues surrounding the quality and robustness EP economic evaluations, the very small pool of evidence seems to suggest that there may be potential financial benefits related to EP adoption in the hospital setting. Other benefits may provide value to patients through reducing errors, improving quality, and increasing efficiency. However, it is difficult to reach any definitive conclusion as to whether EP provides value for money due to uncertainty surrounding the costs and outcomes, as well limitations in study design. Ensuring better quality and reporting in future economic evaluations is necessary to fill the knowledge gap and inform policy makers' future decisions.

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*Author Contributions

ZA, NB & BDF contributed to the conception and design of this study. ZA, SG, YJ and BDF contributed to the acquisition of the data. All authors contributed to the analysis and interpretation of data, drafting the article, and final approval of the version to be submitted.

AUTHOR DECLARATION




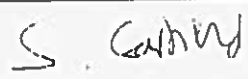
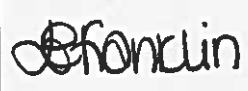
We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from (zamzam.ahmed.11@ucl.ac.uk)

Signed by all authors as follows:

Zamzam Ahmed	
Nick Barber	
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What was already known on the topic

- Acquisition costs of health information interventions such as electronic prescribing (EP) systems are high.
- Evidence for the economic benefits of health information technology interventions in healthcare is limited.

What this study added to our knowledge

- Evaluation studies exploring the economic impact of EP in the context of secondary care are scarce
- A small pool of evidence seems to suggest that there are potential financial benefits related to EP adoption, particularly if indirect costs and/or societal health gains are considered.
- Studies varied significantly in quality and transparency of reporting their methods and results
- Ensuring better quality in future economic evaluations is necessary to fill the knowledge gap and inform policy makers' future decisions.

Figure 1:

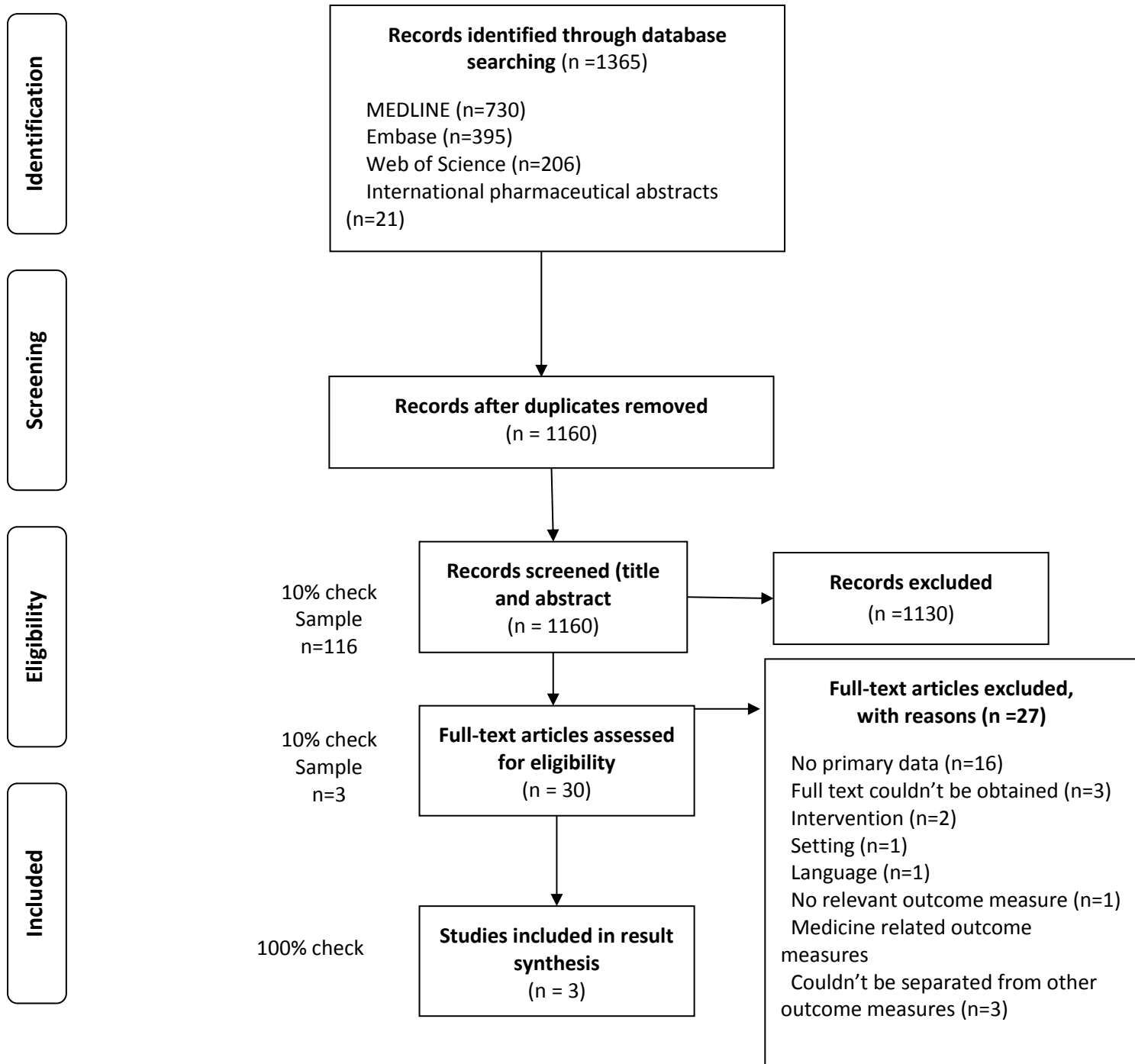


Table 1: Inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Study design	Randomised controlled trials, controlled clinical trials, before/after studies or interrupted time series studies, cohort studies or economic evaluation studies with or without modelling techniques.	-----
Type of economic evaluation	Full and partial economic evaluations	-----
Setting	Secondary and tertiary care settings. This included general hospitals, speciality hospitals, acute and foundation trusts	Primary care, ambulatory care, community hospitals and long term care facilities such as nursing or residential homes
Participants	Any patient group was included e.g. general hospital populations or specific populations such as paediatrics.	
Intervention	Electronic prescribing (EP) systems or computerised provider order entry (CPOE) systems used for prescribing a wide range of drugs for in-patients and/or at discharge from hospital.	EP or CPOE systems introduced at the same time as other interventions e.g. electronic health records where the impact couldn't be separated. Prescribing packages or software used only for a specific class of drugs.
Outcome measures	Any economic outcome measure related to medicines.	Non-monetary outcomes. Monetary outcomes of CPOE use where outcomes measures related to medicines couldn't be separated from outcomes of other aspects of the system.
Language	English	All other languages
Data extraction	Full text could be obtained	Only abstract could be obtained

Table 2: Summary of the articles reporting economic outcomes directly related to medication

Year Author country	Type of economic evaluation	Study aim	Study design & setting	Intervention & comparator (system name and version)	Time horizon	Population	Effect measures	Currency (year) & cost elements	Main economic findings
2008 Karnon et al UK [18]	Full economic evaluation (Cost utility analysis)	To estimate the potential costs and benefits of three key interventions that aim to reduce the impact of medication errors	Modelling structure developed to describe the incidence and impacts of medication errors on hospitals' costs. This model included a decision tree to describe a series of error points and subsequent error detection points in pathways through the medication process. No actual setting (A theoretical model of a 400- bed acute hospital)	CPOE/CDSS vs. ward pharmacists vs. bar coding theoretical system	5 year time horizon	The model was populated with quantitative estimates of the incidence and impacts of MEs. The potential effectiveness of interventions was described by estimating its impact on error incidence and detection rates.	Quality of life utility decrements associated with experiencing a pADE	UK. sterling (2006) Interventions, efficiency savings, treatment of, and the health effects of pADEs.	Health service costs only: CPOE was associated with no probability of producing positive net benefits. Monetary value of lost health included: Estimated monetary valuations of the health effects of pADEs A net benefit with a mean estimate of around £31.5 million for CPOE over five-years.
2007 Wu et al Canada [19]	Full economic evaluation (Cost effectiveness analysis)	To determine the potential incremental cost- effectiveness of an e-MOE/MAR system	An incremental cost- effectiveness analysis was performed comparing an MOE/MAR to the standard system used University Health Network is an association of three University of Toronto teaching hospitals (700 beds in total)	MOE/MAR with CDSS vs. standard paper ordering (misys CPR® , Misys Healthcare Systems) version not specified	a 10- year time horizon with 5% discount rate)	Reduction of pADEs and associated mortality (from literature)	USD (2004) Implementation costs (software, project management, clinical team involvement and training); operating costs (support for new interface, training))	The incremental costs for the MOE compared with a conventional approach were \$3 322 000 over the 10- year. The incremental cost- effectiveness of the new system was \$12 700 (USD) per ADE prevented. The cost-effectiveness was found to be sensitive to the ADE rate, the effectiveness of the new system, the cost of the system, and costs due to possible increase in doctor workload.
2006 Kaushal et al USA [20]	Partial economic evaluation	To assess the costs and financial benefits of the CPOE system over ten years	Cost and benefit estimates of a hospital CPOE system 720 bed, adult tertiary care academic hospital. (Brigham and Women's Hospital)	CPOE with CDSS (home grown system) version not specified	10 years (with 7% discount ing)	patients admitted between 1993 and 2002	Reductions in ADEs, LOS, proportion of appropriate prescriptions laboratory and radiology tests (some measures from the literature)	USD 2002 Capital and operational costs, drug costs, hospital costs	Between 1993 and 2002, the Birmingham Women Hospital spent \$11.8 million to develop, implement, and operate CPOE. Over ten years, the system saved BWH \$28.5 million (17.1 million were directly related to medications prescribing) for cumulative net savings of \$16.7 million and net operating budget savings of \$9.5 million given the institutional 80% prospective reimbursement rate.

LOS: length of stay; CPOE: computerized physician order entry; pADEs: preventable adverse drug reactions; e-MOE: electronic medication order entry system; MAR: medication administration record; USD: US dollars; CDSS: clinical decision support system.

Supplementary Material

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Evaluations of EP economics in the context of secondary care are limited

Findings suggests potential financial benefits related to EP use in hospitals

The evidence is weak and not sufficiently robust to establish clear recommendations

Further high quality research is required to better inform policy makers and adopters